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- Jewell BL[8] underlined that as focus in the SARS-CoV-2 pandemic shifts to the emergence of new variants of concern (VOC), characterising the differences between new variants and non-VOC lineages will become increasingly important for surveillance and maintaining the effectiveness of both public health and vaccination programme.

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NCD Risk Factor Collaboration (NCD-RisC). Worldwide trends in hypertension prevalence and progress in treatment and control from 1990 to 2019: a pooled analysis of 1201 population-representative studies with 104 million participants. Lancet 2021; 11; 398(10304): 957-80.

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CONTENTS Page

Presacral myelolipoma: A gynaecological disorder mimicry

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SUMMARY

Presacral myelolipomas are benign and do not warrant surgical resection unless symptomatic. If the mass exhibits suspicious imaging features or if there are any lingering suspicion, percutaneous biopsy can be performed to aid in the diagnosis. Our patient had classic CT and MRI imaging features of presacral myelolipoma. The percutaneous biopsy was performed due to the clinical suspicion of liposarcoma. The pathology was hence extremely helpful in determining the subsequent management of the patient, who was otherwise considered for preoperative radiotherapy for suspicion of pelvic liposarcoma.

INTRODUCTION

Myelolipoma is a benign tumour consisting of mature fat tissue and normal haemopoietic elements that is commonly found in the adrenal glands. It also can occur outside the adrenal glands—extra-adrenal myelolipoma (EAM). EAM is commonly localised in retroperitoneum, particularly in the presacral region. Myelolipoma is usually a slow-growing and asymptomatic tumour but they can become symptomatic when the size exceeds 10 cm.[1] Herein, we present a case of a 7 cm presacral myelolipoma in a 69-year-old female who presented with painful post-menopausal per vaginal bleeding.

CASE PRESENTATION

A 69-year-old female presented with 3 months history of post-menopausal per vaginal bleeding and suprapubic abdominal pain with pain score of 0 at rest, 3 during strenuous activity. She had no fever, constitutional symptoms, lower urinary tract symptoms, bowel symptoms and bone pain. Her past medical and surgical history were unremarkable. She is a mother to three sons with a single partner. On physical examination, she was hemodynamically stable, abdomen was soft and no mass was palpable. Per vaginal examination was normal. Serum full blood count, renal profile, coagulation profile, erythrocyte sedimentation rate and C-reactive protein were normal. Serum tumour markers such as carcinoembryonic antigen, CA19-9, CA125, beta-human chorionic gonadotrophin (bhCG) and alpha-fetoprotein were normal as well.

An initial ultrasound of the pelvis was performed and demonstrated uterine fibroids as well as a solid mass posterior to the uterus, which appeared to be arising from the left adnexa and was thought to be ovarian in origin (Figure 1A). A computed tomography (CT) study showed that the lesion was presacral in location and measured approximately 3.8 × 4.1 × 2.9 cm. The mass was predominantly of fat attenuation and some soft tissue components (Figure 1B). The magnetic resonance imaging (MRI) study showed a 4.8 × 3.4 × 7.3 cm well-circumscribed, lobulated, predominantly fatty mass in the presacral space extending from the level of the mid S1 to the mid S5 vertebral bodies. The sacral nerve roots were not involved, and no bony extension was appreciated. Internal soft tissue component which does not suppress fat saturated sequences was seen with questionable mild enhancement. The impression was that the imaging features were most consistent with a myelolipoma, although a liposarcoma could not be excluded (Figure 1C).

A CT-guided core needle biopsy of the presacral mass was performed, and the tissue samples were submitted for histology (Figure 2A). Microscopy sections show a fatty tumour containing areas of erythropoiesis featuring scattered megakaryocytes, erythroblasts and differentiating myeloid cells. The trilineage haematopoiesis present is most consistent with a myelolipoma (Figure 2B and 2C). Additional stains showed some of the larger mononuclear cells present within the infiltrate are positive for haematopoietic precursors. These stains confirmed the impression of a myelolipoma (Figure 2D). Fluorescence *in situ* hybridisation (FISH) analysis for Mouse Double Minute-2 Homolog (MDM2) was negative for amplification and thus supported the impression of myelolipoma.

Her per vaginal bleeding was treated with 1 week of oral route Tranexamic Acid 500mg TDS and Celecoxib 200mg BD. Pap smear test was negative. She was offered surveillance versus surgical resection since it was a biopsy-proven benign disease and the symptoms had already resolved. She opted for surveillance. She had undergone her 5th year of surveillance as of this writing. She was asymptomatic, and serial (yearly) ultrasound study showed no interval changes.

DISCUSSION

Myelolipomas are benign lesions which contain mature adipose cells and trilineage haematopoietic cells (red blood cells, white blood cells and platelets).[2] The adrenal glands are the most common site of occurrence, and the pre-sacral region is the most frequent extra-adrenal location. Other extra-adrenal locations include the pelvic retroperitoneum, mediastinum, musculofascial tissue, liver, kidney and stomach.[3] Presacral myelolipomas classically occur in older patients with a female predominance of approximately 2:1.[4] The incidence at autopsy ranges from 0.08% to 0.4%.[5] These lesions are usually asymptomatic and incidentally

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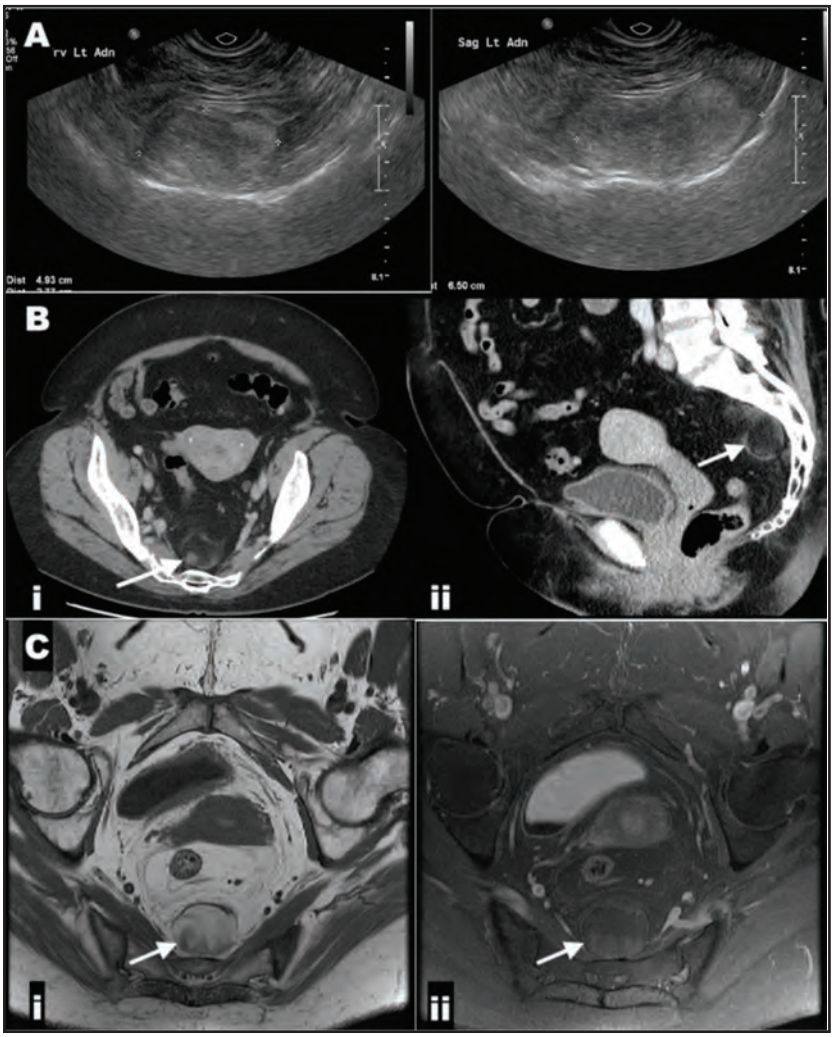

Fig. 1: Multimodality diagnostic imaging to assess the presacral tumour. (A) Ultrasound of the pelvis demonstrated a solid hyperechoic lesion posterior to the uterus. (B) Contrast-enhanced CT IN (i) axial and (ii) sagittal views demonstrated pre-sacral fat-containing lesion. The arrow illustrates the soft tissue component. (C) Axial T1-weighted MR image of the presacral tumour. (i) The arrow shows high-signal-intensity presacral lesion with some regions of intermediate signal intensity within. (ii) Axial T1-weighted fat-saturated gadolinium-enhanced MR image, arrow shows mild enhancement of tissue within the presacral lesion

discovered, as in our case. However, the lesion could exert a mass effect on adjacent structures, including the bladder, ureters, sacral nerve plexus and rectum. These lesions have an association with Cushing syndrome, Addison disease, adrenal hyperplasia and chronic exogenous steroid usage.[4]

The imaging appearances of a presacral myelolipoma is that of a well-encapsulated round or ovoid mass containing varying amounts of fat and soft tissue within. The soft tissue component may enhance post-contrast enhancement and small areas of haemorrhage within the lesion may give rise to calcifications on imaging. The lesion typically does not invade the surrounding bony architecture. As such, the lesion typically appears hyperechoic on ultrasound due to the varying fat content. On CT imaging, the fat-containing component of the myelolipoma will be of low attenuation (≤ –20HU). On MRI, the lesion will appear hyperintense on T1W sequences and hypointense on fat-suppressed T1W sequences.[6]

The main differentials for a fat-containing lesion in the pre-sacral region would be that of a liposarcoma, teratoma, extramedullary haematopoiesis or neurogenic tumour.[3,7] A combination of imaging findings and the clinical history aids in the diagnosis. Liposarcomas are the most common fat-containing retroperitoneal tumour. A liposarcoma typically has ill-defined margins with no surrounding capsule.[7] Neurogenic tumours are the second most common type of presacral tumours; they contain neural elements which are not seen in myelolipomas. On imaging, macroscopic fat is also not typically seen for neurogenic tumours.[8] A teratoma may contain areas of fat, soft tissue and calcium. However, they contain mesenchymal tissue elements on microscopy, which helps differentiate this from a myelolipoma.[6] Extramedullary haematopoiesis may resemble myelolipoma microscopically; however, imaging characteristics are typically ill-defined, multifocal lesion with a lack of macroscopic fat.[9] Clinically, these also occur with a male preponderance, in association with myeloproliferative disorders and chronic haemolytic anaemias.

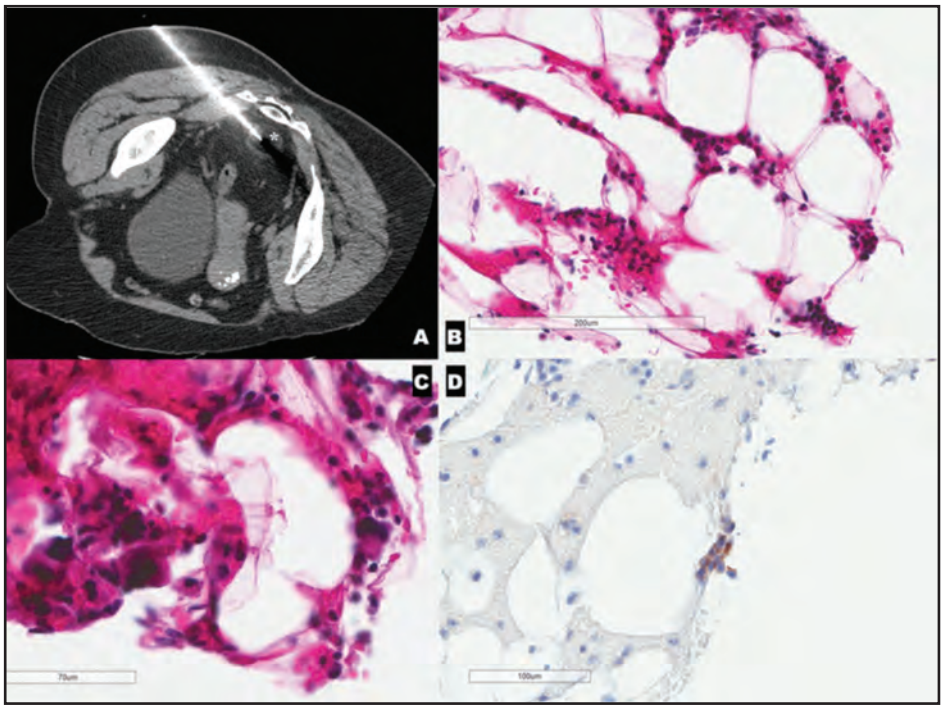

Fig. 2: Histopathological examination of the biopsied presacral tumour specimen. (A) CT-guided biopsy of the presacral lesion (asterisk). (B) Photomicrograph from the obtained biopsy specimen using hematoxylin and eosin (H&E) staining (200× magnification) showing haematopoietic cells in the background of fat. (C) Photomicrograph from the obtained biopsy specimen using H&E staining (200 × magnification) showing megakaryocytes. (D) Photomicrograph from the obtained biopsy specimen using immunostain for E-Cadherin (400× magnification) labelling a cluster of erythroblasts

With respect to management, The AACE/AAES Guideline (2009) recommends that myelolipomas that are observed (not receiving surgical excision) should undergo radiological evaluation at 3 and 6 months, continued by an annual interval for 1–2 years. Accepted indications for the surgical excision of myelolipomas are symptomatic tumour, size > 4 cm, metabolically active tumour, and a suspicion of malignancy on an imaging study. Malignant degeneration has not been documented.[10]

CONCLUSION

Presacral myelolipomas are benign and should be considered in the differential diagnosis during the evaluation of presacral fatty masses. The definitive diagnosis of presacral myelolipoma relies on histopathologic evaluation. Biopsy is necessary to exclude other malignant pathology that requires more aggressive management.

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CASE REPORT

Case series of multisystem inflammatory syndrome in adults in Melaka, Malaysia

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SUMMARY

Multisystem inflammatory syndrome in children (MIS-C) is a post-viral immunological or hyperinflammatory complication of severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) infection commonly seen in older children.[1] During the course of COVID-19 pandemic, reports of new MIS-C cases have been increasing worldwide since it was first described in April 2020. Since June 2020, several cases of Multisystem Inflammatory Syndrome in Adults (MIS-A) have been reported by Chau et al.[2], Magro et al.[3] and Oxley et al.[4] The first MIS-A case in Malaysia was diagnosed in July 2021 and reported on January 2022, by Seow et al.[5] This review describes in detail three additional MIS-A cases up to February 2022 that were subsequently diagnosed since the first reported case in Hospital Melaka, Malaysia. All cases were diagnosed via case definition by Centers for Disease Control and Prevention (CDC).

CASE PRESENTATION

Case Report 1

A 45-year-old gentleman who was an active smoker with no known medical illness was diagnosed with COVID-19 infection Category 1 through contact screening. He was then quarantined for 2 weeks in a low-risk COVID-19 quarantine centre as per Malaysian protocol at that time. The quarantine was uneventful, for he did not develop any symptoms or warning signs or require any medical intervention, and he was discharged well.

On day 13 of his illness, he developed intermittent low-grade fever, non-productive cough, sore throat, abdominal discomfort and diarrhoea. Despite a short course of empirical antibiotics for presumed infective diarrhoea prescribed by a general practitioner, his symptoms persisted, and he sought medical attention from the Emergency Department of Hospital Melaka, Malaysia. There, he required inotropic support due to hypotension that did not respond to fluid resuscitation, albeit still able to saturate well under room air. Blood parameters revealed thrombocytopenia, raised inflammatory markers and evidence of multi-organs damage, including raised cardiac enzymes, hepatitis and non-oliguric acute kidney injury (KDIGO-AKI Stage 2).

Despite the initiation of empirical broad-spectrum antibiotics, his condition did not improve, and there were no positive bacterial cultures to suggest an acute infection. As he fulfilled the MIS-A diagnostic criteria (one primary clinical criterion [a] + three secondary clinical criteria [b, c, d] + two laboratory criteria [A, B]), he was given a dose of intravenous immunoglobulin (IVIg) on day 2 of admission. There were remarkable clinical and biochemical improvements, where the inotropic support was weaned off on day 4 after the given IVIg dose, improving transaminitis and kidney injury. Inflammatory markers also showed a decreasing trend. He continued to improve and was discharged after seven days of hospitalization.

Case Report 2

A 73-year-old Malay gentleman who was an active smoker with no known medical illness was diagnosed with COVID-19 infection Category 1 through contact screening and subsequently quarantined for 2 weeks at a quarantine centre. His quarantine was uneventful, and he did not require any medical intervention.

He was asymptomatic and well until day 17 of the illness, when he developed a fever with chills and rigours, gradual onset of shortness of breath and lethargy for three days at home. As symptoms worsened, he was brought to the emergency department, where he was intubated and started on inotropic support due to severe acute respiratory distress syndrome (ARDS with PaO_2/FiO_2 < 100) and cardiogenic shock. Blood investigations reported thrombocytopenia, raised inflammatory markers and evidence of multi-organ damage, including raised cardiac enzymes, hepatitis and non-oliguric acute kidney injury (KDIGO-AKI Stage 2).

He was started on empirical broad-spectrum antibiotics and anticoagulant for venous thromboembolism prophylaxis. However, his condition did not improve, and there were no positive bacterial cultures to suggest an acute infection. With a recent history of COVID-19 infection and overall clinical picture suggestive of hyperinflammatory syndrome, the diagnosis of MIS-A was considered, and he was later found to fulfil the diagnostic criteria (one primary clinical criterion [a] + two secondary clinical criteria [b, d] + two laboratory criteria [A, B]). He was given a dose of IVIg on day 2 of admission with corticosteroids. Despite the reduction in inflammatory markers, he succumbed to death on day 3 of admission due to fulminant multi-organ failure.

Case Report 3

A 55-year-old Malay gentleman who was an active smoker with underlying hypertension was diagnosed with RVD disease during his current admission. He was initially treated for COVID-19 pneumonia Category 5, for which he was intubated for severe respiratory distress. In view of his newly diagnosed retroviral disease (RVD) with low CD4 counts, compatible chest X-ray changes and difficulty weaning

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Table I: Case definition of Multisystem Inflammatory Syndrome in Adults (MIS-A)

Definition of MIS-A by CDC[6]
A patient aged ≥21 years hospitalised for ≥24 hours, or with an illness resulting in death, who meets the following clinical and laboratory criteria. The patient should not have a more likely alternative diagnosis for the illness (e.g., bacterial sepsis, exacerbation of a chronic medical condition).
Clinical criteria
Subjective fever or documented fever (≥38.0 C) for ≥24 hours prior to hospitalisation or within the first 3 days of hospitalisation* and at least three of the following clinical criteria occurring prior to hospitalization or within the first 3 days of hospitalization*. At least one must be a primary clinical criterion.
A. Primary clinical criteria
1. Severe cardiac illness Includes myocarditis, pericarditis, coronary artery dilatation/aneurysm or new-onset right or left ventricular dysfunction (LVEF<50%), 2nd/3rd degree A-V block or ventricular tachycardia (Note: cardiac arrest alone does not meet this criterion)
2. Rash AND non-purulent conjunctivitis
B. Secondary clinical criteria
1. New-onset neurologic signs and symptoms include encephalopathy in a patient without prior cognitive impairment, seizures, meningeal signs or peripheral neuropathy (including Guillain-Barré syndrome)
2. Shock or hypotension not attributable to medical therapy (e.g., sedation, renal replacement therapy)
3. Abdominal pain, vomiting or diarrhoea
4. Thrombocytopenia (platelet count <150,000/ microliter)
Laboratory evidence
The presence of laboratory evidence of inflammation AND SARS-CoV-2 infection.
A. Elevated levels of at least TWO of the following: C-reactive protein (CRP), ferritin, IL-6, erythrocyte sedimentation rate and procalcitonin
B. A positive SARS-CoV-2 test for current or recent infection by RT-PCR, serology or antigen detection

NOTE: *These criteria must be met by the end of hospital day 3, where the date of hospital admission is hospital day 0.

oxygen support, he was also treated for *Pneumocystis Jirovecii pneumonia*. He had a prolonged history of ventilation during this hospitalization, complicated by severe COVID-19 infection and sequential ventilator-associated pneumonia. He also developed pulmonary embolism (PE), as evidenced by computed tomography pulmonary angiogram (CTPA), with additional findings of bronchiectasis and fibrotic lung changes, which were suggestive of underlying chronic lung disease. He responded well to treatments given for infections and PE thus was subsequently planned for tracheostomy, followed by a period of rehabilitation to optimise his conditions prior to discharge.

Towards the end of the sixth week from the date his SARS-CoV-2 PCR was positive, he suddenly deteriorated as he developed fever and breathlessness, followed by cardiac arrest, and required cardiopulmonary resuscitation. During resuscitation, he had refractory ventricular tachycardia that required multiple electrical and chemical cardioversions. A repeat CTPA showed worsening of pre-existing PE with new emboli seen in another pulmonary artery branch, despite being on a therapeutic dose of anticoagulant. In view of poor GCS recovery post-resuscitation, computed tomography (CT) brain imaging was performed and showed features of vasculitis with intraparenchymal bleeds and thrombus within intracranial vessels. An echocardiogram showed akinesia over the mid-apex anteroseptal wall; in this case, it might be contributed by coronary artery involvement.

Blood investigations showed raised inflammatory markers, coagulopathy and evidence of multi-organ damage, including raised cardiac enzymes, hepatitis and acute kidney injury. Overall clinical, biochemical and radiographical findings were suggestive of possible vasculitis affecting multiple organs (brain, heart and lungs), although acute kidney injury and transaminitis might be multifactorial due to post-cardiac arrest and/or vasculitis.

In view of his recent SAR-CoV-2 infection, the diagnosis of MIS-A was considered. IVIg was not given due to concerns about multiple thrombosis; thus, he was given high-dose steroids; unfortunately, he succumbed to death after three days of steroids.

Case Report 4

A 65-year-old Malay gentleman with type 2 diabetes mellitus was hospitalized and treated for COVID-19 infection Category 4 with a short course of corticosteroids. He was discharged home on day 17 of his illness after weaning off oxygen support.

On day 27 of his illness, he was admitted again with a fever (40 °C), shortness of breath for 2 days, and clinically in shock, resulting in multi-organ dysfunction. Despite elevated inflammatory markers, platelet count and troponin-I were still within normal range. He was initially treated for septic shock secondary to pneumonia with an empirical antibiotic, but there was no improvement and no positive bacterial culture.

Subsequent blood investigations showed a reduction in platelet count with an increase in inflammatory markers. Cardiac dysfunction was evident by the pericardial effusion noted on the echocardiogram with a markedly raised repeated troponin-I level. A retrospective review concluded that he had MIS-A as he fulfilled the criteria (one primary clinical criterion [a] + two secondary clinical criteria [b, d] + two laboratory criteria [A, B]) on day 3 of admission. In view of his poor kidney function and urine output and the fact that he was intolerable of dialysis, physicians opted for high-dose steroids instead of IVIg. Unfortunately, he succumbed to death soon after the initiation of high-dose steroids due to irreversible multi-organ failure.

Table II: Summary of all cases with investigations

Summary of the MIS-A cases									
Date of admission	**Age (years), sex, race, COVID-19 vaccination status**	**Underlying medical conditions**	**Clinical signs/ symptoms**	**Previous SARS-CoV-2 testing and disease category (CAT)***	**SARS-CoV-2 testing on MIS-A admission**	**Laboratory studies (upon diagnosis)**	**Imaging/ other diagnostic studies**	**Treatments given**	**Outcome**
13/7/2021	45, male, Malay, not vaccinated	Nil	Fever, cough, sore throat, abdominal bloating, diarrhoea for 1 week Admitted with signs of shock associated with multi-organs dysfunction including myocarditis, hepatitis and acute kidney injury (KDIGO-AKI stage 2).	Yes/PCR (+) CAT 1 20 days prior to MIS-A presentation	Yes/PCR (-)	Platelet 85 cells/μL, CRP 260 mg/L, Ferritin 7830.2 pmol/L, Procalcitonin 24.35 ng/mL, Trop-I 5700.51 ng/L	CXR: clear lung fields ECHO: mild global hypokinesia with ejection fraction 45%, no pericardial effusion ECG: sinus tachycardia with mild T inversion at precordial leads USG Abdomen: no significant abnormality detected	IVIg x1, corticosteroids, empirical antibiotic, inotropes, anticoagulants	Liver and kidney injury started to improve on day 2 post-IVIg Off inotrope on day 4 post-IVIg Discharged after 7 days of admission
23/8/2021	73, male, Malay, not vaccinated	Nil	Fever (38°C) with chills and rigours, dyspnoea, lethargy x 3 days Admitted with respiratory distress and cardiogenic shock, complicated with acute kidney injury (KDIGO-AKI stage 2) and hepatitis	Yes/PCR (+) CAT 1 20 days prior to MIS-A presentation	Nil	Platelet 80 cells/μL, CRP 155 mg/L, Ferritin 9287 pmol/L, Trop-I 3275 ng/L	CXR: cardiomegaly, bilateral peripheral ground glass opacity ECHO: posterior wall hypokinesia with ejection fraction 45%, no pericardial effusion, no signs of pulmonary PE, all valves were normal. ECG (serial): sinus tachycardia, dynamic and ischemic changes over II, III, aVF, v2 to v6	IVIg x1, corticosteroids, empirical antibiotic, inotropes, antiplatelet, anticoagulants	Deceased on day 3
6/11/2021	55, male, Malay, not vaccinated	HTN, RVD	Admitted initially for COVID-19 CAT 5 and PJP, complicated with VBP and PE, which was well treated. On 7th weeks from last positive SARS-CoV-2 PCR result, developed sudden onset of fever (38°C), breathlessness, cardiac arrest and refractory VT that required multiple cardioversions. Poor GCS recovery post-resuscitation.	Yes/PCR (+) CAT 5 6 weeks prior to MIS-A presentation	Nil	Platelet 223 cells/μL, ESR 45 mm/hr, Ferritin 36300 pmol/L, Trop-I 1449 ng/L	CXR: bilateral diffuse reticular opacification CTPA (7th week admission): PE involving segmental branches of bilateral descending pulmonary artery (previously only right descending). ECHO: Akinesia over mid-apex anteroseptal wall, consisted with severe CAD ECG: ventricular tachycardia CT brain: features of vasculitis with intraparenchymal bleed and thrombus within intracranial vessels	corticosteroids, empirical antibiotic, inotropes, antiplatelet, anticoagulants	Deceased on day 3

cont..... pg 7

cont from..... pg 6

Table II: Summary of all cases with investigations

Summary of the MIS-A cases									
Date of admission	**Age (years), sex, race, COVID-19 vaccination status**	**Underlying medical conditions**	**Clinical signs/ symptoms**	**Previous SARS-CoV-2 testing and disease category (CAT)***	**SARS-CoV-2 testing on MIS-A admission**	**Laboratory studies (upon diagnosis)**	**Imaging/ other diagnostic studies**	**Treatments given**	**Outcome**
11/2/2022	65, male, Malay, not vaccinated	Type 2 DM	Lethargy and poor oral intake for 2 weeks, fever and shortness of breath for 2 days Admitted with severe respiratory distress and signs of distributive shock, complicated with oliguric acute kidney injury (KDIGO-AKI stage 3) and hepatitis	Yes/PCR (+) CAT 4 27 days prior to MIS-A presentation	Nil	Platelet 103 cells/μL, CRP 61.6 mg/L, Ferritin 3807.2 pmol/L, Trop-I 3735.62 ng/L	CXR: bilateral ground-glass opacity ECHO: hyperdynamic heart with ejection fraction 49%, pericardial effusion ± 0.5cm ECG: sinus tachycardia USG Abdomen: fatty liver with hepatomegaly, bilateral renal parenchymal disease	Corticosteroids, empirical antibiotic, inotropes, anticoagulants, diuretics	Deceased on day 6

*Disease category (CAT) by Malaysia clinical practise guidelines for COVID-19 infection
- CAT 1: asymptomatic
- CAT 2: symptomatic, no pneumonia
- CAT 3: symptomatic with pneumonia
- CAT 4: symptomatic with pneumonia and require supplemental oxygen
- CAT 5: critically ill with or without other organ failures

Abbreviations: PCR, polymerase chain reaction; CRP, C-reactive protein; Trop-I, troponin-I; CXR, chest X-ray; ECHO, echocardiogram; ECG, electrocardiogram; USG, ultrasonography; IVIg, intravenous immunoglobulin; HTN, hypertension; RVD, retroviral disease; DM, diabetes mellitus; PJP, Pneumocystis Jirovecii pneumonia; VAP, ventilator-associated pneumonia; ESR, erythrocyte sedimentation rate; CTPA, computed tomography pulmonary angiography; CT brain, computed tomography of brain.

DISCUSSION

With the surge of SARS-CoV-2 infection cases worldwide due to the global pandemic, clinicians and public health officers are not only dealing with the disease itself but also the complications that follow. MIS-A is a rare yet life-threatening condition that follows the SARS-CoV-2 infection. Its fatality is due to multi-organ dysfunction resulting from hyperinflammation. Three out of four patients who have been diagnosed with MIS-A reported in this review are deceased. In our review, which consisted of patients aged between 45 and 73 years old, all were Malay males. In the case series of MIS-A in UK, the findings show that adults of all ages who were infected with SARS-CoV-2 are at risk of developing MIS-A.[7] A study concerning the race and ethnicity of COVID-19 MIS-C was conducted, and it reports a disproportionate burden of MIS-C among Black and Hispanic children in NYC.[8] However, there was also a disproportionate burden of COVID-19 hospitalisations among Black and Hispanic children; thus, it is still unclear whether this signifies a fact. As Malays are the majority of the Malaysian population, it is not clear whether Malays have a relatively increased risk or burden of MIS-A, although all cases in our review are Malays.

The pathophysiology of MIS in both adults and children remains elusive. "Updated Management Protocol for MIS-C" concluded that the most postulated mechanism is the abnormal immune or inflammatory response triggered by SARS-CoV-2 infection.[1] This theory is evidenced by the manifestation of MIS signs and symptoms two to six weeks after SARS-CoV-2 infection, multisystemic involvement of cytokine storms and hyperinflammation, positive SARS-CoV-2 serology in the majority and prompt response to immunomodulation therapy.[1]

While MIS-A also mimics the presentation of extrapulmonary manifestations in severe SARS-CoV-2 infection with elevated inflammatory markers and coagulopathy associated with damaged organs, it is distinct in that it presents with new symptoms after an acute infectious illness that is often followed by a period of recovery.[9] As the studies on the disease nature are still ongoing, the case definition of MIS-A has been revised, and the latest version was published by CDC in May 2021 (Table I). All the patients described here were proven to be infected with SARS-CoV-2 prior to their current illness and developed a new onset of fever and signs of cardiac, kidney and liver damage, with one of them having diarrhoea that suggested gastrointestinal system involvement and one of them having multifocal thromboembolic events (cerebral and myocardial infarction and PE). Although the patient from case 3 did not fulfil the CDC criteria for MIS-A (clinical criteria did not occur within the first three days of hospitalization), there were definite clinical, biochemical, and radiological signs of multisystemic (cardiovascular, pulmonary and neurological) hyperinflammation and coagulopathy, which is highly supportive for the diagnosis of MIS-A as all other possible pathologies had been well treated. Case 3 patient had been fit and planned for discharge prior to the new onset of clinical deterioration, which happened around 6 weeks post-SARS-CoV-2 infection. Consequently, the diagnosis of MIS-A should be considered among patients with signs of hyperinflammation and severe extrapulmonary multiorgan dysfunction, particularly cardiovascular, occurring within 2-5 weeks after the initial SARS-CoV-2 infection, when alternative diagnoses for the illness are excluded. RT-PCR and serologic testing for SARS-CoV-2 antibodies may aid in the diagnosis of MIS-A.[9]

In contrast with MIS-C, there is no existing management protocol or guideline for MIS-A.[7] As the hypothesised pathophysiology of both MIS-A and MIS-C is the dysregulation of immune or inflammatory responses, immunomodulators have become the pillar of treatment. Evidenced by the anti-inflammatory and beneficial effects of reducing coronary artery aneurysm in Kawasaki's disease, in COVID-19 fulminant myocarditis, and in various case reports of MIS-C, IVIg is especially widely recommended.[10] Combination of IVIg with glucocorticoids in a stepwise approach has also proven to have faster recovery of myocardial function and reduced length of hospital stay.[10] A systemic review reported the application of these treatments as well for MIS-A.[9] In our review, there were two patients given a combination of IVIg and corticosteroids, while the other two received only corticosteroids. Only one of the patients who received combination therapy survived, who had a milder degree of organ damage at presentation.

The true incidence of MIS-A is unknown, which is highly likely to be underreported, given that there is difficulty in distinguishing it from sepsis at initial presentation. During this COVID-19 pandemic era, clinicians should maintain a high index of suspicion for MIS-A among patients who present with hyperinflammatory syndrome and thus should investigate for current or previous SARS-CoV-2 infection at presentation. Earlier identification of disease and prompt initiation of appropriate treatment will improve outcomes. Further study of the pathophysiology of MIS in both adults and children is desired for a better understanding of the disease, thus more targeted therapy can be applied. Clinical trials for the use of biological agents are required, thus providing more alternate treatment options, especially in adults where we still have limited data for the efficacy of IVIg and corticosteroids.

CONCLUSION

This review describes four cases of MIS-A diagnosed in Malaysia, and one of them shows good clinical outcomes with a trial of IVIg combined with corticosteroids. Hopefully, this review will be able to raise awareness of MIS-A among clinical practitioners, and thus, more clinical trials on treatment will be made to improve survival.

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CASE REPORT

Malaria and filariasis: An unusual coinfection in South East Asia

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SUMMARY

Coinfections are infrequently reported and rare in literature. Tropical infections such as malaria, leptospirosis and filariasis are endemic in a temperate country such as Malaysia. Most of the studies pertaining co-infections centres on Malaria, as it is one of the most prevalent infectious diseases in the world. All three disproportionately affect low-middle-income countries with poor sanitation and vector control. We report with us a Bangladeshi man who was infected with malaria and filariasis, with also serological evidence of previous leptospirosis infection. He was successfully treated with local protocols.

INTRODUCTION

In tropical countries, malaria and leptospirosis are typically characterised as acute infections. Patients typically present with fever and progress rapidly, with potential complications such as acute kidney injury, acute liver failure, acute respiratory distress syndrome and disseminated intravascular coagulopathy. Death is a real possibility. Diagnosis is easily made with Thick and thin blood films (BFMP) for malaria, while leptospirosis is typically screened via ELISA upon clinical suspicion, with MAT titre ≥400 or a demonstration of fourfold rise between acute and convalescent serum or PCR as follow-up confirmation. Filiariasis, on the other hand, while endemic in Malaysia, is uncommonly seen in day-to-day practice as it presents chronically and is identified by Clinicians only when complications such as elephantiasis have set in. Additionally, it can be difficult to diagnose as periodicity is typically exhibited by parasites, which can be difficult to pick up via microscopy. Generally, PCR has been advocated as a gold standard for leptospirosis and filariasis but is not feasible inresource-limited settings.

CASE PRESENTATION

A Bangladeshi man in his 30s presented with fever, chills, rigour, vomiting and lethargy for the past 3 days prior to admission. He is a migrant worker at a local oil palm plantation, his main occupation involving harvesting and gathering of the palm oil kernel, with frequent exposure to mosquitoes during dusk and dawn. He otherwise denies any ill contacts, travel history, chest pain, and shortness of breath. He is not known to have any medical illness and is not on any medications, with no previous hospitalisation or surgeries. Upon arrival, he was lethargic, but otherwise conscious, not in any respiratory distress. He is also hemodynamically stable. Cardiovascular and lung examination was unrevealing, but Splenomegaly of 2 finger breath (4 cm) was noted on abdominal palpation, with no hepatomegaly or lymph nodes appreciated. The patient has no meningismus or rashes and is fully cooperative with a normal neurological examination. FBC was significant for thrombocytopenia (Plt: 94 × 10^9/L), while Hb was 13 g/dL, as was WBC 8 × 10^9/L. Renal profile and liver function test were found to be normal (Table I). CXR is clear, and ECG revealed only normal sinus rhythm. He was then started on IV Drip for maintenance and IV Ceftriaxone 2g STAT and OD to cover for acute undifferentiated febrile illness and blood cultures drawn. Point of care testing for dengue, the most prevalent anthropod disease, proved negative.

In view of patients' clinical presentation and nature of occupation, atypical infections were at the forefront of suspicion. As such, blood film for malarial parasites, peripheral blood film (taken at 11 pm on admission), leptospiral IgM was sent. Few hours later, thin blood films confirmed the presence of Plasmodium Vivax (Asexual 708 counts; Sexual 2124 counts) (Fig. 1). The same blood film also confirmed the presence of 6 counts of *Wucherceria bancrofti* (Fig. 2). The laboratory also confirmed a positive Leptospiral IgM (MAT was sent to MKAK). Oral Riamet 4/4 Tabs were started immediately at 0, 8, 12 hours for the *Plasmodium vivax*, while oral albendazole 400 mg STAT and oral diethylcarbamazine (DEC) 6 mg/kg (total: 350 mg OD) were started for the filariasis. IV Ceftriaxone 2g OD was continued as a treatment for leptospirosis.

Fortunately, he responded well to therapy and was gradually then transitioned to Tablet Doxycycline 100 mg BD as a continuation of therapy for the leptospirosis. He was eventually discharged from our centre after 1 week. No malarial and wuchereria parasites were seen on blood film upon discharge. Discharge medications include tablet primaquine 30 mg OD, tablet diethylcarbamazine (DEC) 100 mg TDS and tablet doxycyline 100 mg BD for 2 weeks each for hypnozoite, filariasis and leptospirosis eradication, respectively. He was then referred to a local clinic for directed observed therapy under the supervision of a health inspector and completed treatment successfully.

DISCUSSION

Since 2000, Malaysia has aggressively tackled filariasis by initiating massive drug administration (MDA) upon identification of at-risk areas.[1] While Malaysia has not attained a lymphatic filariasis-free status, it is gradually getting there due to steadily reducing cases. The presence of *Wuchereria bancrofti* in our patient is thus unsettling. 90% of

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Table I: Summary of blood investigations

Day of admission	1 Admission	3	5	7 Discharge
Hb (g/dL)	13	13.2	12.2	12.2
WBC (/mm3)	8	4.5	5.6	10.7
Plt 10^3/µL	94	158	198	304
Htc (%)	-	40.3	37.9	37.2
Urea (mmol/L)	3.8	3.6	4.0	3.7
Cr (mmol/L)	67	83	81	83
Na (mmol/L)	141	140	142	138
K (mmol/L)	3.98	3.38	3.69	3.28
Cl (mmol/L)	103	97	101	99
Albumin (g/L)	39	42.7	36.6	38.3
Globulin g/L	43	42.3	36.3	34.6
Bilirubin (umol/L)	30.5	28.7	13	31
ALT (units/L)	22	24	-	-
ALP (units/L)	85	82	-	-
CK (units/L)	-	58	-	-
LDH (units/L)	-	375	-	-
ESR (ng/mL)	35	-	-	-
Malaria	Plasmodium Vivax Asexual : 708 Sexual : 2124	Not detected	Not detected	Not detected
Filariasis	6 counts of Wuchercia Bancrofti	2 counts of Wuchercia Bancrofti	Not detected	Not detected

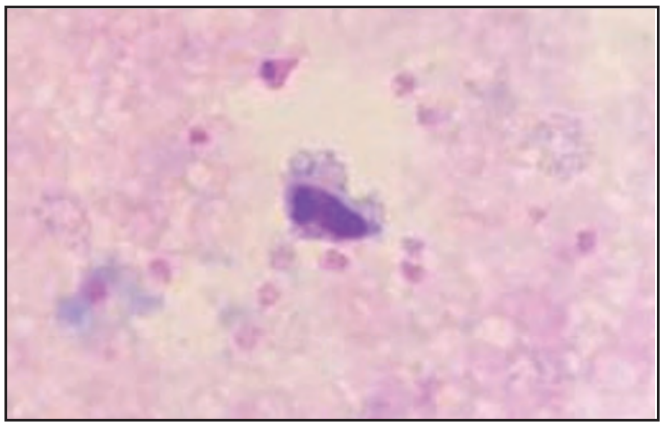

Fig. 1: Peripheral thin blood film confirmed the presence of Plasmodium Vivax

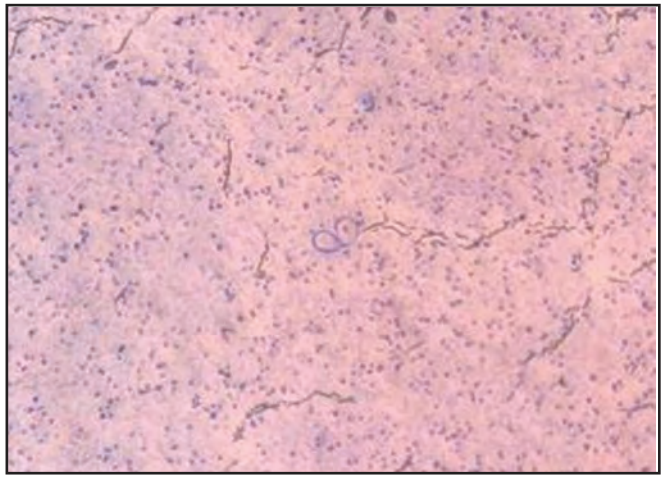

Fig. 2: The peripheral blood film confirmed the diagnosis of filariasis by identifying the presence of *Wucherceria bancrofti*

all filariasis worldwide is Bancroftian in origin. It is endemic in both Malaysia and Bangladesh. In Malaysia, however, WB constitutes only 2% of all filariasis cases reported. The predominant microfilaria is *Brugia malayi*.[2] It is thus likely our patient was first infected with *Wuchereria bancrofti* in his home country. Such cases are termed 'imported filariasis' and have previously been reported during health screening of incoming migrant workers.[3] Gatekeeping is thus imperative as immigrants have the potential to reintroduce pathogens that have been previously eradicated or controlled in the host country. This is paramount, as the vector for filariasis, the mosquito *Anopheles or Culex* is present in Malaysia.[1]

Our patient has resided in Malaysia for almost 2 years prior to presentation, with no previous medical illness and hospitalisation noted. Given the incubation period of Malaria, he was likely infected locally.[4] Comprehensive health screening is mandatory for all blue-collar foreign workers as per FOMEMA (Foreign Workers Medical Examination Monitoring Agency); this includes Malaria screening (but not filariasis). It is unlikely he would have been allowed to work in Malaysia were Malaria screening has proven to be positive.[5] While it is easy to assume that - infection portends more severe infection, co-infection of malaria with microfilariae is actually associated with lower parasite density and less severe anaemia. This is due to the upregulation of IFN g (a Th1 response) which is responsible for clearing malaria parasites. At the same time, upregulation of IL 10 (a Th2 response) is important for filarial parasite survival.[6,7] The net effect between these two responses, pro-inflammatory (Th1) versus anti-inflammatory (Th2), ultimately results in less inflammation, translating to less anaemia and parasitemia.[8]

While co-infections of malaria and Wuchereria bancrofti are a possibility, they occur by chance (pooled prevalence of

0.7%, n = 83863). The Africa continent reports a higher prevalence coinfection (1.7%), while the prevalence in Asia is low (0.2%). The low prevalence of coinfection in Asia further lends weight to our suspicion that our patient was likely infected in stages, likely *bancroftian* filariasis first in his home country, followed by *Plasmodium Vivax* in Malaysia. In Malaysia, *Anopheles* species mosquitoes are a major concern, as they can transmit both pathogens. Our patient's nature of outdoor work likely predisposed him as such for *Plasmodium Vivax*. Blood film microscopy is cheap and effective in identifying *plasmodium species*; however not as effective in identifying *Bancroftian* parasites, as they exhibit periodicity, and patients are generally asymptomatic. A better tool for identifying the latter would include molecular methods (PCR) or even rapid test kits. To be cost-effective, screening should be limited to male foreigners originating from countries in which both pathogens and vectors are abundant.[6]

Despite the term coinfection, each pathogen is dealt with individually with specific antimicrobials. Mass Drug Administration (MDA) utilises weight-based diethylcarbamazine (DEC) 6mg/kg and a single dose of albendazole 400 mg to eradicate filariasis. This mode of therapy has been highly efficacious in many countries.[1] Plasmodium Vivax is treated with weight-based Chloroquine and Primaquine, with Riamet in lieu of Chloroquine in areas known to have high resistance. 14 days of primaquine is required as Plasmodium Vivax is known to produce hypnozoites in the liver, which can cause recurrence. G6PD testing is recommended prior primaquine to prevent haemolytic anaemia. Leptospirosis is typically treated with IV ceftriaxone or doxycycline. In our patient, we opted for the latter option as objective evidence of malaria and filariasis was demonstrated.[9] Additionally, ELISA IgM for leptospirosis remains elevated for 6 months since the onset of infection and is poorly discriminant of present or past infection. Our patient's final confirmatory MAT is only 1:100 and does not satisfy the criteria for Acute Leptospirosis (MAT 1:400).[10] Pragmatically, treatment should still be initiated upon a positive serology, particularly in resource-limited settings as confirmatory MAT istime-consuming. In a compatible clinical presentation, treatment delay might result in adverse outcomes.[11] Fortunately, clinical improvement was noted after the initiation of therapy.

CONCLUSION

Coinfection of atypical infections is most certainly possible in Malaysia. Gatekeeping via proper screening at borders is thus the backbone of disease management. Additionally, clinicians should have a high degree of suspicion of coinfections when investigating febrile patients, particularly male patients from endemic areas and treat them accordingly.

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CONFLICT OF INTEREST

This study has no conflict of interest.

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Iatrogenic parapelvic urinoma post-proximal uretero-calyx anastomosis: The role of dynamic renal scintigraphy

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SUMMARY

A woman in her mid 30s presented with recurrent right-sided abdominal swelling, which was initially diagnosed as a right parapelvic renal cyst. She had undergone laparoscopic deroofing with proximal uretero-calyx anastomosis. Post-operatively, as the swelling had recurred, a 4-phase contrast-enhanced renal CT scan was performed and revealed gross right hydronephrosis, proximal hydroureter and a large cyst-like lesion at the anastomotic site. The patient was then referred to our nuclear medicine department for further assessment of urinary outflow obstruction and characterisation of the cystic lesion because the differential diagnosis was suspected urinoma. On 99mTechnetium-Mercaptoacetyltriglycine (^{99m}Tc- MAG3) dynamic renal scintigraphy, there was progressive tracer accumulation in the right kidney with tracer hold-up noted at the inferior part of the cystic lesion located adjacent to the inferior pole of the right kidney. This confirmed the communication between the pelvic-calyceal system of the right kidney with the collection. Thus, the diagnosis of urinoma was confirmed with the ^{99m}Tc-MAG3 renal scintigraphy. Renal scintigraphy can aid in the assessment of renal function as well as confirm the presence of a urinoma, which may at times be difficult to be determined on conventional radiological imaging.

INTRODUCTION

Urinomas occur as a result of leakage of urine into a contained collection in the retroperitoneal cavity as a result of blunt or penetrating abdominal injury leading to rupture anywhere along the urinary system. The aetiology of urinomas includes tumours or calculi causing urinary obstruction and damage to the urinary outflow tract, or rarely caused by iatrogenic injury to the pelvicalyceal system (PCS).[1] Usually, a urinoma starts as a small collection and does not require any intervention. In cases of significant injury or trauma, however, urinomas can increase in size and lead to other complications. Failure to decompress a urinoma can lead to compression of other organs, the development of abscess, hydronephrosis, electrolyte imbalance and even urosepsis.[2] Radiological imaging such as contrast-enhanced computed tomography (CECT) with delayed imaging or CT urography (CTU) and retrograde urethrography are the diagnostic imaging modalities of choice to help make the diagnosis.[3] In some cases, urinomas can be missed or mistaken for exophytic renal cysts. Thus, in certain instances, dynamic renal scintigraphy may be useful to aid in the diagnosis of a urinoma masquerading as a parapelvic cyst.[4]

CASE PRESENTATION

A woman in her 30s with no known medical illness presented with a non-tender right abdominal swelling, which increased in size over a period of 1 year. Ultrasound abdomen was performed at our hospital and detected a large right renal cyst. Subsequently, she underwent a four-phase contrast-enhanced renal CT scan, which revealed a large right parapelvic renal cyst with no complex features.

Hence, our urology team decided to perform aspiration of the cyst and proceeded with laparoscopic deroofing operation with proximal uretero-calyx anastomosis. At 2-week post-operative period, the patient again presented with a recurrence of the swelling at the right lumbar region.

A post-operative CT scan was performed to investigate the recurrent mass, which revealed right hydronephrosis and proximal hydroureter as well as a large cystic lesion anterior to the anastomotic site, measuring 3.6cm × 4.1 cm × 5.1cm. There was no communication between the mass and the dilated proximal ureter. Therefore, the patient was managed conservatively as a recurrence of right parapelvic cyst. However, due to persistent abdominal swelling and discomfort after 6 months post-surgery, the patient was arranged for a follow-up CT scan.The scan revealed worsening right hydronephrosis whereas the cyst was essentially unchanged in size, measuring 3.5cm x 3.9cm and 5.0cm (APxWxCC). Subsequently, the urology team referred the patient to our nuclear imaging department for a dynamic renal scintigraphy to rule out urinary outflow obstruction and characterisation of the cyst in view of worsening hydronephrosis.

Thus, we performed dynamic renal scintigraphy with F+20 protocol using ^{99m}Tc-Mercaptoacetyltriglycine (^{99m}Tc-MAG3). Whereby F+20 is a protocol for administration of IV Lasix at 20 minutes post-radiotracer injection for achieving diuretic renal stress. After post-processing, the differential renal function was calculated by creating a region of interest around each kidney. Subsequently, the renogram curve was generated.

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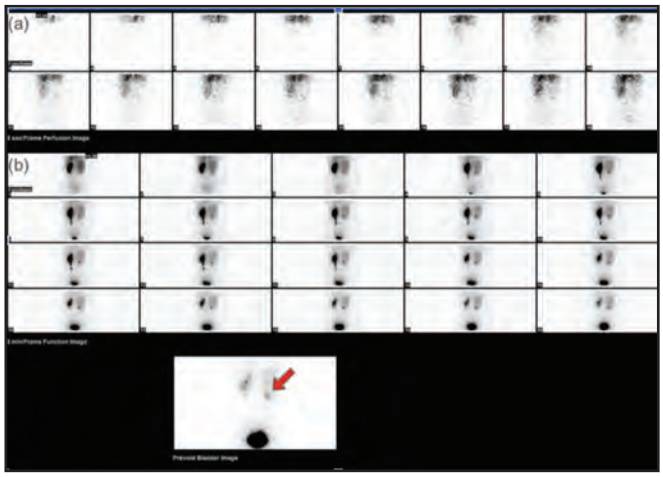

Fig. 1: Dynamic renal scintigraphy image. (a) Perfusion images. (b) Functional images. In image (a) demonstrating good and prompt tracer perfusion in the left kidney but poor and delayed perfusion in the right kidney. The red arrow highlights one of the images in the functional scan demonstrating faint uptake in the enlarged right kidney with tracer hold-up noted in the collection at the lower pole of the right kidney.

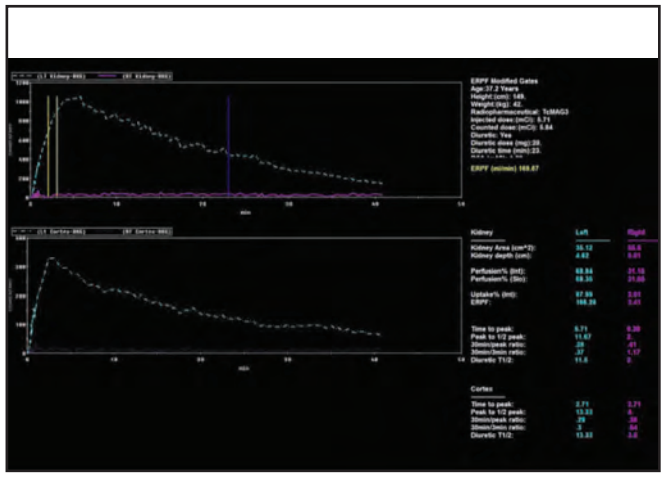

Fig. 2: Summary of renal scintigraphy with renogram showed a non-functioning of the right kidney with severely reduced perfusion and function.

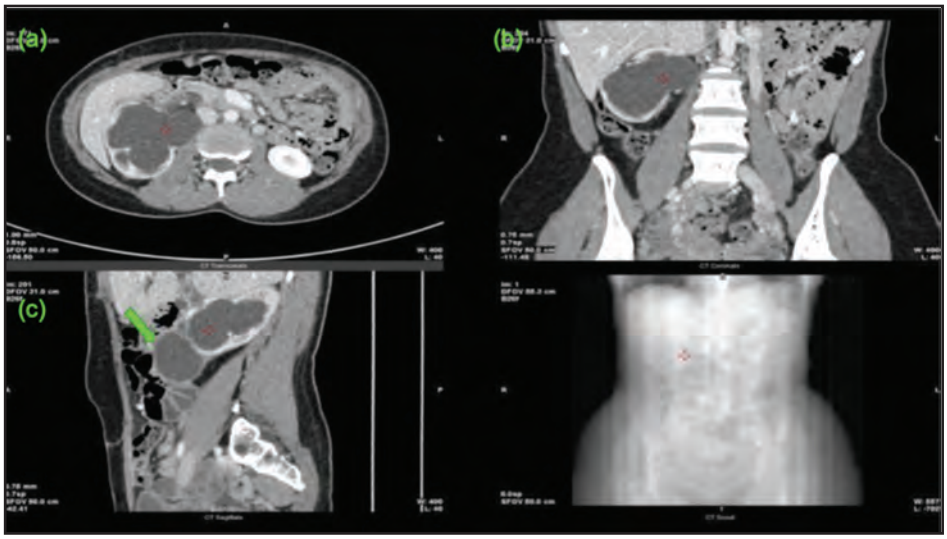

Fig. 3: A four-phase renal contrast enhanced CT scan in (a) axial, (b) coronal and (c) sagittal views during the nephrographic phase, which revealed a large cystic lesion (green arrow) arising from the right parapelvic region.

^{99m}Tc-MAG3 dynamic renal scintigraphy revealed markedly reduced perfusion of the right kidney, which was compressed and displaced superiorly by a large cystic mass located at the right parapelvic region and extending to the right lumbar region. Hence, the urodynamic status of the right kidney was indiscernible due to severely impaired function. As the study progressed, there was an apparent large area of mild tracer accumulation seen at the right renal fossa, which corresponded to a huge hypodense cystic mass seen on a previous CT. We also observed a hold up of tracers at the inferior pole of this large mass (red arrow) (Figure 1). The renogram illustrated a clinically non-functioning right kidney, with a solitary good-functioning left kidney having no scan evidence of urinary outflow obstruction (Figure 2). On further evaluation of the previous CT imaging, the cystic lesion measured 12.2 x 9.2 x 11.8 cm (AP x W x CC) and a communication between this mass and the ruptured renal calyx at the mid-segment of the right kidney was identified (Figure 3). Moreover, we concluded that the hydronephrosis and severely impaired right renal function were due to the right ureteric compression caused by the large urinoma in the parapelvic region.

Outcome/Follow-up

Definite management by the urology team was for right nephrectomy in view of non-functioning right kidney and increasing size of the urinoma. The patient, subsequently, underwent an open right nephrectomy and was well post-operatively. She was discharged with empirical antibiotics for a week. Follow-up physiotherapy was planned for the patient during the recovery period.

DISCUSSION

Post-traumatic urinomas are a rare complication, occurring in less than 1% of cases of abdominal injury. The differential diagnoses include parapelvic renal cysts and perirenal haematomas. Nevertheless, a history of preceding trauma or surgery may point to the correct diagnosis with the aid of radiological imaging. The delayed phase of a contrast-enhanced CTU is usually helpful in clinching the diagnosis. Three factors are required for the development of a urinoma, which includes a tear in PCS, the presence of a functional kidney and underlying distal urinary outflow obstruction.[3]

Four-phase contrast-enhanced renal CT scan is the modality of choice to diagnose a urinoma as extravasation of contrast from the renal PCS or ureter indicates urinary leakage. However, this radiological modality is unable to measure renal function or elucidate on the presence of urinary obstruction in the individual kidneys. Repeated exposure to radiation and intravenous iodinated contrast media that may cause adverse reactions are also factors to be considered.

Renal scintigraphy uses a lower dose of effective ionising radiation compared to contrast-enhanced CT. It can also be used in patients with compromised renal function. Severe allergic reaction to contrast media can also be prevented.[4] As in our patient, the decision to perform the renal scintigraphy to aid in the evaluation of renal function and renal outflow obstruction was made due to the initial diagnosis of a large parapelvic cyst compressing the right pelviureteric junction. Nevertheless, the scan revealed a free communication with the collection and PCS with radiotracer hold-up evident in the collection as the scan progressed. The right renal parenchyma was slightly functioning, albeit with reduced intensity. The Single Photon Emission Computed Tomography/Computer Tomography (SPECT/CT) imaging further helped to localise the ruptured PCS that communicated with the large urinoma. This multi-modal assessment in a single investigation allows clinicians to decide on a definitive management by appropriate evaluation of the size of the urinoma as well as the status of the kidney function. Early diagnosis of urinomas, the assessment of renal function and identification of urinary outflow obstruction can give a better prognosis by enabling the urologist to decide on definitive surgical intervention.

Dynamic renal scintigraphy is a simple, non-invasive, outpatient procedure that can be safely performed in paediatric as well as adult age groups and even in patients with poor renal function. It does not produce serious adverse effects and carries minimal radiation exposure to patients. In comparison with four-phase contrast-enhanced renal CT scan, which gives an effective radiation dose of approximately 10 mSv, dynamic renal scintigraphy gives only 2.7 mSv of effective radiation dose.[5] Thus, performing dynamic renal scintigraphy carries lower ionising radiation risk because its effective dose is 30% lower than conventional CT imaging. Furthermore, if SPECT/CT is performed, only a low dose CT is utilised, and it can help to delineate the site of leakage and estimate the rate of leakage. This will be helpful in assisting the decision-making towards formulating the optimal management strategy and is indispensable for the selection of a conservative versus a surgical approach.[6] First line of treatment is the drainage of the urinomas with empirical antibiotics. If the catheter fails to drain, a percutaneous nephrostomy tube is placed to facilitate drainage. Surgical reconstruction will be performed only if the other measures fail to resolve the collection.

CONCLUSION

Renal scintigraphy can aid in the assessment of renal function as well as confirm the presence of a urinoma, which may be missed on conventional radiological imaging.

LEARNING POINTS

- Urinomas can occur as a complication of blunt or penetrating abdominal injury, with iatrogenic causes being a rare aetiology.
- Radiological imaging such as contrast-enhanced CTU or retrograde urethrography is first-line modalities of choice that help make the diagnosis.
- The presence of a triad of factors predisposes to the formation of urinomas, which include a tear in PCS, the presence of a functional kidney and underlying distal urinary outflow obstruction.
- Radionuclide imaging such as dynamic renal scintigraphy may aid in the diagnosis of urinomas and exclude other differential diagnoses such as parapelvic renal cysts or perinephric haematomas, by demonstrating leakage and accumulation of the radiotracer within the urinoma collection.

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CASE REPORT

A case report of congenital chylothorax

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SUMMARY

Pleural effusions in a neonate are generally congenital in about one third of the cases and acquired in the remaining two thirds. The incidence of congenital chylothorax is 1 in 12000 to 1 in 15000 making it rare. This case describes the complexity and challenges that are faced in diagnosing a case of congenital chylothorax in the newborn. The article also highlights the current management as well newer forms of management for congenital chylothorax.

INTRODUCTION

The thoracic duct function is to transport close to 70% of ingested fat at a concentration of 0.4–6 g/dl from the intestine to the circulatory system. A total of 2.4 L of chyle is transported through the lymphatic system.[1] Chyle is constituted by cholesterol, triglycerides, chylomicrons and fat-soluble vitamins. In addition to this, chyle is also made up of lymph, which consists of immunoglobulins, enzymes, digestive products and between 400 and 6800 white blood cells/ml.[1]

Chylothorax is characterised by the accumulation of chylous fluid in the pleural space. It is the most common cause of pleural effusion in the foetus and neonates. The causes of chylothorax can broadly be classified into traumatic as well as not traumatic.

The presentation can range from asymptomatic cases to non-immune hydrops fetalis. Congenital chylothorax (CC) can lead to poor lung development, which in turn leads to respiratory distress in the newborn period.[2] Occasionally CC has been associated with certain syndromes. In most cases, the outcome is a favourable prognosis, except in hydropic neonates.

The authors would like to present a case of CC that was managed medically and has been on regular follow-up with any complications.

CASE PRESENTATION

A 22-year-old Malay woman, gravida 2 with a maternal history of being overweight, and previous admission at 28 weeks for leaking liquor, underwent emergency caesarean section (EMLSCS) due to poor progress. The newborn delivered was a late premature at 36 weeks with a birth weight of 3380 g. APGAR score was 9 in 1 minute and 10 in 5 minutes with stable vitals. He was then admitted to the post-natal ward and started breastfeeding.

On day 2 of life, the patient developed physiological jaundice and was admitted to special nursery care (SCN) in Hospital Sultan Abdul Halim (HSAH). Phototherapy was initiated. On day 5 of life, it was noted that the patient was tachypnoeic (respiratory rate; RR > 70/minute) associated with subcostal recession. It was noted that the patient had been given his scheduled feeding an hour before. He was supported with nasal prong oxygen, and his saturation ranged between 90% and 91%. Prior to transferring him, he was kept nil-by-mouth and was presumptively covered for aspiration pneumoniae according to HSAH NICU protocol.

In NICU, the oxygen support was increased to nasal continuous positive airway pressure (nCPAP). A chest x-ray revealed left lower zone opacity/consolidation (Figure 1).

He was started on full intravenous maintenance fluid (IVD). Feeding was resumed the following day with close blood sugar monitoring. A trial of weaning the patient to nasal prong oxygen was unsuccessful as the patient developed respiratory distress in the form of subcostal recession and tachypnoea. He was then placed back on NcPAP for oxygen support.

On day 7 of life, patient had on-and-off desaturation associated with subcostal recession. Spo2 ranged between 82% and 83% under NcPAP support. He was thus intubated and was supported with synchronised intermittent positive-pressure ventilation (SIPPV). A repeated CXR post-intubation was done, demonstrating left pleural effusion and right loculated pneumothorax (Figure 2). Subsequently, an ultrasound (USG) thorax was done, showing a left huge simple pleural effusion.

Based on the USG findings, we revised our diagnosis to CC. We continued the feeding according to the age.

A left intercoastal chest drain (ICD) was inserted, and an initial drain of 70 ml of milky yellow was drained. Subsequent CXR showed there was marked resolution of the left-sided pleural effusion/collection after insertion of the left-sided chest drain (Figure 3).

The pleural fluid resulted in exudative pleural fluid. The pleural fluid was sent for further analysis which resulted in a yellowish coloured jelly like consistency with scanty amount of white blood cells. The labarotary analysis also revealed albumin, lactate dehydrogenase, protein as well as triglycerides.

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Table I: Summary of feeding and ventilation support.

Days	Feeding	Respiratory status
0–2	Breastfeeding on demand	Self-ventilating in air
2–4	Feeding according to age via cup	Self-ventilating in air
4–5	Nil by mouth	NcPAP Fio_2 30%, PEEP 5cmH_20
6–7	Started on half feeding and was increased to full feeds	NcPAP Fio_2 25%, PEEP 5cmH_20
7	Full feeding	SIPPV FiO_2 pressure 20/5
8–9	Nil by mouth	SIPPV FiO_2 pressure 20/5
9–2 months of life	MCT formula milk (basic F formula)	SIPPV FiO_2 pressure 18/5

Table II: Differences between congenital chylothorax, simple pleural effusion and pneumothorax

Characteristics	Congenital chylothorax	Pleural effusion	Pneumothorax
Definition	Accumulation of lymph in the pleural cavity	Accumulation of extra fluid around the lungs and the membranes around the lungs	Abnormal accumulation of air in the space between the thin layer of tissues that cover the lung and chest cavity
Clinical Findings	*(Depends upon the rate of chyle loss)* - hypovolaemia - respiratory difficulty secondary to pleural space fills with fluid - dyspnoea - malnutrition due to loss of proteins, fats, and vitamins	- respiratory distress - dyspnoea - dullness to percussion - decreased breath sounds	- reduced chest expansion - reduced air entry - hyper resonant on percussion
Radiology findings	Chest X-ray - homogeneous density obligating costophrenic angle and cardio phrenic angle Thoracic ultrasound - isodense echoic region without any septation or loculation Chest CT scan - low-attenuation tubular area in the posterior mediastinum MRI - shows cisterna chyli	Chest X-ray - blunting of costophrenic and cardio-phrenic angle - fluid within the horizontal or oblique fissure Thoracic ultrasound - Definite is by identifying the quad sign sinusoid sign Chest CT scan	Chest X-ray - hyperlucent hemithorax sign in case of anterior pneumothorax - medial stripe sign in case of medial pneumothorax

In view of the pleural fluid biochemistry confirming the diagnosis of CC, we kept the patient NBM with IVD maintenance according to age.

He was successfully extubated on day 4 of chest tube insertion and was weaned to room air support the following day.

He was kept NBM, till the availability of medium chain triglycerides (MCTs) based formula milk. On day 4 of chest tube insertion, we were able to restart the feeding for the patient with MCT-based formula.

Clinically the patient's condition showed improvement evident by the successful extubation of the patient; however, chest drainage was still approximately 30 ml/kg/day of chyle.
Hence, it was decided to start the patient on octreotide infusion at 1 mcg/kg/min and was titrated to a maximum dose of 2 mg/kg/h.

The addition of the octreotide infusion resulted in the reduction of the intercostal drainage to which allowed for the removal of the intercostal drain on day 17. The drain was removed after 17 days. He was continued on MCT-based formula for 6 weeks after which we introduced normal milk at 2 months of life (Table II). The introduction of formula milk was well tolerated by the patient, and he has been growing well. We are currently still following up in our outpatient paediatric clinic. At the first consultation in the paediatric clinic after discharge, a CXR was done, and it was noted there was no residual right pneumothorax present.

DISCUSSION

Congenital chylothorax is the most common form of pleural effusion during the new-born period. CC is defined as the accumulation of lymph in the plural cavity.[2] Criteria for the diagnosis of CC are the following: pleural fluid protein concentration >20g/L, triglyceride concentration > 100 mg/dl, number of cells per millilitre >100 with lymphocyte predominance and sterile culture.

The presence of milky appearance of the fluid with positive Sudan III test results is diagnostic in orally fed infants.[3] CC

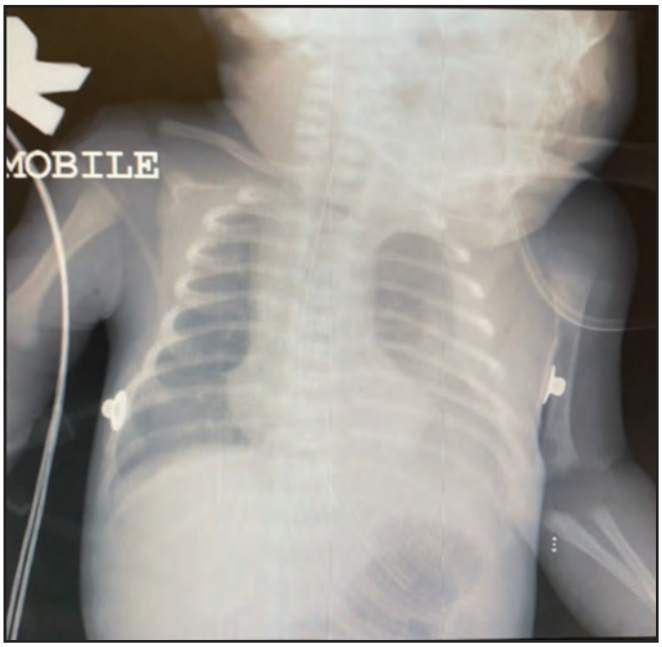

Fig. 1: A chest x-ray of the neonate given oxygen supplementation revealed left lower zone opacity/consolidation

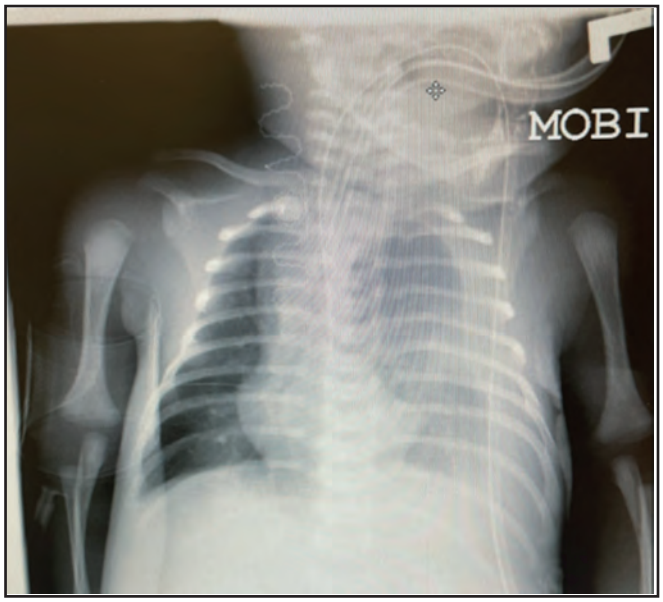

Fig. 2: Repeat CXR several days later (post intubation), revealed that there was a large left-sided pleural effusion, likely increasing in size from birth and a small loculated pneumothorax at the right lower zone. Thus, a provisional diagnosis of congenital chylothorax was made

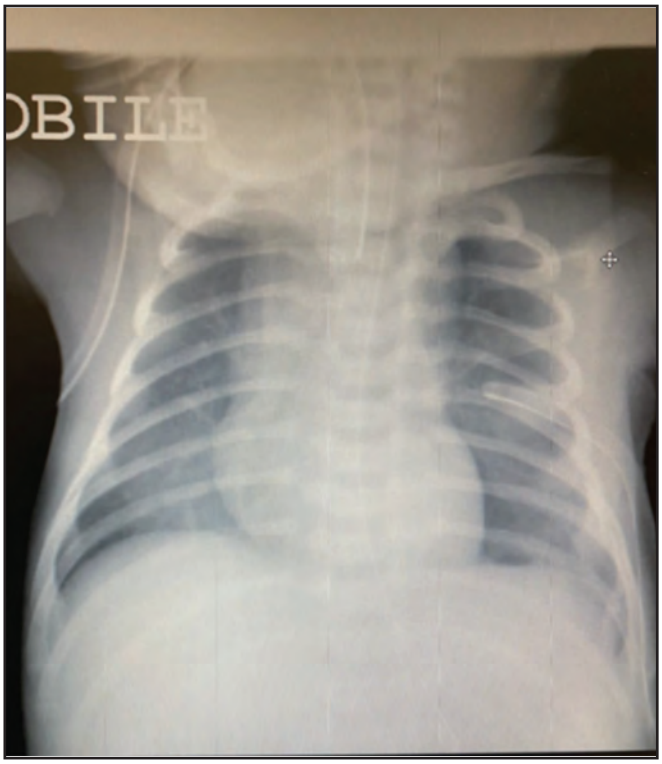

Fig. 3: CXR showed there was marked resolution of the left sided pleural effusion/ collection after insertion of the left-sided chest drain

can be idiopathic due to congenital lymphatic malformations, atresia or hypoplasia of the thoracic duct. It can also associate with syndromes such Down's, Turners, and Noonan.

The main goal of the treatment for CC is removing the chyle, preventing re-accumulation, managing the complications, and looking for the underlying aetiology. If not treated appropriately, it is a potentially a life-threatening disorder that can lead to serious respiratory distress, metabolic disorder, immunodeficiency, and nutritional complications.[4] The percentage of mortality increases depending on associated findings, gestational age and the duration and severity of chylothorax.

One of the most challenging aspects is the initial diagnosis of CC. The diagnosis requires a high degree of suspicion as radiographically the appearance may mimic pleural effusion or pneumothorax. The main diagnostic tool is thoracic ultrasound. Mainly in CC, the USG thorax will appear as an isodense echoic region without any septation or loculation. The differences between CC, pleural effusion and pneumothorax are summarised in the table below (Table II).

The management of CC can be conservative or surgical. The conservative approach involves replacing lost nutrients, draining the accumulated chyle and administering low-fat medium triglycerides (MCTs) orally.[5] By introducing MCT formulation, we bypass the intestinal lymph system, and in return, this reduces the flow of chyle into the thoracic duct, which in turn allows it to heal. The success rate of the MCT diet in CC is up to 75%.[2] However, failure of the MCT

formulation to plug this gap may result in complete nil-by-mouth and full total parental nutrition being initiated.[5] In addition to the MCT formulation, the infusion of octreotide has been proven helpful as a tool in the conservative approach. The octreotide can be administered either via venous infusion or subcutaneously. Being a somatisation analogue, the splanchnic blood flow is reduced by mild vasoconstriction, leading to less intestinal secretion and absorption. Hence, this decreases the thoracic duct flow.[2]

Surgical intervention is often required if the drainage from the ICD is more than 100ml/body weight/day or if the chyle flow is present for more than 2 weeks. Another indication for surgical intervention is the rapid decline in nutritional status despite conservative management.

Another new approach to the management of CC cases is by administrating Picibanil (OK-342) during the in-utero period. Tanemura et al. reported the usage of Picibanil (OK-342) in a patient who was scanned at the 20th week gestation period and showed severe pleural effusion, ascites, skin oedema and polyhydramnios. The Picabanil (OK-342) was administered in utero at 23, 24 and 25 weeks of gestation. The pleural effusion started to subside by 28th week of gestation and completely disappeared by the 34th week of gestation [6]. This resulted in the delivery of a healthy neonate.

Conversely, CC cases that persist for more than 2 weeks or have a high-volume leak of more than 1000–1500 ml/day, are usually managed surgically. The surgical techniques include thoracic duct ligation, mass ligation of the tissue, pleurodesis and pleuroperitoneal shunting. The surgical method that is most preferred is the ligation of the thoracic duct, as it has a higher rate of success and a lower rate of failure.

CONCLUSION

CC is a diagnostic challenge for the neonatologist. The presentation may closely resemble other common lung pathology during the neonatal period. However, an early diagnosis with prompt intervention can determine the course of management and improve outcomes. In most reported cases, a favourable outcome can be achieved with a conservative approach. We report one such case.

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CASE REPORT

Sézary syndrome: Unravelling the mystery behind erythrodermic manifestations - A case report

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SUMMARY

Sézary syndrome (SS) is a rare, aggressive leukemic variant of cutaneous T cell lymphoma (CTCL). It is often difficult to differentiate from benign inflammatory disorders such as atopic eczema, psoriasis and chronic eczema, especially in its early stages. The diagnosis relies heavily on a strong clinico-pathological association. Early diagnosis is crucial as inappropriate treatment, such as immunosuppressants, can lead to unfavourable outcomes. This article focuses on the diagnostic challenges faced and the subsequent management approach.

INTRODUCTION

Sézary syndrome (SS) is a rare leukemic variant of cutaneous T cell lymphoma (CTCL), characterised by the triad of erythroderma, generalized lymphadenopathy and neoplastic T-cells (Sézary cells) in peripheral blood.[1,2] Majority of CTCL (75%) can be classified as mycosis fungoides (MF) or SS.2 The relative frequency of SS as per World Health Organization–European Organization for Research and Treatment of Cancer (WHO-EORTC) is 2%; whereas the 5-year disease-specific survival rate of SS is 36%.[1] Another multicentre registry study in Asia reported 0.6% of SS among peripheral T cells lymphoma.[3] MF and SS often share overlapping features clinically and histopathologically, yet are considered two distinct diagnoses with separate memory T cell subset.[2,3,4] SS manifests with severe symptoms, unfavourable response to treatment and poorer survival rate in comparison to MF.[5] Its rare manifestation as generalised erythroderma poses a diagnostic challenge and impacts patient management.[1] Herein, we present a rare case of SS presenting as generalised erythroderma, discuss the diagnostic challenges faced and the subsequent management approach.

CASE PRESENTATION

A 27-year-old male of Indian ethnicity was referred by a local clinic to a tertiary hospital for dermatology consultation and evaluation of a 10-year history of diffuse, pruritic hyper-pigmented skin eruptions. He had visited multiple general practitioners prior for this troubling condition as he was disabled by its severity and could not hold onto his job. The longstanding lesions initially commenced over the trunk as dermatitis-like lesions. The lesions gradually spread over his face, bilateral limbs, and flexural area with worsening thickness and pain over the past 2 years despite followed up under dermatology clinic. Sweating and sun exposure further aggravated the skin lesions. He had a history of childhood asthma and dry skin. There was no significant family history of any malignancy, autoimmune or familial disorder. The patient was an active smoker and a non-alcoholic drinker.

Despite multiple courses of topical creams and antibiotics, the skin eruptions persisted. During the first dermatology consultation, hidradenitis suppurativa and atopic dermatitis were diagnosed. He was started on topical emollients and doxycycline. After 6 months of treatment, his lesions waxed and waned. The surface of plaques increased with new nodules over his scalp, and he developed alopecia. Accompanied by systemic symptoms such as weight loss, anorexia and reduced effort tolerance, the clinical picture was intriguing.

On examination, he had generalised hyper-pigmented plaque-like and nodular lesions with scratch marks over his face, trunk, upper and lower limbs, accounting for about 95% of his body surface area. Diffuse alopecia and infiltration over facial skin were present (Figure 1). There was an absence of lymphadenopathy and hepatosplenomegaly. Other examinations were unremarkable.

The preliminary laboratory investigations showed an elevated white cell count of 17.3 109/L and lactate dehydrogenase level of 285 U/L. Peripheral blood smear showed leukocytosis with eosinophilia without any blasts seen, indicating a potential inflammatory or infectious condition. His total IgE was >5000 kU/L. The Viral screening panel was negative. Flow cytometry immunophenotyping of peripheral blood showed a small cluster of 3.5% aberrant T cells expressing c3, 3 dim, TCRab dim, 2 dim, 5 bright, 4 dim and lacking all other antigens including 7, 8, 26, 25, 30, cyTCL-1, 34 and nTdT alongside 47% cluster of eosinophils.

A biopsy of skin over his back presented with epidermotropism with Pautrier microabscess, a feature suggesting CTCL[4] (Figure 2). The atypical lymphoid cells expressed CD2, CD3, CD4, CD5, CD7 and GATA3 diffusely

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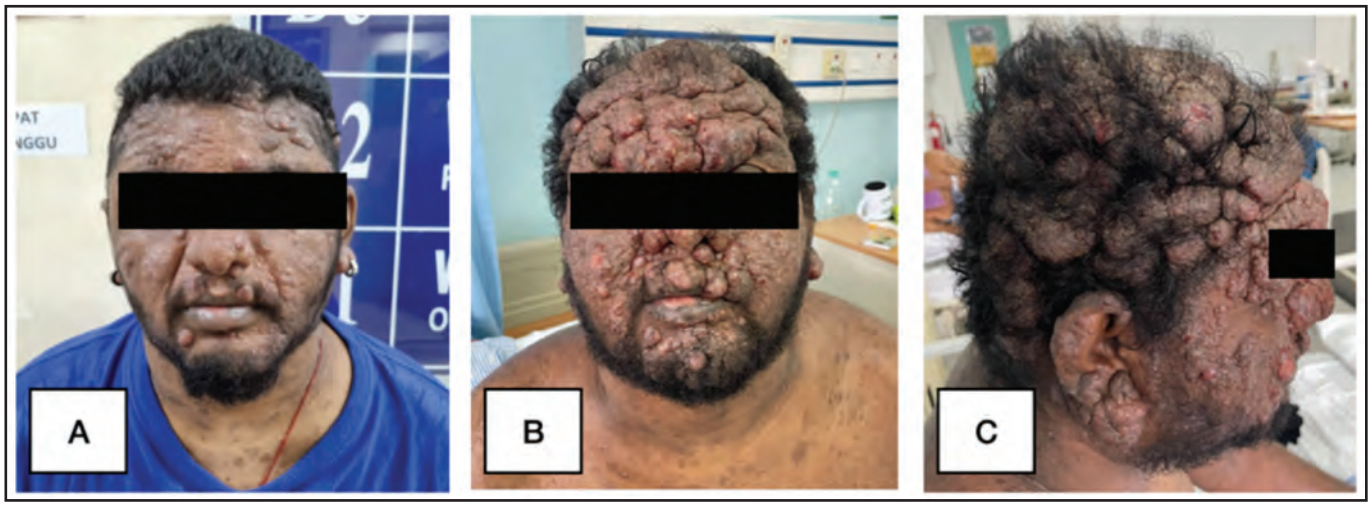

Fig. 1: Clinical images of the patient with cutaneous findings. A. 2 years ago (front view): Scattered plaques-like and nodular lesions over bilateral temporal region and nasolabial folds. B. Current (front view) : Infiltration over facial skin—leonine facies. C. Current (side view): Diffuse alopecia and nodules over scalp; infiltration over ears

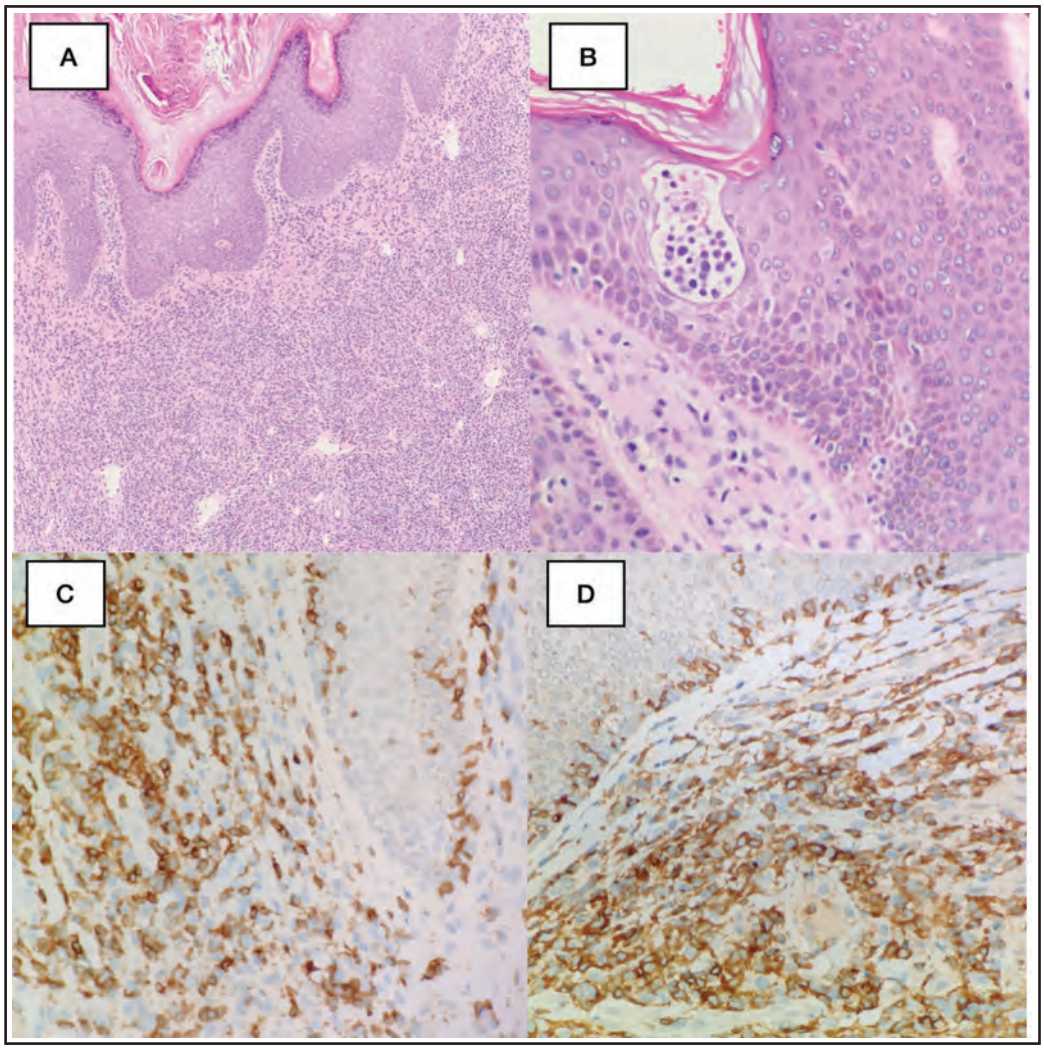

Fig. 2: Histological findings from the skin biopsy. A.Diffuse lymphoid infiltrates in the dermis along with occasional epidermotropic lymphocytes(H&E with 100× magnification). B. The case showing Pautrier microabscess (H&E with 400× magnification). C. Neoplastic CD3-positive T-cells can be seen in the epidermis and dermis (CD3 immunostain 400× magnification). D. Neoplastic CD4-positive T-cells can be seen in the epidermis and dermis (CD4 immunostain 400× magnification)

(Figure 2). There was a smaller number of those cells expressing BCL6, CD8, CD30, CD56, T1A1 and PD1. The cells stained negative for CD10, CD20, CD21, EBER (ISH), MPO, TDT and granzyme B. The Ki67 proliferative index was reported to be about 30%. Computed tomography of thorax, abdomen and pelvis revealed multiple skin thickening and nodules, but no visceral organ involvement, hence the tumour, node, metastasis, and blood (TNMB) staging was determined to be stage 3A T4N0M0B0.[1]

Collectively, the clinical and histopathological features were suggestive of SS.

A multidisciplinary approach was taken in the management of the patient in order to minimise the side effects of the long-term treatment and improve quality of life.[4,5] He was started on standard combination therapy of chemotherapy oral Methotrexate 10mg once a week and oral prednisolone 20mg OD.[2,6] There was limited response to oral chemotherapy. First cycle of intravenous infusion of methotrexate treatment was complicated by septic shock secondary to methicillin-sensitive *Staphylococcous aureus* bacteraemia. Subsequently, he was switched back to low-dose oral methotrexate. Ultraviolet phototherapy (Psoralen plus Ultraviolet A), an effective adjuvant therapy was started alongside with skin-directed topical treatments for symptom control.[4-6] His condition remained stable on this regime; however, he has yet to achieve a complete skin clearance. He was planned for total skin electron beam therapy, with future plans for subcutaneous interferon and brentuximab vedotin as the next steps in management.

DISCUSSION

This case highlights the importance of recognising uncommon presentations of SS. The common non-classic signs of SS were palmoplantar keratoderma, onychodystrophy, alopecia, leonine facies, and ectropion. Erythroderma, although a rare presentation, should be considered in patients with long-standing, progressive skin lesions and systemic symptoms.[8] Unless there is an exacerbation of pre-existing dermatoses, the final diagnosis of erythroderma depends on the individualised evaluation of clinical, biochemical, and histological findings of each patient. A 12-year-prospective study by Miyashiro and team reported the most common aetiology of erythroderma is eczema (20.7%), followed by psoriasis (16.8%), SS (12.3%), drug eruption (12.3%), atopic dermatitis (8.7%) and MF (5.5%).[9] The prevalence of CTCL can be as high as 18% in patients with erythroderma, not including the idiopathic erythroderma (16.8%) that may represent a pre-SS or not yet diagnosable erythrodermic CTCL.[9]

Erythroderma in SS can develop with or without the background of pre-existing cutaneous lesions.[4] The diagnosis of SS is challenging, particularly in the early stages. SS can masquerade as benign inflammatory disorders.[9] Patients may have other dermatologic symptoms (nonspecific dermatitis, poikiloderma or erythroderma) for years to decades, diagnosing as MF/SS.[5] It is difficult to further differentiate between SS and erythrodermic CTCL.[9,10] This can be due to clonal T cells occasionally being present in benign skin conditions and older subjects secondary to the ageing process. Furthermore, not all SS patients fulfil the criteria of CD4: CD8 ratio ≥ 10 at presentation.[9] In such cases, it is crucial to have unequivocal identification of Sézary cells in blood or skin.[10] It is strongly recommended for clinicians to be highly suspicious of CTCL and lower threshold to proceed with skin biopsy over the most indurated area after stopping topical treatment for >2 weeks in these patients, if the clinical course raised suspicion with the initial skin biopsy, is nondiagnostic.[5]

Immunostaining of specimens and flow cytometry of peripheral blood can aid in clonal cell detection to facilitate the accurate diagnosis of SS.[5,9] In SS, clonal T cells are generally CD3+CD4+ and CD8-.[2,4,5] The loss of CD7 and/or CD26 is highly specific for SS.[2] In contrast, MF have immunophenotypic characteristics of skin-resident effector memory T cells (CCR4+, CCR7–) compared to SS's phenotype of circulating central memory CD4+ T cells.[4,5] Alternatively, clonal gene rearrangement of T-cell receptors in skin or blood for clonality.[4,5]

The treatment of SS is stage-dependent; thus, early recognition can guide therapeutic strategy and potentially improve prognosis.

CONCLUSION

SS can present with a myriad of clinical manifestations.5 Recognising the atypical manifestation is key for early diagnosis and appropriate prompt management.5 Furthermore, standardising the evaluation of erythrodermic patients is the first step to better define the management and understand the evolution of this severe skin condition.[1] This case highlights the implication of taking into consideration SS in the diagnosis of erythroderma.

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ETHICAL CLEARANCE

Ethical clearance has been obtained from NMRR Secretariat (NMRR ID-23-02134-8R3). Informed consent was obtained from patient/ patient's family members in line with COPE standards for his/her images and other clinical information to be reported in this journal. Due efforts are made to conceal their identity.

DECLARATIONS

The authors declare no conflict of interest.

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CASE REPORT

Scrofuloderma: An arduous diagnosis

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SUMMARY

Cutaneous tuberculosis is a rare occurrence. It comprises 1 to 1.5% of all the extra-pulmonary tuberculosis cases. Scrofuloderma, also known as tuberculosis colliquativa cutis, is a form of cutaneous tuberculosis that was frequently observed prior to the availability of effective treatment for tuberculosis. We reported a case of scrofuloderma in an elderly male who presented with chronic non-healing ulcerative nodules over the left axilla and upper limb. His condition did not improve with empirical antibiotics and anti-fungal agents. The diagnosis was made based on the skin punch biopsy suggestive of scrofuloderma.

INTRODUCTION

According to World Health Organization (WHO) 2022 data, extrapulmonary tuberculosis constituted 17% of the ten million incident cases in 2021.[1] Cutaneous tuberculosis presents in a wide range of clinical manifestation. The causative agents are Mycobacterium tuberculosis, Mycobacterium bovis and the Bacille Calmette-Guérin vaccine. Scrofuloderma results from the direct extension of the infection from deep structures (e.g., lymph node, bone, joint or epididymis) to the overlying skin. It typically starts with slow growing subcutaneous nodules that may eventually ulcerate and drain caseous or seropurulent content.[2] Scrofuloderma mimics a wide differential diagnosis. Without treatment spontaneous healing may occur, but it may take years before lesions are completely replaced by scar tissue.[3]

CASE PRESENTATION

A 65-years-old male rubber tapper presented with multiple skin lesions over left upper limb for 2 months. The lesions initially started as multiple swellings over his left axilla which spontaneously ruptured with purulent discharge. Multiple similar swellings subsequently appeared over the left inner arm and the left shoulder. They were associated with redness of overlying skin and mild pain. He did not report fever, chronic cough, or weight loss. His comorbidities are hypertension and dyslipidaemia. His grandson had received treatment for pulmonary tuberculosis 4 years ago. Physical examination showed multiple ulcerated, indurated, erythematous skin nodules over the affected areas (Figure 1a and b). The skin lesions failed to improve after completion of two weeks of tablet ampicillin/sulbactam 375 mg BD and 4 weeks of capsule itraconazole 200 mg BD. The empirical treatment was initiated by surgical and dermatological department while awaiting skin biopsy report. Mantoux test was positive (17 mm). Skin tissue was tested negative for acid-fast bacillus (AFB), mycobacterium tuberculosis (MTB) culture, MTB PCR, fungal culture and fungal PCR. Biopsied skin specimen reported granulomatous inflammation (Figure 2a, b, c and d). His chest X-ray was normal. Patient was treated with the standard regimen of anti-tubercular therapy consisting of rifampicin (R), isoniazid (H), pyrazinamide (Z) and ethambutol (E) for 2 months continued by rifampicin (R), isoniazid (H) for the next 7 months. Patient tolerated the therapy well and the skin lesions healed gradually leaving scar tissue (Figure 1c, d and e). No new skin lesions were identified during the subsequent follow up.

DISCUSSION

Cutaneous tuberculosis was first described in 1981 by Beyt et al Scrofuloderma is increasingly recognised as one of the most common forms of cutaneous tuberculosis.4 Scrofuloderma has a broad differential diagnosis such as atypical mycobacterium infection, actinomycosis, sporotrichosis, botryomycosis, nocardiosis, coccidioidomycosis and hidradenitis suppurativa.

Scrofuloderma is more commonly seen among the children, adolescents and older adults.[2] Cervical lymph nodes are the most common source of infection. The disease is typically dominated by granulomatous necrosis, scarring and sinus tract formation.[5] Mantoux test is a useful screening test for tubercular infection. There has been increased utilisation of PCR because of its rapidity, sensitivity, and specificity.[3]

The diagnosis of scrofuloderma often requires detection of the causative organism by culture, smear, or skin biopsy. However, the causative organism may not always be detectable in all cases. According to Amar et al., a case of scrofuloderma was diagnosed and successfully treated based on physical examination findings and typical histopathological changes.[6] Soeroso et al. reported another similar case of scrofuloderma with additional regional lymph node involvement.[7] Both the cases were diagnosed without detection of mycobacterium tuberculosis by culture or molecular method in the background of strongly positive Mantoux test.

Pulmonary tuberculosis/other forms of extrapulmonary tuberculosis infection should be looked for as soon as cutaneous tuberculosis is diagnosed. A full physical

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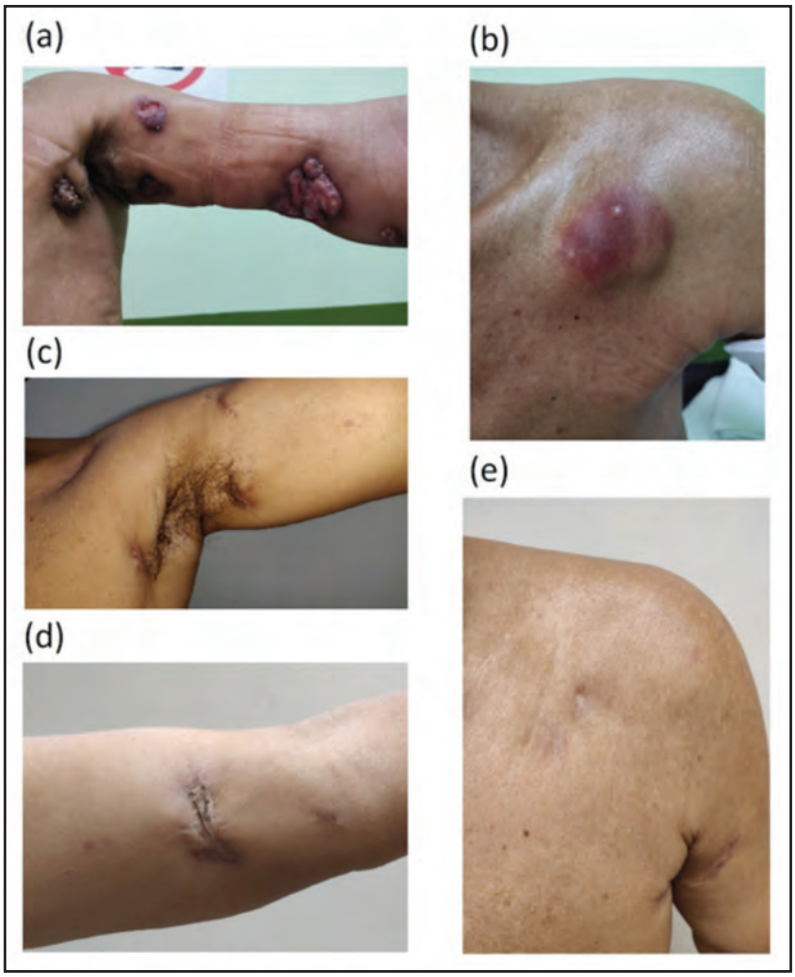

Fig. 1: (a) Multiple ulcerated skin nodules over left axilla and left arm. (b) Erythematous nodule over left shoulder. (c) Resolved skin lesions over left axilla after completion of anti-tubercular treatment. (d) Resolved skin lesions over left inner arm after completion of anti-tubercular treatment. (e) Resolved skin lesion over left shoulder after completion of anti-tubercular treatment

examination and chest radiograph should be performed. The general approach to treatment of cutaneous tuberculosis is similar to the approach to systemic tuberculosis, which can be treated with a short course of four-agent chemotherapeutic regimen given for two months followed by a two-drug regimen for the next 4 months.

In our case, patient presented with sole cutaneous lesions without any constitutional symptoms. The diagnosis was delayed, and he had failed the empirical treatment targeting at possible deep skin bacterial/fungal infection. During follow up, the Mantoux test and histopathological study of skin biopsy showed diagnosis in favour of cutaneous tuberculosis in the form of scrofuloderma. Standard guidelines suggested 6 to 9 months of anti-tubercular therapy in all forms of cutaneous tuberculosis. Our patient received 9 months of anti-tubercular therapy as he had developed extensive skin lesions and subsequently recovered well.

CONCLUSION

Diagnosis of scrofuloderma is challenging and requires correlation of clinical findings and appropriate diagnostic tests in the background of high clinical suspicion. An accurate diagnosis is essential before anti-tubercular therapy could be initiated timely.

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None.

ETHICAL APPROVAL

The research is registered under National Medical Research Register in Malaysia (NMRR ID-23-00592-PIL). Ethical approval is not required as per The Medical Research & Ethics Committee (MREC) protocol.

PATIENT CONSENT

The patient was properly informed and had provided consent for the clinical information to be included in the publication of this case report and the accompanying images.

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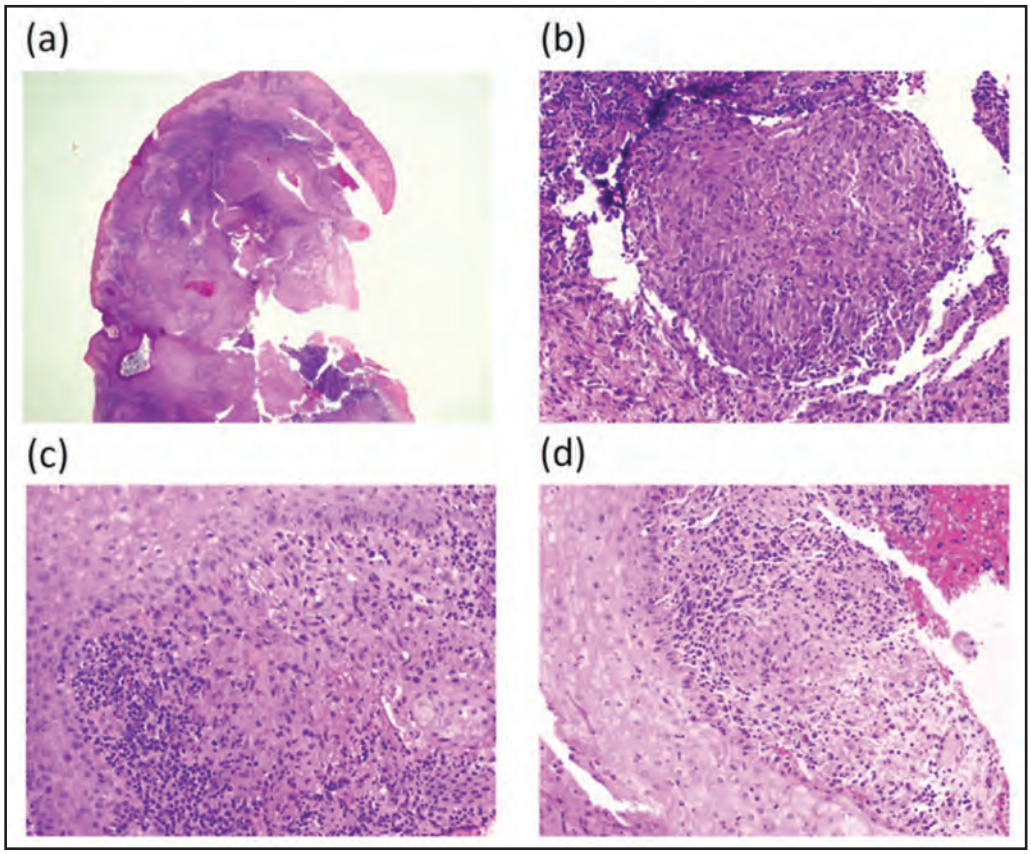

Fig. 2: (a) Skin biopsy tissue displaying pseudoepitheliomatous hyperplasia. (b) Granuloma with central necrosis. (c) Granuloma surrounded by lymphoplasmacytic cells at subepidermal area. (d) Granuloma surrounded by lymphoplasmacytic cells and Langhans type multinucleated giant cells

CONFLICTS OF INTEREST

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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Beaver tail liver: An uncommon presentation

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SUMMARY

The beaver tail liver represents an anatomical variation where the left lobe extends beyond the midline, reaching laterally into the left side of the abdomen and occasionally enveloping the spleen. This uncommon variation in liver anatomy has clinical implications, including potential diagnostic challenges and increased susceptibility to trauma or iatrogenic injury. Diagnosing this variant can be intricate due to its similar echogenicity in ultrasound (USG) and density in computed tomography (CT) images. We present a case where a beaver tail liver manifested as an extraluminal mass, causing compression on the gastric fundus during an oesophagogastroduodenoscopy examination. This report aims to underscore the diverse presentation of this clinical condition.

INTRODUCTION

The anatomical variant known as the beaver tail liver, or liver sliver, is characterised by the left lobe extending laterally to make contact with and enclose the spleen, resembling the tail of a beaver. This feature is more prevalent among females. Radiologically, ultrasound (USG) may exhibit similar echogenicity with the spleen. However, the use of colour Doppler is valuable in identifying the hepatic vascular structures, aiding in the differentiation from perisplenic haematoma or renal structures.[1]

CASE PRESENTATION

A 36-year-old male presented to the emergency department with per chronic rectal bleeding and symptomatic anaemia. Physical examination revealed grade 1 haemorrhoid without signs of recent bleeding. Oesophagogastroduodenoscopy identified an extraluminal mass causing partial compression at the gastric fundus (Fig. 1). The upper scope easily passed, reaching duodenum D2 with no significant findings, and colonoscopy revealed no abnormalities. A computed tomography (CT) abdomen showed a homogeneously enhanced liver with a smooth margin. However, the left lobe of the liver was elongated, extending laterally in contact with the spleen (Fig. 2). The biliary system and liver vasculatures appeared normal, with no other reported abnormalities. Rubber band haemorrhoidal banding was performed, and the patient was discharged in good condition after optimising the haemoglobin level.

DISCUSSION

The beaver tail liver, more commonly found in middle-aged females, is often asymptomatic and discovered incidentally through CT imaging for unrelated reasons. Limited literature, particularly in paediatrics, documents its incidence and geographical distribution.[2]

There have been cases of misinterpretation during trauma assessments, where it was initially mistaken for splenic subcapsular hematoma or perisplenic fluid collection.[3] In an unusual presentation, it resembled an organised haematoma during coronary artery bypass graft surgery (CABG).[4] This report is the first to identify the beaver tail liver causing an extraluminal mass compressing the gastric fundus.

While the beaver tail liver does not pose additional pathological risks, it can impact patient management. The Focused Assessment with Sonography for Trauma (FAST) scan, crucial for evaluating blunt abdominal trauma, may incorrectly identify the extended left liver lobe as a splenic haematoma. Careful sonographic examination of the perisplenic region, including assessing hepatic and portal veins, helps differentiate the liver variant from perisplenic haematoma.[5]

Due to its extension into the left lateral abdomen, trauma to this area increases the risk of injury. Lack of awareness about this anomaly may lead to complications during operative interventions,[6] such as percutaneous gastrostomy tube or percutaneous endoscopic necrosectomy.[7]

In the context of liver transplantation, ensuring donor safety is crucial. Studies suggest that individuals with a liver extending to the left hypochondrium have a secure postoperative remnant volume. The beaver tail liver feature, indicating an extended left liver lobe, could be a positive marker for safe transplantation, especially when 3D volumetric evaluation is not possible. Living liver donors with this feature may have a safer recovery and better outcomes due to a larger remaining liver volume.[8]

Hence, the beaver tail liver feature emerges as a potential positive marker for safe transplantation, emphasising the importance of further research in assessing its incidence, geographical distribution, and impact. The classification of the beaver tail liver anatomy, especially in terms of the extent of contact and enclosure between the left liver lobe and spleen, could prove valuable for future clinical applications.

CONCLUSION

The beaver tail liver is often discovered incidentally but presents with diverse manifestations and potential

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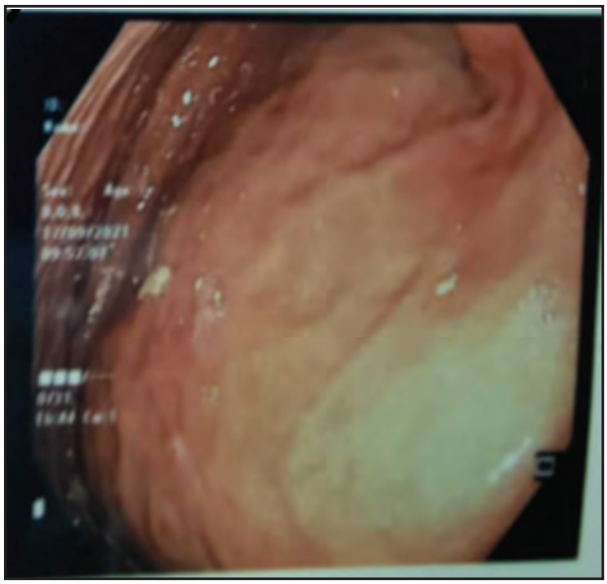

Fig. 1: Oesophagogastroduodenoscopy image shows the presence of extraluminal mass (arrow) causing compression at the gastric fundus

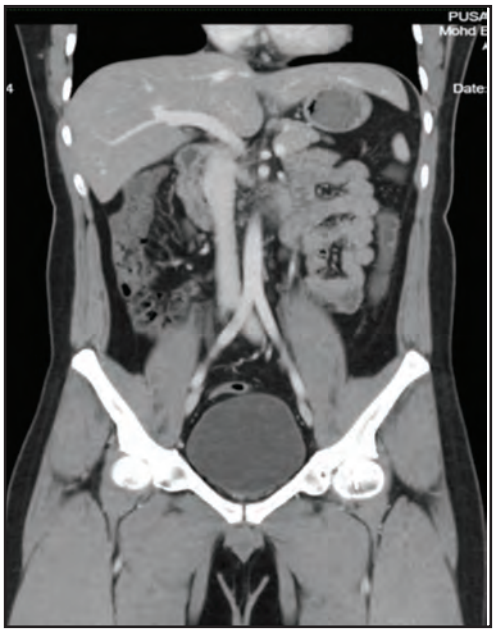

Fig. 2: Oesophagogastroduodenoscopy image shows the presence of extraluminal mass (arrow) causing compression at the gastric fundus

misinterpretations during trauma assessments. While not posing additional pathological risks, its implications for patient management, underscore the need for awareness.

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CONFLICT OF INTEREST

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Head and neck arteriovenous malformation: A rare case and review of literature

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SUMMARY

Arteriovenous malformation (AVM) of the head and neck region is an extremely rare existence. This condition can lead to various complications due to the surrounding complex anatomical structures of the head and neck. From the clinical manifestation, AVM mass can be easily mistaken for other soft tissue masses. The gold standard diagnostic procedure for AVM is angiography. The current approach in managing AVM involves a combination of conventional surgical technique and endovascular procedure. The ultimate goal is to achieve either complete removal of the nidus or total occlusion of its blood flow. The management of head and neck AVM demands a comprehensive, multidisciplinary approach involving various medical specialties.

INTRODUCTION

Arteriovenous malformation (AVM) of the head and neck region is an extremely rare existence. This condition can lead to various complications due to the surrounding complex anatomical structures of the head and neck. From the clinical manifestation, AVM mass can be easily mistaken for other soft tissue masses. The gold standard diagnostic procedure for AVM is angiography. The current approach in managing AVM involves a combination of conventional surgical technique and endovascular procedure. The ultimate goal is to achieve either complete removal of the nidus or total occlusion of its blood flow. The management of head and neck AVM demands a comprehensive, multidisciplinary approach involving various medical specialties.

CASE PRESENTATION

A 20-year-old male presented with a mass on the right neck. The patient said that the swelling initially was as big as a peanut and had been present since childhood. However, the swelling started growing larger until it reached the size of a tennis ball within a period of 4 months. The patient felt difficulty and pain during swallowing but denied any difficulty of breathing or hoarseness. Physical examination revealed significant swelling within the right neck region with clear margin and soft consistency upon palpation. From the cranial nerve examination, all was within normal limits. The patient was haemodynamically stable with normal vital signs.

Laryngoscopy showed a vascularised mass at the right vallecula, deviating the epiglottis to the left. The mass extended into the supraglottic region (Fig. 1). The vocal cord movement was symmetrical during adduction and abduction. A contrast-enhanced computed tomography (CT) of the neck demonstrated a well-margined amorphous mass with the dimension of 4.1 × 5.3 × 5.6 cm in right neck region with density of 41 Hounsfield units (HU) precontrast and lined up to 58 HU postcontrast. The mass drawing vascularisation from right external carotid artery and superior right thyroid artery was also seen from the CT result. Thus, a high vascularised mass was suspected.

A multidisciplinary meeting with the interventional radiologist and anaesthesiologist was held to decide the best approach to treat the patient. Because of the suspicion of highly vascularised mass in the neck which extend into the supraglottic region, it was then decided for the patients to have tracheostomy to secure the airway before angiography. the interventional radiologist would confirm the AVM during angiography and proceed with the embolisation.

Embolisation under general anaesthesia was carried out. The procedure involved a right femoral approach to access the right common carotid artery. After digital subtraction angiography (DSA) was assessed, selective catheterisation of the right external carotid artery branches was then carried out in a systemic fashion, followed by transarterial embolisation using polyvinyl alcohol (PVA) sequentially under fluoroscopic guidance (Fig. 2).

During recovery, there was no significant pain except around the recent tracheostomy site. No visual or neurological deficit was found. Within one night, the patient's symptoms of dysphagia had significantly improved with almost complete devascularisation of the mass radiologically, the patient was then discharged home one day after.

Follow up was done 1 month after the embolization to detect any early signs of recurrence and to plan possible decannulation procedure when the airway was completely safe. At follow-up, there was no clinical complaints nor any enlargement of the neck and no signs of complication from the embolisation procedure (Fig. 3). A follow up, contrast-enhanced CT angiography of the neck was done for evaluation and detected shrinkage of the mass by 32%. There was a hypovascularised mass with size of 3.6 × 4.6 × 5 cm without airway narrowing. Thus, patient was instructed to undergo routine long-term follow-up to assess the progress of his condition.

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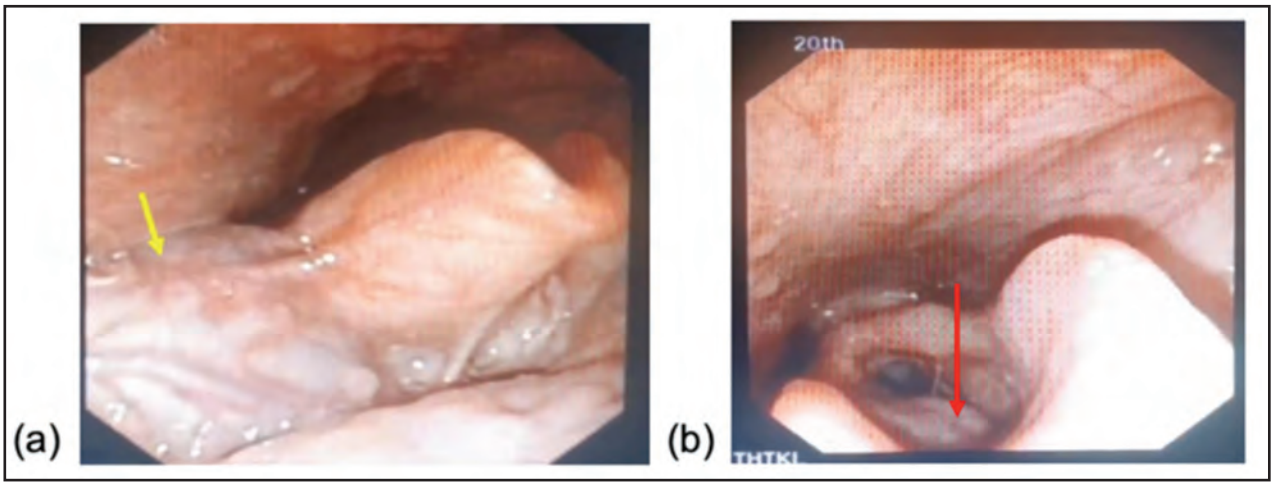

Fig. 1: Laryngoscopy a) a mass on the right vallecula deviating the epiglottic to the left (yellow arrow), b) a mass on the supraglottic area, the vocal cord showed symmetrical movement (red arrow)

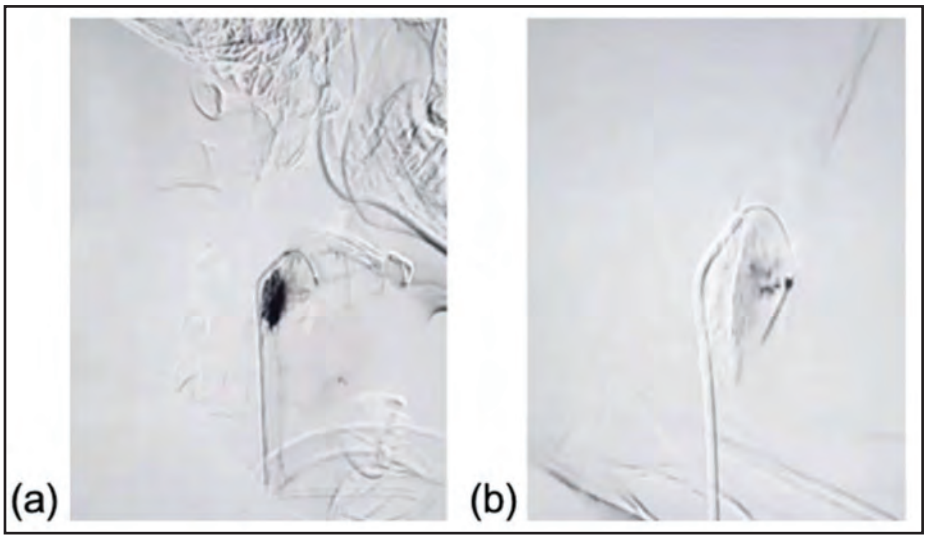

Fig. 2: Angiogram showing the AVM nidus drawing from right carotid artery and right superior thyroid artery. a) Pre-embolisation – showing tumour blush appearance. b) Post-embolisation – showing no visible blushing

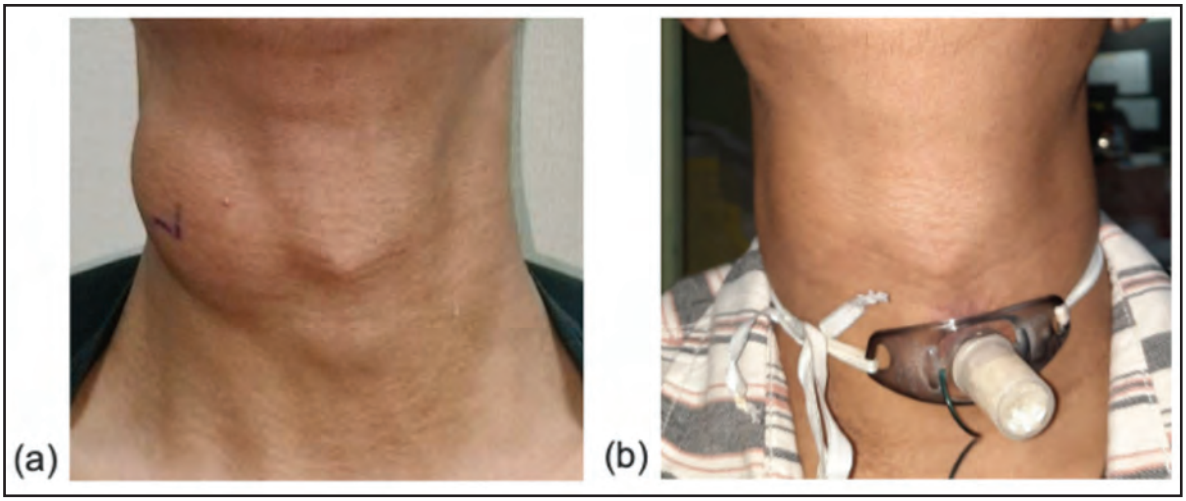

Fig. 3: Clinical picture of the patient before and after embolisation. a) Pre-embolisation. b) Post-embolisation

DISCUSSION

AVMs fall under the category of congenital high-flow vascular anomalies, constituting a mere 4.7% of all vascular irregularities. While AVMs most frequently occur within the central nervous system, they are seldom found extracranially.[3] AVMs usually exist as clinically dormant but may become progressively symptomatic until adulthood, leading to disfiguring and life-threatening complications. Contributing factors might include infection, injury, or hormonal imbalances during phases like pregnancy or puberty.[2] Their diagnosis relies on complete patient history, clinical assessment and specific imaging traits. There are various classification systems for AVMs (Table I).[4]

AVMs have diverse clinical presentations and pose challenges to manage due to high rates of recurrence irrespective of therapeutic approach. The classification and management of AVMs have considerably changed in the last few years. Endovascular treatment is currently almost always part of the treatment of AVMs often combined with surgical resection.[1] AVMs within the head and neck poses a unique challenge given the proximity to vital structures.[5]

In our case, for radiological imaging we use contrast-enhanced CT scan and angiography. CT scan was a useful diagnostic imaging tool for its high spatial resolution and quick scanning time, it also could detect soft tissue abnormalities and bone involvement. It provided detailed evaluation of the angiographic structure of the mass which in our case was originated from right external carotid and right superior thyroid artery. Head and neck AVM may be fed by multiple or bilateral arteries including external and internal carotid, vertebral, or subclavian artery depending on the distribution around the region. Arteriography remains the gold standard to diagnose AVM is mainly characterised by tortuous, dilated arteries with arteriovenous shunting and enlarged draining veins. Even though in this case we did not use ultrasonography with colour doppler, it is an accessible and inexpensive modality to assess disease progression and treatment outcomes.[1] Biopsy is not necessary to diagnose AVM and should be avoided as far as possible due to the risk of bleeding and the possibility of triggering growth of an AVM.[6]

The available literature highlights instances of high success rates in treating head and neck AVM using a singular treatment approach, particularly emphasising embolisation. Various embolic material can be used for the endovascular treatment of the AVM. It has been recommended that transarterial embolisation with slow injection with penetration to draining veins along with shunt points using low concentration n-butyl-2-cyanoacrylate (NBCA) can achieve better embolisation effect of AVMs.[7] Although there had been many results reported of a vast variety of embolic agents for transarterial embolisation, the use of NBCA had become the most commonly utilised due to its proven properties and effectiveness. This liquid embolic material was frequently used for its permanent embolic effect and wide blockage from the vascular feeder to drainers via fistula. NBCA is considered to depict high thrombogenicity compared to other liquid embolic materials.[7]

The application and selection of embolic agents in the management of head and neck AVMs depend on several factors like the vascular characteristics, the AVMs classification, the expertise of the treatment team, and the availability of the embolic agents, also the main goal of the procedure. We used transarterial PVA which is a permanent type of agent used worldwide. In our case, we use PVA because it was readily available, inexpensive, and has good capillary control.[7] Thus, the outcome of our case still obtains quite satisfactory results in the aspect of function and appearance. The main focus of our treatment was to preserve the surrounding anatomical structure of the neck region in order to avoid potential complication with swallowing and breathing. Ischemic complications in the nervous system may arise due to the migration of embolic materials into the cerebral arteries or the vessels that supply the cranial nerves, known as the vasa nervorum. Such occurrences can result in mortality or severe neurological deficits. To mitigate these risks, particularly in embolisation involving liquid embolic material, it is crucial to carefully observe and address angiographic findings demonstrating the neural arteries. Injection of liquid embolic material or small-sized particles is contraindicated in the head and neck arteries that have anastomotic channels with cerebral arteries and vasa nervorum.[7]

Surgical treatment alone might be considered the initial treatment choice for smaller, isolated AVM characterised by well-defined feeding vessels and without any involvement of bones. For larger or previously treated AVM, a combination of super selective embolisation and surgical intervention has been shown to yield better intraoperative management and the highest rates of success.[1]

The patient was instructed to undergo routine long-term follow-ups because of the possibility of recurrence, as reports suggest that it can occur in as many as 80% of cases following embolisation or resection. Incomplete removal or embolisation of the nidus can stimulate aggressive growth of the remaining lesion, leading to a risk of progression as high as 50% within the initial five years. Furthermore, recurrences have even been observed a decade after treatment, underlining the necessity of extended post-treatment follow-up for timely detection. It's important to consider that the interpretation of the term 'cure' varies within the literature and reported instances of 'cure' might be influenced by limited follow-up periods. Some reported cases of 'cure' refer to an asymptomatic state following embolisation, rather than a complete absence of the condition.[1]

CONCLUSION

Head and neck arteriovenous malformations (AVMs) are rare vascular abnormality that is not commonly found in clinical practice. Because they come with such dire consequences often associated with both cosmetic issues as well as serious consequences including life-threatening bleeding, swallowing problem and airway obstruction. Awareness of the clinical appearances and correct choice of modalities is important to uphold swift diagnosis and accurate management. Our case demonstrated head and neck AVM treatment based on multidisciplinary decision for a single

Table I: Overview of various classification systems for AVMs.[4]

Focal vs diffuse		Schobinger	Suen-Richter
Focal	Diffuse	Stage I: Quiescence, cutaneous blush, warmth	T: Size of AVM T_1: 1 Cervicofacial subunit T_2: 2 Cervicofacila subunit T_3: 3 Ccervicofacila subunit T_4: Bilateral/multifocal disease
Discrete border with central nidus	Multiple or no discrete nidus	Stage II: Expansion; active growth, pulsations, bruit	D: Depth of AVM invasion D_1: Skin and/or subcutaneous involvement D_2: Subcutaneous and muscle involvement D_3: Subcutaneous, muscle, and cartilage or bone involvement D_4: Skull base or intracranial extension
Firm to palpation	Compressible with rapid rebound	Stage III: Destruction; same as stage II but symptomatic (pain, bleeding, disfigurement)	S: Schobinger stage modified: Kohout and colleague S_0: Quiscence S_1: Expansion (Bruit, pulsation, rapid growth S_2: Destruction (Ulceration, bleeding, pain)
1-2 arterial feeders	Multiple arterial feeders	Stage IV: Decompensation; same as stage III but with high- output cardiac failure	Stages: Stage I: $T_{1\text{-}2}$ D_1S_0, $T_1D_1S_1$, $T_1D_2S_0$ Stage II: $T_1D_3S_0$, $T_2D_{1\text{-}2}$ $S_{1\text{-}2}$, $T_2D_2S_0$ Stage III: $T_1D_3S_{1\text{-}2}$, $T_3D_{1\text{-}2}S0$, $T_2D_3S_{0\text{-}2}$ Stage IV: $T_3D_3S_{0\text{-}2}$, any D_4, any T_4
Good treatment outcomes	Higher risk of recurrence	-	-

endovascular approach with an optimal functional and cosmetic outcome.

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DECLARATION

The authors declare no conflict of interest.

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Unveiling the potential fatality of refeeding syndrome in malnourished patients: A case series

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SUMMARY

Detecting refeeding syndrome is always challenging unless a thorough assessment is conducted. In some cases, despite all efforts for replenishment, the condition remains refractory. We present three cases of upper gastrointestinal cancer patients with severe malnutrition who were fed without prior electrolyte replenishments and succumbed to severe refeeding syndrome. The discussion emphasises the importance of precautionary measures in managing such cases. A high index of suspicion, especially given the background of severe malnutrition, is pertinent to detecting potential cases of refeeding syndrome. Initiation of hyperosmolar, hyperglycaemic parenteral or enteral feeds shall be withheld before any electrolyte replenishment or vitamin supplementation. Current guidelines emphasise screening followed by diligent resuscitation, replenishment, and supplementation.

INTRODUCTION

Refeeding syndrome is a potentially lethal condition that occurs among malnourished patients who are fed immediately after a period of prolonged starvation with high volumes of calories.[1] It is a spectrum of clinical manifestations as a result of fluid and electrolyte shifts from the intravascular space into the intracellular space. This fatal shift results from the metabolic requirement of a sudden increase in calories in the background of depleted body resources.[2] The biochemical hallmarks of refeeding syndrome are hypophosphatemia, hypomagnesaemia and hyopokalaemia.[3] Untreated, refeeding syndrome will cause a myriad of clinical consequences due to protracted depletion of thiamine, phosphate, magnesium, potassium and on the contrary fluid and sodium overload.[4] Replenishments of thiamine, phosphate, magnesium, potassium, vitamins and trace elements are crucial before any provision of feeding or calories.[5] Once stable feeding or calorie provision can be initiated or increases slowly. Available guidelines in the management of potential or overt refeeding syndrome incorporate risk stratifications, specific risk factors (e.g., cancer, chronic alcoholic, post bariatric surgery), nutritional assessment, baseline electrolyte checks and thorough monitoring during the treatment and provision of calories.[6] Three cases of severe refeeding syndrome are presented here to highlight precautionary steps and pertinent points in managing such fatal but commonly missed cases.

CASE PRESENTATION

As standard protocol, all upper gastrointestinal cancer patients referred to the National Cancer Institute Putrajaya Malaysia for definitive treatment were screened for malnutrition and the risk of refeeding syndrome before any nutritional and physical rehabilitation. Throughout 2022, there were 236 cases of upper gastrointestinal cancer, and among them, three cases were identified suffering from severe refeeding syndrome. Refer to Table I for their characteristics and risk stratifications.

Case 1

A female with stage III obstructed adenocarcinoma of the stomach was diagnosed after 12 weeks of post-prandial vomiting, inadequate oral intake and 16% weight loss. Cancer confirmation and staging by endoscopy, histopathological report and CT imaging was done. She had severe hypophosphatemia, hypomagnesaemia, and borderline low potassium. Total parenteral nutrition was initiated by the referring hospital without any electrolyte replenishment. We withheld the feeding, resuscitated her, and replenished the phosphate, magnesium and potassium. Intravenous vitamins and trace elements were given concomitantly. She succumbed to cardiac failure, which is one of the most common sequelae of severe refeeding syndrome.

Case 2

A case of non-familial gastric polyposis who suffered post-prandial vomiting and 20% weight loss over a period of 2 months. Immediate enteral tube feeding was initiated up until 86% of his total energy requirement without prior electrolyte assessment and replenishment. We withheld the feeding and resuscitated him with intravenous vitamins and trace elements. He responded well initially; thus the low-calorie provision was reinitiated at 13 kcal/kg/day. Concurrent electrolyte replenishment was continued with cautious monitoring. Further increments of calories did not progress well, evidently with the deterioration of his electrolytes. He succumbed to cardiac arrhythmias and cardiac arrest.

Case 3

Stage III obstructed adenocarcinoma of the stomach was diagnosed after 6 weeks of post-prandial vomiting and 19.0% weight loss. Cancer confirmation and staging by endoscopy, histopathological report, and CT imaging. She was initiated

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Table I: Characteristic of the severe refeeding syndrome cases encountered among the upper gastrointestinal cancer patients

Demographic and risk stratifications	Case 1	Case 2	Case 3
Gender	Female	Male	Female
Age	62	46	66
Cancer	Stage III gastric cancer	Non-familial gastric polyposis	Stage III gastric cancer
Symptoms	Malnourished and post-prandial vomiting	Malnourished and post-prandial vomiting	Malnourished and post-prandial vomiting
Weight and BMI	56 kg, 23.4	50 kg, 19	42 kg, 17
Unintentional weight loss	16% over 12 weeks	20% over 8 weeks	19% over 6 weeks
Little/no nutritional intake	Very high risk	Very high risk	Very high risk
Nutritional screening	SGA C	SGA C	SGA C
Electrolytes deficiency	Phosphate 0.56 Magnesium 0.60 Potassium 3.3	Phosphate 1.34 Magnesium 0.75 Potassium 3.7	Phosphate 0.94 Magnesium 0.49 Potassium 2.7
Calorie provision before electrolytes replenishment	TPN 30% of TEE	EN 86% of TEE	TPN 34% of TEE

BMI – Body mass index, SGA – Subjective global assessment, TPN – Total parenteral nutrition, EN- Enteral nutrition, TEE- Total energy expenditure

on total parenteral nutrition without proper electrolyte assessment and replenishment prior to referral to our centre. She had severe hypomagnesaemia and hypokalaemia. Feeding was withheld, and she was resuscitated with intravenous vitamins and trace elements. We were very cautious with fluid and sodium retention, as she has manifested evidence of peripheral oedema. She responded well; hence a modest calorie provision was reinitiated at 10 kcal/kg/day. However, her condition slowly deteriorated, and she finally succumbed to cardiac and respiratory failure.

DISCUSSION

During periods of prolonged fasting or severe malnutrition, the body adapts by utilising stored energy sources such as glycogen, fat, and protein. This adaptation results in decreased body weight, reduced basal metabolic rate, and altered metabolic pathways. When nutrition is abruptly reintroduced, there is a rapid shift in metabolism from catabolism to anabolism, which can overwhelm the body's compensatory mechanisms. Pourhassan et al. reported that the majority of hospitalised patients who are malnourished are at high risk of developing refeeding syndrome.[7] Current updated nutritional protocols strongly recommend nutritional screening as mandatory to enable the timely implementation of refeeding protocols.[8] Patients shall be stratified according to the potential risk of developing refeeding syndrome based on the nutritional screening, severity of starvation and weight loss. Provision of intravenous thiamine 100 to 200 mg should take precedence before any provision of calories, even in the simplest form of intravenous dextrose in maintenance fluid therapy.[9] Electrolyte depletion (phosphate, magnesium and potassium) shall be replenished accordingly as suggested by Freidli et al. Following electrolyte replenishment, supplementation of vitamins (lipid-soluble and water-soluble vitamins) and trace elements shall be given too.[10] There are various approaches to the provision of calories, but most guidelines recommend cautious increments depending on the severity of the potential risk of refeeding syndrome. Basically, the pathophysiological changes of refeeding syndrome are as follows:

1. Electrolyte and fluid imbalances: Rapid delivery of calories or refeeding leads to increased insulin secretion, which promotes cellular uptake of glucose, electrolytes, and water from the extracellular into the intracellular space.
2. Thiamine deficiency: Malnourished patients often have depleted thiamine (vitamin B1) stores. Thiamine is important for the metabolism of glucose; hence, with the abrupt provision of calories, there will be increased demands for thiamine.

The recurring issues that we encountered in the reported cases were almost similar, as summarised below:

1. There was no nutritional screening; hence, the risk of refeeding was not highlighted.
2. Electrolyte assessment (magnesium and phosphate) was not a standard practice prior to the initiation of feeding.
3. Vitamin and trace element supplementation were not a standard practice in severely malnourished patients fed with either enteral or parenteral feeding.
4. In Case 2, calorie provision was given at 86%, which is considered too high and too fast for a severely malnourished patient.

As described by the NICE guideline, the ASPEN guideline, and Freidli et al.,[10] all malnourished patients shall have the following assessment and treatment:

The management of refeeding syndrome as outlined by NICE guideline, ASPEN guideline and Freidli et al.[10] focuses on gradual and cautious refeeding, close monitoring, and correction of electrolyte imbalances and other metabolic abnormalities. Key management strategies include:

1. Risk assessment includes significant weight loss, low body mass index, prolonged fasting or other risk factors such as cancer patients and post-bariatric surgery.
2. Gradual feeding: initiate feeding at a low caloric intake of 10 to 20 kcal/kg/day and gradually increase the energy intake over 3 to 4 days while closely monitoring electrolyte levels and other clinical responses.
3. Electrolyte supplementation: correct and replenish phosphate, magnesium and potassium.
4. Thiamine deficiency: administer thiamine (vitamin B1) to all at risk patients.

CONCLUSION

Malnutrition is highly prevalent among hospitalised patients. Any intended treatment plan may be hampered by the patient's poor general well-being or progress. Refeeding syndrome is one of the teething issues that often accompany severe malnutrition, as showcased here. Unless precautionary steps are taken in vigilant screening, we often miss the opportunity to salvage them and proceed with the intended treatment plan. Basic nutritional knowledge and protocols should be made mandatory for all clinicians handling frail and malnourished patients. Implementing these strategies in clinical practice can help mitigate the risks associated with refeeding syndrome and improve patient outcomes and chances of survival.

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CASE REPORT

A case report of recurrent pterygium in a paddy farmer following occupational risk exposure to solar radiation

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SUMMARY

Occupational-related pterygium, specifically among paddy farmers, was rarely discussed in the literature. However, given that they are outdoor workers exposed to direct solar ultraviolet, which is known to induce pathophysiological pterygium formation, the risk of pterygium development cannot be disregarded. To date, there is no standard assessment guideline for the ocular exposure hazards of Malaysian outdoor workers to prevent chronic eye diseases. We reported a case of recurrent left-eye pterygium due to chronic occupational ultraviolet radiation (UVR) exposure during paddy cultivation. This case report provides in-depth insight and valuable information regarding risk assessment and management for outdoor workers, particularly paddy farmers.

INTRODUCTION

Pterygium is a chronic eye disorder mainly induced by long-term exposure to solar ultraviolet (UV), particularly among outdoor workers.[1] Globally, extremely high UV-risk countries had the highest prevalence of pterygium, accounting for up to 52%, followed by very high UV risk (30.8%), high UV risk (9.4%), and moderate UV risk (up to 7.1%).[1] While solar UV radiation (UVR) has long been recognised as a major risk factor for pterygium, it remains under-researched in occupational fields, especially among paddy farmers. A similar issue was found in Malaysia. This case report focused on the case of a paddy farmer with recurrent left eye pterygium with a history of chronic exposure to solar UVR in rural West Peninsular Malaysia. This is a preliminary case report of occupation-related pterygium in this country. The findings reported here provide information on establishing ocular risk assessment.

CASE PRESENTATION

A 59-years-old Malay woman complained of painless left eye discomfort and gradual poor vision for 6 months. She denied eye redness, swelling, itching, irritation and floaters. The patient had initially noticed an elevated lesion of her left eye, which was presumably due to recurrent pterygium tissue growth approximately 2 years ago. In 2017, she was diagnosed with bilateral pterygium, where she underwent left eye excision and conjunctival autograft due to blocked vision. Further investigation determined that she and her husband were farming a 5-acre paddy field situated on one of the regions on the western coast of the peninsular Malaysia. Her job responsibilities focused on the paddy growth process, which included pre-planting, growth and post-production. Her regular schedule included 3 days of duty and 1 day off, with a total of 4 to 6 hours of labour per day that included 1 to 2 hours of rest. Depending on the sun rising and setting in this reported region, her shift began between 7.30 am and 8.00 am which was around sunrise (7.30 am) and ended between 11.30 am and 3 pm which was around 5 to 8 hours before sunset (7.30 pm). She often wore a wide-brimmed hat but not sunglasses while performing her farming tasks. Otherwise, she denied possible UVR exposure caused by either previous employment or outdoor hobby activities. She also denied any eye trauma such as exposure to rice husk dust or episodes of hypersensitivity when working. On further history, she stated that her husband had also complained for years of bilateral vision blurring. Nonetheless, he had not sought treatment as his symptoms were mild and tolerable.

Slit-lamp examination revealed a fleshy nasal triangular membrane 4.6 mm away from the limbus covering part of the corneal pupillary area of her left eye. Her right eye showed right pterygium at the nasal side 2 mm away from the limbus, which was not significantly increased as compared to 5 years ago. Her corrected vision with spectacles was 6/36 (left eye) and 6/9 (right eye). Fundoscopy for both eyes were normal.

The workplace hazard assessment was conducted using solar UVR hazard assessment tool for ocular exposures (2007) from the International Labour Organisation (ILO), the International Commission on Non-Ionising Radiation Protection (ICNIRP) and the World Health Organisation (WHO) (Table I).[2] The calculation of this value was performed using the formula provided:

Ocular exposure factor = (f_1) x (f_2) x (f_3) x (f_4) x (f_5) x (f_6).

In the present case, as Malaysia is situated at an approximate latitude of 30ºN and experiences an average annual temperature of 25.4°C, which is comparable to the temperature observed during the summer season, the Geographical Latitude factor (Factor f_1) was assigned a score of 9. The score of 1.5 for Factor f_2 (cloud cover) determined that the workplace environment had partial clouds, sometimes covering the sun. The assigned score for the duration of exposure (Factor f_3) was 0.3, given that this

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Table I: Hazard assessment factors for ocular exposure

Season	Geographical latitude (Factor f_1)		
	>50°N or S	>30° - >50°N or S	<30°N or S
Spring/summer	4	7	9
Autumn/winter	0.3	1.5	5
Cloud cover		**Factor f_2**	
Clear sky		1	
Partial cloud sometimes covering sun		1.5	
Overcast sky		0.8	
Duration of exposure		**Factor f_3**	
All day		1	
An hour or two around midday		0.35 – 0.5	
Four to five hours around midday			
Early morning or late afternoon		0.2	
Ground reflectance		**Factor f_4**	
Fresh snow		1.0	
Dry sand, sea surf, concrete		0.1	
All other surfaces, including open water		0.02	
Eyewear		**Factor f_5**	
None		1	
Sunglasses without hat		0.5	
Clear spectacles without brimmed hat		0.2	
Sunglasses or spectacles with brimmed hat		0.02	
Shade		**Factor f_6**	
No shade e.g., open fields, tundra, beach, ocean		1	
Horizon blocked by hills, housing, scattered trees		0.3	
Horizon and lower sky blocked by tall buildings/terrain		0.02	

patient had worked for approximately one and a half hours at midday. The ground reflectance (Factor f_4) score was 0.02, which represented 'all other surfaces'. The patient's score for the eyewear factor (Factor f_5) was 1 due to the patient's usage of sunglasses while working was infrequent. The shade factor (Factor f_6) assigned score was 1, representing open fields. Thus, by considering these risk factors, the ocular exposure factor value in this case is:

Ocular exposure factor = 9(f_1) x 1.5(f_2) x 0.3(f_3) x 0.02(f_4) x 1(f_5) x 1(f_6) = 0.081 (low)

Although her UV exposure risk was low (0.081), this value should be interpreted with caution, as the score was calculated based on perceived information from the patient's history and clinical findings. Considering her strong occupation-related clinical history and suggestive clinical findings, at the same time, other non-occupational causes for pterygium, which were infection symptoms, hobby, trauma and hypersensitivity, had been ruled out, the treating ophthalmologist diagnosed the patient with recurrent left eye pterygium secondary to chronic occupational solar UVR exposure. Successful excision of the left eye pterygium with conjunctival autograft under local anaesthesia was performed in June 2022. Nevertheless, further details about workplace management were not available in the patient's medical reports or from deep interviews with both the patients and the treating doctor.

DISCUSSION

To date, many epidemiological studies have reported the association between outdoor work and pterygium.[2–5] Several studies conducted in Asia reported significant findings between occupational pterygium prevalence and solar UVR exposure.[4-5] Studies conducted in Singapore suggested that occupational pterygium prevalence was 10.1 to 12.3%. [4-5] Unsurprisingly, a study in Thailand reported that more than 50% of respondents diagnosed with pterygium were farmers,[3] while Ang et al. reported that severe pterygium was detected only among outdoor workers.[4] These findings are predictable, as most Asian countries, including Malaysia, have extremely high ultraviolet index risk (UVI ≥ 11). Although recent local epidemiology data on pterygium among outdoor workers are not available, we strongly believe that the country faces a similar issue.

Our patient was notably involved in a high-risk occupation that exposed her to solar UVR, with cumulative solar UVR exposure, for approximately 25 years. Compared to other individuals who do not perform outdoor work, she was 20 times more likely to develop pterygium.[6] Consequently, the significant cumulative UVR exposure caused eye damage, which increased the likelihood of limbal stem cell and fibroblast proliferation and subsequently triggered the pterygium formation. Furthermore, UVR also induces proinflammatory cytokines, growth factors and matrix metalloproteinases, which promote the progression of pterygium.[6] The above path mechanism might possibly apply to both the patient's primary and recurrent pterygium growth.

Table II: Ultraviolet radiation exposure limits and relative spectral effectiveness

Wavelengtha (nm)	Exposure limit ($J.m^{-2}$)	Exposure limit ($mJ.cm^{-2}$)	Relative spectral effectiveness S_λ
180	2500	250	0.012
190	1600	160	0.019
200	1000	100	0.030
205	590	59	0.051
210	400	40	0.075
215	320	32	0.095
220	250	25	0.120
225	200	20	0.150
230	160	16	0.190
235	130	13	0.240
240	100	10	0.300
245	83	8.3	0.360
250	70	7.0	0.430
254[b]	60	6.0	0.500
255	58	5.8	0.520
260	46	4.6	0.650
265	37	3.7	0.810
270	30	3.0	1.000
275	31	3.1	0.960
280[b]	34	3.4	0.880
285	39	3.9	0.770
290	47	4.7	0.640
295	56	5.6	0.540
297[b]	65	6.5	0.460
300	100	10	0.300
303[b]	250	25	0.120
305	500	50	0.060
308	1200	120	0.026
310	2000	200	0.015
313[b]	5000	500	0.006
315	1.0×10^4	1.0×10^3	0.003
316	1.3×10^4	1.3×10^3	0.0024
317	1.5×10^4	1.5×10^3	0.0020
318	1.9×10^4	1.9×10^3	0.0016
319	2.5×10^4	2.5×10^3	0.0012
320	2.9×10^4	2.9×10^3	0.0010
322	4.5×10^4	4.5×10^3	0.00067
323	5.6×10^4	5.6×10^3	0.00054
325	6.0×10^4	6.0×10^3	0.00050
328	6.8×10^4	6.8×10^3	0.00044
330	7.3×10^4	7.3×10^3	0.00041
333	8.1×10^4	8.1×10^3	0.00037
335	8.8×10^4	8.8×10^3	0.00034
340	1.1×10^5	1.1×10^4	0.00028
345	1.3×10^5	1.3×10^4	0.00024
350	1.5×10^5	1.5×10^4	0.00020
355	1.9×10^5	1.9×10^4	0.00016
360	2.3×10^5	2.3×10^4	0.00013
365[b]	2.7×10^5	2.7×10^4	0.00011
370	3.2×10^5	3.2×10^4	0.000093
375	3.9×10^5	3.9×10^4	0.000077
380	4.7×10^5	4.7×10^4	0.000064
385	5.7×10^5	5.7×10^4	0.000053
390	6.8×10^5	6.8×10^4	0.000044
395	8.3×10^5	8.3×10^4	0.000036
400	1.0×10^5	1.0×10^5	0.000030

[a]Wavelength chosen are representative; other values should be interpolated at intermediate wavelengths.
[b]Emission lines of a mercury discharge spectrum.

Our patient's likelihood of recurrent pterygium was possibly aggravated by her previous surgical history, although the detail was not clear. Several factors such as preoperative pterygium features (size, vascularity index, active growth of the pterygium), surgical factors (insufficient conjunctival graft size and inadequate peripheral dissection), postoperative graft retraction due to inadequate fixation, caruncle abnormality and genetic factors are also the factors of recurrent pterygium.[7-8] Furthermore, postoperative lesion is also a possibility, with greater extension of fibrovascular growth than its primary presentation depending on the preoperative condition and operative approach.[7] Therefore, we postulated that one of the above factors could be the underlying reason for the progressive unilateral pterygium growth in her left eye.

Despite her significant clinical history and suggestive clinical manifestations mentioned previously, the ICNIRP, ILO and WHO assessment tool [2] deemed that our patient had low UV risk. The tool has been recognised as the main reference for ocular hazard assessment in occupational fields to date. However, in certain instances, the UV risk assessment results might not be reliable, particularly for countries with tropical climates, as the tool was designed for temperate countries. As one of the elements used to determine UV risk assessment, the ground reflectance value must be carefully tailored to the employment environment. Due to the lack of a standard reflectance value, it was difficult to ascertain the value of the paddy field earth surface in the case. Therefore, we firmly believed that the discrepancy between the patient's risk assessment score and clinical history and manifestations was due to the limitations of the tool.

In Malaysia, ocular hazard assessment with an established assessment tool and the use of personal protective equipment (sunglasses or wide-brimmed hat) are uncommon practices, especially among paddy farmers, due to certain circumstances. For example, based on the ICNIRP guideline, the actinic UV (UV-B and UV-C) spectral region value is 180 to 135 nm on unprotected eyes within an 8-hour period (Table II).[2] Hence, the maximum safe UVR exposure in the tropics throughout the summer and under clear skies would be reached in approximately 6 minutes at solar noon.[2,9] However, determining an adequate UVR dose in a natural outdoor context is difficult for a number of reasons. For example, the brow ridge, the upper lid, squinting reactions and behavioural responses to sunshine limit the amount of UVR that reaches the eyes.[2,9] The amount of UVR exposure to the eyes might be significant when the sky is overcast because the eyelids are open widely.[9] Contrastingly, the retina is protected from direct sunlight when the person squints under clear skies, particularly when the sun angle > 10°. The fact that eyes are naturally drawn downward and forward during work presents another issue. Consequently, radiant energy from ground reflectance, rather than direct UVR exposure, dominates ocular exposure.[2,9] Given these considerations, it is likely impractical to adhere to the aforementioned exposure limit. Another option is to use the WHO Global Solar UVI, which is a simple tool for protecting against and preventing the dangers associated with solar UVR overexposure. Nevertheless, the tool does not provide useful information regarding a person's actual UV exposure. Instead, it is aimed at assessing the dangers of sun exposure for recreational purposes and to raise public awareness about the importance of taking precautions against UVR.

We firmly believe that prolonged UVR exposure and aggravation by surgical history were the main reasons for the pterygium recurrence in the present case despite the low solar UVR assessment score. Pterygium is also considered as an occupation-related disease because our patient was mostly exposed to solar UVR at her workplace, excluding other non-occupational risks such as family history, trauma, hypersensitivity and outdoor activity. To prevent negligence among outdoor workers, Malaysia requires a standardised national hazard assessment tool for workplace solar UV ocular exposure. A walkthrough survey is crucial to identify spatial and temporal factors to develop an effective risk assessment tool. A detailed work task is required via photographs or videos to observe details concerning the workplace, the exposed people, the existing engineering, administrative procedures and protective outfit practice.[2] Despite the recent growing interest in epidemiology studies on UV exposure in occupational medicine, analytical studies specifically involving paddy farmers remain limited in Southeast Asia. Although the role of UVR exposure in occupational pterygium has not been consistently reported, some evidence from previous studies strongly recommended that paddy farmers wear sunglasses and wide-brimmed hats to protect themselves from solar UVR hazards. Furthermore, appropriate solar UV protection was followed by a statistically significant decrease in pterygium recurrence.[10]

CONCLUSION

Our patient is an example of a recurrent pterygium case secondary to chronic occupational solar ultraviolet radiation (UVR) during paddy farming. To derive our conclusion, we considered certain occupational factors that increase the risk of recurrent pterygium, namely outdoor work in a high-solar UVR risk region and non-compliance with the use of self-protective equipment such as sunglasses. We also did not identify any other related causal factors such as history of trauma, hypersensitivity or possible UVR exposure outside the patient's occupational activities or hobbies. To date, Malaysia does not have a national standardised hazard assessment and management guideline for occupational ocular exposure. Although it has long been associated with occupational eye disease, occupational ocular exposure has received less attention from local medical professionals and other relevant parties. Hopefully, the new information in our case report will benefit the development of a standard hazard assessment for ocular solar UVR exposure among paddy farmers in Malaysia.

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CONFLICT OF INTEREST

The authors declare no conflict of interest. Informed consent on patient participation in this investigation and publication of any data included in this article has obtained.

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Pyoperitoneum: An unusual presentation of advanced carcinoma cervix

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SUMMARY

Pyometra is the accumulation of pus inside the uterus due to blockage of drainage of uterus. It is a known that pyometra can lead to pyoperitoneum. A 65-years-old postmenopausal woman, para three (three children) presented with symptom of carcinoma cervix. However, spontaneous rupture of pyometra leading to pyoperitoneum is a rare phenomenon. Spontaneous perforation of pyometra resulting in generalised peritonitis can pose diagnostic dilemma to the clinician and these patients may need emergency surgery due to acute presentation compromising the outcome due to inadequate workup and suboptimal treatment. High index of suspicion and multi-disciplinary approach is needed to manage such patients to reduce the related morbidity and mortality. We present one case of undiagnosed cervical cancer presenting as acute abdomen due to spontaneous perforation with acute abdomen and signs of generalised peritonitis. After a clinical evaluation, a provisional diagnosis of cervical cancer stage IIA with pyoperitoneum was made. Ultrasound and contrast enhanced computerised tomography confirmed the diagnosis of pyometra with uterine perforation and moderate ascites. Emergency laparotomy was planned. Around 1000 ml of pus was drained. A circular defect of 0.5 × 0.5 cm with pus oozing out was found at the anterior wall of the uterus, around 1.5 cm below the fundus. Total abdominal hysterectomy with bilateral salpingo-oophorectomy was done. Lymph node sampling could not be attempted due to friable tissue. Histopathological examination confirmed diagnosis of squamous cell carcinoma of cervix.

INTRODUCTION

Cervical cancer is the fourth most common gynaecological cancer affecting women globally. The association of cervical carcinoma with human papilloma virus (HPV) is well established, and the presence of HPV vaccination makes primary prevention of the disease possible. Long latency period from HPV infection to development of the cancer and availability of various screening facilities makes it possible to diagnose and treat the precancerous lesions of cervix and prevent progression to cervical cancer. Yet, cancer cervix is one of the leading cause of deaths among women. WHO reported 604,000 new cases of cervical carcinoma with 342,000 deaths worldwide in 2020. Around 90% of deaths occurred in lower middle-income countries.[1] Such high rate of mortality can be attributed to poor infrastructure, improper implementation of screening programs or unavailability of vaccination and screening services in these countries. One case of undiagnosed cervical carcinoma presented as acute abdomen as a result of spontaneous perforation of pyometra is being reported here.

CASE PRESENTATION

A 65-years-old woman, para three, menopausal since past 12 years, presented to surgical emergency with the complaints of dull pain abdomen, vomiting and constipation for past 3 days. Pain suddenly increased in intensity for last 3 hours of her presentation to the hospital. She also gave history of low-grade fever on and off since past 1 week. Patient was extremely uncomfortable and was tossing in bed due to pain. Her last childbirth was 42 years ago, all three children delivered vaginally. She did not practice any form of family planning. There was no history of any gynaecological examination or cervical cancer screening done in the past. No significant past medical and surgical history was present. On examination she was anxious with pulse rate of 106 bpm, blood pressure 100/60 mmHg, respiratory rate 22 bpm and oxygen saturation 90 to 94% at room air. Mild pallor was present. Her abdomen was distended, tense and tender. On palpation guarding, fluid thrill and shifting dullness were present. Bowel sounds were present but sluggish. Her haemoglobin was 8.9 gm/dl, total leukocyte count was 10.51 thousand/µl. Liver function test, kidney function tests and electrolytes were normal. X-ray abdomen erect and supine was suggestive of dilated bowel loops. Patient was being prepared for emergency exploratory laparotomy for acute abdomen with features of peritonitis and an ultrasound was ordered to confirm the probable aetiology. From ultrasound there was heterogenous bulky uterus with echogenic contents and septations. Moderate ascites with echogenic content was seen in the abdominal cavity. In view of these ultrasound findings, gynaecological opinion was sought to workup for gynaecological cause. On per-speculum examination an ulcerated growth was seen on the anterior lip of the cervix with minimal purulent foul-smelling discharge coming though the cervix. Bimanual examination of pelvis revealed hard cervix that bled on touch. Uterus was retroverted, bulky and relatively soft in feel. Vagina and bilateral parametrium was free. On per rectal examination rectal mucosa appears to be free. With above clinical findings a provisional diagnosis of cervical cancer stage IB1clinically was made. Differential

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Table I: Summary of cervical cancer patients presenting with acute abdomen due to spontaneous perforation of pyometra leading to pyoperitoneum.

Study	No. of cases	Age (years)	Parity	Presenting symptom	Duration of symptoms	Provisional diagnosis	Site of perforation	Management	Final diagnosis
Imachi M et al. (1993)	One	67	*P3L3	1. Pain abdomen, abdominal distention, genital bleeding and fever	2 weeks	Cervical cancer stage IV B	Anterior wall of uterine fundus near right horn	Subtotal hysterectomy with bilateral salpingo-oopherectomy with peritoneal lavage	Squamous cell carcinoma keratinising type
Chan LY et al. (2000)	Two	34 and 72	Not mentioned	1. Pain abdominal and fever 2. Pain abdomen and fever	Not mentioned	Generalised peritonitis	1. Left cornual region 2. Uterine fundus	Exploratory laparotomy with drainage of the pus	Cervical cancer
Shahid N et al. (2006)	One	80	--	Pain abdomen	Not mentioned	Gastrointestinal perforation	Uterine fundus	Exploratory laparotomy with drainage of pus with repair of the perforation with TAH with BSO	Not mentioned
Lee SL et al. (2007)	One	60	P4	Acute pain abdomen, fever and cold sweats	Not mentioned	Gastrointestinal perforation	Uterine fundus	Exploratory laparotomy with drainage of pus with TAH with BSO Followed by radiotherapy	Poorly differentiated cervical cancer stage Ib
Vyas S et al. (2009)	One	60	P5L5	Lower abdominal pain and vomiting	Initial symptoms 4 months Presentation of acute abdomen	Histo-pathologically confirmed case of moderately differentiated adenocarcinoma cervix stage IIIB	Uterine fundus	Pigtail drainage of large pelvic and sub-hepatic pus collection under antibiotic cover	Moderately differentiated adenocarcinoma cervix stage IIIB
Ou YC et al. (2010)	Two	80 & 73	Not mentioned	1. Pain abdomen Pain abdominal and fever	Not mentioned	Gastrointestinal perforation with pneumoperitoneum	Site not mentioned	Drainage + total abdominal hysterectomy + bilateral salpingo-oopherectomy + lymphadenectomy	Not mentioned
Agarwal R et al. (2011)	One	60	P2	Acute central abdominal pain, abdominal distension and fever **Presenting symptom**	12 hours fever × 3 days	Enteric perforation with peritonitis	Uterine fundus	Exploratory laparotomy with abdominal lavage by surgeons and prevaginal pyometra drainage followed by radiotherapy	Advanced stage of cervical carcinoma

cont..... pg 39

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Table I: Summary of cervical cancer patients presenting with acute abdomen due to spontaneous perforation of pyometra leading to pyoperitoneum.

Study	No. of cases	Age (years)	Parity	Presenting symptom	Duration of symptoms	Provisional diagnosis	Site of perforation	Management	Final diagnosis
Jeon HS et al. (2012)	One	78	P6	Fever, vomiting and diffuse abdominal pain	4 hours	Perforated pyometra/GI perforation	Uterine fundus	Exploratory laparotomy + peritoneal lavage +TAH + BSO Followed by radiotherapy	Squamous cell carcinoma of the cervix with large cell keratinising cervical cancer stage Ib
Ikeda M et al. (2013)	One	80	Not mentioned	Pain abdomen and fever	Not mentioned	Perforated pyometra	Anterior uterine wall	Exploratory laparotomy with TAH + BSO	Not mentioned
Alakananda et al. 92015)	One	60	P11	Severe abdominal pain, abdominal distension, vaginal bleeding for 25 days followed by vaginal discharge for 1 month and foul smelling discharge for 1 week	2 days	Pyoperitoneum due to perforated pyometra	Site not mentioned	Exploratory laparotomy with pan-hysterectomy	Keratinizing squamous cell carcinoma
Konishi Y et al. (2015)[3]	One	64	P3	Sudden pain abdomen and vomiting	Not Mentioned	Squamous cell carcinoma cervix Stage IIB	Uterine Fundus	Exploratory laparotomy with drainage of pus with intrauterine indwelling silicone catheter left in situ	Squamous cell carcinoma cervix Stage IIB
Rao SVM et al. (2015)	One	60	P4L4	Pain abdomen, fever, constipation and decreased urinary output	1 day	Generalised peritonitis	Site not mentioned	Emergency laparotomy with biopsy from perforation site closure of perforation followed by chemoradiotherapy	Well differentiated squamous cell carcinoma
Kroon HM et al. (2016)	One	65	Not mentioned	Sudden onset pain abdomen	Not mentioned	GI perforation squamous cell carcinoma stage IIA1	Uterine fundus	Exploratory laparotomy with drainage of pus with radical hysterectomy	Not mentioned
Oumayma L (2023)[5]	One	60	P2	Severe pain abdomen, persistent vomiting, obstructive syndrome with no bowel movements and fever	2 days	Squamous cell carcinoma Stage IIIB	Multiple perforations	Exploratory laparotomy with TAH +BSO with peritoneal lavage	Invasive cervical cancer
Our study	One	65	P3L3	Severe pain abdomen, vomiting, constipation and fever	3 days	Generalised peritonitis	Uterine fundus	Exploratory laparotomy with drainage of pus with TAH with BSO followed by external beam radiotherapy + cisplatin-based chemotherapy	Squamous cell carcinoma stage III A1

*P-Para, L-Live

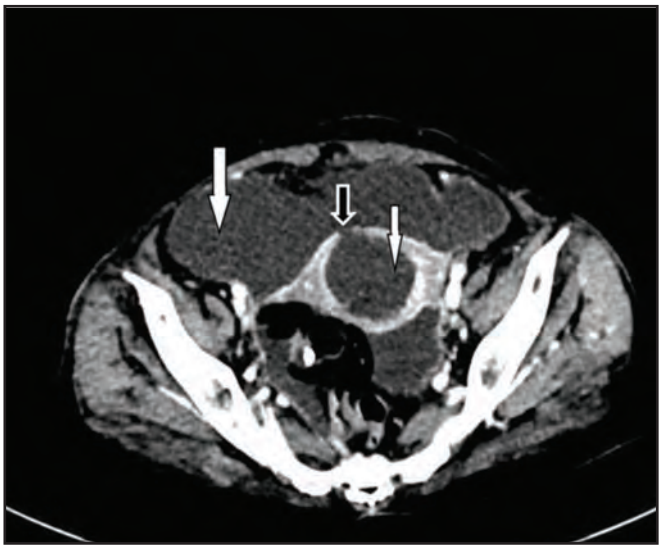

Fig. 1: Axial view (pelvic level) contrast enhanced CT scan demonstrating distended fluid filled endometrial cavity (white solid arrows) consistent with pyometra. Loculated collection (hollow white arrow) consistent with pyoperitoneum is seen in lower abdomen. Also seen is a small defect along anterior wall of uterine corpus marked by black arrow

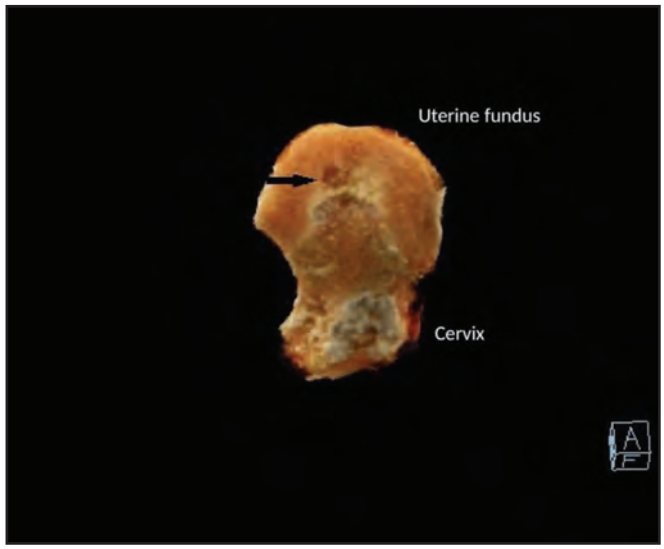

Fig. 2: Coronal post contrast and volume rendered image demonstrating en-face view the perforation (black arrow)

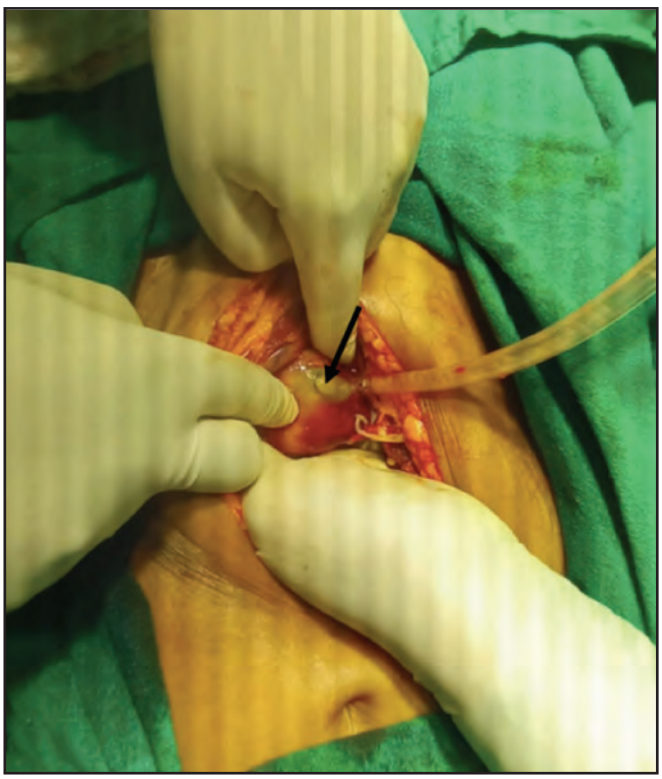

Fig. 3: Intraoperative image showing perforation at the fundus of the uterus with pus oozing out

diagnosis was tuberculosis of cervix, due to ultrasonographical features and history of low-grade fever. An urgent contrast enhanced computerised tomography (CECT) abdomen was ordered which was suggestive of distended abdominal cavity (hydro/pyometra) with evidence of focal area of gross wall thinning along recto-uterine pouch/pelvis/para-colic gutter (Figure 1). A defect (0.3 × 0.5 cm) along anterior aspect of uterus corpus is seen (Figure 2). Loculated collection along pelvis and lower abdomen (15 × 5 × 5.5 cm) with few small air foci present suggesting infected collection. Bulky cervix (3.0 × 3.1 × 3.6 cm) with relatively irregular serosal margins with heterogenous post-contrast enhancement and irregular peritoneum. Omental fat stranding and regional small bowel wall thickening was present. No enlarged lymph nodes were seen.

After initial stabilisation, decision for emergency laparotomy with pyo-peritoneum drainage was taken. Inter-operatively 1000 ml of foul-smelling pustular discharge was drained (Figure 3). Omentum and bowel were matted with pus. Pus was sent for culture, acid fast bacilli (AFB), adenosine deaminase (ADA), cytology and biochemical evaluation. Around 0.5 × 0.5 cm circular defect was present in the anterior wall of the uterus around 1.5 cm below the fundus. Pus was oozing out from the defect. Uterus was distended and thinned out. Bilateral fallopian tubes and ovaries were adherent to the bowel. A decision for total abdominal hysterectomy with bilateral salpingo-oopherectomy (type 1) was taken. Intraoperatively tumour was extended towards the left side but was not extending till lateral pelvic wall. The tissue was extremely friable hence lymph node sampling could not be done. Patient was given two units of blood intraoperatively. Pus for culture sensitivity was sterile, AFB negative ADA raised (110.4), cytology was negative for malignant cells.

Histopathology confirmed the diagnosis of squamous cell carcinoma NOS, grade 2, moderately differentiated, with middle third stromal invasion with involvement of

ectocervix. Final clinic-surgical stage assigned was stage III A1. Her postoperative period was uneventful. Patient was referred to medical oncologist for further management and was planned for external beam radiotherapy and chemotherapy.

DISCUSSION

Pyometra is collection of pus in the uterine cavity due to obstruction to the natural drainage to the uterine secretions/content. Pyometra is more common in postmenopausal women due to increased chances of cervical canal stenosis at this age. The risk further increases by 1.5 to 4% in presence of cervical or uterine malignancy. Patients with pyometra can remain asymptomatic for long time. Postmenopausal bleeding, foul-smelling vaginal discharge and lower abdominal pain are the usual manifestations of symptomatic pyometra.

Very rarely, pyometra causes spontaneous perforation due to degeneration of the uterine walls. Formation of pyoperitoneum results in clinical features of acute abdomen. Reported incidence of generalised peritonitis because of spontaneous perforation of pyometra in both benign and malignant condition is nearly 0.01 to 0.05%.[2] Abdominal pain (96.3%), fever (44.44%), vomiting (30.8%), purulent vaginal discharge (7.4%) and genital bleeding (3.7%) were among the common symptoms reported in such cases.[5] In a case report and literature review by Konishi Y et al.,[3] authors reported 11 cases of spontaneous perforation of pyometra in patient with cervical carcinoma. All the cases presented with features of generalised peritonitis (abdominal pain in 100% and fever in 63%).

The most common site for perforation was uterine fundus in 72.72% (08/11 cases). Cornual region in 0.09% (01/11 cases), anterior uterine wall 0.09% (01/11 cases) were the other sites mentioned. In 18.18% (02/11 cases) the site of perforation was not documented.[4] Most of these cases like our case remain undiagnosed and present for the first time in emergency and require urgent surgical management owing to their acute symptoms compromising final outcome because of suboptimal workup and management. Emergency laparotomy followed by drainage of pus with total abdominal hysterectomy with bilateral salpingectomy is most common surgical management done in such cases. In cases where total abdominal hysterectomy cannot be done drainage of pus followed by peritoneal lavage with or without repair of the perforation is also acceptable.[5]

The final management depends upon the histopathological confirmation of the diagnosis and final stage of the disease. Many patients require second surgery and others are candidates for radiotherapy or chemoradiation. Our patient presented to the surgical emergency with acute abdomen requiring surgical management and finally was confirmed as squamous cell carcinoma cervix stage III A1 and hence required external beam radiation therapy with cisplatin-based chemotherapy. A summary of previously published cases of spontaneous perforation of pyometra resulting in pyoperitoneum in women with cervical cancer is provided in Table I.

CONCLUSION

Pyoperitoneum due to spontaneous perforation of pyometra is a rare complication of cervical cancer. Most of the times these patients require emergency surgical management due to acute presentation of the symptoms that can compromise patients haemodynamically. High index of suspicion is required, and a multidisciplinary approach is mandatory to optimise management and improve the outcome. In short, reinforcement of the vaccination and cervical screening programs are utmost crucial to reduce overall incidence of cervical carcinoma.

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CONFLICT OF INTEREST

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CASE REPORT

Bullous cutaneous larva migrans: An atypical presentation

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SUMMARY

Migratory, erythematous, serpiginous skin lesions of cutaneous larva migrans caused by parasitic hookworms is a typical dermatological case faced by primary care clinicians. The condition spreads through direct contact with soil contaminated with hookworm larvae, particularly in tropical and subtropical climates. The classical clinical features of the infection are intense pruritus and serpiginous skin lesion, primarily occur in the lower limbs. Nevertheless, it can present with atypical features such as papular eruption, nodules and bullae that may cause confusion, misdiagnosis and subsequently delayed treatment. Although cutaneous larva migrans can naturally resolve within weeks, early recognition and prompt treatment with effective anti-helminthic medication is recommended to rapidly alleviate the symptom of severe itchiness, prevent excoriation due to excessive scratching, which may lead to secondary bacterial infection and even Loeffler syndrome. We report a case of cutaneous larva migrans in a woman who developed a rare blistering skin lesion following a short vacation to a beach.

INTRODUCTION

Cutaneous larva migrans (CLM), also known as creeping eruption, is a common skin infestation caused by animal hookworms. These nematodes are transmitted via infected cat or dog faeces and are highly prevalent in tropical and subtropical climates. CLM commonly occurs from direct contact of human skin with contaminated soil in which the hookworms penetrate and migrate in the epidermal layer.[1] The distinctive linear tracks and intense itching are vital clinical features that point towards the diagnosis, especially in individuals with a history of contaminated soil or sand exposure.[1]

Without intervention, the infection often resolves naturally within 5 to 6 weeks following exposure.[1] Nevertheless, it can cause skin damage due to severe itching, potentially leading to bacterial superinfection or even Loeffler syndrome; hence, it is recommended to use the very effective oral albendazole or ivermectin treatment to reduce the intense symptoms and infectious period, preventing potential complications.[2] Occasionally, the disease may present with unusual characteristics such as eczema-like lesions, papules or blisters.[3-5] Rare presentations such as oedema, local swelling and vesiculobullous lesions are reported in approximately 3.3 to 10% of CLM patients.[4,8] Secondary scratching frequently complicates these features, making the diagnosis more challenging. As a result, there is a risk of misidentifying the disease and causing undue anxiety.[6] This report describes a case of CLM on the left leg that developed after a beach vacation. We discuss the initial misdiagnosis and the subsequent evolution into bullous CLM, detailing the condition's clinical presentation, diagnosis, management and prevention.

CASE PRESENTATION

A 32-year-old woman presented to the government health clinic with a pruritic, erythematous rash on her left leg for a week. She recently came back from a short seaside vacation a week ago. She has no prior medical illness or history of allergy. She denied any insect bite or sustained any injury at the location of the lesion. This was her third medical visit, having previously visited two different clinics where the lesion was first diagnosed as a skin allergic reaction, given topical hydrocortisone cream and oral antihistamine. On the second visit, she received a topical antifungal cream. However, the medications did not alleviate the symptoms and her skin condition. Due to escalating severe itchiness that disrupts her sleep at night and the development of a small blister along the lesion, she sought for the third medical attention at a government health clinic. She showed her initial photo of erythematous, creeping skin lesions before the bullous formation, which is associated with intense itchiness and discomfort, as shown in Figure 1. The patient took this photo when she first noticed the skin lesion before the first and second clinic visits. Due to the classic initial lesion and history of exposure to the probable parasites, she was then diagnosed with bullous CLM. The disease was explained to her, and she was prescribed oral albendazole 400 mg daily for 5 days.

After 2 days of taking oral anti-helminthic therapy, she observed the enlargement of the bullae on the same site with surrounding hyperpigmentation. Nonetheless, she did not experience any symptoms, and fresh lesions were not found elsewhere. She returned to the clinic to convey her concern and seek advice about the evolving nature of the lesion. The examination of the lesion revealed a well-defined, hyperpigmented bullae measuring approximately 7 cm long and 5 cm wide, superimposed the serpiginous track, partially ruptured containing clear serous fluid (Figure 2). She was reassured regarding the nature of the disease and the possibility of this rare presentation of hyperpigmented bullae and advised to finish the entire course of the medication as prescribed for 5 days.

At a follow-up appointment 2 weeks later, there was a complete resolution of the bullae and pruritus. A barely noticeable scar from a healing wound was seen at the lesion

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Table I: Differential diagnoses for blistering (bullous) skin disorder

Disease	Clinical/diagnostic characteristics
Infectious aetiology	
Bullous impetigo	• Typical pathogens are staphylococcal aureus and streptococcus pyogenes. • Bullae usually appear relatively quick, spreading locally on the face, trunk, extremities, buttocks, or perineal regions. • Commonly rupture spontaneously to leave a yellow crust.
Herpetic infection	• Have preceding pain before developing into red papules. • In herpes zoster, the papules evolved into vesicular and/or pustular bands following dermatomes whereas in herpes simplex, it commonly affects mouth and genitalia. • Lesions occasionally become bullous and necrotic.
Parasites: tinea, scabies	• Can occasionally cause bullae formation due to local reaction with the parasites.
Non-infectious aetiology	
Bullous pemphigoid	• A chronic autoimmune skin disorder characterised by large, tense blisters that often occur in older adults.
Drug-induced bullous dermatoses	• A number of drugs may result in extensive bullous skin reactions, such as Stevens-Johnson syndrome or toxic epidermal necrolysis.
Contact dermatitis	• Exposure to irritants or allergens can lead to blister formation.
Bites and stings	• Can produce local skin reactions, including small and large bullae.

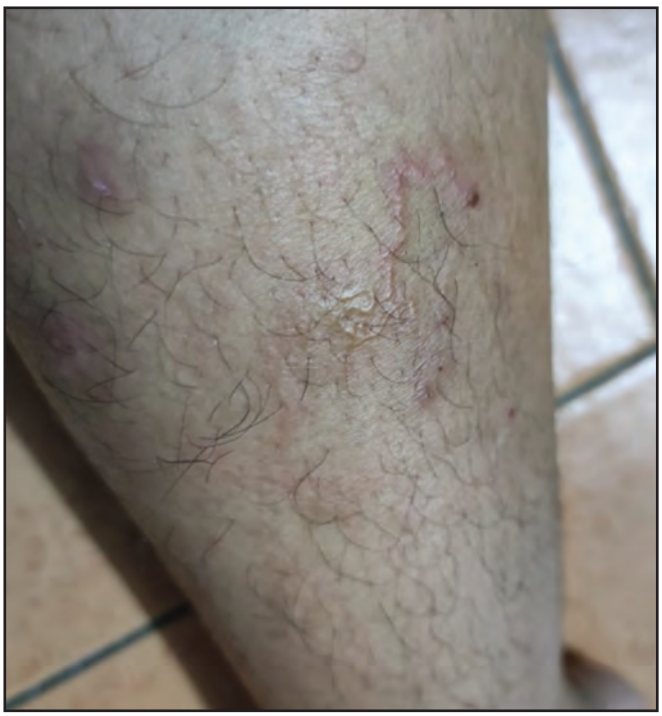

Fig. 1: The appearance of erythematous, tortuous, serpiginous tracks on the left leg with few papular eruptions when the patient first sought medical attention.

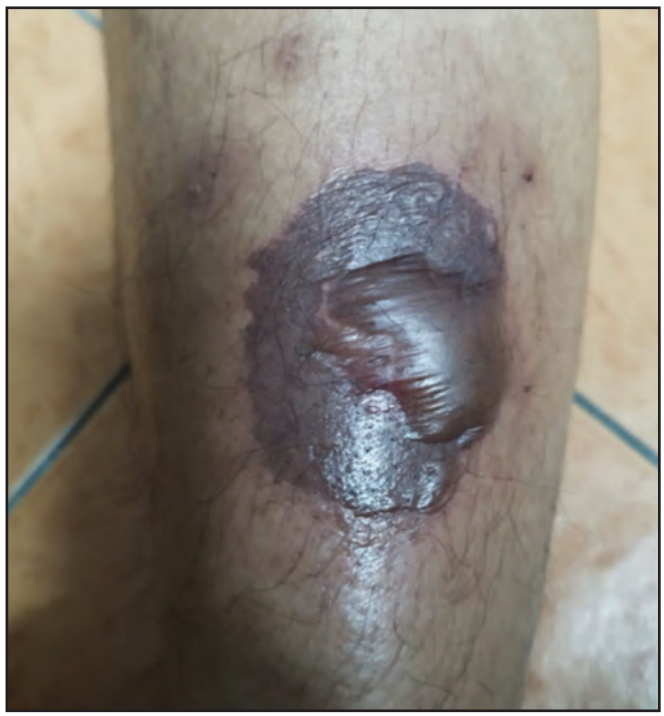

Fig. 2: A hyperpigmented, well-defined, partially ruptured bullae superimposed the serpiginous track during her second visit, day-2 of oral anti-helminthic therapy.

site. The patient expressed her gratitude as the disease was utterly cured, leaving a very minimal resolving scar.

DISCUSSION

CLM is a skin infestation caused by parasitic hookworms, with the most common species responsible for this infection being *Ancylostoma braziliense* and *Ancylostoma caninum*.[1] These parasites are transmitted through the faeces of an infected host and are widespread in tropical and subtropical areas due to favourable climatic conditions and moisture levels. The incidence of CLM in Malaysia is currently unknown. However, one cross-sectional study in Brazil estimated that CLM prevalence ranges from 6.3 to 10.1%.[6,7]

In favourable environmental conditions like fields, gardens and beaches, hookworm eggs hatch and mature into rhabditiform larvae, where these larvae can survive for three to four weeks.[1,9] Within a week, these larvae undergo metamorphosis into filariform larvae, able to secrete a lytic enzyme to penetrate human skin when in contact.[9] In this case report, she was probably exposed to contaminated sand during her vacation at a beach.

These hookworms typically inhabit the intestines of primary hosts, such as dogs and cats, while humans are only incidental terminal hosts.[1,7] The larvae cannot fully mature or reproduce within human hosts. After entering human skin, the larvae migrate within the epidermis, creating characteristic serpiginous lesions usually located a few centimetres away from the penetration site.[1,7] Normally, the larvae cannot traverse the human basal membrane and are incapable of invading visceral organs or reaching the intestines to reproduce.[5] The symptoms of CLM may manifest within hours or up to 15 days after exposure to contaminated soil or sand.[9] The individual experiences intense pruritus, followed by local papular eruption due to an inflammatory reaction towards the parasitic larvae, which subsequently progresses into an erythematous, tortuous, serpiginous track that spreads a few centimetres per day,[2,9] The most common site of infection is the lower limb, although theoretically, any part of the body that had contact with contaminated soil can be affected. Some individuals may experience the conditions at unusual locations, such as on the scalp, penis and chest or have atypical presentations, such as oedema, vesiculobullous lesions or folliculitis.[3-5]

The pathogenesis of bullae in CLM is unknown. Still, it has been suggested that it could be due to a delayed hypersensitivity reaction caused by the release of lytic enzymes (such as metalloproteases and hyaluronidases) and unidentified antigens by the larvae.[3,4] Differential diagnoses for blistering skin disorder are stated in Table I, which includes bullous impetigo, herpetic infection, etc.[10]

Although most patients with CLM exhibit a distinct clinical picture, it is sometimes incorrectly diagnosed, especially in cases with atypical features. According to a retrospective analysis conducted in Hospital Kuala Lumpur, it was discovered that primary care doctors inaccurately diagnosed 54.8% of patients with CLM.[6] Inopportunely, it may lead to the unnecessity of multiple doctor consultations, delayed treatment and regretfully causing distress to patients.[6] Fortunately, our patient received the correct diagnosis and treatment before the worsening of the bullae, which could have led to further confusion and consequences of cellulitis and abscess.

In most cases, CLM naturally heals within a few weeks and typically does not cause permanent scarring.[1,2] Yet, anti-helminthic therapy is indicated to stop the intense pruritus and prevent secondary bacterial infections such as cellulitis, impetigo and abscess, in addition to the unpleasant feeling of a parasite living beneath the skin.[5] Serious complications of untreated CLM are rare, for example, Loeffler's syndrome, which is believed to involve a systemic immune response, with the presence of hookworm under the skin, thus leading to generalised sensitisation. The lungs react to the larval antigen, resulting in eosinophilic pulmonary infiltration and symptoms like cough, difficulty breathing and wheezing.[2] However, in our case, the patient experienced the classical erythematous serpiginous skin lesion before evolving into the bullous formation without any respiratory symptoms.

Albendazole and ivermectin are the treatment of choice for CLM, with 94 to 100% curative rates.[1,8] Albendazole is administered orally at a dosage of 400 mg per day for 3 to 7 days. In contrast, ivermectin is administered orally at 200 mcg/kg as a single dose.[1,9] Due to their contraindication in pregnant women and children under 2 years old (or under 15 kg for ivermectin), alternative treatments include topical thiabendazole or topical ivermectin. However, their effectiveness is inferior compared to systemic therapy.[1,7] Prior to this, cryotherapy was employed as a treatment for CLM, but further research has demonstrated its ineffectiveness.[1,3] As with our case, bullous CLM was successfully treated with a 5-day course of oral albendazole, which is low-priced and readily obtainable at government health clinics.

Effective vaccinations and chemoprophylaxis are not presently available for CLM. The most recognised and important prevention method involves safeguarding the skin against contact with potentially contaminated soil or sand through protective footwear and using towels and mats while sitting at the beach.[7] Additionally, in the context of public and environmental health, preventing the excretion of stray animals in public areas apart from sheltering, neutering and regular deworming of stray animals is beneficial to minimise the environmental reservoir of infective larvae.[1,7] However, in the local Malaysian context, mass neutering of stray animals may not be plausible as it is costly and needs adequate resources. Perhaps the public should be encouraged to adopt sheltered animals to ensure better care and regular deworming of these animals.

Considering the increased interest in travel post-COVID-19 pandemic, raising awareness about tropical infectious diseases like CLM among primary care doctors and the general public is essential. The rate of correct diagnosis of CLM was lower in Malaysia (45.2%) compared to developed countries such as Canada (63.3%) and the United Kingdom (72.5%), although CLM infections are non-endemic in these countries.[5]

For most Malaysian graduate doctors, the only formal dermatology exposure they received was during their 1 to 2 weeks of undergraduate dermatology posting, which is possibly inadequate.[5] Thus, perhaps it is imperative to increase dermatology exposure by providing regular, continuous medical education (CME) sessions or short courses in dermatology for health professionals, especially those working in high-risk areas close to beaches and agricultural fields. This will aid in early recognition, accurate diagnosis, and prompt treatment of CLM infection or other infectious dermatological conditions, thus minimising unnecessary distress among patients, ensuring timely and effective management, and preventing complications. Apart from that, this condition is also an important travel-related dermatologic infection, and it is recommended to educate travellers coming to endemic areas by providing health educational material or pamphlets on parasitic skin infections such as CLM and should also be included in travel websites that are easily accessible to the general public and tourist.

CONCLUSION

Cutaneous larva migrans (CLM) is a common skin problem presented to primary care. Nevertheless, bullous CLM is not a typical presentation, and it may cause misperception in the diagnosis among primary care doctors, leading to delayed effective treatment. This case report showed that vigilant inspection and sound clinical knowledge are imperative in recognising and managing dermatological cases with rare presentations such as bullous CLM in primary care. Therefore, primary care doctors must have some awareness of the diseases for early recognition and correct diagnosis to treat them promptly. CML oral treatment, alongside good hygiene and avoiding wound injury, will promote optimal healing with no scars. Currently, there are no effective vaccinations or chemoprophylaxis methods available. Hence, providing health education on parasitic infections to the public and tourists is imperative to protect them from this condition.

CONFLICT OF INTEREST

There was no conflict of interest.

CONSENT

Informed consent was obtained from the patient before preparing this case report.

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CASE REPORT

Magnesium sulphate as primary intervention for persistent pulmonary hypertension of the newborns at limited settings in West Papua, Indonesia: A case report

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SUMMARY

Persistent pulmonary hypertension of the newborn (PPHN) is characterised by sustained elevation of pulmonary vascular resistance (PVR), leading to right to left shunting across foetal circulatory pathways. It is one of the main causes of neonatal mortality. There have been studies suggesting standard and advanced managements of PPHN. However, many developing countries do not have access to some of those therapies. Magnesium sulphate (MgSO4), a potent vasodilator, has the potential to reduce high pulmonary arterial pressures. Due to its unspecific action site, its usage in PPHN is still uncommon. We reported a case of PPHN that was managed using MgSO4 in a limited setting district hospital in West Papua, Indonesia. Patient was a normal weight, term baby boy, delivered spontaneously with risk factors of prolonged labour and meconium stained-amniotic fluid (MSAF). Respiratory distress was found shortly after birth with >10% difference of pre- and post-ductal sites. Hyperoxia test was positive. Following his diagnosis of PPHN, he was given oxygen therapy and first-line antibiotics. Standard medications to lower the PVR were unavailable in our setting, so we could only give continuous MgSO4. On the 5th day, improvement was seen in respiratory distress and MgSO4 was stopped. The baby was discharged with a total of 11 days of stay after successfully weaning from oxygen therapy. In this report, we would like to highlight the usage of MgSO4 as an alternative treatment to lower PVR at limited healthcare facilities and haemodynamic monitoring for hypotension and bradycardia that should be conducted.

INTRODUCTION

Persistent pulmonary hypertension of the newborn (PPHN) is a condition characterised by sustained elevation of pulmonary vascular resistance (PVR) and is frequently associated with normal or low systemic vascular resistance (SVR), resulting in right to left extrapulmonary shunting across foetal circulatory pathways (patent ductus arteriosus, PDA, and patent foramen ovale, PFO).[1] It prevents the increase in pulmonary blood flow (PBF), which is essential for extrauterine oxygenation and survival, leading to severe hypoxemia which may not respond to conventional respiratory support.[1,2] The incidence of PPHN is 1.8 2/1,000 live births.[2] Despite the availability of advanced neonatal care, PPHN remains one of the major causes of neonatal morbidity and mortality with poor prognosis. The mortality rate is 4 to 33%.[2]

There have been several neonatal cardiorespiratory studies that provided us with better understanding about the pathophysiology and management of PPHN. The management of PPHN, including supportive care and pharmacotherapy to reduce PVR, has been practiced all around the world. Pharmacotherapy's administration routes for pulmonary vasodilators consist of oral, intravenous, and inhalation such as nitric oxide and prostacyclin analogue.[3] Many developing countries, however, do not have access to some of the advanced and costly therapies, including some areas of our country. Previous studies have reported the benefit of magnesium sulphate ($MgSO_4$) as a potent vasodilator and thus having the potential to reduce high pulmonary arterial pressures associated with PPHN. Nonetheless, due to its unspecific action, its usage in PPHN remains uncommon.[4] We reported a case of PPHN managed with MgSO4 at a district hospital with limited facilities in West Papua, Indonesia.

CASE PRESENTATION

A 31-year-old woman gave birth to a normal-weight, term baby boy with a risk factor of prolonged labour and meconium stained-amniotic fluid (MSAF). The baby did not cry immediately after birth and was given initial steps of neonatal resuscitation. Apgar score was five in the first minute and seven in the fifth minute. Upon evaluation, the heart rate was 120 bpm but we found respiratory distress in the baby, characterised by nasal flaring, tachypnoea, cyanosis, severe chest indrawing, grunting and peripheral oxygen saturation (SpO_2) that was only 70% at 5 minutes of life with more than 10% difference between preductal and post-ductal sites. Total Downe's score was seven. The results of other physical examinations were within the normal limits. Hyperoxia test was performed and there was an increase of SpO_2 to 80 to 85%. Unfortunately, arterial blood gas analysis and echocardiography were unavailable in our hospital and the baby's condition was not transportable for a chest X-ray. Based on those limited findings, we concluded that the baby suffered PPHN, which may have been induced by meconium aspiration syndrome (MAS) or perinatal hypoxia due to the prolonged labour.

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Supportive oxygen therapy with continuous positive airway pressure (CPAP) was given to the baby, but there was no improvement even with the highest setting of CPAP. The oxygenation was subsequently switched to non-invasive ventilation (NIV) with peak inspiratory pressure (PIP) 30 cm H_2O, positive end-expiratory pressure (PEEP) 8 cm H_2O, respiratory rate 50, fraction of inspired oxygen (FiO_2) 100%. Surfactant and inhaled nitric oxide (iNO) were inaccessible, and due to our setting's limitation, other pulmonary vasodilator such as sildenafil or inhaled prostacyclin analogue were unavailable either. As an alternative, we gave loading dose of $MgSO_4$ 200 mg/kg BW in 30 minutes, followed by maintenance dose 20 mg/kg BW/hour to the baby. Ampicillin and gentamicin were also given as the first line antibiotics. The baby's vital signs, including blood pressure, SpO_2, and scoring of respiratory distress using Downes score were closely monitored. We decided to increase the $MgSO_4$ level to 50 mg/kg BW/hour and the SpO_2 increased to 92 to 95% after 6 hours of $MgSO_4$ infusion even though the Downes score was still five.

Routine follow-up showed improvement of the respiratory distress condition. Magnesium sulphate was reduced gradually and stopped on the fifth day of hospitalisation. At first, we encountered a problem in which the baby developed desaturation every time the FiO_2 was weaned, however, on third day of treatment, the baby's condition became more stable and the FiO_2 could be weaned, followed by the PIP and PEEP. Oxygen therapy with NIV was given for 7 days and switched to CPAP for 2 days. Fortunately, there were no side effect of hypotension or deterioration of respiratory distress in the baby. The baby was then discharged with the total 11 days stay in hospital. Further follow-up was conducted at the outpatient clinic which showed a good neurodevelopmental screening status the first three months.

DISCUSSION

PPHN is commonly present shortly after birth, precipitating severe respiratory distress and hypoxemia.[2,5] It may also be induced by a variety of primary disorders such as MAS, respiratory distress syndrome (RDS), congenital diaphragmatic hernia (CDH), neonatal sepsis, pneumonia or it can be also idiopathic.[3] In this case, MAS was thought to be the risk factor for the baby to develop PPHN due to the presence of MSAF. MAS occurs in approximately 2 to 10% of infants born with MSAF and is generally found in 25 to 40% patients with PPHN.[1,6] It can cause PPHN through maldevelopment of pulmonary vasculature pathogenesis, in which disturbance occurs in lungs that are otherwise structurally normal.[1] In such cases, infants will typically have respiratory distress with marked tachypnoea and cyanosis immediately after birth.[6] Respiratory distress is indicated with increased respiratory rate, chest indrawing, abdominal (paradoxical) breathing and is frequently accompanied with grunting and nasal flaring, which we identified in our patient. Moreover, we also found low SpO_2 with more than 10% difference of the pre- and post-ductal oxygen saturation. Hyperoxia test were also positive in our patient. It was proved by increased of SpO_2 after the patient got oxygen supplementation with 100% FiO_2. Although definitive diagnosis of PPHN is made by echocardiography, we could not perform echocardiography due to our setting limitation. Echocardiography itself is an essential test in any infant with unremitting cyanosis that is unexplained by parenchymal lung disease, to exclude structural heart disease and confirm a diagnosis of PPHN.[1] Based on those limited clinical signs and symptoms, we considered the diagnosis of PPHN and provided therapy accordingly.

The course and response to therapy in patients with PPHN vary substantially. Therefore, individualised management and frequent reassessment are critical.[3] The main goal is to decrease PVR and reduce the magnitude of the right to left shunt, mainly by administering pulmonary vasodilators.[2] Unfortunately, the standard therapies used for reducing PVR were unavailable in our hospital. Neither iNO, inhaled prostacyclin analogue, or phosphodiesterase type 5 inhibitors (sildenafil) were accessible at that time. The only choice of treatments that we had was $MgSO_4$. It is infrequent to use $MgSO_4$ as the treatment for PPHN because although it is a natural calcium channel blocker that antagonises Ca ion entry into smooth muscle so that it has the effect to dilate constricted muscles in the pulmonary arteries, its action is not specific and when given intravenously, it will act on other arteries.[4,7]

In a systematic review on MgSO4 usage in PPHN cases based on clinical grounds, all the studies demonstrated a substantial improvement in oxygenation, as measured by changes in partial oxygen pressure, alveolar-arterial oxygen index, oxygen index and alterations in mechanical ventilation needs.[4] Hypotension was seen in 16% of PPHN cases treated with $MgSO_4$.[8] A temporary drop in blood pressure 2 hours after starting the infusion was observed, which normalised after 8 hours. In several studies, inotropic agents were administered to most of the patients.[4] Dopamine commenced at 5 to 10 µg/kg BW/minute was used before the loading dose of $MgSO_4$ to prevent the systemic hypotension in one of the studies.[8] Other adverse effect was also observed, including a transient bradycardia that was corrected by dobutamine infusion, urinary retention and altered gastrointestinal tract function in about 8% of patients.[4,8]

Therefore, close monitoring should be done in patients with $MgSO_4$ therapy for any life-threatening adverse events such as bradycardia, hypotension and cardiorespiratory failure.[4] We decided to give $MgSO_4$ loading dose 200 mg/kg BW three hours after birth, followed by maintenance dose started from 20 mg/kg BW/hour and titrated up the dose per one to two hours. The upper limit that we used was 50 mg/kg BW/hour because there had been an improvement in the SpO_2 level >92%. Blood pressure measurement by auscultation was done because neither invasive method or non-invasive method using automated oscillometric device were available. We did not find bradycardia or hypotension in the baby during treatment. The improvement in SpO_2 was seen in about 6 hours after continuous $MgSO_4$. That result was in accordance with previous studies that showed significant improvement of oxygenation and decrease in PVR at 72

hours after the use of $MgSO_4$.[8] We closely monitored the patient's condition using a modified protocol that involved checking the patient's vital signs, including blood pressure, every hour and assessing respiratory status using Downe's score. In an ideal setting, we should also have monitored the serum level of magnesium and adjusted the dosage accordingly to maintain the magnesium concentration between 7 and 11 md/dL.[10]

Comparison between MgSO4 with the standard treatments such as iNO, extracorporeal membrane oxygenation (ECMO), and sildenafil was still limited. Studies comparing clinical efficacy of intravenous $MgSO_4$ and oral sildenafil in PPHN showed that sildenafil was more effective in terms of the time for oxygenation improvement, duration of mechanical ventilation, and fewer requirements of inotropic support. Both groups showed a significant improvement in their pulmonary artery pressure 48 hours after therapy as compared to their baseline measurements. However, the estimated pulmonary arterial pressure was significantly lower 5 days after therapy in neonates receiving sildenafil as compared to those receiving $MgSO_4$.[7,10] iNO is widely recognised as the primary and extensively studied treatment for PPHN, acting locally as a pulmonary vasodilator in pulmonary artery smooth muscle cells. A meta-analysis of several randomised controlled trials compared the use of iNO with control in term or late preterm newborns with PPHN. The analysis revealed no significant difference in mortality; however, there was a notable decrease in the requirement for ECMO. Furthermore, oxygenation significantly improved, leading to a reduced risk of neurodevelopmental sequelae and pulmonary complications.[2]

Furthermore, surfactant as the treatment for MAS was also unavailable in our hospital. Meconium is thought to have negative impact in the production of endogenous surfactant, and it is thought that administration of exogenous surfactant reduces ventilation-perfusion mismatch as well as PVR. However, surfactant is not routinely administered to all patient with MAS, but current study showed the benefits of giving surfactant to patient with severe disease who are mechanically ventilated and require high FiO_2 (>50%) and high mean airway pressure (>10 to 12 cm H_2O).[9] Due to the unavailability of surfactant, we could only give supportive therapy in our patient such as oxygenation and empiric antibiotics with ampicillin and gentamicin. Although antibiotic therapy is still debatable for its beneficial in MAS, we thought it would be more beneficial to give empiric antibiotics to the patient because we didn't have the laboratory examination for blood culture to distinguish the condition with neonatal sepsis.

Newborns with PPHN could have significant long-term morbidity, irrespective of the treatment modality. These infants are at high risk of neurological injury, multiorgan dysfunction, long-term sequelae such as neurodevelopmental, cognitive and hearing abnormalities, and even death.[1,2,5] The majority of studies reported one-year outcome of patients with PPHN treated with $MgSO_4$. None of the studies conducted a formal neurological assessment, but all reported that all survivors were developing normally.4 We were able to follow up the patient for three months after birth that showed good neurodevelopmental status. However, further follow up for the patient's condition and development in later childhood are still needed.

Although $MgSO_4$ showed good results in this case, the results may differ for each patient, depending on the underlying cause of PPHN and its severity. The limitation of our experience was that we could not do a proper monitoring for the estimated pulmonary artery pressure and patient's oxygen index (OI) which are needed for determining the severity of PPHN and adjusting the dose of $MgSO_4$. Thus, we did not have the precise time of adequate clinical response of $MgSO_4$ therapy. Serum magnesium level also could not be measured in our case.

CONCLUSION

In conclusion, treatment with magnesium sulphate ($MgSO_4$) can be considered beneficial to be used in persistent pulmonary hypertension of the newborn (PPHN). Nevertheless, in facilities that may be more equipped, the use of inhaled nitric oxide (iNO) remains the first choice for PPHN.[4] Sildenafil is also superior to $MgSO_4$ in terms of shorter duration of mechanical ventilation, interval to improvement of arterial blood gases, lowering estimated pulmonary artery pressure, and also the need of inotropic agent.[7,10] Vital sign, including blood pressure, SpO_2, and worsening of respiratory distress should be monitored during $MgSO_4$ infusion. This case is expected to be a reference for the beneficial effect of $MgSO_4$ usage in PPHN in other limited healthcare facilities.

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DECLARATIONS

The authors have no conflict of interest to declare.
Consent for the publishing of this case report was obtained from the patient's parents

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CASE REPORT

The tale of COVID-19 survivor: Primary care physician's management strategies for mental health and chronic disease during pandemic COVID-19 era

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SUMMARY

The coronavirus disease 2019 (COVID-19) pandemic has impacted the mental health of those with chronic illness since its declaration. Primary care physicians play an essential role in the fight against the disease. They are the first point of contact for a significant proportion of patients. It is very important to be holistic and emphasise the importance of early mental health screening among primary care physicians in managing post-COVID-19 patients, especially those with comorbidities. This is to improve the detection rate for mental illness at the primary care level and subsequently assist in managing the disease accordingly. Low detection of mental illness among COVID-19 patients has resulted in serious implications and an increased morbidity. Managing post-COVID-19 patients with mental and multiple comorbidities require good family support along with the involvement of a multidisciplinary team to ensure diseases controlled and prevent further complication. This case illustrates the diagnosis and management of a 67-year-old woman with underlying diabetes mellitus and depression, where she had been recently infected with the COVID-19. Based on the latest evidence, the key element in managing the aforementioned patient is via a holistic approach, pharmacological treatment and supportive care from primary care physician and family members.

INTRODUCTION

In December 2019, China reported the first case of a new coronavirus (SARS-CoV-2). The World Health Organisation (WHO) subsequently named the disease 'the 2019 novel coronavirus disease' (COVID-19) and declared it a pandemic subsequent to its global outbreak.[1] This virus has the potential to cause acute infectious pneumonia. The COVID-19 pandemic has impacted the mental health of those with chronic illness since its declaration. Hence, the identification of this condition and its appropriate management is essential to ensure that this group of patients is being screened and given early psychological first aid. This case describes how an elderly woman with an underlying history of depression and diabetes mellitus developed a relapse of her major depressive disorder (MDD) episode following the COVID-19 infection, and the challenges faced by medical team and her family in managing this patient.

CASE PRESENTATION

A 67-year-old postmenopausal lady with multiple comorbidities, which include COVID-19, diabetes mellitus, hypertension, dyslipidaemia, and a history of depression in the past, was treated in a post-COVID-19 clinic. She was diagnosed with depression in 2016 and was started on an antidepressant. She was stable after 2 years of treatment and subsequently in remission and no longer on follow-up and medication. Two weeks after being discharged from the ward, she began to experience depressive symptoms. She had low mood, lost interest engaging in any activity, poor sleep, diminished appetite and lost weight for almost 2 weeks. Initially, the patient was reluctant to attend the clinic because she was concerned about contracting another infection, but her daughter persuaded her. The symptoms have moderately impaired her social activity and function. She denied having any suicidal thoughts or intentions. There was no psychotic, anxiety or manic symptoms. In addition, she did not consume alcohol, smoke or take any substances. She has good family support and stays with her daughter, where the daughter financially supports her. There is no family history of mental illness among her family members.

On physical examination, her height, weight and BMI were 153 cm, 66 kg, and 28.2 (obese), respectively. All her vital signs were normal. The Patient Health Questionnaire-9 (PHQ-9) score was 10, which indicates moderate depression; and the GAD-7 score was 0, which indicates no anxiety. The mental status examination indicates that her consciousness was clear. She was not cooperative throughout the conversation, where she demonstrated reluctance to talk and was avoiding eye contact. Her mood was low, but there were no signs of hallucination and delusions. No other abnormalities were noted.

Blood investigations showed a high HbA1c of 7.5%, triglyceride (TG) level of 1.2 mmol/L, low density lipoprotein (LDL) of 2.2 mmol/L, high density lipoprotein (HDL) of 1.1 mmol/L and total cholesterol (TC) of 7.0 mmol/L. The liver, renal and urine tests were all normal. Both the annual eye examination and baseline electrocardiogram were also normal.

Both the patient and the daughter were informed about the diagnosis. Initially, the daughter could not accept the diagnosis of depression, as she thought the disease was resolved in the past. The initial management was to educate

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the patient and the daughter regarding the disease. Following clarification, both the patient and the daughter agreed that the former is to be started on an antidepressant treatment. The patient started with a low-dose tablet of fluvoxamine (50 mg), a selective serotonin reuptake inhibitor (SSRIs) antidepressant medication group, via oral administration once a day. Starting antidepressants at low doses will reduce side effects and improve adherence. The side effects of SSRI medications, such as stomach disturbance, sleep disturbance and nervousness, were explained to the patient. A short course of benzodiazepine lorazepam (1 mg/day) was also prescribed to the patient due to her sleep disturbance. The benzodiazepine tablet was prescribed for a short duration, as it may cause dependence in the long term. Its side effect has been addressed to the patient as well. In addition, a separate consultation with the daughter was done to assess for psychological impact on the caregiver. It was reported that the daughter could cope, as she received support from her other siblings as well.

A second visit was done after 2 weeks, which showed that the patient's mood had improved after starting the medication. She is more responsive to questions and her mood lifted. Additionally, she became talkative and answered questions readily. Following her medication, she is able to sleep at night and converse more. Her sugar profile was normal during the visit, as she was compliant with her medication. Her daughter supervised her mother's medication daily. Her antidepressant and diabetes medication were continued, and a 1-month follow-up was given.

During the third visit after 1 month, the patient's depression significantly improved. Her sugar level was also normalised. Her mother was compliant with all her medications under supervision. During the visit, the patient asked about the COVID-19 vaccine, as she was concerned about contracting another infection in the future. Subsequently, vaccine was given to the patient, considering she was a high-risk patient. In this case, virtual consultation was recommended to the patient, as her condition had improved and become stable. This was also a request by the daughter to avoid another infection, as she was aware of the increased risk for the elderly.

DISCUSSION

The rising number of depressions among COVID-19 patient with comorbidities has revealed serious implications and resulted in increased morbidity. It is very important for primary care physicians to be holistic and emphasise the importance of early mental health screening in managing a post-COVID-19 patient, especially those with comorbidities, in order to improve the detection rate for depression at the primary care level and subsequently manage the disease accordingly. It is important to detect depression early to prevent delay in management. The first step is to screen depression among post COVID-19 patient.

Moreover, primary care physicians should be well-equipped and responsible for managing COVID-19 in Malaysia. This case is an example of inspiration, whereby during the COVID-19 pandemic, people are prone to stress, anxiety and depression. Some groups are more likely to be affected than others, as they have a poor ability to tolerate stress and are more likely to experience a relapse of depression. Studies have suggested the need for surveillance and care for people with pre-existing psychiatric disorders during the COVID-19 pandemic.[2]

Therefore, it is essential to emphasise on psychological first aid to patients who have suffered from COVID-19. Primary care physicians need to assess patient's psychological status during every consultation post-COVID-19 infection. Patients discharged from the ward should be psychologically evaluated using a simple mental health screening tool. These tools include the Whooley test, Patient Health Questionnaire (PHQ) or the Generalised Anxiety Disorder (GAD). Whooley test is commonly used to screen depression at primary care setting, as it is very simple to use, with a specificity of 99 and 78%.[3] Similarly, the PHQ could be incorporated to screen depression due to its good sensitivity and specificity at 97 and 67%, respectively. Moreover, the GAD screening tool, which has a sensitivity of 86% and a specificity of 83%, can be used to screen for anxiety.[3] All these tools are simple and easily applicable at primary care clinics.

Besides that, non-pharmacological therapies for depression are equally important. These include psychoeducation, relaxation therapy from the occupational therapist, support groups from people who have survived depression and yoga or mindfulness activities, which may ease stress and anxiety. The incidence of depression could also affect the caregiver. Caregiver of patient with depression is more likely to develop depression, a strong risk factor for depression. Hence, psychoeducation is beneficial for the caregiver as well. Families who have undergone psychoeducation showed a significantly lower rate of depression.[4]

During the pandemic, primary care physicians find it difficult to manage chronic diseases, as some patients may find it challenging to attend the clinic, particularly during a Movement Control Order (MCO). These concerns indicate the need for improvement in chronic care management during the COVID-19 pandemic. Alternatively, consultation and psychological counselling via telephone call or virtual follow-up can be done. The Ministry of Health (MOH) embarked on a virtual clinic project in order to improve chronic care management. This concept enables patients to communicate with healthcare professionals at their homes via a virtual approach application. The Malaysian Medical Council (MMC) has developed a virtual consultation guideline during the COVID-19 pandemic, which ensures that medical services comply with medical ethics, laws and legislation. Obtaining the information, consent, and maintaining the medical records of patients must be established in accordance with professional and ethical requirements. During virtual consultations, doctors can follow up with their patients, review their blood test results, provide interactive consultation and order an investigation. However, the virtual clinic provides neither an online prescription nor a diagnosis during consultation. It can only be offered to those with a stable chronic disease case, consented to use virtual consultation and reachable with internet connection.

CONCLUSION

In conclusion, early identification and holistic management of depression among coronavirus disease (COVID-19) patients with multiple comorbidities are essential to be enhanced among primary care clinicians. The increase in the prevalence of mental health problems among COVID-19 survivor has coincided with severe disruptions to mental health services, leaving huge gaps in care for those who need it most. Concerns about the potential increase in mental health conditions among COVID-19 survivors make it important to include mental health and psychosocial support in their COVID-19 response plans, but major gaps and concerns remain.

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COMPETING INTEREST

There was no conflict of interest.

CONSENT FOR PUBLICATION

Written informed consent was obtained from the patient for publication of this case report.

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Malignant transformation of mature cystic teratoma: An uncommon encounter

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SUMMARY

Malignant transformation in a mature cystic teratoma (MT-MCT) of the ovary is a rare condition which poses a great challenge to diagnose it preoperatively and hence, a hindrance to proper treatment planning. In most cases, definitive diagnosis is achieved postoperatively via histological examination of the specimen. Here we report a case of MT-MCT to squamous cell carcinoma (SCC) with intra-abdominal keratin flake seeding.

INTRODUCTION

The most frequent ovarian germ cell tumours are mature cystic teratoma (MCTs), comprising 10 to 25% of all ovarian neoplasms. MT-MCT of the ovary is rare and has been reported to occur in 0.17 to 2% of MCT,[1] predominantly in women in their fifties.[2] SCC is the most common transformation.[3]

CASE PRESENTATION

A 53-year-old, parity 5, post-menopausal housewife presented with abdominal distension and constitutional symptoms with altered bowel habits for 2 weeks. She denied pain, bowel or urinary symptoms. Family history was insignificant and there was no past surgical history. Physical examination revealed a 20-week size non-tender, immobile pelvic mass. Breast, speculum and digital bimanual vaginal examinations were unremarkable.

An abdominal ultrasound assessment revealed a complex multiseptated solid-cystic ovarian mass of 14 × 10 × 14 cm with minimal ascites. The uterus and cervix were normal in appearance and size with endometrial thickness of 24 mm. Both kidneys showed no hydronephrosis.

A contrast-enhanced computed tomography of thorax, abdomen and pelvis (CTTAP) showed a multiloculated cystic enhancing mass in the pelvis measuring 12.5 × 10.7 × 15.8 cm, with septations and calcification within the mass with thickened wall in some areas (Figure 1B). Normal ovaries were not seen while the normal uterus was anteverted and displaced to the right side due to the mass. The urinary bladder and rectum were also displaced to the right with a clear fat plane.

Diffuse enhancing heterogenous fat-containing soft tissue mass was seen at the anterior lower abdomen, suggestive of omental caking measuring 2 × 18 × 13 cm with enhancement of peritoneal lining (Figure 1A). Moderate ascites with enhancing peritoneal lining were noted in the lower abdomen.

There were sub-centimetre mesenteric nodes and an enhancing peritoneal nodule at the left hypochondrium measuring 1 cm. There was also prominent left renal pelvis with mildly dilated proximal and mid ureter.

The overall features were suggestive of advanced ovarian malignancy.

Patient underwent pigtail insertion for drainage of ascites and ultrasound guided omental biopsy. The peritoneal fluid cytology showed no malignant cells.

Histological examination of the omental biopsy showed granulomatous inflammation with foreign body reaction and presence of keratin materials (Ziehl-Neelsen (ZN), Periodic acid-Schiff (PAS) and Congo red stains were negative). There was no immature teratomatous element.

Her cancer antigen-125(CA125) was 377.2U/ml while serum carcinoembryogenic antigen (CEA) was 82.5 U/ml. Her alpha fetoprotein was < 1.3 ng/ml while her beta-human chorionic gonadotropin (beta-hCG) was < 2 mIU/ml. Her infective screening was negative while the erythrocyte sedimentation rate (ESR) was 86, with normal chest X-ray, liver and renal profiles.

A second repeated laparoscopic biopsy of the peritoneal nodules and omentum was done. Intraoperative findings revealed a pelvic mass with minimal ascites, omental caking, extensive peritumour adhesions resulting in inadequate visualisation of the uterus and lower pelvis. The peritoneum fluid cytology taken also showed no malignant cells.

Histological examination of the peritoneal nodules and omentum biopsies were similar to previous biopsies.

GeneXpert and mycobacterium tuberculosis polymerase chain reaction tests were not performed as all the specimens were preserved in formalin solution. Pulmonary tuberculosis was deemed unlikely after assessment and workup by a physician.

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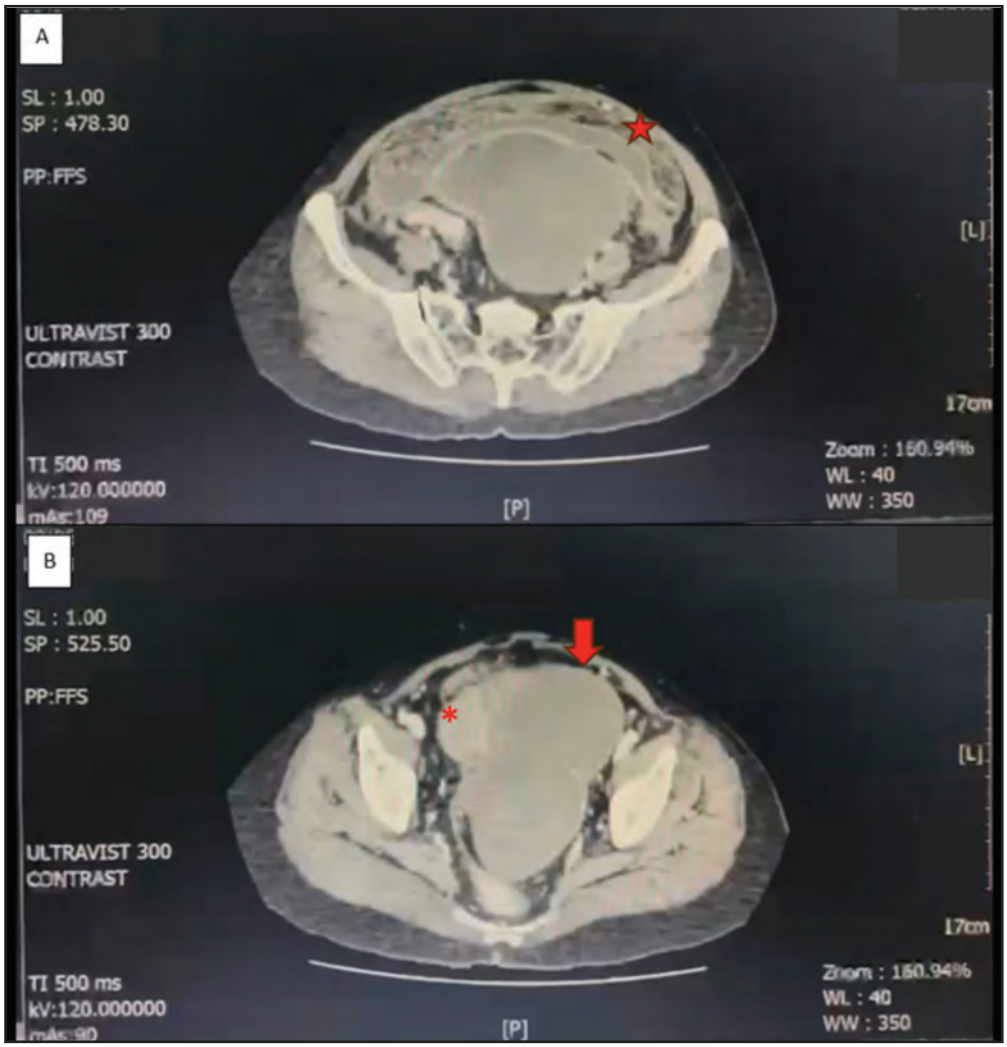

Fig. 1: A: CT of abdomen showing feature (star) suggestive of omental caking with moderate ascites and enhancing peritoneal nodules. B: CT of pelvis showing large multiloculated ovarian cystic enhancing mass (arrow) with septations and calcifications. Uterus (*) was anteverted and displaced to the right side

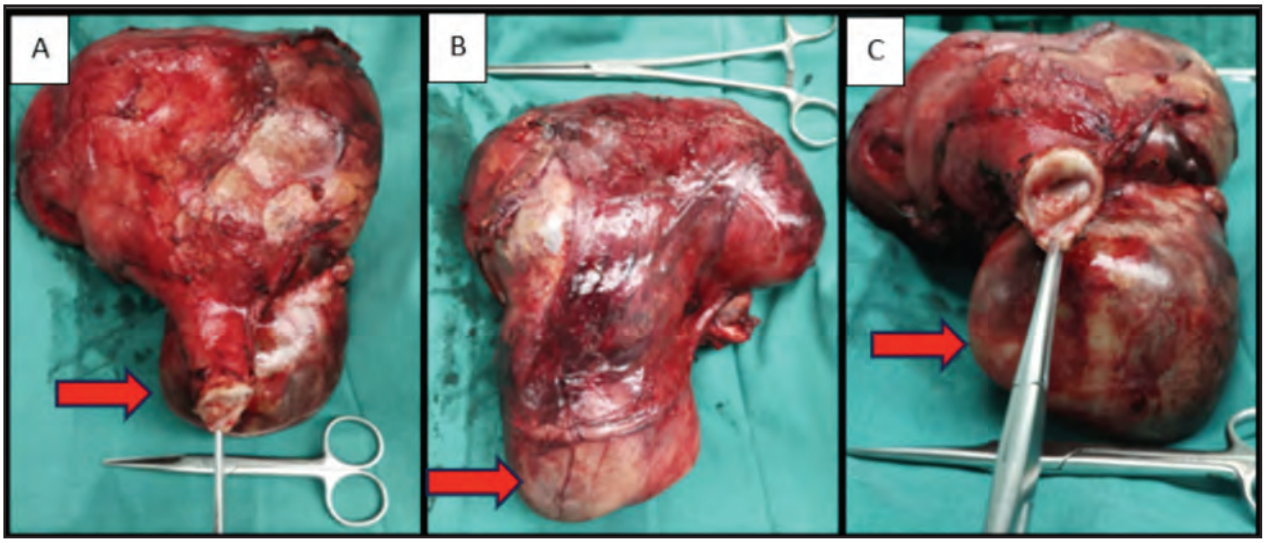

Fig. 2: A: Anterior view; B: Posterior view; C: Inferior view of the specimen. Red arrow: left ovarian mass

Patient then underwent primary debulking surgery (midline supraumbilical staging laparotomy, total abdominal hysterectomy, bilateral salpingo-oophorectomy, pelvic, para-aortic lymph node dissection, appendicectomy and omentectomy). Intraoperatively, the left ovarian tumour was adhered to the pararectal space and posteriorly to the pouch of Douglas. Right ovary appeared unaffected. Multiple nodules exceeding 2 cm were noted on the omentum and few smaller nodules approximately 2 to 3 mm on the peritoneal surface.

Pathological assessment showed that the left ovarian tumour (18 × 17 × 10 cm) was intact, multiloculated, with thickened cyst wall, patchy plaque at the inner surface and Rokitansky protuberans (2 × 1.5 × 0.8 cm). Histologic examination showed ovarian stroma containing all three embryonic layers, ectoderm (skin and appendages, nerve and glial tissue), mesoderm (fat, cartilage, bone and muscle) and endoderm (glandular and ciliated epithelium). The left ovary showed non-keratinising SCC arising from mature cystic teratoma, in which the malignant cells showed moderate to marked pleomorphic vesicular nuclei with prominent nucleoli. Occasional intercellular bridges were noted with absence of keratin pearls. Capsule was intact. Foci of lymphovascular invasion were seen at the right fallopian tube and left ovary. Sections from cervix, omentum and nodules from various sites (small bowel surface, small bowel mesenteric, pararectal, peritoneum) showed foreign body granulomatous inflammation. Omentum, peritoneal and small bowel serosal nodules showed malignant cells with foreign body granuloma. Malignant cells were also seen at appendiceal serosa. Malignant cells were highlighted by CK 5/6, p63 (diffuse), GATA 3 and CAM5.2 (patchy). Right ovary was normal. Bilateral pelvic and para-aortic lymph nodes were negative for malignancy.

Patient was staged as stage 3C (FIGO staging 2014) in view of presence of tumour exceeding 2 cm on the omentum as well as involvement of the bowel serosa surface.

Patient was treated with adjuvant chemotherapy 8 weeks post-surgery consisting of carboplatin and paclitaxel for six cycles in which she completed without issues.

Her tumour markers showed a decline in values compared to the values prior to surgery. Her CEA reduced to 15.3 U/mL from 82.5 U/ml, while her CA125 showed a reduction from 377 U/ml to 32 U/ml. However, CTTAP done 2 weeks post adjuvant chemotherapy showed multiple enlarged peritoneal nodules, mesenteric and paracaval lymph nodes. There were also multiple liver lesions suggestive of liver metastasis indicating disease progression.

Patient was then planned for second line chemotherapy.

DISCUSSION

According to Malaysia National Cancer Registry Report 2012 to 2016, ovarian cancer ranked tenth in Malaysia and fourth in females. MCT (also known as dermoid cyst) is the most common benign ovarian tumour, composed exclusively of mature tissues from two or three germ layers (endoderm, mesoderm and/or ectoderm) with MT-MCT has been reported to occur in 0.17 to 2% of MCT.

Preoperative suspicion of malignant transformation is difficult, thus posing a great challenge and dilemma regarding ways of surgical resection and need of adjuvant therapy. It is commonly accepted that potential malignancies should be suspected in all ovarian tumours, until proven otherwise. There were no specific clinical symptoms, but abdominal pain was the most frequent complaint and abdominal swelling placed second.[4] In most cases, definitive diagnosis is achieved postoperatively via histological examination. Risk factors for malignancy in a teratoma include age, tumour size,[2] imaging characteristics and serum tumour marker levels, which concur with the current case. It has been reported that malignant transformation occurs in a relatively older population, predominantly in fifties.[2] According to Kikkawa et al.,[8] tumours more than 9.9 cm in diameter or grow rapidly may be associated with malignant transformation. Presence of a solid component with contrast enhancement, evidence of adherence to surrounding structures, necrosis and haemorrhage are important radiographic parameters to suspect malignant transformation in mature teratoma.[5] Chiang et al.[6] found out that in cases of MCT with malignant transformation to SCC measuring greater than 15 cm in diameter were more aggressive than those measuring less than 15 cm.

The importance of serum tumour markers in the diagnosis of ovarian malignancies has been acknowledged in earlier studies. CEA is the best screening marker, followed by SCC antigen for SCC arising from MCT.[2] A combination of age above 40 years and serum SCC antigen levels above 2.5 ng/ml were 77% sensitive and 96% specific for malignant squamous transformation in a teratoma, therefore is considered a suitable marker for diagnosis.[7] Kikkawa et al.[2] recommend that serum SCC and CEA levels be tested in patients aged 45 years or older and the tumour is more than 99 mm in greatest dimension. However, testing of SCC antigen is not readily available in our setting.

This patient had laparoscopic biopsies done to establish the diagnosis as advanced ovarian malignancy was suspected and initially planned for neo-adjuvant chemotherapy. In view of the presence of multiple miliary-like intra-abdominal nodules seen during the laparoscope and histological report of granulomatous inflammation, extrapulmonary tuberculosis was suspected. However, histological examinations showed foreign body reactions (presence of giant cells engulfing keratin flakes) and presence of keratin materials expressing CKAE1/AE3, negative ZN and PAS stains. These findings further support the differential diagnosis of teratoma with squamous components. Combined with the radiological findings, patient's age and tumour size, advanced ovarian tumour became the most suspected diagnosis. However, the biopsy results were not diagnostic. The patient then underwent primary debulking surgery to stage, obtain definite histopathological diagnosis and to further guide her adjuvant treatment.

In a case series, 83% of MT-MCT had obvious large solid

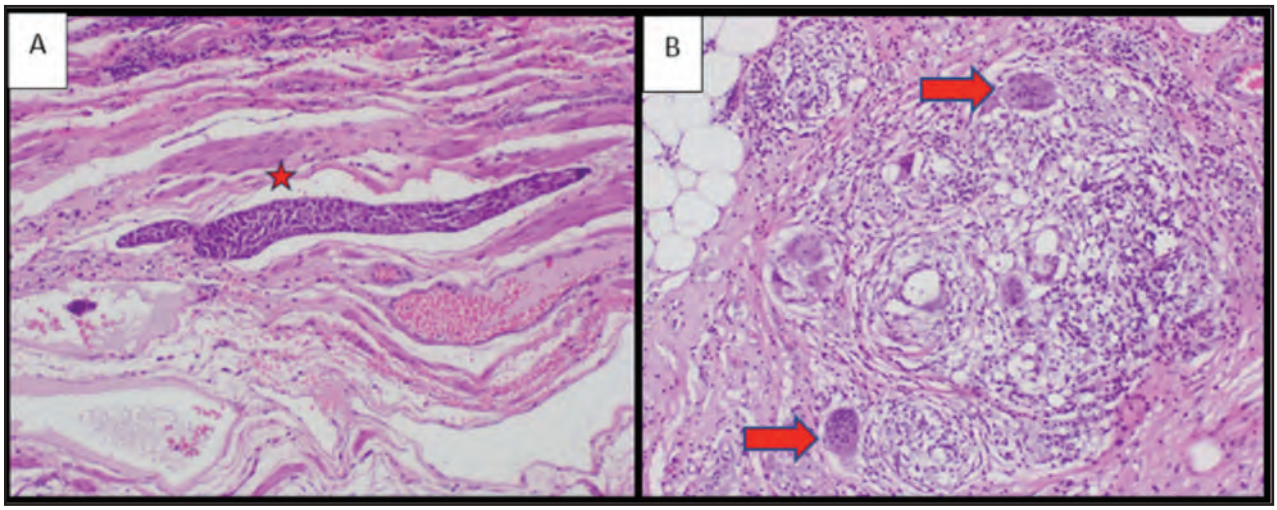

Fig. 3: A: Vascular infiltration by malignant squamous cells (star); B: Foreign body granulomas associated with squames are seen at omentum (arrow)

components in gross pathological examination.[5] However, in this patient, the tumour has no obvious solid component. The malignant component of MCT sometimes exists in only a part of the lesion, causing difficulty in its identification grossly, thus emphasising the importance of careful examination of the MCT specimens.

The occurrence of the keratin flake seeding could be due to focal tearing, localised rupture or penetration of capsule by the tumour, leading to the deposition of keratin debris and/or formation of keratinous nodules in the peritoneal cavity or adjacent organs, and may be easily mistaken for tuberculosis.[9] The diagnosis of MC-MCT is mainly based on the morphology[10] and immunohistochemical (IHC) stains are supportive rather than diagnostic.

Chen et al.[4] revealed that tumour stage, patient age, tumour size, positive preoperative CA 125 and SCC antigens level and optimal debulking affects survival, with tumour stage and optimal debulking being the most significant. They reported that the 5-year survival rates for stages I, II, III and IV were 75.7, 33.8, 20.6 and 0%, respectively. The other factors that may affect prognosis are capsular invasion, ascites, rupture or spillage, adhesions and vascular space invasion.[1] Interestingly, it was reported that patients with increased SCC antigen and CA125 markers had a worse 5-year survival rate, while a high CA125 level is a more reliable prognostic marker than SCC antigen.[4]

Due to the scarcity of literature, adjuvant treatment has yet to be defined, not to mention neoadjuvant therapy. Chen et al.[4] revealed that for stage II-IV cases, instead of radiotherapy, the advanced cases may be better treated with optimal debulking with cisplatin-based chemotherapy.

Pelvic and para-aortic lymph nodes (retroperitoneal lymph nodes) assessment for ovarian carcinoma is recommended and is an important component of staging and debulking, according to the National Comprehensive Cancer Network (NCCN guideline V1.2024). In this patient, pre-operative diagnosis of MT-MCT was not established and there were enlarged pelvic nodes on the CT scan. Hence a full staging for ovarian cancer was performed and no neoadjuvant chemotherapy was able to be given to her.

In general, follow-up for ovarian malignancy is life-long with the interval between follow-ups gradually increasing in correlation with the duration from treatment completion. NCCN recommends every 2 to 3 months with CTTAP every 3 to 4 months in the first year. Unfortunately, in this patient, a follow-up CT scan done 2 weeks after completion of treatment showed disease progression.

CONCLUSION

Malignant transformations of mature teratoma are rare, with squamous cell carcinoma being the most common malignant transformation. With the knowledge of the risk factors, preoperative risk assessments and imaging correlation, teratomas in older women, especially if it is large-sized, should raise clinical suspicion. They should be carefully and adequately sampled to attain accurate diagnosis to decide on appropriate management of the patients.

CONFLICT OF INTEREST

None

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CASE REPORT

Spontaneous globe rupture in a patient with anaplastic spheno-orbital meningioma

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SUMMARY

Anaplastic meningioma is rare and has always been linked to a grave prognosis. We present a case of unilateral anaplastic spheno-orbital meningioma (SOM), which was complicated by spontaneous globe rupture and invasive recurrences. A 55-year-old female presented with extreme non-axial proptosis in the right eye with lateral globe displacement a month post-radiotherapy following the fourth surgery for the right SOM. Compressive optic neuropathy led to non-perception of light (NPL) in the right eye, while the left eye vision remained at 6/6. Refusing evisceration, the patient experienced spontaneous right globe rupture after 1 month. Brain magnetic resonance imaging showed an advanced exophytic right infiltrative SOM. Bevacizumab therapy failed, necessitating a fifth surgery. Six months postoperatively, SOM infiltration caused NPL in the left eye. The patient's general health declined, leading to death after 3 months. SOM is a blinding condition that can be associated with high morbidity and a poor prognosis for survival.

INTRODUCTION

Meningiomas are primary intracranial neoplasms arising from arachnoid cap cells and constitute about one-third (37.6%) of all primary brain tumours, with an incidence rate of 8.81 in 100 000.[1-2] They are typically slow-growing tumours which can be invasive. SOM is a unique subset of meningioma that arises from the sphenoid ridge with an orbital extension, accounting for 2 to 9% of all intracranial meningioma and only 2% of all orbital lesions.[3-4] The vast majority of SOMs are benign. Anaplastic SOMs are rare and potentially manifest itself with an aggressive clinical course. We reported an advanced presentation of anaplastic SOM with spontaneous globe rupture, followed by invasive recurrences, leading to bilateral vision loss and finally loss of life.

CASE PRESENTATION

A 55-year-old female was diagnosed with right SOM at the age of 40. The patient has no other medical comorbid and had four previous surgeries for SOM with histological transformation from World Health Organisation (WHO) grade I to grade III. Her right proptosis significantly reduced after each debulking surgery and a prior course of radiotherapy (Table I). However, her right visual acuity (VA) had declined from 6/6 to non-perception of light (NPL) after 5 years of disease onset due to tumour compression into the right optic nerve. She presented with right severe proptosis 1 month after undergoing radiotherapy following her fourth surgery. This occurred around 3 months after the fourth surgical procedure (Figure 1A). The proptosis rapidly worsened with a complete inability for eyelid closure and eye irritation. Examination showed right severe non-axial proptosis, dry ocular surface with intraocular pressure (IOP) of 22 mmHg and total restriction of right ocular motility (fifth recurrence). Left eye examination was unremarkable. The patient was counselled for evisceration but opted for moist chamber, intensive lubrication and IOP lowering agents. She defaulted her subsequent appointment and only presented after 1 month, complaining of serous eye discharge for 3 days. She also had intermittent generalised headaches, nose block and anosmia, but denied having trauma to the right eye, reduced hearing, shortness of breath, loss of appetite or loss of weight.

Examination showed a huge orbital mass occupying the right periorbital area, with some lobulations medially. There was a spontaneous right globe rupture with no visible anterior segment structure, leaving the posterior sclera exposed, surrounded by severe conjunctiva chemosis (Figure 1B-C). The residual posterior eyeball structure was distorted and was pushed laterally by the orbital mass. There was a reduced sensation on the right ophthalmic and maxillary distributions of the trigeminal nerve. Left eye VA remained 6/6 with normal anterior segment, intraocular pressure, fundus findings and ocular motility. Other neurological and systemic examinations were normal.

Magnetic resonance imaging (MRI) brain and orbit revealed marked tumoral growth of the SOM with lobulated exophytic component. The mass extends to the ethmoid and sphenoid sinuses, right cavernous sinus, anterior and medial cranial fossae causing mass effect on the anterior temporal and inferior frontal lobes (Figure 2A). The patient was put on Gutt

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Table I: Patient's clinical course in chronological order prior to presentation

Date	Age	Clinical presentation	Clinical status	Management	Histopathology
2015 (Aug)	49	Right proptosis VA RE 6/6, LE 6/6, No RAPD IOP BE normal BE full ocular motility	First presentation	RE lubrication Right craniotomy and tumour debulking (30/10/2015) - First surgery - Simpson grade 4 - Proptosis resolved	WHO grade I meningioma
2018 (May)	52	Recurrent right proptosis VA RE 6/7.5, LE 6/6 RE RAPD positive Grade 1 IOP BE normal BE full ocular motility	First Recurrence	RE lubrication Radiotherapy 60Gy 30 fractions (24/6-3/8/2018) - Proptosis improved	NA
2020 (Oct)	54	Worsening right proptosis Loss of right eye vision VA RE NPL, LE 6/6 RE RAPD positive grade 4 IOP BE normal Ophthalmoplegia with restriction on temporal, superior and inferior gaze	Second recurrence	RE intensive lubrication Right craniotomy and tumour debulking (17/11/2020) - Second surgery - Simpson grade 4 - Proptosis improved	WHO grade II meningioma
2021 (Jan)	55	Worsening right proptosis VA RE NPL, LE 6/6 IOP BE normal Ophthalmoplegia with restriction on temporal, superior and inferior gaze	Third Recurrence	RE intensive lubrication Right craniotomy and tumour debulking (16/2/2021) - Third surgery - Simpson grade 4 - Proptosis improved	WHO Grade II meningioma
2021 (Jul)	55	Worsening right proptosis Headache Nose block and loss of smell VA RE NPL, LE 6/6 IOP RE 22 mmHg, LE normal Ophthalmoplegia with restriction on all directions of gaze	Fourth Recurrence	RE intensive lubrication Gutt Latanoprost 0.005% nocte RE Right craniotomy and tumour debulking, combined with endoscopic excision of tumour and skull base reconstruction (12/8/2021) - Fourth surgery - Simpson grade 4 - Proptosis improved	WHO Grade III meningioma

BE: Both eyes; IOP: Intraocular pressure; LE: Left eye; NPL: Non perception of light; RE: Right Eye; VA: Visual acuity; WHO: World Health Organisation

chloramphenicol four times a day, and swab culture and sensitivity from the right residual globe showed no growth. A course of seven cycles of intravenous bevacizumab 10 mg/kg 2 weekly was given for treatment-refractory SOM. However, repeated MRI brain after completing bevacizumab showed a marked increase in size of the spheno-orbital mass, fungating beyond the right bony orbit (Figure 2B). The mass infiltrated the right middle and superior nasal meatus, bilateral posterior ethmoidal sinuses, right maxillary sinus, anterior cranial fossa and right temporal fossa, resulting in white matter oedema and midline shift.

The patient opted for another craniotomy and tumour excision after multi-disciplinary team discussions were held. A preoperative-tumour embolization was done prior to the surgery, with approximately 90% of the tumour with the feeders mainly from the right internal maxillary artery and right facial artery were embolised. Bifrontal craniotomy and tumour excision were carried out. Maximum safe resection surgery (Simpson grade 4) was done, to remove the soft tissue component that occupied the entire intraconal cavity, along with the excision of the intradural tumour that was attached to the right sphenoid wing and extradural component that infiltrated the anterior and posterior ethmoid sinus, as well as the sphenoid sinus. Histopathology showed epithelioid neoplastic cells with prominent nucleoli, ill-defined cytoplasmic borders and brisk mitotic figures ranging from 14- to 7/10 hpf with aberrant form identified which consistent with anaplastic meningioma, CNS WHO grade III (Figure 3A-C).

During an ophthalmology review at 6 months after the fifth tumour debulking surgery, the patient mentioned that her left eye VA had gradually deteriorated over a period of 1 month. Examination revealed right anophthalmia with a clean and well-healed surgical wound. The left eye VA was NPL with pale disc on the left eye on fundus examination. Left eye IOP was 12 mmHg and there was no demonstrable left proptosis or restriction in ocular motility. Neuroimaging confirmed the recurrence of the tumour (sixth recurrence), extending into the left orbit, encasing and compressing the left optic nerve (Figure 2C). The patient opted for conservative management, but ultimately became bedridden due to disease progression, leading to her demise 3 months later.

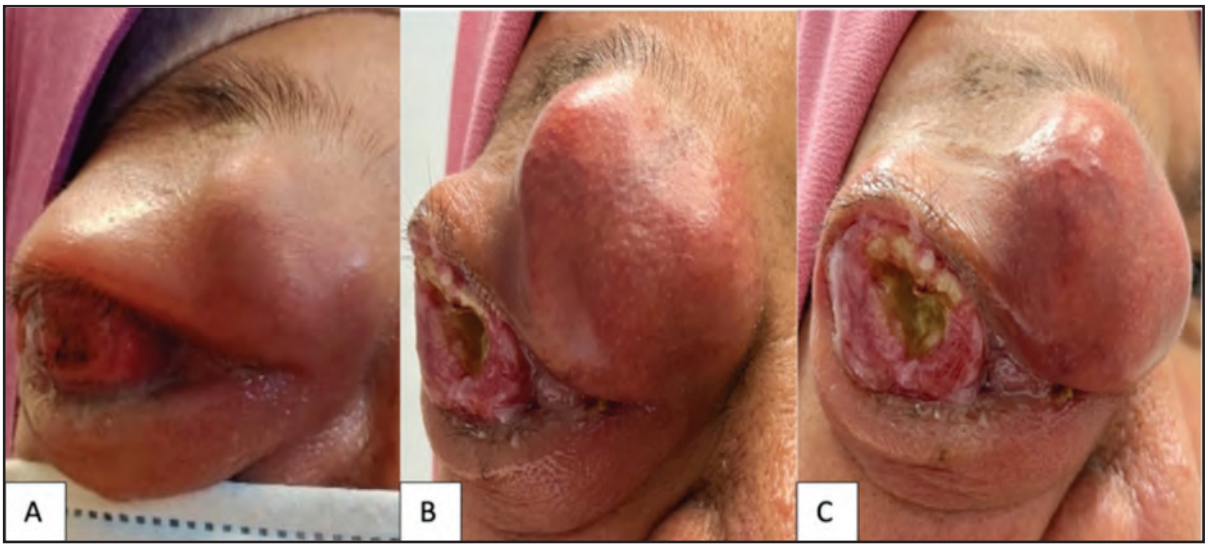

Fig. 1: Patient's photo (A) at presentation of fifth recurrence shows right severe non-axial proptosis with exposure keratopathy, (B) anterior view and (C) lateral view shows spontaneous globe rupture with worsening exophytic component of the right orbital mass

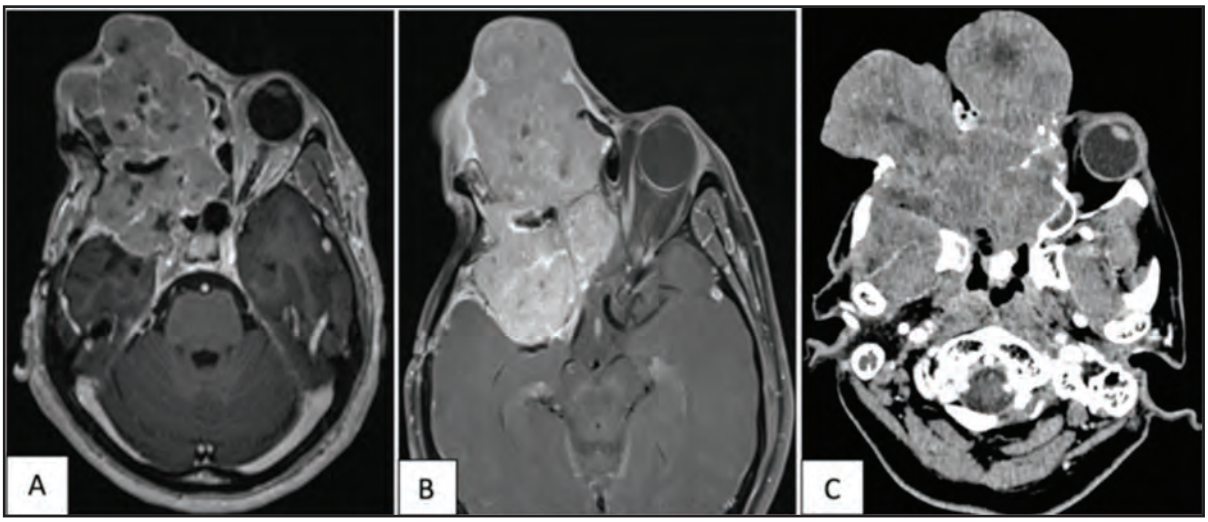

Fig. 2: Spheno-orbital meningioma in axial contrast-enhanced T1-weighted MRI reveals (A) marked tumoral growth with lobulated exophytic component at fifth recurrence. The mass extends to the ethmoid and sphenoid sinuses, right cavernous sinus, anterior and medial cranial fossae causing mass effect to the anterior temporal and inferior frontal lobes, (B) marked infiltrative tumour recurrence with heterogenous exophytic component, worsening locoregional and intracranial extension despite of a course of bevacizumab therapy prior the fifth surgery, (C) axial computed tomography (CT) image reveals further progression of infiltrative exophytic tumour recurrence in the right orbit, nasal cavity and paranasal sinuses with increasing degree of intracranial extension to bilateral anterior and right middle cranial fossae at sixth recurrence

DISCUSSION

SOMs are defined as primary en plaque tumours of the lesser and greater sphenoid wings. It is uniquely categorised as invasive tumour characterised by pathological hyperostosis and a widespread, carpet-like soft-tissue growth at the dura that may invade the orbit, optic canal, superior orbital fissure and other critical neurovascular structures.[3,5] SOMs are more common in women than in men (6:1 ratio), particularly in middle age of onset with incidence increases with age.[6] Anaplastic SOMs are rare, consist of 1 to 2% of all meningioma, which approximately half of this originate de novo, while the other 50% are the result of anaplastic transformation of lower-grade meningioma.[7]

Risk factors for anaplastic meningioma include childhood exposure to radiation and genetic mutation for NF2.[2] Our patient had none of the clinical features of neurofibromatosis type 2 including the absence of plaque-like skin lesions and hearing loss. Additionally, there was no family history, and genetic testing has excluded the genetic mutation for NF2. She had a triad of classic presentations of SOM, including proptosis, vision loss and restricted ocular motility, similar to other previously reported cases.[3-5] She developed headache, nasal block, anosmia and anaesthesia along the right ophthalmic and maxillary distribution of the trigeminal nerve as sequelae of further tumour progression, as similarly found in other cases.[1,7] Spontaneous globe rupture in SOM is

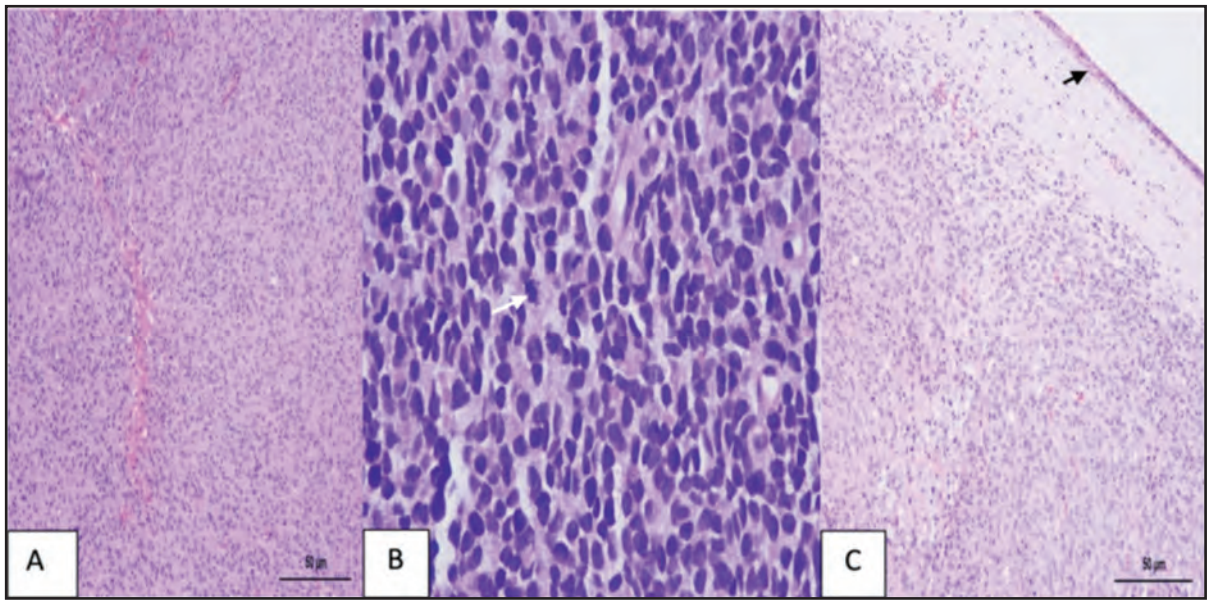

Fig. 3: Histopathology showed features of anaplastic meningioma. (A) Tumour cells arranged in diffuse sheath with interlacing fascicles infiltrating the bony trabeculae and adjacent connective tissue. Extensive areas of geographical tumour necrosis seen. (B) The epithelioid tumour cells display markedly pleomorphic nuclei and prominent nucleoli with ill-defined cytoplasmic borders. Mitotic figures are easily seen (indicated by white arrow). (C) Tumour with overlying respiratory type epithelium (indicated by black arrow). No whorling pattern, psammoma bodies or macrocalcifications observed

a rare entity. Cases of spontaneous globe rupture in orbital tumours have been reported in Group E retinoblastoma and choroidal melanoma, presumed to be related to raised intraocular pressure.[8,9] Such cases have also been reported in orbital metastasis from breast cancer, with evidence of severe keratitis leading to corneal perforation.[10] Spontaneous globe rupture in our patient possibly resulted from a combination of reduced corneal sensation, severe proptosis, raised intraocular pressure and the severe infiltrative nature of the SOM, causing disruption of the globe's integrity. Others have also reported that patients with SOM may also experience various neurological symptoms, such as sensorineural hearing loss, facial palsy, seizures, cognitive impairment, limb weakness, vertigo or dizziness, ataxia and gait changes.[1-3,7] However, these symptoms were not observed in our patient.

The combination of extensive bony hyperostosis and orbital extension are distinct characteristic imaging features of SOM. The common sites for hyperostosis are typically the greater and lesser sphenoid wings, the clinoid process and the roof and lateral walls of the orbit. Hyperostosis is best visualised on a high-resolution CT scan. T1-weighed MRI with gadolinium enhancement and fat suppression is necessary to define the limits of the dural tail and intraorbital extension.[11] Neuroimaging in our patient showed progressive lesions of both components that worsen at locoregional with intracranial extension. The majority of SOMs are grade I WHO lesions (90%), typically regarded as benign and slow growing. A small percentage of SOMs are composed of WHO grade II lesions (borderline), whereas WHO grade III SOMs (malignant) are very rare.[6,12] In our case, the initial WHO grading of meningioma was grade I, then progressed to grade II, and finally to grade III, an anaplastic subtype that poses a more rapid disease recurrence with a more aggressive disease presentation.

Due to the anatomical complexity of this region in proximity to many critical neurological and vascular structures, SOMs present a surgical difficulty.[13] The extent of resection, is determined by the Simpson grade which is based on the surgeon's evaluation during the surgery with considerations that affect the overall safety of surgery. Gross total resection was defined as Simpson grade I, II and III, whereas subtotal resection is defined as Simpson grade IV.[11] Our patient underwent maximum safe resection surgery for each craniotomy and two courses of fractionated radiotherapy. Fractionated radiotherapy (at least 54 Gy given in 1.8 to 2.0 Gy per fraction) has been recommended for WHO grade III tumours, regardless of gross total or subtotal resection.[2,11] After the fourth craniotomy that confirmed WHO grade III tumour, our patient was immediately subjected to radiotherapy. Unfortunately, she developed the fifth tumour recurrence after 1 month completion of radiotherapy treatment. The tumour continued to grow aggressively despite targeted therapy with bevacizumab. Bevacizumab is a vascular endothelial growth factor (VEGF) inhibitor with antiangiogenetic properties. It disrupts the binding and signal transduction processes that are essential for tumour vascularisation, resulting in the regression of the tumour's blood supply.[14] Other targeted therapies such as α-Interferon, sunitinib, everolimus and somatostatin receptor agonists, have also been administered to patients with recurrent or progressive meningiomas that no longer respond to surgery or radiotherapy.[6] Although some successes were reported in several case reports, the use of targeted therapy for meningioma is under level C evidence, and limited efficacy is anticipated.[11]

Recurrence rate for SOM is as high as 33 to 59%.[13] Our patient had a total six recurrences within a period of eight years, with rapid and advanced recurrences more pronounced after being diagnosed with anaplastic meningioma. She succumbed to her illness after one and half years of histological finding of anaplastic transformation. Anaplastic meningiomas are aggressive tumours with a dismal prognosis with a median overall survival period of one and half years and 10-year overall survival rate of 0%.[2,7] Literature has shown that distant extracranial metastases may occur in 0.18% of patients with meningioma, commonly found in the lung, bone, liver, kidney and spine.[15] However, further confirmation of any metastasis was not done in our patient as her condition deteriorated and she became bedridden, and the family opted for conservative and palliative care.

CONCLUSION

Anaplastic SOMs are fast-growing tumours, highly aggressive and associated with a poor prognosis. It leads to considerable cosmetic deformity, visual impairment, high morbidity and ultimately fatality. Decision-making for the management of advanced SOM is challenging, and it must be tailored to each patient, taking into consideration its impact on daily life and the patient's wishes.[3]

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COMPETING INTEREST

No potential conflict of interest was reported by the author(s).

ETHICAL CLEARANCE

This article was registered via the National Medical Research Register Medical Research, Ministry of Health Malaysia with ID NMRR ID-23-02036-XE5.

No ethical clearance was required as this is a case report.

CONSENT FOR PUBLICATION

Written informed consent was obtained from the legal guardian.

AUTHORSHIP

All authors attest that they meet the current ICMJE criteria for Authorship.

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A medical student with undiagnosed HbE-beta thalassemia and cholelithiasis

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SUMMARY

HbE/β- thalassaemia is the most common form of β-thalassaemia. The clinical presentation of HbE thalassaemia is heterogeneous, symptomatic individuals may vary significantly, while the onset can occur later in adulthood. This report illustrates a medical student with a long history of anaemia who finally got his diagnosis right after he was noticed to have jaundice and pallor by a physician. He also developed cholelithiasis as a complication due to his poor health-seeking behaviour, even though he is studying medicine. Therefore, early diagnosis of thalassaemia, including the genotype and proper management, is vital as this condition might be noticed and progress with the proper investigation and intervention.

INTRODUCTION

Thalassaemia, which includes α- and β- thalassaemia, is one of the Malaysia's most common genetic diseases. Almost 5% of the Malaysian population were reported to be carriers of this disease, and up to 40% were HbE carriers.[1] The clinical phenotype of HbE-thalassaemia is heterogeneous, with haemoglobin levels ranging from approximately 3 to 14 g/dL. HbE-beta0 thalassaemia can range from a β-thalassaemia intermedia phenotype to a transfusion-dependent, severe β-thalassaemia. Individuals with a less severe phenotype are also referred to as having non-transfusion-dependent β-thalassaemia (NTDT), where they typically do not require regular transfusions. These individuals are often homozygous or compound heterozygous for a β- + thalassaemia variant or heterozygous for a β- 0 thalassaemia variant.

The typical age of presentation is 2 to 4 years old or later in adolescence.[2] As insignificant thalassaemia, HbE-thalassaemia patients may also face complications such as anaemia, hepatomegaly, splenomegaly and pulmonary hypertension due to haemolysis and ineffective erythropoiesis.[3] Cholelithiasis has been described as one of the common complications of thalassaemia. Gallstone prevalence (detected by ultrasonography) in patients with β-thalassemia ranged from 17 to 57%.[8]

CASE PRESENTATION

A 22-year-old year, single male student at a local university was doing his primary care clinic attachment in Kuantan, Pahang. A resident physician accidentally noted that he looked pale and jaundiced. He admitted to experiencing intermittent symptoms of easily lethargy and palpitation for the past 3 years, which usually come on exertion. However, he has no symptoms of fever, chills, myalgia, arthralgia, diarrhoea, bleeding tendencies, headache, calf pain or shortness of breath. He also denies symptoms of no abdominal pain, dark-coloured urine, pale-coloured stool, bloating, nausea, vomiting, belching, early satiety, regurgitation or retrosternal burning. He also has no history of recent travel to the jungle or water activities, and he does not live in a dengue-endemic area.

He also noticed yellowish discolouration of the sclera and palpable abdominal mass, possibly hepatosplenomegaly, since he was in his second year of medical school. However, he had never sought further professional help. In 2022, he had a history of admission to a tertiary teaching hospital in Kuantan, Pahang, for fever and anaemia. He presented with a fever for 2 weeks, which was associated with daytime somnolence, fatigue and headache. During that time, his Hb was 3.3 g/dL, and he was transfused with two units of packed cells and later discharged with Hb of 7 g/dL. He was told that he might have thalassaemia intermedia, but the confirmed diagnosis was never known since his Hb analysis is still pending during that time. The medical department did defaulter tracing, but he was uncontactable. He attributed his busy academic schedule and negligible symptoms to his ignorance of medical care.

Upon further history taking, the fourth-year medical student affirmed that his mother told him that he had been diagnosed with 'thalassaemia trait' when he was 10 years old. He was unsure what test was performed as the report was eventually lost in a flood. According to him, his brother and mother were also found to have similar diagnoses during the check-up at that time. However, they do not portray symptoms like him. There was no history of anaemia in the family, and both his parents are non-consanguineous.

On examination, he was pale-looking and jaundiced. He was afebrile, and his other vital signs were normal. His BMI was 18 kg/m^2, with a height of 171 cm. There was no frontal bossing, conjunctival suffusion, fetor hepaticus, palmar erythema, finger clubbing or calf tenderness. The cardiorespiratory examination was unremarkable. Per abdomen revealed soft, non-tender abdomen with palpable hepatosplenomegaly. There was no ascites. Cutaneous stigmata of chronic liver disease or skin rashes were absent.

A basic laboratory workout in the clinic results showed mild hypochromic microcytic anaemia and mild hyperbilirubinemia with normal liver enzymes.

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Table I: Result for full blood count and liver function test

Parameters	Unit	Result	Reference
FBC			
RBC	10^{12}/L	4.57	4.5 to 5.50
HB	g/L	83	130 to 170
MCH	pg	18.1	27 to 32
MCV	fL	61	77 to 97
RDW	%	32	12 to 14
Liver function test			
Total bilirubin	mmol/L	98	5 to 21
Direct bilirubin	mmol/L	10.8	<3.4
Indirect bilirubin	mmol/L	87.2	3.4 to 12.0
AST	U/l	33	<50
ALT	U/l	11	<50
ALP	U/l	83	30 to 120
Random Blood Sugar	mmol/L	8.8	

Further investigation was sent to find out the cause of his current condition.

Table II: Result for iron study

Parameters	Unit	Result	Reference
Iron study			
Se iron	mmol/L	30.7	12.5 to 32.2
Se ferritin	Ug/L	198.8	23.9 to 336.2

Table III: Result for full blood picture and Hb analysis

Full blood picture	The haemoglobin level is moderately low. The absolute reticulocyte count is raised. The red cells are hypochromic microcytic. Marked anisopoikilocytosis. Presence of tear drop cells, target cells, cigar shaped cells. Nucleated RBC seen.
Hb Analysis	The HbA2 level is raised (HPLC) The HbF level is raised (both HPLC and CE). Abnormal peak HbE is observed (51.1%) No HbA Haemoglobin analysis: HbE-β thalassaemia
DNA analysis	The predicted genotype/phenotype is β0βE No pathogenic variants of HBA1 and HBA2 genes detected, significantly reduced the probability of alpha thalassaemia trait.

The iron study was normal, while Hb analysis showed HbE-β-thalassaemia (HbE/B-thalassaemia). DNA analysis and the result showed HbE- thalassaemia.

Because of the hepatosplenomegaly, hepatobiliary system ultrasonography was performed. The liver was enlarged with a craniocaudal length of 18.3 cm. The liver parenchymal echogenicity was normal, with no focal liver lesion. The gall bladder was well distended, with several small calculi seen within. The largest calculus was 0.7 cm in diameter. Otherwise, the gallbladder wall was not thickened and had no pericholecystic collection. Common duct and intrahepatic bile ducts were not dilated. The spleen was significantly enlarged, measuring 18.8 cm craniocaudally, with no focal lesion seen. Pancreas showed a normal appearance. The student was later referred to the surgical team. However, due to his asymptomatic status, he was not offered any surgical intervention.

DISCUSSION

HbE results from a β-globin mutation that reduces β-globin production. Individuals who are heterozygous for HbE are asymptomatic carriers. Individuals with homozygous HbE have mild microcytic anaemia. At the same time, HbE, in combination with β-thalassaemia, can range from mild to moderate to severe anaemia, depending on the other beta globin variant. More than half of patients with HbE plus β0 thalassaemia are transfusion-dependent.

In Southeast Asia, HbE/β-thalassaemia is the most common form of β-thalassaemia. According to the Thalassaemia Registry Malaysia, in 2019, the distribution of HbE-thalassaemia was 35.19%.[1] The HbE/β- thalassaemia forms the largest group of thalassaemia patients in Malaysia with 2878 (35.19%) patients, followed by β-thalassaemia major with 2671 (32.66%) patients, HbH disease with 1593 (19.48%) patients, β-thalassaemia intermedia with 738 (9.02%) patients. In contrast, the remaining 298 (3.64%) patients have other forms of thalassaemia.[1]

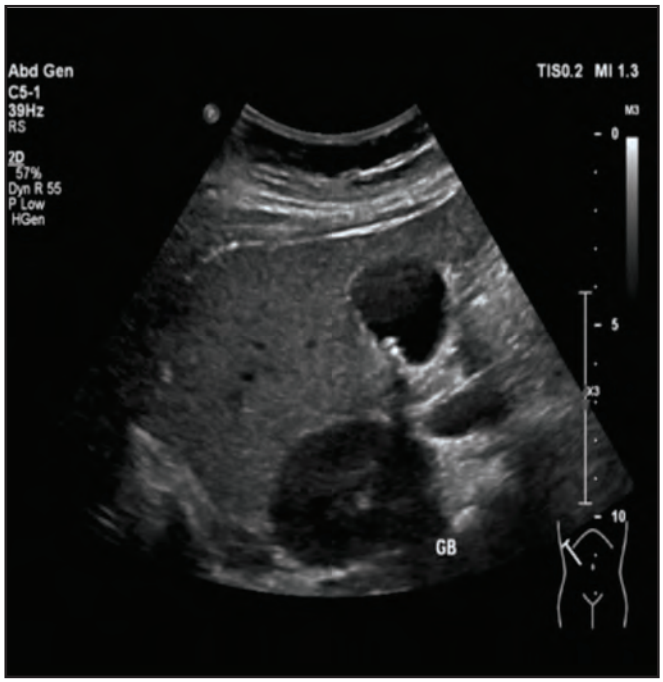

Fig. 1: Ultrasound hepatobiliary showed several small calculi within the gallbladder

Symptomatic individuals are typically homozygous or compound heterozygous for a clinically significant variant. Symptoms generally start in childhood, but in some cases, the initial presentation may occur later in adolescence or adulthood.[7] Heterozygous HbE individuals are not usually anaemic but may have minimal degrees of microcytosis and hypochromia. Homozygous (Hb E disease, Hb EE) meanwhile have minimal anaemia, prominent microcytosis, hypochromia and target cells along with jaundice. Sometimes, incidental findings of heterozygous individuals could happen when a complete blood count, haemoglobin analysis, or genetic testing is done for reasons other than clinical symptoms, such as in evaluation for another condition and reproductive testing.[5] HbE β-thalassaemia usually will be milder when the concomitant alpha thalassaemia trait exists, hence the importance of further diagnostic testing using DNA analysis.

Thalassaemia patients may face multiple complications with their disease, such as cholelithiasis due to chronic haemolysis and ineffective erythropoiesis.[5,6] Gallstone prevalence (by ultrasound) in β-thalassaemia patients was 17 to 57% in different countries, with lower incidences occurring among non-transfusion-dependent thalassaemia. Meanwhile, 23 to 57% of cases of cholelithiasis among β-thalassemia Intermedia were reported in Malaysia.[9] Significant predictors of gallstone prevalence include age and the presence of the Gilbert allele.[2] Most individuals with incidental findings of gallstones on abdominal imaging are asymptomatic. Most of them will remain asymptomatic, while those who develop symptoms typically report biliary colic. The occurrence of cholecystitis or cholangitis among thalassaemic is rare. It is also important to note that the development of pigmented gallstones among Non-Transfusion Dependent Thalassaemia (NTDT) significantly raises the risk of complex cholecystitis and iron buildup in the liver parenchyma, which can cause liver damage that may progress to fibrosis and eventually cirrhosis.[7]

Another issue that needs to be discussed is how medical students seek health care. Self-prescription is the most typical behaviour among medical students.[4] They frequently self-diagnose and self-treat themselves because they see symptoms and sickness differently. Refusal to consult doctors and self-treatment are evident when they start their careers as junior doctors.[4] This group of students is more likely to seek informal counsel from friends and family members, particularly regarding mental health care.

A variety of factors influence students' behaviour in seeking health care. Their primary source of influence over their health-seeking behaviours is their study of medicine. Ironically, their knowledge of the available health services, level of medical knowledge, or stage of study could either encourage the student to seek prompt care or overlook their health problem.[4]

CONCLUSION

HbE-β-thalassaemia can range from asymptomatic carrier status to severe clinical complications. Therefore, early diagnosis and determination of the specific type of thalassaemia are essential, as with proper tests, thalassaemia's clinical syndrome can be noticed and not misdiagnosed.[6] Primary care doctors may face challenges in diagnosing thalassaemia as the clinical symptoms are non-specific. In public primary care settings, the diagnostic test for thalassaemia must go through a strict procedure, i.e., be approved by a family medicine specialist. Hence, many suspected cases are left without testing. Hence, a good and focused history taking, and a targeted physical examination are required to justify the indication for the test.

Adequate training on this topic should also be conducted to increase primary care doctors' awareness and knowledge. For most of the population in Malaysia, the FBC screening program at secondary school and the pre-marital screening are preventive programs aimed at identifying those at risk of thalassemia. Cascade screening among family members of thalassaemic is a standard practice. For this case, even though some of his family had done the test in the past, accurate information and documentation are critical as this will prevent unnecessary repeat testing in the future.

Thalassaemia patients may develop jaundice due to ineffective erythropoiesis. However, jaundice in adults is generally caused by a wide range of diseases, including biliary system infections, pancreatitis, and cancers. Therefore, primary care doctors must include thalassaemia in the list of differentials for jaundice.

As safety netting, it is imperative to inform thalassaemic individuals regarding the signs and symptoms of anaemia and complications such as cholelithiasis, as early detection may lead to the initiation of medical care and prevent potential severe complications. Patient-centred and comprehensive health education should be given during the initial consultation to avoid late-seeking behaviour.

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CONFLICT OF INTEREST

None to declare.

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Unusual presentation of isolated right abducens nerve palsy followed by elevated intracranial pressure and pendular nystagmus in the case of myelin oligodendrocyte glycoprotein antibody-associated disease

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SUMMARY

We describe the case of a female patient with underlying acute lymphoblastic leukaemia in remission who initially presented with isolated right abducens nerve palsy. A month later, she further deteriorated with development of myelopathy and brainstem syndrome, which required ventilatory support due to respiratory failure. A lumbar puncture was performed, revealing evidence of elevated intracranial pressure. Subsequently, she presented with an unusual clinical symptom of pendular nystagmus while on a ventilator. She received treatment with intravenous methylprednisolone, intravenous immunoglobulin and plasma exchange for her myelopathy and brainstem syndrome. As a result, she was successfully weaned off the ventilator, and experienced full improvement in her upper limb functions. Nevertheless, she had remaining bilateral visual impairment and paraplegia. Furthermore, the pendular nystagmus resolved following treatment with gabapentin and memantine.

INTRODUCTION

Myelin oligodendrocyte glycoprotein (MOG) is a glycoprotein expressed selectively in oligodendrocytes, which are glial cells of the central nervous system.[1] Serum antibodies directed against MOG are found in patients with acquired central nervous system demyelinating syndrome that are distinct from multiple sclerosis and aquaporin-4-seropositive neuromyelitis optica spectrum disorder, thus requiring a different treatment management.[2]

CASE PRESENTATION

A 38-year-old female with underlying migraine and acute lymphoblastic leukaemia that was diagnosed since 1996, and completed chemotherapy in 1998, had her last haematology follow-up 5 years ago. Subsequently, she first presented at our department with sudden onset diplopia, that worsened when gazing to the right. Five days later, she started to have occipital headache, which was throbbing in nature and radiated to the frontal region having pain score of 6/10. Initial neurological examination revealed right abducens nerve palsy without cerebellar signs. The other cranial nerves were grossly intact. Fundoscopy finding showed normal visual acuity with no papilloedema. Power for all limbs was full (MRC scale 5/5) with normal tone, reflexes, and sensation. A non-contrast enhanced CT brain at that time was normal. She was given paracetamol and subsequently headache was improving. She was discharged home and early appointment for contrast enhanced CT brain has been arranged for her. However, she defaulted contrast enhanced CT brain appointment. One month later, she visited the emergency department due to acute urinary retention. Her right abducens nerve palsy persisted. Visual acuity and relative afferent pupillary defects were negative, and there was no nystagmus. She also had weakness of bilateral lower limbs with sensory level at T10. She was admitted to the ward and subsequently developed sensory level at T4, upper limbs weakness and respiratory failure. Post intubation, patient required high ventilator support. Magnetic resonance imaging of brain and spine showed patchy areas of T2WI/FLAIR hyperintensities in parasagittal bifrontal cortex, bilateral periventricular and left peritrigonal region, corpus callosum, bilateral medial temporal lobes including the hippocampi, bilateral cerebral peduncle, visualised bilateral proximal optic radiations, midbrain, and pons (worse on right), vermis, bilateral cerebellar lobes and bilateral cerebellar peduncles (Figure 1). A few of these lesions showed corresponding hypointense signal on T1WI. There were extensive patchy ill-defined T2WI hyperintensities (Figure 2) in the medulla oblongata and along the spinal cord, causing cord expansion at the cervical, lower thoracic cord and the conus medullaris (Figure 3). These spinal cord lesions also showed enhancement post contrast.

Lumbar puncture was performed, revealing a high opening pressure of > 50 cm H_20. Cerebrospinal fluid (CSF) results showed a protein level of 659 mg/L (normal range: 150-400 mg/L), glucose level of 2.8 mmol/L (normal range: 2.2-3.9 mmol/L) and having no cell count. CSF results showed no evidence of bacterial or viral meningitis and cytospin showed no malignant cells. The serum aquaporin-4 receptor antibody test was negative. Serum anti MOG antibody was detected by Euroimmun Indirect Immunofluorescence Test. Subsequently, she was given IV methylprednisolone 1 g OD for 5 days, intravenous immunoglobulin 0.4 g/kg for 5 days with plasma exchange for five cycles. After a month she was able to wean off ventilator and regain full strength in her bilateral upper limbs, with residual weakness in her bilateral lower limbs. She also developed pendular nystagmus while

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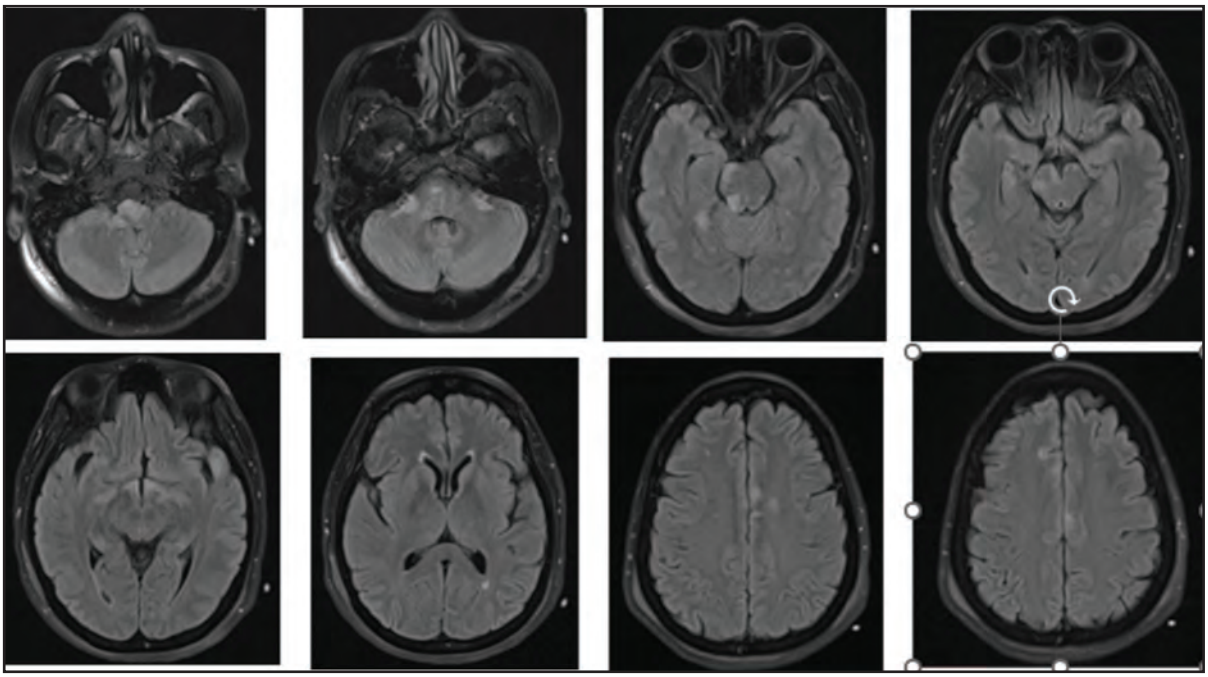

Fig. 1: Axial FLAIR brain images showed patchy hyperintensities at medulla (A), bilateral cerebellar peduncles (B), pons (C), midbrain (D), third ventricle and hypothalamus (E), peritrigonal region (F), parasagittal bifrontal cortex (G) & (H)

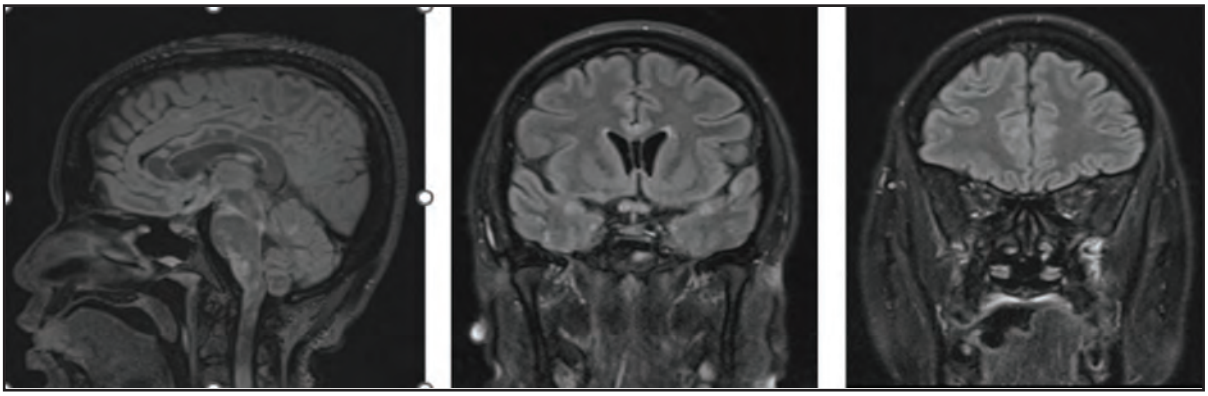

Fig. 2: Sagittal FLAIR brain images showed patchy hyperintensities at corpus callosum (A), bilateral medial temporal lobes (B), frontal region (C)

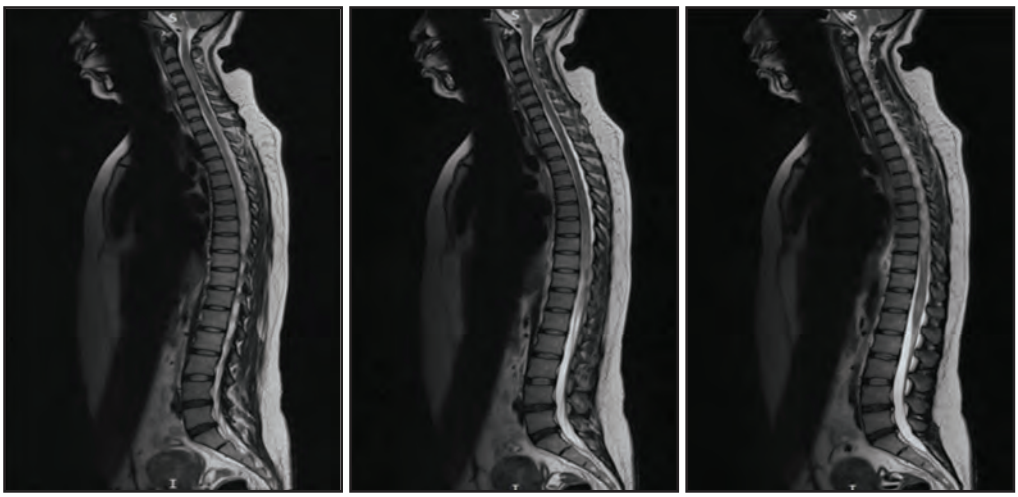

Fig. 3: Sagittal T2WI spine images showed longitudinal hyperintensities and cord expansion at cervical cord (A), lower thoracic cord (B), conus medullaris (C)

on the ventilator, which did not respond to gabapentin treatment but resolved after given memantine for a month. She was subsequently put on oral prednisolone as maintenance therapy.

DISCUSSION

Our patient presented with subacute onset of brainstem syndrome and myelopathy. Our initial differential diagnosis includes demyelinating disease, haematological malignancy relapse, or central nervous system infection. In her case, a full blood count shows normal lymphocyte counts, and no blast cells are detected in a full blood picture. Cytospin of cerebrospinal fluid showed no malignant cells, thus relapse of haematological malignancy in the central nervous system was excluded. Central nervous system infection was also unlikely, as the infective screening of the cerebrospinal fluid was negative. Subsequently, MOG antibodies were detected in her serum via a fixed cell-based assay. Hence, in combination with the clinical features, the diagnosis of myelin oligodendrocyte glycoprotein antibody-associated disease (MOGAD) was made. The diagnosis was guided by the proposed criteria set by the International MOGAD Panel.[3]

There were a few interesting features that we detected in our patient with MOGAD. Firstly, our patient had an isolated right abducens nerve palsy without signs of raised intracranial pressure. We suspect that the initial isolated right abducens nerve palsy might be due to a small lesion at the abducens nerve region in the pons. Brainstem involvement in MOGAD is common, although isolated nerve palsies are not common as due to the typical involvement of diffuse lesions in medulla, pons, or midbrain in MOGAD.[4] This was evidenced by a case series of MOGAD involving cranial neuropathies reviewed by Du et al. In their study, the majority of their patients had multiple cranial nerve involvement.[5] Isolated abducens nerve palsy as the first presenting sign of multiple sclerosis had been reported[6] wherein short peripheral lesion predominates in multiple sclerosis. However, there is no case report regarding isolated cranial nerve involvement in MOGAD noted so far.

Secondly, our patient developed acquired pendular nystagmus. This occurrence has not been reported in the case of MOGAD. Nonetheless, a case of acquired pendular nystagmus secondary to multiple sclerosis and ocular palatal tremor has been reported.[7] We postulated that the acquired pendular nystagmus of our patient was due to instability of neural integrator which are distributed across the brainstem and cerebellum especially at the paramedian tracts, dorsal pontine tegmentum in the brainstem and the anterolateral pons and midbrain.[8]

On the other hand, our patient exhibited an elevated opening pressure during lumbar puncture, yet there was no evidence of central nervous system infection. We concluded that the increase in intracranial pressure was attributable to MOGAD, given its temporal association with the detection of MOG antibodies in the patient. Elevated intracranial pressure is an uncommon presentation of MOGAD. Chaudhuri et al[9] reported a MOGAD case with relapsing remitting course, each time presenting solely with symptoms of raised intracranial pressure, without developing any typical clinical manifestations of MOGAD. In contrast, our patient developed elevated intracranial pressure alongside brainstem syndrome and myelopathy, which aided in the diagnosis.

She was administered a high dose steroid, intravenous immunoglobulin, and plasma exchange after the diagnosis of MOGAD was confirmed, which led to partial neurological improvement. She was able to sit up and carried basic daily activities on her own. The pendular nystagmus showed reduction upon taking gabapentin 600 mg TDS, but it fully resolved only upon the use of memantine 10 mg bd. Both gabapentin and memantine have been reported as effective in decreasing acquired pendular nystagmus and enhancing functional visual outcomes.[10]

CONCLUSION

In conclusion, our patient presented with subacute brainstem syndrome and myelopathy. After malignancy and infection were excluded, coupled with serum MOG antibody detection, she is confirmed to have MOGAD. Along with common presentations such as brainstem syndrome and myelopathy, this case broadens the clinical spectrum to include unusual presentations such as isolated abducens nerve palsy, elevated intracranial pressure and pendular nystagmus.

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