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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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Eikenella corrodens necrotising myositis in an immunocompetent adolescent

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SUMMARY

A case of a rare organism of *Eikenella corrodens* in an immunocompetent adolescent is described. A previously healthy 17-years-old student has a persistent non-healing wound post-operatively following Compartment Syndrome after being diagnosed with a closed right radius styloid fracture. No history of human bite prior to the incident. Tissues sample intra-operatively grew *Eikenella corrodens* identified by Bruker® Maldi-TOF which is sensitive to ampicillin, amoxicillin/clavulanic acid, penicillin, ceftriaxone, imipenem and meropenem. The patient was prescribed intravenous ceftriaxone and responded well to the treatment.

INTRODUCTION

A rare but potentially lethal condition, necrotizing soft tissue infections have a high mortality rate with a death incidence of 25 to 30 %.[1] *Eikenella corrodens* is a bacterium of the HACEK group, belonging to the *Eikenella* of the Neisseria family. Although initially thought to be non-pathogenic as it can be normal commensals of the oral cavity, it has been established that the *Eikenella* species can cause serious human infections.[2]

Eikenella corrodens are a rare cause of necrotising soft tissue infections. To our knowledge, there were three case reports on necrotising fasciitis following elective inguinal hernia surgery and one retroperitoneal necrotising fasciitis post-endoscopic retrograde cholangiopancreatography caused by *Eikenella corrodens*.[3,4] Most cases of necrotising soft tissue infections are caused mainly by polymicrobial organisms with Gram-negative aerobe involved more often than Gram-positive organisms. In monomicrobial infection, the causative agent is usually *Streptococcus pyogenes*. Thus, we present a case of necrotising myositis by *Eikenella* following fasciotomy.[3]

CASE PRESENTATION

A previously healthy 17-year-old gentleman presented to the hospital with a complaint of right upper limb pain for one week that started after a series of 'push-ups'. The pain was associated with swelling over the right wrist. He accidentally hit his right hand on the wall the day before. He denied any animal or human bites. X-ray showed a closed right radius styloid fracture (Figure 1). Right hand above elbow back slab was applied and he was discharged home. Four days later, he presented with worsening swelling, redness and skin tightness. Otherwise, he had no fever, shortness of breath, or recent fall or trauma.

On examination, he was alert, conscious and afebrile. There was a generalized swelling of the hand extending to the midarm that was tender upon palpation. The compartment is tense with non-palpable brachial, radial or ulnar pulse. The sensation was also reduces over radial and median nerve distribution. He was then planned for emergency right-hand fasciotomy and carpal tunnel release in view of associated Compartment Syndrome. Post-operatively, there was foul-smelling pus discharge with necrotic patches on the skin. He underwent second extensive wound debridement and a necrotizing myositis was diagnosed. Intraoperatively, 600ml seropurulent pus was drained from the intermuscular plane.

Two tissue samples from deep muscle were cultured on Blood Agar (BA), MacConkey Agar (MAC) and Blood Anaerobic Agar (Baano2), in aerobic and anaerobic conditions. The gram-stain of tissue samples showed occasional pus cells with few gram-negative rods. The blood agar showed tiny colorless colonies with pitting appearance and no growth on the MacConkey agar (Figure 2). Colonies were identified as *Eikenella corrodens* by Bruker® Maldi-TOF with a score value of 2.04. The isolate was susceptible to ampicillin, amoxicillin/clavulanic acid, penicillin, ceftriaxone, imipenem and meropenem.

The laboratory examination indicated a normal full blood count but hyponatremia, hypoalbuminemia, mild transaminitis and elevated erythrocyte sedimentation rate (ESR) (Table 1). These findings are possibly due to the underlying ongoing muscle inflammation. Infective screenings for Hepatitis B, Hepatitis C, Human Immunodeficiency Disease (HIV) and syphilis were non-reactive. The blood culture for aerobes and anaerobes revealed no growth after five days of incubation.

The patient was initially started on intravenous piperacillin/tazobactam 4.5g QID and intravenous clindamycin 600mg QID. Upon identification of the tissue culture, intravenous ceftriaxone was commenced and he was transferred to another referral facility for the continuation of care. After another wound debridement, his condition improved and the limb was able to be salvaged.

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Table I: Summary of patient's investigations. Blood parameters show features of underlying inflammation

Indices	Value	Normal value
Haemoglobin (g/dL)	13.0	1.5 - 15.5
White blood cell (x10^9/L)	12	5.00 - 13.00
Absolute Neutrophil (x10^9/L)	10.42	2.00 - 8.00
Platelet (x10^9/L)	178	170 - 450
Erythrocytes Sedimentation Rate (mm/hr)	51	0 - 10
Sodium (mmol/L)	124	136 - 145
Potassium (mmol/L)	3.7	3.5 - 5.1
Urea (mmol/L)	9.7	3.2 - 8.2
Creatinine (umol/L)	114	62 - 115
Albumin (g/L)	27	32 - 48
Total Bilirubin (umol/L)	42	5 - 21
Direct Bilirubin (umol/L)	30	0 - 5
Aspartate Transaminase (U/L)	104	0 - 34
Alkaline Phosphatase (U/L)	182	46 - 116
Alanine Transaminase (U/L)	58	10 - 72
HbA1C (%)	5.7	< 5.7
HBsAg	Non-reactive	
Anti-HCV	Non-reactive	
HIV-Combo	Non-reactive	
Syphilis serology	Non-reactive	

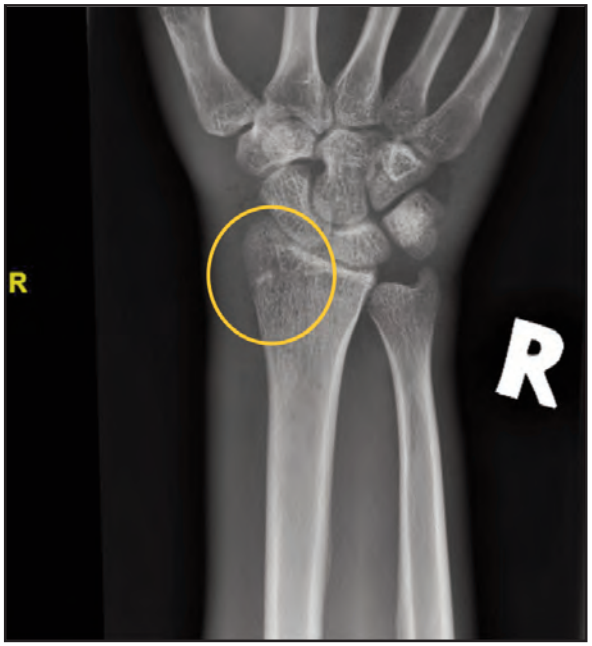

Fig. 1: X-ray of right wrist joint show a closed right radius styloid fracture as marked by the orange circle

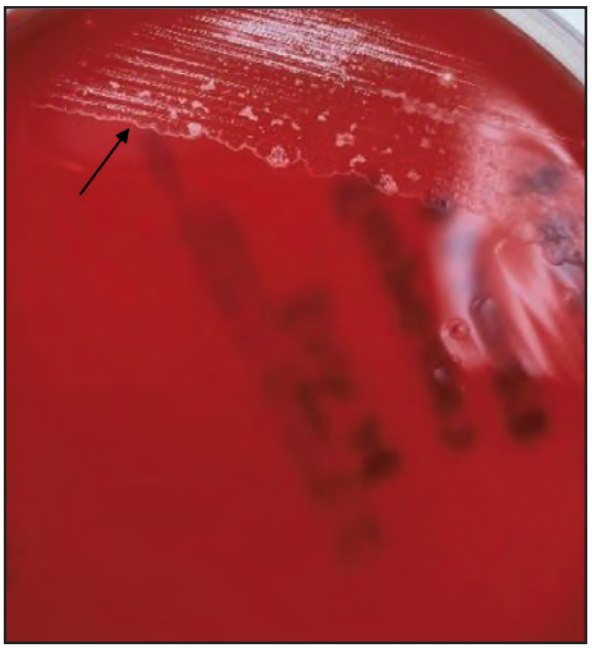

Fig. 2: Tiny irregular colourless colonies with pitting appearances (black arrow) of *Eikenella corrodens* on blood agar

DISCUSSION

Necrotizing soft-tissue infections (NSTIs) are rare, life-threatening bacterial infections with a high morbidity and fatality rate. It is estimated that between 0.3 and 15 cases of necrotising fasciitis occur per 100,000 people.[5] Necrotizing soft tissue infections can be divided into three types based on the depth of the tissue necrosis and infection. Necrotizing cellulitis affects the dermis and subcutaneous tissue, necrotizing fasciitis affects the fascia, and necrotizing myositis affects the muscle layer with intact overlying skin.[1] Necrotizing fasciitis and clostridial myonecrosis, are more easily diagnosed than necrotizing myositis, which requires a high index of suspicion. The infection spreads along the fascial planes, eventually affecting deeper muscles, causing myositis and myonecrosis.[5]

Certain variables increase a patient's risk for NSTIs, such as any skin or mucosal break and many surgical procedures.[5] In this case, the patient initially had a closed fracture that was complicated with compartment syndrome causing him to undergo fasciotomy and carpal tunnel release. Once there was a break in the skin integrity, the risk for any organism to invade the muscle is high. Immunosuppression conditions, cancer, vascular disease, diabetes, alcoholism, and obesity enhance the risk of NSTIs leading to severe sepsis and septic shock.[5] However, in this case, the patient did not have any

comorbidities but he had a persistent non-healing wound that required multiple wound debridements. However, he did not progress to fulminant sepsis due to early surgical intervention.

The genera *Haemophilus* (except for *H. influenzae*), *Aggregatibacter, Cardiobacterium, Eikenella, and Kingella* (HACEK) comprise a group of gram-negative bacteria that are normal flora of the oral cavity and gastrointestinal tract and are known to cause infective endocarditis.[6] *Eikenella* is a tiny, non-sporulating, facultatively anaerobic, and non-motile bacterium. It grows slowly in blood agar or chocolate agar at 35 to 37°C and 5% carbon dioxide and is able grow under aerobic conditions. The colonies are rough with irregularly shaped, grey and non-hemolysis.[2]

Eikenella corrodens is most associated with head and neck infections even though some of the literature also did report bite wound infections, respiratory tract infections, abdominal infections, gynaecologic infections, meningitis, spinal infection, endocarditis, osteomyelitis and urinary tract infections.[2,6] It can cause infection in susceptible individuals with aspiration, alcoholism, immunosuppression, cardiovascular disease, and diabetes, among others. However, in this case, the patient was a healthy young man with no previous hospitalization. He had surgery that led to an open wound that allowed this fastidious organism to invade his muscle tissue. Most likely the source of the infections would be the oral cavity or saliva. This organism led to a chronic non-healing wound despite multiple wound debridements and consistently produced pus collections.

Even so, *Eikenella corrodens* as a causative agent for necrotising soft tissue infection is quite uncommon. A literature review of *Eikenella corrodens* infections in children and adolescents revealed that head and neck infections account for the majority of causes which are mostly abscesses in nature followed by extremities abscesses and central nervous system abscess.[7] None of the cases reported a necrotising infection. However, there was a reported case of necrotising fasciitis that occurred after the elective inguinal hernia repair in a middle age man without no obvious cause of contamination during the surgery.[3]

Diagnosis of these fastidious organisms was previously difficult because they need prolonged incubation time with specific temperatures and environments. Because of their complex nutritional requirements, they only grow on blood agar and chocolate agar. Not able to grow on differential media or MacConkey agar. They are biochemically inactive, do not ferment glucose or carbohydrate or produce any acid. This makes the microbiological diagnosis challenging. However, the introduction of Bruker® Maldi-TOF, an identification tool that uses a laser to vaporize and ionize molecules in the organism and generate mass spectrum using spectrometry that would be compared to a database and identified the unknown organism. The score value of 2.00 to 3.00 gives a high confidence identification up to the species level.[8]

The preferred treatment for *Eikenella corrodens* infection suggested by the National Antimicrobial Guideline would be oral amoxicillin/clavulanic acid 625mg TDS for mild infections or intravenous ceftriaxone 2mg OD for severe infections.[9] For this patient, he was started with piperacillin/tazobactam which according to Sanford Guide to Antibiotic Therapy 2022 had shown some activity towards this organism.[10] However, as in vitro antibiotic testing, piperacillin/tazobactam was not included in the panel for primary testing as suggested by the Clinical & Laboratory Standards Institute (CLSI).[11] According to the literature review of six reported cases by Li li (2), two out of six reported cases were treated with piperacillin/tazobactam before the identification of *Eikenella corrodens* was made.[2] Both cases presented with abscesses in different locations that were not resolved solely with antibiotics and surgical intervention. After a change of antibiotic according to the susceptibility tested in the laboratory, the patient's condition improved and was able to be discharged from the hospital.

CONCLUSION

Eikenella corrodens can be associated with severe non-healing necrotizing myositis despite no apparent cause in this case. Maldi-TOF is an excellent tool to identify the rare fastidious organism that can be missed due to inherent difficulties in culture and biochemical tests. Timely results are important to guide treatment decisions apart from prompt wound debridement and compartment release to prevent the extension of the disease. More studies in the diagnostic field of the organism are needed so that these organisms were not under-identified due to it fastidious characteristics.

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CONFLICT OF INTEREST

There was no competing interest exists between authors.

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Disseminated sporotrichosis in a human immunodeficiency virus positive man with upper airway involvement

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SUMMARY

Sporotrichosis is a fungal infection caused by dimorphic fungus Sporothrix. Sporotrichosis can be seen in cutaneous or extracutaneous form. Disseminated form of sporotrichosis with upper airway involvement rarely been reported. We present a case of disseminated sporotrichosis in a HIV-positive young gentleman manifesting as fungemia, lymphocutaneous and upper airway involvement.

INTRODUCTION

Sporotrichosis is a fungal infection caused by dimorphic fungus *Sporothrix*, which is found in decaying vegetation, sphagnum moss, soil, and other environmental niches throughout the world.[1-3] Transmission involves subcutaneous inoculation through injury from thorns or animal bites or scratches. It commonly afflicts humans in the lymphocutaneous form. Rarely it might be disseminated involving the lungs, osteoarticular or central nervous system. Here we present a case of a disseminated sporotrichosis in a HIV-positive young gentleman manifesting as fungemia, lymphocutaneous and upper airway involvement.

CASE REPORT

A 24-year-old gentleman presented with diffuse skin lesions and fever for one month. He was newly diagnosed HIV-positive with a CD4 count of 26 and was not on any anti-retroviral (ARV) medication yet. He is working as an administration officer, has no pet and volunteered no history of gardening or exposure to soil. On physical examination there were multiple ulcerous and crusted nodular lesions over the face, bilateral upper and lower limbs along the lymphatic channel, as well as numerous firms, non-tender lymph nodes at the submandibular, submental, and supraclavicular regions. He also had multiple interphalangeal joints swelling over bilateral hands and feet where the x-rays revealed osteopenia over involved joints (Figure 1). Despite treatment for candidiasis, he had persistent dysphagia and odynophagia whereby intraoral inspection revealed many small ulcerated superficial lesions measuring less than 0.5cm each, on the soft palate. During endoscopy, generalized lobulated lesions were also seen in the nasal cavity, laryngeal surface, epiglottis, bilateral arytenoid, and pyriform fossa (Figure 2). Otherwise, he had no respiratory symptoms and had clear chest x-ray.

Provisional diagnosis of systemic fungal infection was entertained and intravenous amphotericin B deoxycholate initiated empirically. Subsequent blood fungal culture grew *Sporothrix schenckii*. Lactophenol cotton blue (LPCB) mount of slide culture demonstrated small budding, round, oval-or-cigar shaped, 2-6µm diameter yeast cells, which is typical of *Sporothrix species*. Histopathology examination of both skin and nasal biopsies also revealed sporotrichosis (Figure 3). The organism was later sent for antifungal susceptibility test and was reported sensitive to Amphotericin B and itraconazole.

The patient responded clinically to the intravenous Amphotericin B with dosage of 1mg/kg/dose for total 14 days with an improvement of skin lesions (Figure 5) and lymphadenopathy, interphalangeal joint swelling also subsided. Subsequent repeated blood fungal culture was negative and inflammatory markers were much improved. Upon discharge, antiretroviral therapy was commenced, and intravenous Amphotericin B was transitioned to oral itraconazole 200mg 3 times per day, treatment was intended till his CD4 count more than 200 cells /uL or HIV viral load suppressed. He remained well during his clinic appointment with further resolution of cutaneous lesions and residual lymphadenopathy.

DISCUSSION

Sporotrichosis is a disease caused by a thermo-dimorphic fungus *Sporothrix* species.[1,3] It is currently reported throughout the world, especially in tropical and subtropical regions as the humid environment favours the fungal growth. It grows as mold in the environment and at temperature below 35°C and assumes the yeast form at temperature above 35°C.[2] The commonest route of transmission is by subcutaneous inoculation of the organism through traumatic inoculation[4], and occasionally inhalation of conidia causing upper airway and pulmonary infection.

Sporotrichosis can generally be classified into cutaneous or extracutaneous form.[1,2] The cutaneous form can manifests as either cutaneous fixed type or lymphocutaneous type, which are both found predominantly in the immunocompetent host.[1,2] Extracutaneous form is rare and usually in immunocompromised patients.[5] It can be divided into disseminated cutaneous type, disseminated or pulmonary sporotrichosis. Laryngeal and nasal sporotrichosis are rarely described. We illustrated here a patient with advanced HIV who was treated for disseminated sporotrichosis involving the nasal, oral, laryngeal, lymphocutaneous and hematogenous systems. In a patient with advanced HIV, the immunocompromised state of the body might aggravate the

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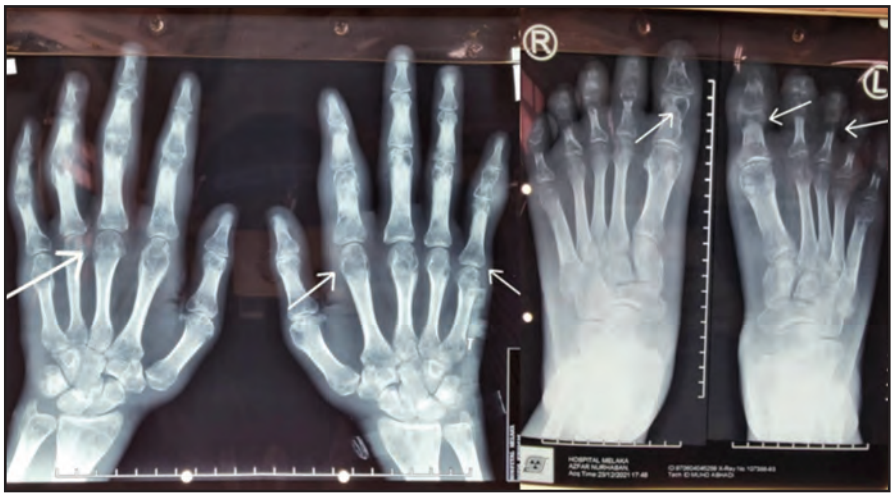

Fig. 1: X-rays osteopenia in all involved joints over bilateral hands and feet.

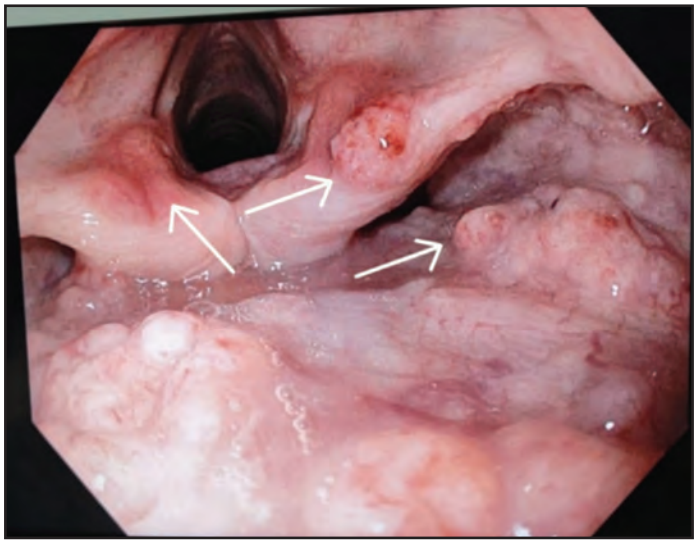

Fig. 2: Endoscopy findings of multiple lobulated erythematous lesions over laryngeal surface, epiglottis and bilateral arytenoid.

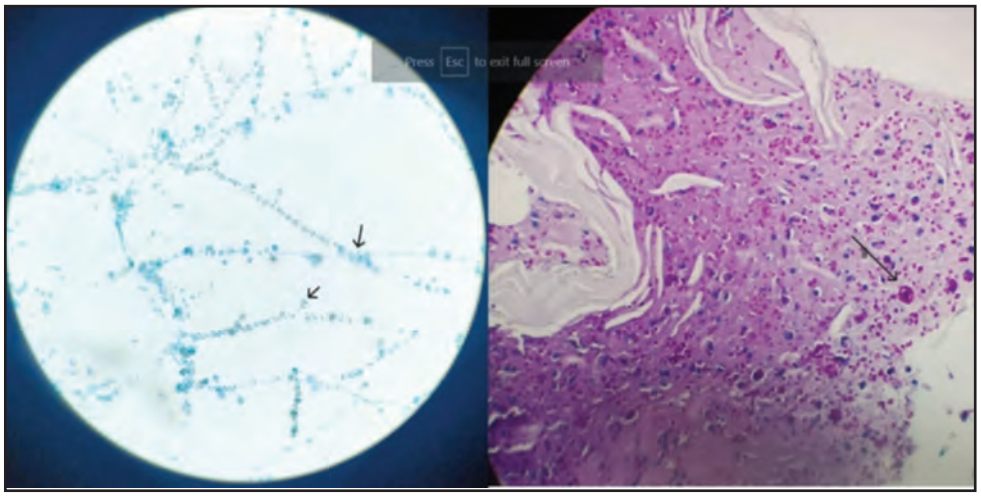

Fig. 3: (Left): Microscopy shows small budding, round, oval-or-cigar shaped, with 2-6μm diameter yeast cells in LPCB mount of slide culture.
(Right): Densely eosinophilic yeast forms with a surrounding ray of eosinophilic material called 'Sporothrix asteroids' seen in the histopathology examination.

sporotrichosis, with higher incidences of severe disseminated form of the disease. Hence, the diagnosis of cutaneous form of sporotrichosis in an immunocompromised host should spark a search for dissemination to the other sites, especially upper airway, as although uncommon, sporotrichosis can be transmitted by inhalation.

So far, we are only aware of two case reports describing laryngeal involvement in adults. Roslle N. described an immunocompetent individual with hoarseness due to laryngeal sporotrichosis.[6] Also described in the literature a HIV positive man who presented with painful intraoral papular-infiltrative lesions and dysphagia, and subsequently found to have laryngeal sporotrichosis.[7]

Although upper airway involvement is rare in sporotrichosis, it is important for clinicians to be aware of the possibility. Among people living with HIV, complaints of odynophagia or dysphagia are often treated as oral candidiasis. However, other diagnosis should not be overlooked and sporotrichosis should also be considered in the evaluation of an immunocompromised patient including newly diagnosed advance RVD.

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CONFLICTS OF INTEREST

The authors declare that they have no conflict of interest.

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CASE REPORT

Exploring the possibility of intravenous modified high dose methotrexate in leptomeningeal metastatic disease treatment: A case series

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SUMMARY

Leptomeningeal metastatic disease (LMD) is a rare complication of advanced cancer, with no standard management and often associated with poor prognosis and short survival time. Current treatment options involve high doses of intravenous (IV) or intrathecal (IT) methotrexate (MTX), which can be associated with significant side effects. To mitigate the adverse effects, this case series aims to highlight the feasibility a reduced IV MTX dosage, which we termed "IV modified high dose MTX" to treat LMD. In the three cases of LMD with underlying breast cancer, we reduced the IV dosage of MTX to 2.5-3 g/m^2 (standard high dose MTX is 3-3.5 g/m^2) and examined the outcomes of clinical symptoms, side effects and overall survival of the patients. In the three LMD cases, the use of IV modified high dose MTX had reduced toxicity, improved neurological symptoms, partially recovered the quality of life, and conferred a survival duration comparable to the conventional high-dose regime. Given the favourable safety profile and comparable treatment effect, our case series highlighted the importance of further investigation to establish the optimal dosing regimen of MTX in the palliative care of LMD.

INTRODUCTION

Leptomeningeal metastatic disease (LMD) is characterised by cancer metastasis to the subarachnoid space in between the pia and arachnoid maters of the brain. Melanoma, breast and lung cancers are common primary tumour origin of LMD.[1,2] It occurs in about 5% of advanced breast cancer with an overall survival of three to four months.[1] Triple negative breast carcinoma, old age, presence of brain metastases and low albumin have been associated to a poorer prognosis.[3]

Symptoms of LMD vary between patients and largely depend on the anatomical site of the metastatic cells. The symptoms develop either due to the obstruction of cerebrospinal fluid (CSF) flow, increased intracranial pressure or direct infiltration of tumor cells. Common manifestations include seizure, headache, nausea, impaired consciousness, radicular pain due to the involvement of spinal roots, or a focal neurological deficit if the cancer cells have infiltrated into the brain parenchyma.[4]

The gold standard of LMD diagnosis remains the demonstration of tumor cells in CSF. The test has an underwhelming sensitivity. Repeating the test up to 3 times may increase its sensitivity beyond 90%.[5] Magnetic resonance imaging scan with gadolinium contrast has become a reliable tool for LMD diagnosis. There is no standard treatment for LMD. Mainstream therapies include focal radiotherapy and chemotherapy with high-dose methotrexate (HD MTX), but for the latter, the optimal administration route either via intrathecal (IT) or intravenous (IV) remains highly debatable. IT MTX is conventionally used, but its effectiveness depends on a good CSF flow and the adverse reactions are significant, leading to the increased popularity of IV HD MTX. As most LMD patients eventually succumb to the disease, current treatment strategies aim to prolong survival and improve quality of life by stabilizing and delaying neurological deterioration. Given the palliative nature of the treatment approach, it is possible to further reduce the dosage of IV MTX if it can minimise the side effect without comprising the drug efficacy. Here, we would like to showcase three patients with LMD originated from breast carcinoma and discuss the possible improvement on the chemotherapy strategies by reducing the systemic dosage of MTX, which we termed "IV modified high dose MTX".

CASE REPORT

Case 1

The patient was a 58 years old Chinese female diagnosed with right breast carcinoma in 2013 and treated with right mastectomy and axillary clearance. Histopathology examination (HPE) demonstrated a stage 3A, T2N3 invasive lobular carcinoma, ER+, PR+, and HER2-. She underwent 6 cycles of chemotherapy comprised of 3 cycles 5-Fluorouracil, Epirubicin and Cyclophosphamide (FEC) and 3 cycles of Docetaxel followed by adjuvant radiotherapy. Upon completion, she was treated with Tamoxifen since November 2013. The patient had been in remission until December 2019, when she developed headache and vomiting. A magnetic resonance imaging (MRI) showed multiple tiny low signal modules that scattered in T2-T11, which confirmed leptomeningeal metastasis. Bone metastases at T2 and T7 were also noted. The patient received palliative radiation to the spine and started on Letrozole and Palbociclib. The symptoms worsened in September 2020 and a restaging imaging demonstrated a progressive leptomeningeal carcinomatosis with gadolinium enhancement. She remained Eastern Cooperative Oncology Group performance

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status (ECOG) 1 with Karnosky performance status (KPS) grade 90. Lumbar puncture with cerebrospinal fluid (CSF) cytology analysis was positive for metastatic breast cancer, positive for ER, negative for PR and HER/neu IHC stain. She received 8 cycles of IT MTX, which was 12mg twice weekly for 4 weeks, followed by 12mg once weekly for 4 weeks. Repeated cerebrospinal fluid cytology in January 2021 showed no malignancy cell. However, the disease continued to progress with worsening of headache and left-sided body weakness in February 2021. Her performance status deteriorated to ECOG 3 (KPS grade 50). She then received 5 cycles of systemic chemotherapy with IV modified high dose MTX administered 2 weekly. The dosage ranged from 2.5-3 g/m^2, with the first two cycles (C1 and C2) using 2.5 g/m^2, the third cycle (C3) using 2.8 g/m^2, and the fourth cycle (C4) using the maximum dose of 3 g/m^2. She was able to tolerate the regime relatively well without significant complications. At the point of writing, her condition stabilized at ECOG 3 (KPS grade 50). Symptoms like vomiting and pain improved after the first cycle of IV MTX. The patient survived 8 months with good quality of life. Subsequently, she defaulted the follow up.

Case 2

A 60 years old female with hypertension, type II diabetes mellitus and dyslipidemia was diagnosed with metastatic right breast invasive lobular carcinoma, pT3N3M1(bone), triple negative disease, underwent right mastectomy and axillary clearance (MAC) followed by adjuvant chemotherapy and radiotherapy which were completed in 2016. In October 2020, she presented with generalized body weakness, vomiting and headache. She had bilateral eyes optic disc swelling with bilateral 6th nerve palsy, facial asymmetry and reduced power of all limbs. Contrast enhanced computed tomography (CECT) brain showed chronic ischaemic changes with no brain lesion. MRI brain showed an empty sella sign with no obstructive hydrocephalus. Computed tomography (CT) of the thorax, abdomen and pelvis showed no other new visceral metastasis. A lumbar puncture analysis was unremarkable. The patient was referred to neuromedical team for further investigations. Her condition deteriorated to ECOG 2 (KPS 70) in November 2020 with worsened headache, vomiting, neck stiffness, blurring of vision, seizure. Repeated lumbar puncture revealed occasional atypia cells characterised by cells with eccentric nuclei and large rounded nuclei and moderate amount of cytoplasm. Her MRI brain and neck revealed multiple tiny nodules in the cervical vertebral bodies. Together, the results were suggestive of LMD. She was treated with IV MTX (2.5 g/m^2) administered 2 weekly in December 2020. The dose was gradually increased to 3 g/m^2 during the third cycle of chemotherapy. However, the chemotherapy caused grade 3-4 toxicity, including myelosuppression, elevated serum hepatic transaminases and prolonged MTX clearance. The highest alanine transaminase (ALT) and alkaline phosphatase (ALP) levels recorded exceeded the upper limits by 3 and 1.5 times, respectively. Due to the severe side effects, her chemotherapy was deferred multiple times, and the interval of her chemotherapy regime was prolonged to once in every 3 weeks with a dose reduction to 2.8 g/m^2. Post cycle 4 IV MTX, an improvement in performance status to ECOG 1 (KPS 80) was noted. Repeated CSF was free of atypia cells. However, her liver function test remained deranged and the typical side effects of MTX persisted. She completed a total of 7 cycles of IV MTX by April 2021. CT imaging post chemotherapy showed an overall stable disease with diffuse nodular leptomeningeal enhancement through the cauda equina. Nonetheless, her condition deteriorated in May 2021 with cord compression symptoms and ECOG 3 (KPS 40). MRI spine confirmed disease progression. She was then started on palliative hormonal therapy letrozole. The patient transitioned to end-of-life care and died in August 2021. The patient lived a total of 9 months after the initial diagnosis of LMD.

Case 3

A 62 years old Malay lady was diagnosed with metastatic right breast invasive carcinoma, pT3N0cM1 (lungs-small volume, bone), triple negative disease. She underwent right mastectomy and axillary clearance and adjuvant anthracycline-based chemotherapy followed by radiotherapy in 2016. In November 2019, she complained having progressive bilateral limb weakness. MRI spine showed a conus medullary lesion. She then underwent laminectomy and excision of the lesion. HPE showed malignant spinal cord tumour consistent with breast metastasis. Five fractions of palliative radiotherapy to the spine were given in December 2019. The tumour recurred 2 months later and re-excision was done. HPE was consistent with the previous disease. She completed 6 cycles of chemotherapy Paclitaxel in July 2020. Positron emission tomography (PET) scan in December 2020 showed a new ^{18}F-fluorodeoxyglucose avid enhancing lesion at T12/L1 level, measuring 0.94cm x0.72cm, highly suspicious of metastasis, with no other visceral metastasis. CSF analysis found no malignant cells. However, in view of recent radiotherapy treatment received, patient was suggested to commence on 3 weekly chemotherapy MTX in January 2021. She received total 5 cycles of IV MTX ranging from 3-3.5 g/m^2. However, treatment was frequently delayed due to recurrent urinary tract infections. Her ECOG status remained stable (ECOG 3, KPS 50) throughout the treatment. Repeated PET CT imaging post cycle 5 IV MTX noted worsening spine metastasis characterized by larger and more intense lesion extending from T9 to L1. Palliative therapy with Eribulin was given to the patient and discontinued at Cycle 5 due to intolerance. Her disease has been under controlled for 7 months since the initial diagnosis of LMD.

DISCUSSION

Our case series highlight two aspects in the treatment of LMD: (1) the tolerability and efficacy of IV MTX and (2) the optimal dosage of IV MTX for LMD originated from breast carcinoma. All our LMD patients were treated with IV modified high dose MTX which was well-tolerated, effective and able to maintain quality of life. Conventionally, IT MTX is the primary therapy although its efficacy compared to systemic chemotherapy is not well-established. IT MTX causes significant neurotoxicity especially when CSF flow is obstructed, thus limiting its use in patients with bulky LMD, hydrocephalus and dural-based or parenychemal disease. The administration of IT MTX is an invasive procedure and highly operator dependent which can be associated with procedural complications such as meningitis, myelopathy,

myelosuppression, encephalopathy.[2] In contrast, IV HD MTX has increasingly used due to its convenience, high tolerability and ability to attain good serum and CSF cytotoxic levels.[6] In line with our cases, the effectiveness of IV HD MTX in LMD originated from breast carcinoma has been previously reported.[7-9]

The optimal MTX dose, infusion duration and leucovorin rescue of IV regimen are disease- and protocol-specific. Most studies utilised an IV HD regime of 3-3.5 g/m^2 of MTX fortnightly which can achieve comparable or even higher CSF concentration than IT administration.[6] In two larger series, the rate of stable disease ranged from 30 to 45%, with a median survival of five to six months.[7,10] Similarly, Glanz et al. (1998) reported a median survival of 13.8 months with IV HD MTX versus 2.3 months with IT MTX.[6] CSF and serum MTX concentrations were maintained at a cytotoxic level much longer than with IT dosing.[6] Cytologic clearing was seen in 81% of patients compared with 60% of patients treated intrathecally. Prolonged survival has also been described in many reports.[7-9] Here, we used a stepwise increment of IV modified high dose MTX ranging from 2.5-3.5 g/m^2. The regimen was adequate to stabilize the patients' condition for up to 7 months before any major disease progression was detected. At the time of penning down this report, all the patients are still alive, translating to a survival period of at least 9 months. The observations are in line with the overall survival (0.7 – 33.9 months) of IV HD MTX-treated LMD patients7 and was much longer than those receiving IT MTX (2.3 months) as reported by Glanz et al. (1998)[6]. Hence, our cases are supportive to the use of IV modified HD MTX in LMD, especially those originated from the breast carcinoma.

Low toxicity is a key advantage of IV modified HD MTX. We observed that a slightly lower of at 2.5-3 g/m^2 of IV MTX fortnightly demonstrated good tolerability and minimal toxicity. The therapeutic effect was not compromised by the dose reduction. Likewise, according to Bazan et al (2019), a dosage of 3 g/m^2 of systemic IV HD MTX demonstrated an acceptable toxicity profile without compromising efficacy.[10] In contrast, the typical IV HD MTX may cause significant hepatotoxicity. Elevated serum ALT or AST are observed in 15-50% of the patients receiving IV HD MTX. In view of the better safety profile and comparable efficacy, further investigations on the use of 2.5-3 g/m^2 of IV MTX, especially in high-risk patients, are warranted.

Among the three patients, Case 2 exhibited the least favourable outcome. There was a significant gap (2 months) to acquire her diagnosis because her CSF analyses were repeatedly negative. False negative of the test is not uncommon.[5] Hence, a negative result is insufficient to exclude LMD and repeated test is highly recommended especially when the clinical presentations align well with the diagnosis. CT and MRI are the alternative diagnostic tools. Scanning the brain and whole spine should be performed as LMD can affect any part of the central nervous system.[5] In Case 2, only MRI brain was performed at the early course of the investigation. The false negative result from CSF analysis and incomplete imaging result significantly impeded the diagnosis process. The patient also exhibited poorer performance status and was unable to tolerate the chemotherapy, necessitating modification of the chemotherapy regime. These reasons could contribute to the poor clinical outcome.

LMD is often associated with poor prognosis. Without any treatment, the estimated survival after diagnosis is 6 to 8 weeks. This is prolonged to 8 to 30 weeks in treated cases8.Recent advancements in the targeted therapy of different breast cancer subtypes may further improve the outcome of LMD with underlying breast cancers. For instance, cyclin-dependent kinase (CDK) 4/6 inhibitors such as Abemaciclib and Palbociclib and Poly (ADP-ribose) polymerase (PARP) inhibitors Olaparib and Talazoparib have demonstrated promising intracranial activities in hormone positive Her^2 negative breast cancers and triple negative breast cancers, respectively.[11-14] Larger trials are warranted to examine their feasibility in LMD with underlying breast cancers of the corresponding subtypes. In our case series, the mean period from diagnosis to disease progression were more than 24 weeks. Two of the patients were able to tolerate IV modified high dose MTX of 2.5-3 g/m^2, which conferred lower toxicity, higher tolerability and comparable survival duration to the HD counterpart. The favourable outcomes highlight its feasibility to treat LMD and hence, further investigation to optimize the dosage of IV MTX is pertinent.

CONCLUSION

In conclusion, IV MTX could be a better alternative to the IT counterpart for the therapy of LMD originated from breast carcinoma. The possibility to use IV modified high dose MTX of 2.5-3 g/m2 should be investigated in view of better tolerability and comparable therapeutic efficacy.

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DECLARATIONS

The investigators declare no conflict of interest. Informed consent was obtained from all patients/patients' family members in line with COPE standards.

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CASE REPORT

Tennis Racket sign – an underacknowledged sign of active tuberculosis

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SUMMARY

World Health Organization (WHO) has reported tuberculosis as the thirteenth leading cause of death worldwide. Tuberculosis (TB) is also the second leading infectious killer after COVID-19, surpassing acquired immunodeficiency deficiency syndrome (AIDS).[1] Therefore, it is only prudent that clinicians are equipped with adequate knowledge to diagnose tuberculosis. Cavitation is recognised as a common finding of active pulmonary TB on chest radiographs. However, the 'Tennis Racket' sign which is made up of a cavity, is less frequently acknowledged as a sign of active TB. We present a case series of five patients who visited our TB clinic between January 2021 and January 2022. They presented with various symptoms such as fever, chronic cough, shortness of breath and constitutional symptoms. The chest radiographs of all these patients showed the 'Tennis Racket' sign. We then proceeded with sputum for Ziehl Neelson stain to look for acid-fast bacilli (AFB). Four out of five patients had positive sputum for AFB. The patient with the negative sputum AFB underwent bronchoscopy. This patient's bronchial washing for AFB direct smear and mycobacterial tuberculosis (MTB) Gene Xpert were positive. Hence, all patients were diagnosed with pulmonary TB and started on antituberculosis treatment. They showed significant improvement. The 'Tennis Racket' sign is a feature of active pulmonary TB. The identification of this sign should initiate a search for pulmonary TB and its subsequent management. We hope this article will shed light on how to recognise the 'Tennis Racket' sign and its importance in diagnosing active pulmonary TB.

INTRODUCTION

Since the discovery of *Mycobacterium tuberculosis* in 1882, tuberculosis (TB) has become a global concern, claiming many lives each year, especially in developing nations. The diagnosis of pulmonary TB is conclusively established by demonstration of *Mycobacterium tuberculosis* from sputum, body fluid or tissue. However, chest radiograph remains a crucial tool in suggesting a diagnosis of pulmonary TB. Furthermore, obtaining a positive specimen from patients often takes more time compared to performing a chest radiograph. Hence, it is important that clinicians are well versed with the radiological signs associated with this treatable disease. One of these signs is the underacknowledged, 'Tennis Racket' sign, which will be further discussed in detail in this case series.

Cavitation is frequently seen in post-primary tuberculosis, as much as in 20 to 45% of cases. In post-primary TB, cavity has a predilection for the apical and posterior segments of the upper lobes as well as the superior segments of the lower lobes.[1] Pulmonary cavitation is associated with high bacillary burden.[2,3] The 'Tennis Racket' sign is a damaged bronchus connecting the cavity to the hilum. It has not gained much attention over these years, except for being mentioned in a few case reports and case series.

CASE REPORT

We presented case reports of five patients who visited the TB clinic at our centre between January 2021 and January 2022. These patients were chosen by virtue of their chest radiographs showing the 'Tennis Racket' sign. A total of 285 patients were registered at our TB clinic throughout that time duration. We went through their chest radiographs and those with the 'Tennis Racket' sign were identified.

Case 1

A 40-year-old Rohingya male with no known medical illness previously, presented with non-productive chronic cough for 3 months with loss of appetite and weight. He lived in a crowded house with other foreigners but denied any history of TB contact. Physical examination revealed bronchial breath sound and crepitations over left upper zone. His total white blood cell (TWBC) count was elevated at 14.5×10^9/L. There was no anaemia or thrombocytosis. His renal profile and liver function tests were normal. Erythrocyte sedimentation rate (ESR) was not available for this patient. The chest radiograph showed 'Tennis Racket' sign on left upper lobe (Figure 1a). Anti-TB treatment was started immediately and later sputum for AFB came back as positive (3+).

Case 2

A 70-years-old Malay woman with underlying type II diabetes mellitus, which was poorly controlled with HbA1c of 10.5%, presented with fever for one week which was associated with productive cough and loss of appetite. Clinically, there were bronchial breath sounds and crepitations at the right upper and middle zones. Her TWBC count and ESR both were elevated, 17×10^9/L and 105 mm/hour, respectively. There was also normochromic, normocytic anaemia with haemoglobin (Hb) of 9.7 g/dl. Other blood investigations were within normal limits. Chest radiograph revealed 'Tennis Racket' sign at the right upper zone as well as patchy consolidation over bilateral lung fields (Figure 1b). Anti-TB medications were started right away, and her sputum AFB resulted in a positive result (3+).

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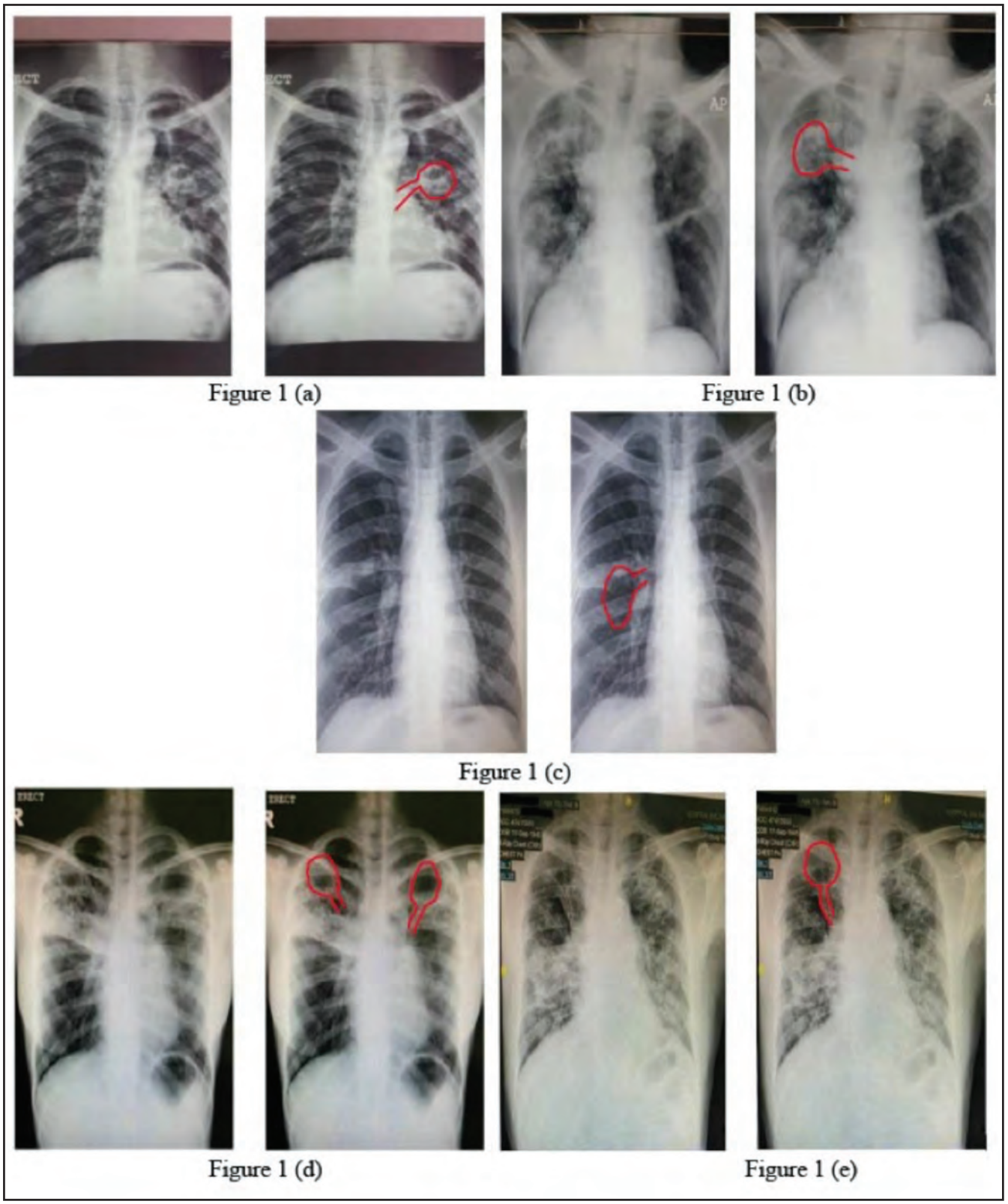

Fig. 1: (a) 'Tennis Racket' sign at left middle zone.
(b) 'Tennis Racket' sign at right upper zone.
(c) 'Tennis Racket' sign at right middle zone.
(d) 'Tennis Racket' sign at bilateral upper zones.
(e) 'Tennis Racket' sign at right upper zone.

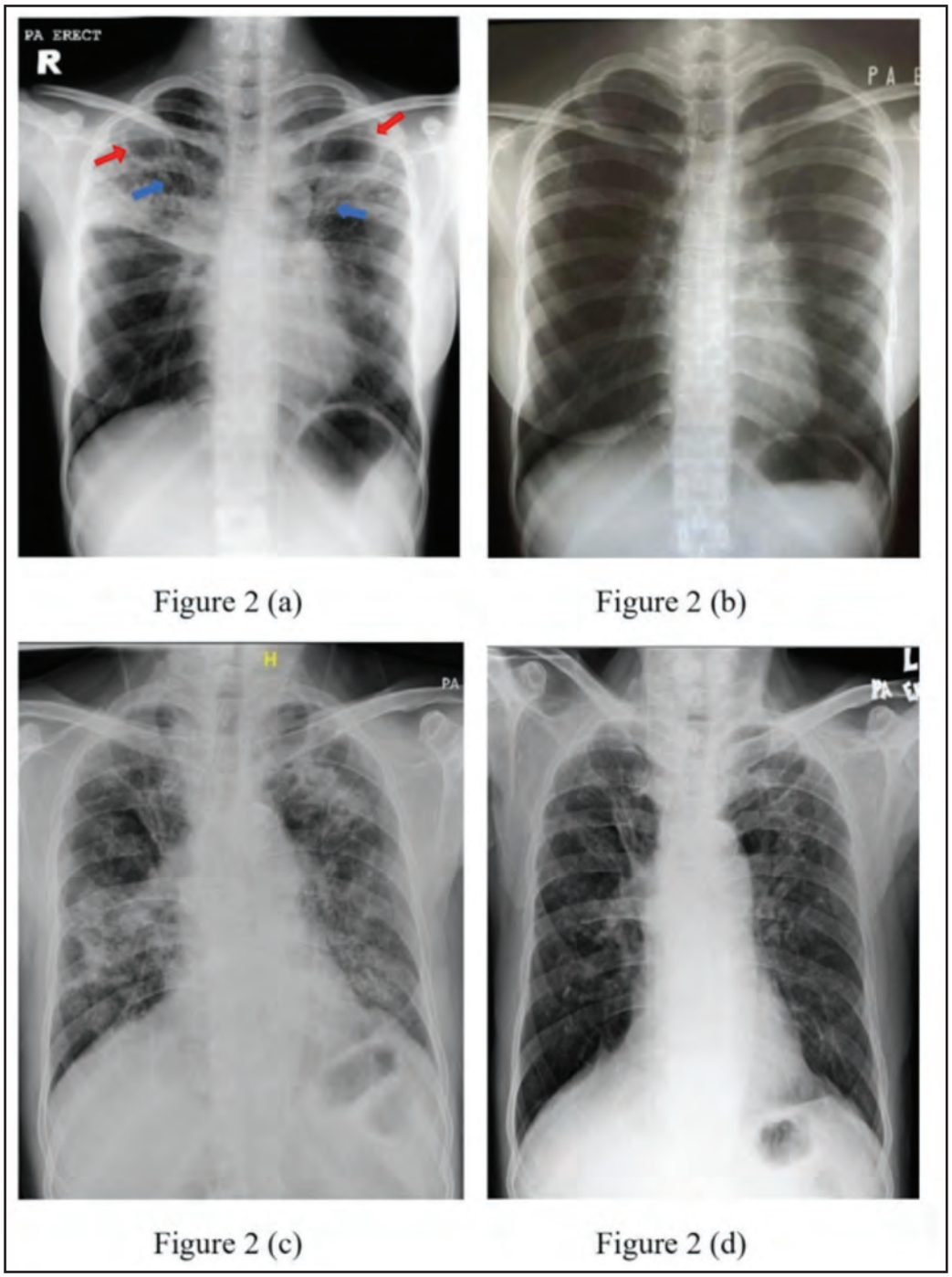

Fig. 2: (a) Pre treatment chest radiograph for Case 4
(b) Post treatment chest radiograph for Case 4
(c) Pre treatment chest radiograph for Case 5
(d) Post treatments chest radiograph for Case 5

Case 3
A 45-years-old Indian man who is an active smoker and consumed alcohol occasionally but no other significant comorbidities, presented with three months history of cough and loss of appetite and weight. There was no history of close contact with another TB patient. On examination, there were crepitations at the right middle and lower zone. His ESR was elevated at 165 mm/hour, but all other investigations were within normal limits. A 'Tennis Racket' sign was seen in the right mid zone on chest radiograph (Figure 1c). Anti TB medications were started while waiting for sputum for AFB which was positive (2+).

Case 4
A 17-years-old Malay student with no known medical illness previously presented with productive cough, fever and loss of appetite for four days. She lived at the hostel of a boarding school but unsure of any TB contact. Physical examination revealed crepitations over bilateral upper zones. Her blood investigations showed leucocytosis and thrombocytosis with TWBC of 18×10^9/L and platelet count of 509×10^9/L. ESR was also elevated at 125 mm/hour. Other blood investigations were within normal limits. Chest radiograph showed 'Tennis Racket' sign over bilateral upper zones (Figure 1d). Her sputum for AFB was positive (3+) and anti-TB treatment was started immediately.

Case 5
A 76-years-old Chinese male with underlying hypertension which was well controlled, presented with shortness of breath and loss of appetite and weight for two months. Clinically, there were crepitations over bilateral lower zones. Blood investigations revelated an elevated ESR (98 mm/hour) and hyponatremia (sodium: 126 mmol/l), other blood investigations were normal. Chest radiograph revealed 'Tennis Racket' sign over right upper zone (Figure 1e). Three early morning samples for sputum for AFB were negative. In view of strong clinical suspicion of TB, we proceeded with bronchoscopy and bronchial washing for AFB direct smear revealed a positive result. MTB Gene Xpert was also positive and showed sensitivity to rifampicin. Anti-TB treatment was started.

Human immunodeficiency virus (HIV) test was negative for all the five patients. They were started on first line anti-TB treatment, which included 2 months of intensive phase with isoniazid, rifampicin, pyrazinamide and ethambutol followed by months of isoniazid and rifampicin. The *Mycobacterium tuberculosis* culture which came out later was sensitive to first line anti-TB medications for all patients. All patients showed remarkable improvement clinically. Sputum smears converted to negative at two months of treatment. There was resolution of the cavities seen in the post treatment chest radiographs that were available. Pre and post treatment chest radiographs of Case 4 and Case 5 are displayed in Figure 2 (a-d). We were unable to trace the chest radiographs of the patients Case 1-3.

DISCUSSION

A cavity is defined by the Fleischner Society as a gas-filled area in a pulmonary mass, nodule or consolidation. The most common infectious cause of persistent cavitary illness is reactivation of TB. The other causes of a pulmonary cavity are pyogenic infections (*Staphylococcus, Klebsiella,* anaerobes), lung abscess, necrotising pneumonia, non-tuberculous mycobacterial infections, septic emboli, fungal pneumonia, primary lung malignancy (most commonly squamous cell carcinoma) and rheumatological conditions such as rheumatoid arthritis and Wegener's granulomatosis.[3]

A pulmonary cavity develops because of liquefactive necrosis and subsequent debris evacuation through the bronchial tree.[3] The 'Tennis Racket' sign reflects TB infection of the bronchus. Narrowing or occlusion of the bronchus results in dilatation distally producing a ring shadow, which forms the cavity (Figure 2 (a), red arrow). The rest of the bronchus, which extends proximally towards the hilum, is often dilated and its wall thickened by TB involvement, resulting in a 'Tennis Racket' shadow4 (Figure 2 (a), blue arrow).

A cavity is known to have a higher number of TB bacilli, i.e., 100 000 times as many as in noncavitary lesions.[5] The direct communication of the cavity with the bronchus explains the high bacterial yield observed with this sign. This is consistent with the findings in our case series, where sputum for AFB was positive in four out of five patients. Three of the patients exhibited strongly positive sputum AFB (3+, more than 60 AFB per high power field) indicating high bacterial yield. The patient in Case 5 who tested negative for sputum AFB was only able to produce a poor sputum sample despite induction with hypertonic saline, hence, explaining the negative results. Subsequently, bronchial washing AFB direct smear and MTB Gene Xpert came back as positive confirming pulmonary TB.

The ESR test is usually sent as a nonspecific test in the initial work-up for TB. It can be raised in multiple conditions such as acute and chronic infections, systemic inflammatory state and malignancy. The most common infection with raised ESR level is TB. Several studies have proven that raised ESR (typically > 100) is more commonly found in symptomatic, smear or culture positive TB.[6-8] Four out of five of our patients had a raised ESR. The ESR value was not available for one of the patients. This shows that the findings in our case series was consistent with other studies.

Initiation of anti-TB treatment resulted in significant improvement both clinically and radiologically in the chest radiographs that were available. There was resolution of the cavities. Similar results were also observed in other case reports.[5] We suggest that the 'Tennis Racket' sign can be used to start anti-TB treatment while awaiting definite microbiological evidence of TB, especially in rural and low resource areas.

CONCLUSION

This case series confirm that the 'Tennis Racket" sign is an important radiological feature of active pulmonary tuberculosis (TB). It is associated with a high bacillary burden. All in all, presence of this sign should instigate a search for TB and its treatment. Hence, it is crucial for clinicians to be able to acknowledge this sign.

CONFLICT OF INTEREST

None.

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A rare hypervascularised giant adult jejunal mesenteric lymphangioma

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SUMMARY

Mesenteric lymphangioma in an adult age group is a rare congenital benign tumour with an incidence of less than one percent. The tumour is biological slow growing. Thus, majority of patient present with non-specific symptoms and inconclusive imaging with mass effect which contributes to the difficulty in achieving the clinical diagnosis. Surgical excision of lymphangioma is the gold standard treatment but remains a surgical challenge due to the giant size intraabdominal lymphangioma. Here we present a rare case of an adult with an extreme sized mesenteric lymphangioma presenting with upper gastrointestinal symptoms. He successfully underwent surgical resection of the lesion which consists of 13 kg in weight and preservation of adjacent bowels.

INTRODUCTION

Mesenteric lymphangioma is an uncommon benign tumour with a reported incidence between 1 in 20,000–250,000.[1] Lymphangiomas are usually located in the head, neck, and axilla in children.[2] Almost 90% are detected by the mean age of two years.[3] Nonetheless, the risk of intraabdominal lymphangiomas which occur in adult age are extremely rare. Lymphangiomas occur at the mesentery in less than one percent of reported cases. The aetiology is unclear, but they are considered primarily to be congenital in origin.[3] Their suggested mechanism of occurrence is an anomalous development of the lymphatic system, which involves the obstruction of developed lymphatic channels due to lack of communication between small bowel lymphatic tissue and the main lymphatic vessels resulting in blind cystic lymphatic spaces. Most of the patients will present with non-specific gastrointestinal symptoms and with a huge sized mass effect obscuring a proper assessment view in imaging which makes it a challenge to make a clinical diagnosis. Surgical resection is the definitive treatment but remains a challenge in complete resection. Here, we present a case report of a giant size adult mesentery lymphangioma that underwent a successful complete resection with preservation of adjacent bowel.

CASE REPORT

A 29-year-old Malay gentleman presented to hospital with abdominal distension and early satiety for the past eight months. He had no vomiting or altered bowel habit to suggest of obstructive symptoms.

His body weight was 61kg. He was clinically thin in built with a grossly distended abdomen occupied by the mass which was non-tender and had the presence of a fluid thrill. Blood parameter showed no abnormality. Ultrasonography showed a large multiseptated cyst filling the whole abdomen. We proceeded with computed tomography (CT) of the abdomen and pelvis which showed a large abdominopelvic cystic mass (average HU of 20) with multiple enhancing septa mass effect to the surrounding structures and compression effect to the retroperitoneal urinary systems (Figure 1a and 1b).

Unfortunately, imaging was unable to determine the origin of the mass due to its large size. In view of its large size and multiple enhancing septa, it raised the suspicion of malignancy.

Tumour markers screening (alpha fetoprotein, carcinoembryonic antigen and CA 199) were normal. Infective screening for hepatitis B, C, HIV (human immunodeficiency virus) and VDRL (venereal disease research laboratory) was also not detected. He preceded with an ultrasound guided biopsy and cytology reported no malignant cells were seen.

He remained symptomatic and underwent laparotomy and tumour excision. Intraoperatively we found a large cystic lesion arising from the jejunal mesentery cyst occupying the entire abdomen. With the size of 41cm × 30 cm × 7cm. It was a hypervascularised lesion, well encapsulated, multilobulate, and multiseptated lesion (Figure 2a and 2b).

Initial working impression was of a mesenteric cyst.

The lesion was successfully excised en-bloc (Figure 2c and 2d) with preservation of major mesentery vessel and preservation of adjacent small bowel. Total cyst weight was 13kg. Colon, small bowel, rectum stomach, liver and spleen were normal with no peritoneal nodules.

Histopathology revealed the lesion was a mesenteric lymphangioma. Microscopically, the cystic lesion was composed of multiple large, irregular vascular spaces lined by flattened, single layered endothelial cells within a fibro-collagenous stroma, with no mitosis, atypia or multilayering of the lining cells seen (Figure 3a-d). In areas, the stroma shows infiltration of moderate lymphoplasmacytic cells and some reactive lymphoid follicle formation. Cholesterol clefts surrounded by foreign body type multinucleated giant cells

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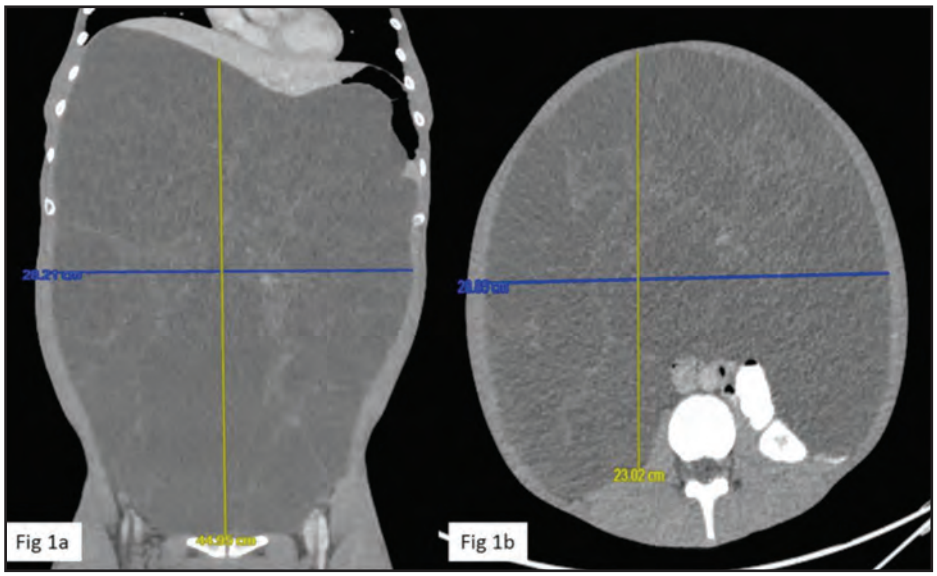

Fig. 1: (a) (CT coronal view)
(b) (CT axial view) showed huge multiple cystic enhancing lesion

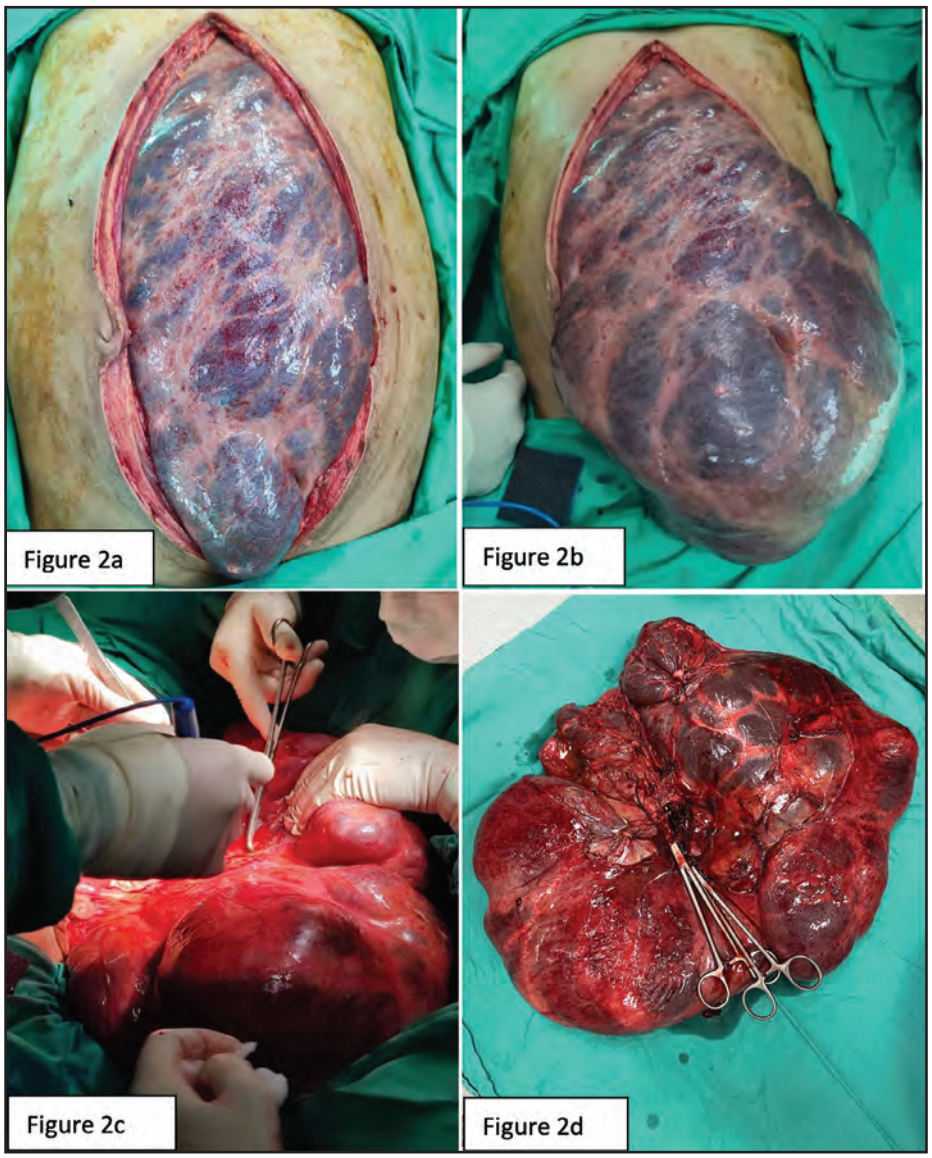

Fig. 2: (a) and (b) Intra-operative lesion prior excision
(c) Resecting the mesenteric lymphangioma
(d) Successful excised the mesenteric lymphangioma specimen

Table I: Classification of mesenteric cystic lymphangioma according to Losanoff and Kjossev

Types	Description et surgical possibilities
Type I	Pediculated with risk of torsion or volvulus. The resection is easy.
Type II	Sessile, less mobile that may require a nearby organ sacrifice
Type III	Includes a retroperitoneal extension (damage to vital structures sometimes) rendering total excision impossible
Type IV	Corresponds to extensive multi-organ damage

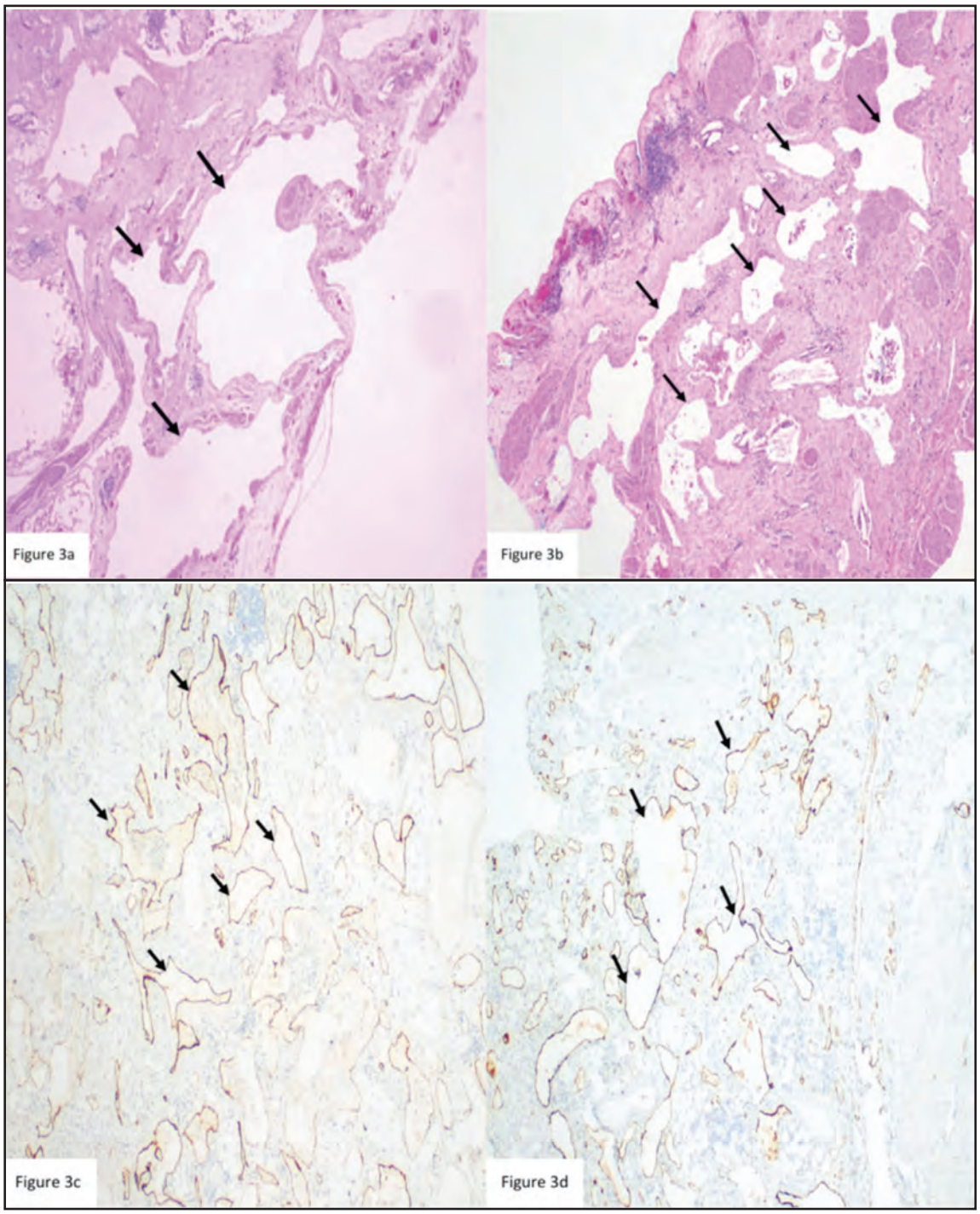

Fig. 3a & 3b : Cystic space lined by flattened, single layered endothelial cells (arrow)
(Figure 3a X20 magnification and Figure 3b X40 magnification)
Fig. 3c & 3d : D2-40(podoplanin) Immunohistochemical stain highlights the endothelial cells (arrow)

are also present. Smooth muscle bundles were seen in areas. No malignancy was identified.

DISCUSSION

Mesenteric lymphangioma are rare benign tumours which preoperative diagnosis is usually difficult due to the frequent silent clinical course. Patients may come with abdominal distension with or without intestinal obstruction and could present as incidental findings in asymptomatic patients.Some may present with acute abdomen such as rupture, infection, haemorrhage, or volvulus (4). Losanoff and Kjossev classification based on the morphotype of lesion is necessary to optimise the surgical treatment (5) (Table I). Radiological investigations are a useful diagnostic tool, but definitive diagnosis is confirmed by histopathology after a complete surgical resection.

Diagnosing an intra-abdominal cystic lesion needs thorough investigation to exclude malignancy and other differentials of an intra-abdominal cystic mass such as enteric duplication cysts, enteric cysts, mesothelial cysts, pancreatic pseudocysts, non-pancreatic pseudocysts, cystic mesotheliomas, cystic spindle cell tumours, and cystic teratomas. (6)

Ultrasound and CT are sensitive in providing structural details of the lesions. On the CT imaging, it appears as either uni- or multi-loculated configuration, size, enhancement of wall and septum.[2] However, ultrasound also can help to identify a cystic liquid lesion by its hypoechogenic and multiloculated morphology. Magnetic resonance imaging (MRI) is a more specific preoperative radiological tool for diagnosis and in surgical planning. It allows better differentiation of cystic and septal structures for comparison of mesenteric cyst and lymphangioma especially in mesenteric cystic lymphangioma. Mesenteric lymphangioma lacks demonstrable fat content by chemical shift and fat saturation.[7] In our patient, we did both CT and US imaging which clearly detailed the morphology and imaging characteristics of a cystic lymphangioma arising from the small bowel mesentery.

Accurate and definitive diagnosis is according to the histopathology and immunochemistry: the lining mesothelial cells are immunoreactive for cytokeratin and negative for factor VIIIIs. Staining with Prox1 and CD31 is the most reliable method for identifying lymphangioma endothelial cells.[8]

The main modality of treatment for mesenteric lymphangioma is adequate surgical excision, because there is a risk of recurrence and malignant transformation, particularly after radiotherapy for the primary lesion.[3] Lymphangiomas can become locally invasive and often require surgical excision, with reported recurrence rates of 12% and 53% when completely or partially resected, respectively.[9] Some cases require small bowel resection, but not in our case. It should be noted that the 10% of postoperative recurrence rate is due to incomplete resection, as evinced by positive microscopic resection margins. To prevent recurrence, complete excision of the tumour with or without intestinal resection is mandatory.

In our patient, we performed a complete surgical excision of the mass, that is the treatment of choice for cystic lymphangioma, even if asymptomatic. The prognosis after adequate excision of the cystic tumour of the mesentery was considered to be excellent.

Drainage has been suggested as a modality of treatment in high-risk patients but is often unsuccessful because of recurrence and for the risk of perforation of the mesentery during the drainage of the lymphangioma.[5] Instillation sclerotherapy with alcohol is being used for ablation, but this method can be destructive to normal tissue. In cases of failed percutaneous sclerotherapy using alcohol, acetic acid has been used with good success in intra-abdominal lymphangioma.[10]

Chen et. al in their study of six patients showed no recurrence during follow-up period of 3 to 12 months.[11] In our case, we follow up the patient three-monthly with a clinical examination and an abdominal ultrasound three months and six months after the operation which showed no recurrence.

CONCLUSION

Mesenteric lymphangioma are benign rare tumour in adults in which need thorough investigation. Surgical resection is gold standard and following up with imaging. Moreover, mesenteric lymphangioma in adult requires further study and clinicians should increase awareness to avoid misdiagnosis.

DECLARATION

The authors declare no conflict of interest with this work.

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CASE REPORT

Prenatal adrenal calcification: A prenatal sonographic feature of congenital cytomegalovirus infection

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SUMMARY

A case of severe congenital cytomegalovirus infection in a healthcare worker is presented. Fetal adrenal calcification is identified as a sonographic finding. Indications for prenatal screening and some aspects of treatment are discussed.

INTRODUCTION

The prevalence of congenital cytomegalovirus infection (cCMVi) is reported to range from 2.6 to 6.8%.[1] of livebirths with the higher end of the spectrum observed in low socioeconomic countries. Congenital CMV infection is the leading cause of nervous system infection in the newborn. It is one of the leading causes of mental restriction, sensorineural deafness and visual impairment in this group.[2]

CASE REPORT

A 34-years-old frontline healthcare worker was referred to our foetal medicine centre with foetal hydrops at week 21 of gestation. This was a planned pregnancy. She had no medical history of note. Her husband is an alpha thalassemia career. The maternal serum free foetal DNA aneuploidy screening at week 12 was low risk for chromosomes 13, 18 and 21 abnormalities. She had a routine level 1 scan at week 16 with the foetus appearing grossly normal with normal biometric parameters. She felt unwell with sore throat, myalgia and low-grade fever lasting two days after this scan. She spent one day at home. There were no localising symptoms or rash. She was back to work the following day feeling fine. The weekly COVID-19 polymerase chain reaction test for frontline healthcare workers were negative. All frontliners work with full protective gear as per national guidelines at the time. A level 2 scan at 20 weeks suggested hydrops fetalis. She presented to our tertiary centre at week 21.

Ultrasound scan findings of the foetus and its environment at the time of assessment are as follows: 1. Small for gestation age (SGA) with biometry symmetrically under the 5th percentile, 2. Ascites was present, 3. No hydrothorax, 4. No skin oedema, 5. Normal liquor volume, 6. Normal placental echotexture, 7. Foetal movements observed but feeble and reduced, 8. Mild cerebral ventriculomegaly with an atrial diameter of 11 mm, 9. Hepatic calcifications, 10. Middle cerebral artery doppler screening for foetal anaemia was negative, 11. Adrenal gland: bilateral extensive echogenic glands of proportionate size suggestive of calcification. There was no evidence of congenital heart defect or dysrhythmia.

Laboratory tests: Red cell antibody screen negative. Kleihauer negative. Blood film and electrophoresis normal. Parvovirus B19 negative. CMV IgM and IgG positive.

Chromosomal study: The couple agreed to an amniocentesis for chromosomal studies. G-band karyotype was normal. Whole exome sequencing (Perkin Elmer Genomics) did not detect any pathogenic sequence variant or variant of unknown significance.

Placental histology: Plasmacytic villitis with positive immunochemistry indicative of CMV infection.

In utero foetal demise was determined 2 weeks after the visit. A perinatal post-mortem was not done respecting the wishes of the couple.

DISCUSSION

A literature search for prenatal adrenal hyperechogenicity or prenatal adrenal calcification and congenital cytomegalovirus infection (cCMVi) did not yield specific papers linking prenatal sonographic adrenal echogenic abnormalities to cCMVi. Adrenal calcification has mostly been described in the postnatal period secondary to other causes.[3] Postnatal causes include birth trauma, foetal acidosis of varying causes, adrenal haemorrhage, Wolman's disease, Niemann-Pick disease and CMV. Prenatal findings for cCMVi are listed in Table I

We report a case of cCMVi with prenatally evident bilateral adrenal echogenicity most probably being calcification.

Serologic CMV IgM and IgG was detected 5 to 6 weeks after the likely episode of illness. This is despite the patient working in a heightened risk aversion manner during the COVID-19 pandemic. Six weeks is the minimum interval between infection/reactivation and foetal infection that becomes serologically detectable.[5] Avidity studies on the IgG if performed would have shed more light on this aspect of the infection. CMV remains lifelong in those infected and exhibits the similar latency characteristics as other herpesvirus family of viruses.[6] A total of 10 to 20% subsequently experience reactivation of disease albeit in milder fashion. Maternal CMV re-activation is the most common scenario in cases of cCMVi. Re-emergence of IgG and IgM is recognised in CMV re-activation. Anti-CMV IgG avidity (level of binding: IgG-viral binding is weaker after primary than re-activation of CMV) testing may help

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Table I: Common ultrasound findings in cCMVi[4]

	Echogenic bowel	**26%**
Non-cranial	Hepatomegaly	14%
	FGR	10%
	Oligohydramnios	7%
	Ascites	4%
	Liver calcifications	3%
	Enlarged placenta	3%
	Pericardial effusion	1%
	Hydrops	1%
	Club foot	1%
Cranial	Calcifications	18%
	Hydrocephaly	18%
	Microcephaly	10%
	Germinative cyst	7%
	Ventriculomegaly	3%
	Cysts	2%
	Polymicrogyria	1%

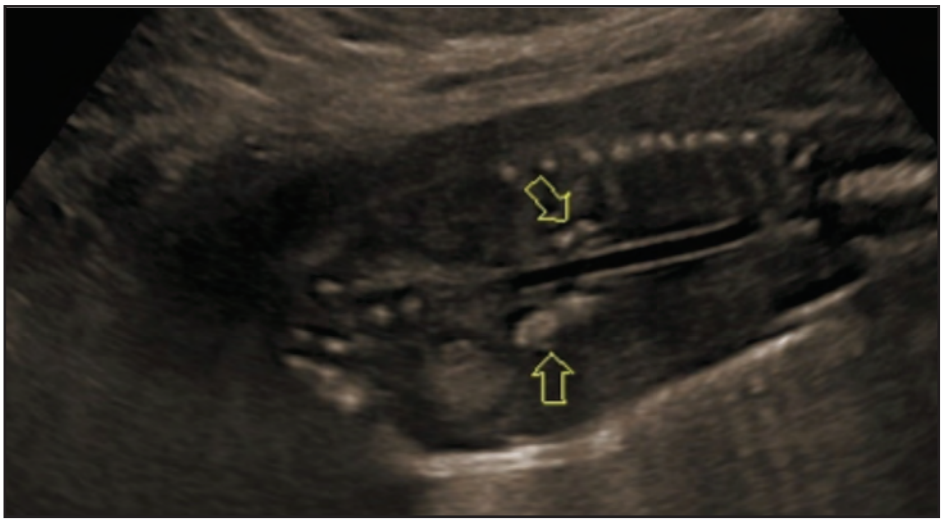

Fig. 1: Large arrows point towards bilateral adrenal hyperechogenicity consistent with calcification

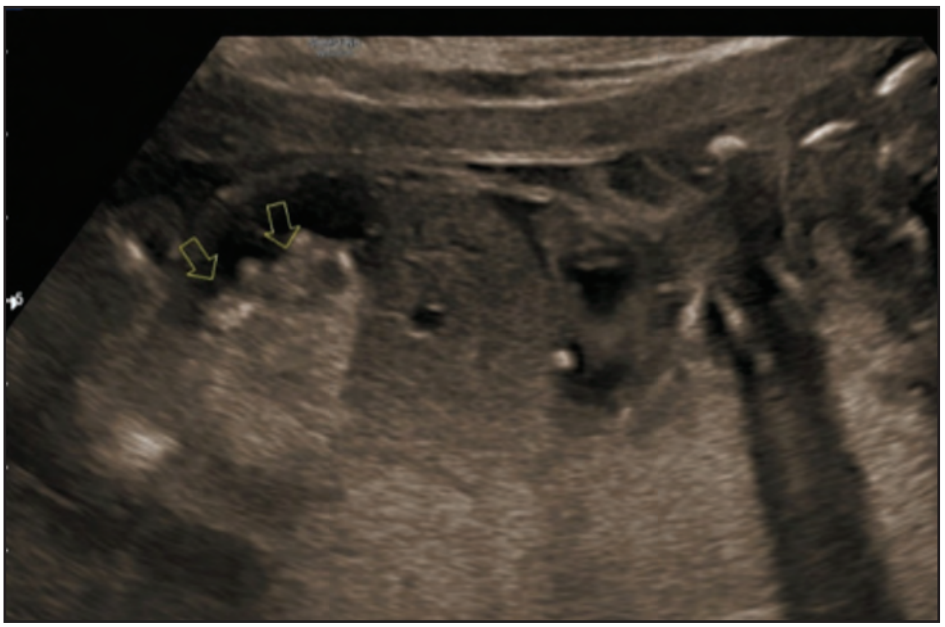

Fig. 2: Large arrows point to echogenic bowel with adjacent ascites.

distinguish primary from a re-activation with high IgG avidity in re-activation cases.[7] Prenatally, amniotic fluid CMV PCR has taken over viral culture as the gold standard for definitive infection as the virus is known to be shed in foetal urine.[8]

It is well known that healthcare workers are at higher risk for CMV infections. Infection requires close contacts with all bodily fluids. Other risk factors for CMV infections include low socioeconomic groups, nursery and childcare settings, and breastfeeding and promiscuity.[9]

CMV screening is currently not routinely recommended even with a prevalence of 2 to 6% of livebirths. CMV infection has a 30 to 40% chance to progress to CMVi and the lack of established treatment is part of why this approach is taken. Furthermore, most cCMVi result in asymptomatic babies. Only 5 to 15% develop symptoms or signs detected prenatally or at birth and this rate is the same in both primary and secondary reactivation cCMVi. Prenatal diagnosis generally confers a poor prognosis. Of babies born with symptomatic cCMVi, 30% will die. In the survivors congenital and perinatal CMV infection remains one of the leading causes of sensorineural deafness, visual impairment and neurologic sequalae including microcephaly, cerebral palsy and neurodevelopmental delay.[10]

CMV can be prevented by simple health measures like sanitising surfaces, use of gloves and hand washing. Serologic screening and surveillance for healthcare workers and other at-risk groups mentioned who are embarking on pregnancy can be recommended. Healthcare workers embarking on pregnancy should have CMV serology baseline taken at booking. Serologic surveillance at regular interval should be advised in the seronegative pool. In pregnant women with a past history of CMV infection viral titres should be monitored or the foetus be subjected to the serial ultrasound scan scrutiny to ascertain possibility of cCMVi. In prenatal CMV confirmed cases, high dose prolonged valacyclovir therapy has the potential to half the neonatal symptomatic rates in a single study.[11] Hyperimmune globulin therapy has not achieved the desired therapeutic effects in a single study but is currently being evaluated under a trial setting.[12] These treatment options, if ultimately proven efficacious, may force a rethink on the merits of screening for cCMVi.

The limitation with this case report is that CMV PCR on the amniotic fluid, foetal autopsy and tissue analysis may have added weight to diagnosis of cCMVi in this case.

CONCLUSION

Fetal adrenal calcification as a consequence of cCMVi has not been reported in the literature. We report a case of fetal adrenal calcification as a sonographic manifestation of cCMVi in a healthcare worker. cCMVi is common and prevalent especially in populations of lower socioeconomic standing. Certain occupations predispose to this congenital infection which is the most common cause of sensorineural deafness/impairment among newborns. Antiviral therapy after prenatal diagnosis has been shown to lower incidence and severity of this morbidity. Screening of at-risk population such as nursery and healthcare workers should be revisited.

DECLARATION

None.

The patient has granted permission for the scientific reporting and subsequent publication of her experience.

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An unexpected presentation of small bowel bleeding from ischaemia, treated with methylene blue-guided surgical resection

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SUMMARY

Acute small bowel bleeding has a high morbidity and mortality rate. Computerised tomography (CT) scan is usually performed and angio-embolisation undertaken if acute bleeding is detected. We present a case where acute bleeding was seen on CT and angiography, but as part of an unexpected underlying bowel ischaemia during the latter. Given the decision to defer embolisation in preference of surgical resection, methylene blue was administered during angiography to demarcate the segment of ischaemic bowel. This is in contrast to much of the literature where the dye was injected peri-operatively, and for bleeding from a vascular lesion. During surgery, the affected ileal segment was identified and successfully resected. No recurrence of bleeding occurred during the remainder of the patient's hospital stay.

INTRODUCTION

Gastrointestinal bleeding from the small bowel (SB) is a challenging condition to diagnose and manage. It is difficult to access and it has a long length, which makes localisation of any source of bleeding with scopes challenging. Other pathology, such as ischaemia, can occur concomitantly and can alter treatment course.

CT angiography (CTA), catheter angiography and endoscopic evaluation remain the mainstay of investigation for acute SB bleeding. Once a source of bleeding is identified, treatment options include embolisation of the culprit vessel or surgical resection. Methylene blue has been used since 1978 to aid in intra-operative localisation of bleeding small bowel segments. In this case report, we described how findings on CTA and catheter angiography in a patient with active SB bleeding altered treatment decision which prompted the use of pre-operative methylene blue injection to aid in subsequent intra-operative localisation of the bleeding SB segment.

CASE REPORT

We present a case of a 76-year-old Chinese gentleman with non-ischaemic cardiomyopathy, reduced ejection fraction and atrial fibrillation. He was admitted to hospital for acute limb ischaemia from an acute saddle embolus of the abdominal aorta which was successfully treated with embolectomy of the distal aorta and bilateral iliac arteries. His atrial fibrillation was adequately controlled, and he was adequately anticoagulated post-embolectomy. However, this was complicated by ischaemic colitis 2 days later for which he required a Hartmann's procedure. He was subsequently put on prophylactic subcutaneous enoxaparin for post-operative venous thrombosis prevention. During his stay in the intensive care unit, about 1 month post-operatively, he was diagnosed with acute per-stomal bleeding. On clinical examination, he did not complain of abdominal pain and there were no sign of peritonism. Serological markers showed a haemoglobin drop from 8.7 to 7.8 g/dL, elevated CRP of 68.2 mg/L, and normal lactate level at 1.3 mmol/L. No abdominal radiographs were performed, with patient proceeding straight to a contrast enhanced CT mesenteric angiogram. This showed arterial phase contrast extravasation (Figure 1a) in a distended loop of ileum with pooling of contrast in the venous phase (Figure 1b) which was reported as active intraluminal bleeding.

Conventional angiography was performed with the intention to embolise the bleeding vessel. Digital subtraction angiography images revealed a focal blush near the anti-mesenteric border of the ileum, with a poorly demonstrated feeding vessel (Figure 2). More importantly, it has been recognised that this loop of bowel has remained aperistaltic and had poor contrast improvement signifying ischaemia. Following discussion with the surgical team, a decision was made not to embolise but instead inject methylene blue to better delineate and identify this loop in preparation for emergency laparotomy afterwards. Approximately 1.5 mls of methylene blue was injected via the microcatheter which was then removed before transferring patient for surgery.

During surgery, a segment of the distal ileum stained with methylene blue was identified. The stained bowel loops were dilated with an area of thinned out bowel wall. Intra-operative indocyanine green with fluorescence imaging was performed to assess the line of demarcation between the healthy and ischaemic bowel for potential anastomosis. This showed small bowel wall hypo-enhancement at the same area, which correlated to the area stained by methylene blue. Approximately 20 cm of ischaemic bowel was resected (Figure 3) and a functional end-to-end small bowel anastomosis was performed. Histology of the resected small bowel revealed acute inflammation with acute ischaemic

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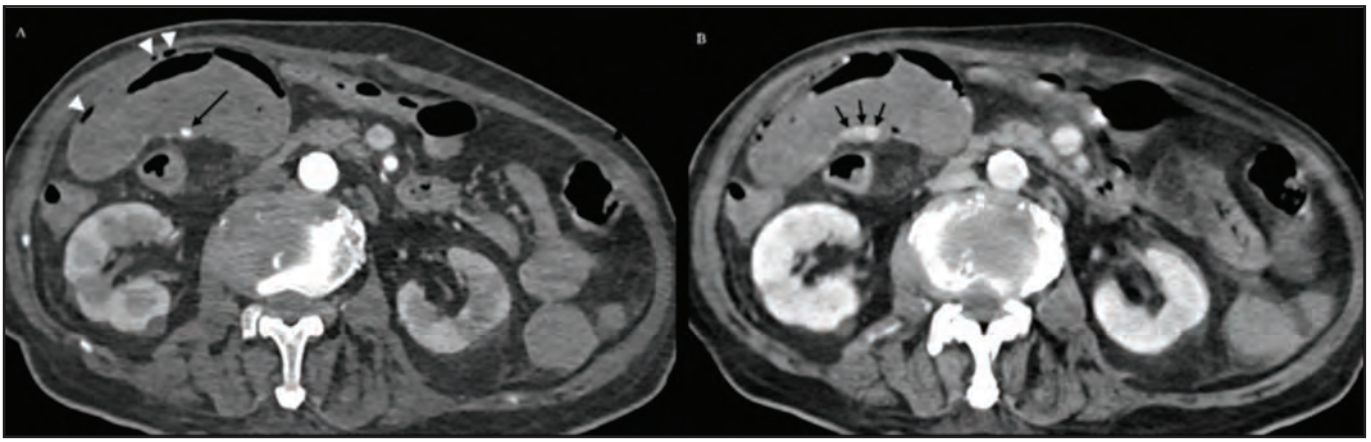

Fig. 1: CT mesenteric angiogram of a 76-year-old patient showing (a) focal contrast extravasation within a distended loop of ileum in the arterial phase (arrow) and intra-mural gas (white arrowheads) as well as (b) pooling of contrast by the venous phase (black arrows).

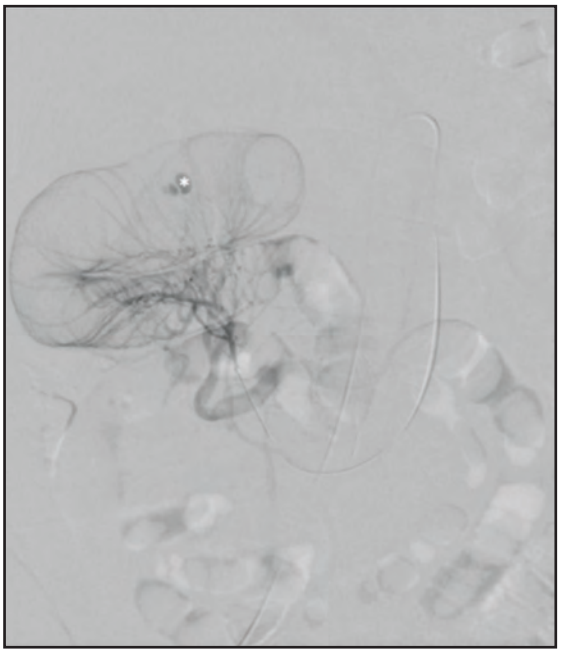

Fig. 2: Digital subtraction angiography image reveals an aperistaltic loop of ileum with focal blush near the anti-mesenteric border (asterix).

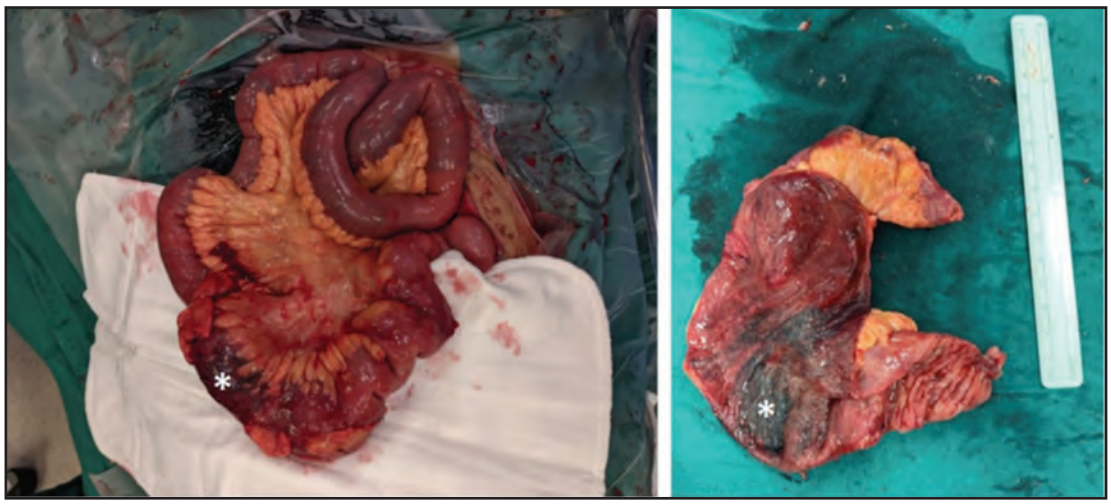

Fig. 3: (a) Intra-operative appearance and (b) resected specimen showing necrotic bowel with areas stained with methylene blue (asterixes).

changes. No recurrence of intestinal bleeding occurred throughout the remainder of the patient's hospital stay. In view of his poor functional status, he kept his colostomy permanently.

DISCUSSION

Small bowel haemorrhage accounts for approximately 5% of gastrointestinal bleeding and has high morbidity and mortality with the inpatient mortality as high as 17%.[1,2] Common aetiologies in the elderly population include vascular abnormalities, ulcers and tumours.[1] Acute bleeding is usually diagnosed using CTA, catheter angiography or endoscopically (oesophago-gastro-duodenoscopy, colonoscopy and more recently, deep enteroscopy) and usually requires active bleeding at the time of investigation for the best chance at detection.[1,3] However, localisation of the acute bleeding source, particularly in the small bowel, is still a challenge as the cause of bleed can be obscure and difficult to locate. The long length of the small bowel, its intraperitoneal location and high motility results in challenging access and inspection with scopes.[1] Furthermore, poor visualisation from suboptimal bowel preparation and slow intermittent bleeding results in delayed presentation and investigation.[4,5] Acute bleeds are usually treated by radiolologic-guided embolisation using coils or glue, endoscopically (e.g. haemoclip application) or surgical resection.[1] The choice of treatment hinges on both patient and clinician factors as well as hospital resources.[1] In general, radiologically-guided angioembolisation is used for regions of haemorrhage beyond the reach of endoscopy, while surgical resection is reserved for recurrent bleeds not amendable to endoscopic or endovascular techniques.[1] Occasionally, radiological and surgical means can be combined as in our case.

Methylene blue dye injection for localisation of the site of intestinal bleeding was first described in 1978 by Fogler and Golembe.[6] A syringe with a 22-gauge needle was inserted directly into the superior mesenteric artery intra-operatively and 10 mls methylene blue was injected. A 10 cm segment of bowel was then stained which guided resection.

A literature review by Gifford et al. in 2012 and Pai et al. in 2013 showed that most authors used the following technique where a microcatheter is left in the culprit vessel during angiography before patient was transferred to the operating theatre.[7,8] Majority were undertaken for bleeding from a vascular lesion. Methylene blue was then injected intra-operatively, usually after the small bowel had been exposed at the time of laparoscopy or laparotomy.[9] Gifford et al. advanced on this method by administering methylene blue peri-operatively.[7]

There have been refinements to this localisation technique. Smaller microcatheters and more super-selective cannulation has resulted in more targeted resection, with the resected bowel length to be as low as 5 to 9 cm.[7,8] The amount of methylene blue required for staining has also decreased, with only 0.5 mls needed in some reported cases.[7] There are however some drawbacks to this technique. One of the risks as described by Gifford et al. is the theoretical risk of catheter migration or dislodgement during patient transfer.[7] This technique may also not be feasible if there is more than one bleeding focus. In addition, there are also some side effects associated with methylene blue. Doses of 500 mg or more (i.e 50 mls) is associated with chest and abdominal pain, nausea, vomiting and altered mental status.[8] There is also a risk of haemolytic anaemia in patients with glucose-6-phosphate dehydrogenase deficiency.[8]

Pre-operative injection of methylene blue during conventional angiography is a viable consideration and has been described in literature. We only found one case where in 2003, Remzi et al. described injection of methylene blue during angiography after identification of the bleeding culprit vessel. This still resulted in accurate identification of the bleeding segment and only 5 cm of small bowel was eventually resected.[10] We employed a similar method where injection of methylene blue during angiography was performed by the interventional radiologist to guide imminent surgery after realisation that embolization was not feasible. There are advantages with this method. The catheter was removed in the angiography suite prior to our patient's transfer to surgery, eliminating the risk of dislodgement.[7,10] Methylene blue injection has been showed to have bowel staining up to six hours in animal models.[7] Hence, in the event of any delay in transfer to surgery, the affected segment will still remain stained. Finally, the process of methylene dye injection during surgery is removed which results in better efficiency and potential time saving.[10]

CTA may be equal or better to catheter angiography in its sensitivity of detecting a bleed.[3] However, the latter is dynamic and has the benefit of providing information regarding bowel peristalsis and perfusion. A pertinent point in our case was that despite performing angiography with embolisation in mind, and detecting the bleeding source, it was crucial to recognise the aperistaltic and poorly enhancing segment of small bowel suggesting ischaemia. This was an unusual presentation given the lack of abdominal pain or peritonism and was an unexpected and subtle finding at the time of angiography. Embolising may have resulted in a satisfying imaging outcome but would have been detrimental to the patient. Hence, we instinctively combined catheter-directed injection of methylene blue to guide surgery. This resulted successful intra-operative localisation and subsequent resection of the affected segment of ischaemic bowel.

CONCLUSION

Recognising potential concomitant pathology in SB bleeding is important. In our case, recognising the concurrent bowel ischaemia changed the treatment course for the patient which resulted in a better outcome. Injection of methylene blue during catheter angiography prior to surgery is a viable alternative technique compared to the conventional technique. Based on our literature review this technique has not been widely used and reported on. We suggest this method be considered as benefits include eliminating the risk of catheter dislodgement and potential time saving.

DECLARATION

The authors declare no conflict of interest.

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Eosinophilic myocarditis: A rare case presentation

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SUMMARY

22-year-old gentleman presented to the emergency department with palpitation and pre-syncope. Initial investigation revealed leukocytosis with a predominant eosinophil count and an exceptionally high troponin level. His electrocardiogram (ECG) showed supraventricular tacycardia with aberrancy. The patient was given intravenous tenecteplase and subsequently underwent coronary angiogram. He was diagnosed with eosinophilic myocarditis after extensive investigation.

INTRODUCTION

Myocarditis is an inflammation of the heart muscle. It is believed that it is most often caused by viruses, bacteria, fungi, parasites or protozoa. They are also known causes of infectious myocarditis. There are other causes of myocarditis such as immune-mediated causes (e.g., systemic lupus erythematosus, Churg-Strauss syndrome, sarcoidosis or Wegener's granulomatosis), toxic causes (e.g., drugs, heavy metals, and snake or scorpion venom), and damage from ionising radiation or electricity.

Eosinophilic myocarditis (EM) is a rare subtype of myocarditis characterised by infiltration of eosinophil which subsequently causes either focal or diffuse myocardial inflammation. To date there are less than 30 published case reports of EM.[2]

CASE REPORT

A 22-year-old gentleman with a previous history of appendicectomy and multiple previous admission for typhoid fever and hypereosinophilic enterocolitis which was confirmed with trephine biopsy presented with vomiting for 2 days duration. There were two episodes of vomiting, and it was non-projectile in nature. The vomiting was associated with pre-syncope prior to presentation. He also experienced palpitation, profuse sweating and dizziness prior to the pre-syncopal episode. The patient denied other symptoms such as fever, shortness of breath, abdominal pain, loose stool and chest pain.

Upon arrival at the emergency department, he was alert, conscious, mildly dehydrated and septic looking. His blood pressure was on the lower side (108/62 mmHg). His heart rate was at 87 bpm and SpO_2 98% under room air. Respiratory and cardiovascular examination was normal.

Initial electrocardiogram (ECG) revealed ST-segment depression over leads I, II, III, aVF and V4-V6. His white cell count was 36.5($x10^9$/L) with eosinophil of 24.47(70%), haemoglobin 15.3 g/dL, while his platelet was 398($x10^9$/L). Troponin level was 3108ng/dL, while renal and coagulation profile was normal. He was empirically treated as typhoid carditis and was started on intravenous normal saline, pantoprazole 40 mg, ceftriaxone 3 g and metronidazole 500 mg.

Patient then developed supraventricular tachycardia with aberrancy which aborted with carotid massage and intravenous calcium gluconate 10% and intravenous magnesium sulphate 2 g.

He was admitted to the coronary care unit (CCU) for close monitoring. Bedside transthoracic echocardiogram showed normal heart with an estimated ejection fraction of 58% with normal valves. Day 2 of admission, computed tomography (CT) abdomen and CT pulmonary angiogram was done which turned out to be normal. He was treated as type II myocardial infarction in view of persistent widespread ST-segment depression and was given intravenous tenecteplase by the cardiology team as emergency coronary angiogram was not available at the time. ECG post thrombolysis showed resolution of ST depression over the anterolateral lead by more than 50%.

The patient also underwent coronary angiogram to find the culprit for the arrhythmias which turned out to be normal. He also had persistent high eosinophil throughout admission and was referred to haematology team for further investigation. Patient was counselled for endocardial biopsy to confirm the diagnosis of eosinophilic myocarditis however patient refused the procedure. He was started on tablet cetirizine 10 mg once daily (OD) and tablet prednisolone 20 mg OD by the haematology team and subsequently patient's eosinophil level reduced to a normal range. He was discharged on day 7 of his admission with oral cetirizine and prednisolone 20 mg once a day, and appointment for cardiac magnetic resonance imaging (MRI). MRI cardiac done later showed myocardial inflammation and fibrosis of basal/mid-apical inferoseptal left ventricle wall with extension to subepicardial layer of apicoseptal indicative of myocarditis.

DISCUSSION

Eosinophilic myocarditis (EM) is a rare form of myocardial inflammation with wide variety of aetiology. In developed

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country, the most common causes of EM are allergic reaction or hypersensitivity. Other possible cause includes infection, malignancies, vasculitis and drugs.

It is characterised pathologically by diffuse focal myocardial inflammation with abnormally high eosinophil infiltration. This infiltration plays an important role in the pathogenesis of eosinophilic myocarditis via release of eosinophilic granule proteins such as eosinophil cationic protein and major basic protein which subsequently causes dysfunction of myocyte mitochondria leading to myocardial lesions such as endocardial necrosis.

Three stages have been reported in EM. The first stage includes myocardial infiltration of eosinophil causing acute necrosis. This is followed by hyper-coagulation state leading to thrombus formation either within the coronary vasculature or the ventricles. Finally stage three which cause permanent cardiac dysfunction due to the formation of scar tissue.

Accurate diagnosis of EM is challenging. The diagnosis is made based on the medical history, clinical findings and laboratory investigation results. However, in some cases it is difficult to differentiate between myocarditis and acute myocardial infarction because of similar clinical presentation. Back to our patient, he was treated as type 2 myocardial infarction in view of the persistent ST-segment depression and changes in his cardiac enzyme level. The patient was given fibrinolytic therapy as coronary angiogram was not available at the time, before further investigation revealed the diagnosis of EM.

The presence of peripheral eosinophilia may indicate a diagnosis of EM. However, in some patients with a confirmed diagnosis of EM, they never develop peripheral eosinophilia throughout the course of the disease. Relying on peripheral eosinophilia to diagnose EM and treat the disease may be misleading. Inflammatory markers such as C-reactive protein and erythrocyte sedimentation rate are often raised together with myocardial injury markers such as troponin T and creatine kinase. This patient was previously diagnosed with hypereosinophilic enterocolitis with histopathological sample taken from trephine biopsy which made the diagnosis of eosinophilic myocarditis likely.

ECG findings in EM may mimic of those with acute coronary syndrome which can cause the delay in arriving to the exact diagnosis of myocarditis. Common ECG findings include sinus tachycardia, ST-T segment abnormalities and conduction delay.[1] However ECG changes were not specific or sensitive for myocarditis. For example, our patient had widespread ST depression and few episodes of arrhythmia which delay an accurate diagnosis of myocarditis. Echocardiography is usually the most readily available imaging modality in most institutions. Common findings on 2D echocardiography include left ventricular dysfunction in up to 69% of cases as evidenced by segmental wall motion abnormalities. Reversible left ventricular hypertrophy can also be observed in 15% of cases while left ventricular cavity dilatation is usually minimal or absent. In addition, only 23% will have right ventricular involvement.[5] In comparison to our patient, the patient had no heart abnormalities in the echocardiography. Cardiovascular magnetic resonance (CMR) is the only non-invasive imaging modality that can assess for endomyocardial involvement and aid in the initial diagnosis of EM prior to endomyocardial biopsy (EMB).[9] Myocarditis is usually characterised by extensive myocardial hyperintensity on T-2 weighted imaging together with subendocardial delayed enhancement. The good diagnostic accuracy of MRI in myocarditis was highlighted in pooled controlled trials with a sensitivity and specificity of 67 and 91% respectively along with positive and negative predictive values of 91 and 69% respectively.[8]

Nuclear imaging has high sensitivity in detecting evidence of myocarditis. However, they are not frequently recommended for the diagnosis in view of its limited availability and risk of radiation exposure to patients and staff involved.

EMB remains the gold standard investigation for the diagnosis of eosinophilic myocarditis. EMB findings include diffuse myocardial necrosis associated with extensive eosinophilic infiltration of the myocardial interstitium, perivascular infiltration, focal myocyte dissolution and myocardial interstitial fibrosis. However, EMB has a low sensitivity (50%) as eosinophilic infiltration is often focal and this can give rise to sampling errors and false-negative results.[1] According to journal of the American College of Cardiology, EMB is associated with a risk of severe complication such as cardiac tamponade (0.5%), perforation (0.1%) and overall risk of complication is 6%.

Initial treatment goal of patient with EM is haemodynamic stability. Treatment of EM include identifying the underlying cause of EM such as stopping the offending drug and treating the parasitic infection as soon as possible. Standard cardiac failure medication and high dose corticosteroid remain therapy of choice. Corticosteroids therapy has been successfully documented in various case reports such as in three cases presented by Wong et al., all the patients demonstrated complete recovery and normalisation of cardiac contractility after treatment with high-dose oral steroids with gradual tapering.[10]

The usage of intravenous methylprednisolone bolus (1 g/day for 3 days) followed by 1 mg/kg/day oral prednisolone, with gradual tapering for one year demonstrated an improvement in symptoms, such as reduction of eosinophil count and increased ejection fraction as reported by a case report.[11] Our patient was started with tablet prednisolone 20 mg for two months and then continued with tapering dose of prednisolone 10 mg. Some patients with milder form of EM may not require corticosteroid therapy. There is no clear guideline regarding the use, dose and duration of corticosteroid therapy in EM.

CONCLUSION

Eosinophilic myocarditis (EM) remain rare type of myocarditis and possibly underdiagnosed. EM characterised by endocardial injury with elevation of eosinophil count. In setting of patient with persistent eosinophilia and presenting with non-specific cardiac symptoms and findings

(electrocardiogram (ECG), troponin elevation and echocardiogram), EM should be added to the differentials. CMR may assist in earlier diagnosis of EM in patient with peripheral eosinophilia. Treatment modality for EM remain to be finalise.

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We would like to acknowledge the patient for agreeing to publish the case report.

DECLARATION

The authors declare no conflict of interest

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CASE REPORT

Genitourinary tuberculosis: A case report with review of literature

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SUMMARY

The second most frequent extrapulmonary tuberculosis is genitourinary tuberculosis (GUTB). The tuberculosis infection can affect multiple areas of the genitourinary tract. As the presentations of the condition is non-specific, various imaging and laboratory procedures to diagnose GUTB should be considered. As it is difficult to perform a GUTB diagnosis due to the vague presentation in patients, this paper aimed to report and discuss the modalities of GUTB diagnostic investigations and its management. We presented a case of a 31-years-old gentleman with 1 month history of lower urinary tract symptoms, and not responsive to antibiotic treatment. Initial plain radiograph showed opacity at the left lower quadrant. Ultrasound of the kidney, ureters and bladder (KUB) reported a left hydronephrosis and hydroureter. Subsequently, computerised tomography (CT) urography reported left obstructive uropathy. Flexible cystoscopy revealed cystitis changes over the bladder wall with severe trabeculation and turbid urine. Investigation for tuberculosis infection was initiated. Although chest radiograph showed clear lung field with no opacity and tuberculin test was negative, the urine acid fast bacilli staining was finally revealed to be positive. The patient was diagnosed as having GUTB and anti-tuberculous medications were initiated. Patients appearing with chronic urinary symptoms who do not respond to antibiotic treatment should be investigated and treated with caution. Early detection is critical to avoid further damage to the urinary system, and to be followed with proper treatment options which include medical and surgery.

INTRODUCTION

Genitourinary tuberculosis (GUTB) is considered uncommon, but it is the second most frequent and severe form of extrapulmonary tuberculosis.[1,2] It accounts 30 to 40% of extrapulmonary tuberculosis cases and occurs in 2 to 20% of patients with pulmonary tuberculosis.[2] GUTB is more common in developing countries with 15 to 20% cases, compared to developed countries with about 2 to 10%.[2] Human immunodeficiency virus (HIV), chronic renal failure and diabetes mellitus patients have higher risks of contracting GUTB.[3] Clinically, it is important to diagnose GUTB as early as possible as it may prevent further renal destruction.

CASE REPORT

This is a case of a 31-years-old gentleman who was previously healthy. The patient presented with a month history of persistent chronic urinary symptoms, such as, dysuria, increase in frequency and hesitancy. He also complained of left loin pain especially when carrying objects and experienced fever even after he had received three courses of antibiotics from general practitioners. He had no hematuria, no abdominal pain, and did not experience loss of weight and appetite. On examination, he was not cachexic and his lymph nodes were not palpable. There was only mild tenderness over the suprapubic region. The respiratory and neurology assessments were unremarkable, whereas the urine microscopy was positive for leucocyte, protein and blood. The patient had no risk factors for pulmonary tuberculosis such as immunocompromised state or history of exposure to any tuberculosis patients.

Initial plain radiograph showed nonspecific finding. Ultrasound of the kidney, ureters and bladder (KUB) reported left hydronephrosis and hydroureter with focal wall thickening. Subsequently, computerised tomography (CT) urography reported bilateral obstructive uropathy more over the left than the right side. Pooling of contrast was also observed over the left side due to distal obstruction, which can be caused by vesicoureteric lesion with probable differential diagnosis of either mass, soft stone or stricture.

The patient was then investigated for tuberculosis infection. Chest radiograph showed clear lung field with no opacity. The tuberculin test showed 5 mm of induration which was interpreted as negative, as well as the urine culture. Eventually, the urine for acid fast bacilli staining was positive. Unfortunately, histopathology of urinary bladder and Mycobacterium tuberculosis culture of urine were not performed. Consequently, the patient was treated as GUTB-positive. Anti-tuberculous medications were started with Akurit-4 four tablets per day and oral pyridoxine 10 mg daily for 9 months. Repeated urine specimen for acid fast bacilli staining after 1 month on treatment reported negative twice.

During the 6 months of anti-tuberculosis therapy, CT urography was performed to assess the patient's response to treatment. Repeated cystoscopy and retrograde pyelogram showed trabeculated bladder; right ureter opening was wide and golf ball-shaped. From the ultrasound, the bladder was

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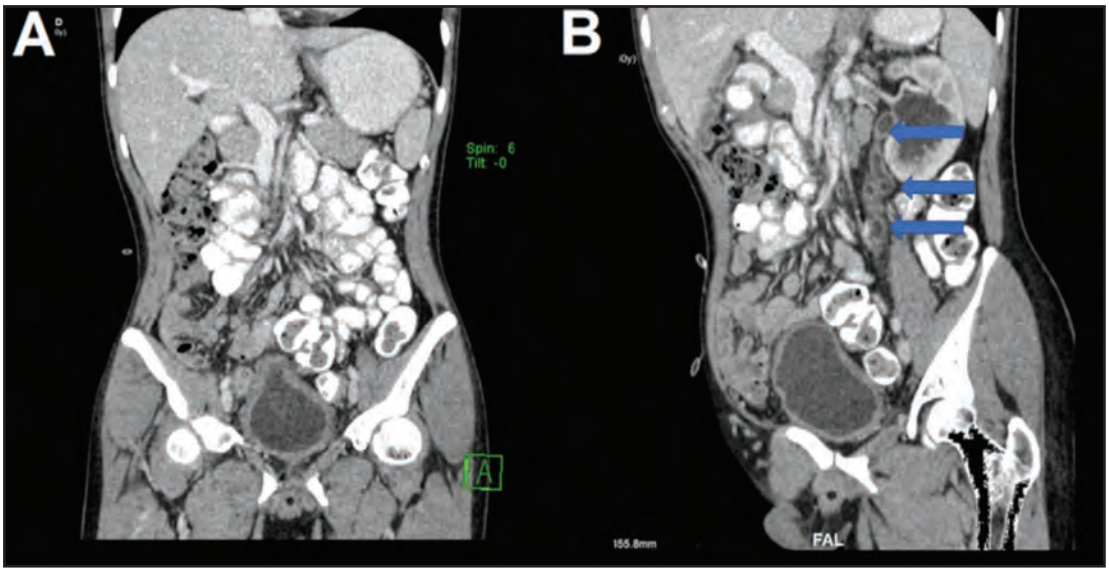

Fig. 1: (A) Image shows abnormal dome-shaped urinary bladder suggestive of neurogenic bladder. (B) The blue arrows in the above picture showed left hydronephrosis.

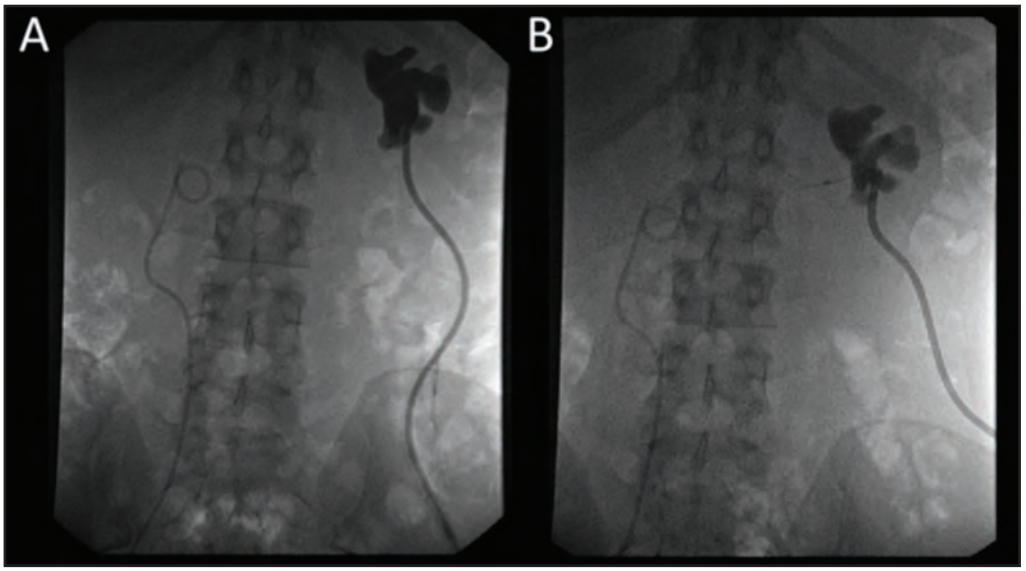

Fig. 2: Left antegrade pyelogram revealed that the patient experienced reducing degree of left hydronephrosis from grade V to grade IV post nephrostomy tube insertion.

found thickened with 430 ml volume which was still within the normal range. Right retrograde pyelogram showed dilated right pelvicalyceal and ureter with kinked proximal right ureter and no ureteric stricture was obvious. However, multiple-length stent was still being used in view of right hydronephrosis. Left retrograde pyelogram was abandoned in view that the left ureter orifice could not be identified during the procedure.

There was a delay in about one month time for left nephrostomy tube in view of the patient having subclinical urinary tract infection. Patient was treated with oral cefuroxime for 1 week. He had nephrostomy tube inserted at the left side. Subsequently, he underwent left antegrade pyelogram which showed left hydronephrosis and hydroureter with abrupt cut off at upper ureter leading to failed antegrade ureteric stenting. This nephrostomy tube is planned for long term. The patient experienced reducing degree of left hydronephrosis post nephrostomy tube insertion (Figure 2). Post-procedure, the patient also developed E. coli ESBL (extended-spectrum beta-lactamases) urosepsis and was treated with intravenous ertapenem for two weeks. White blood cell (WBC) count was initially normal (9 x 10 ^3/uL), but raised to 16 x 10 ^3/uL during the infection and the C-reactive protein (CRP) was high, at 124 mg/L. His CRP later on reduced to 86 mg/L after few days of antibiotic treatment. His previous serum creatinine was 118 umol/L but increased to 155 umol/L during the sepsis episode. But later on, the serum creatinine reduced to 140 umol/L after the infection was controlled. Urine output from

the left nephrostomy tube was also good. No radio-isotope scan was performed to compare both kidney function. We noted that the patient creatinine was increasing in trend from 140 to 200 umol/L in eight months but it remained static after a few months of monitoring. He was planned for a long term left nephrostomy and the tube was changed monthly.

The patient presented eight months later during urology clinic follow up with urinary urgency and acute kidney injury, where serum creatinine increased to 400 umol/L with hyperkalemia but without uremic symptoms. He was still able to pass urine with no abdominal pain and fever. Ultrasound showed echogenic debris within the urinary bladder which may represent cystitis with no significant left obstructive uropathy, and the left nephrostomy tube was in situ. Urine analysis was suggestive of urinary tract infection with WBC in the urine. Complete blood count showed raised WBC 17 x 10 ^3/uL. Urinary catheter was inserted and one litre of urine was drained from the bladder. Urine output from the left nephrostomy tube was around 1.9 L per day. He was treated as neurogenic bladder secondary to GUTB complicated with urinary tract infection. Urine culture grew *Streptococcus, beta-haemolyticus* Group B which is sensitive to penicillin. Intraveneous amoxicillin-clauvenate was started and later changed to oral antibiotic for a duration of one week. He was counselled for clean intermittent self-catherisation (CISC) or suprapubic cystostomy, which he opted for CISC. He was discharged with improved renal profile, where creatinine was reduced to 347 umol/L with good urine output. He was planned to be seen back in the urology clinic after one month but he defaulted urology follow up in view of logistic issues. He subsequently underwent two-weekly changes of urinary catheter in a district hospital. He was also re-diagnosed with hypertension which was probably due to chronic renal disease secondary to GUTB.

DISCUSSION

This case study discussed the diagnosis investigation of GUTB and its management. It is often difficult to infer the diagnosis of GUTB because of the vague presentation in patients. It is important to know the history of previous tuberculous infection either primary pulmonary or extrapulmonary in an individual. There is a latency period that can reach up to 40 years before GUTB is manifested.[2] The symptoms of GUTB are dysuria, nocturia, frequency and chronic urgency of urination; back, flank and suprapubic pain and hematuria. The uncommon symptoms include renal colic, fever, weight loss and night sweat.[4] Patients usually will have abnormal urine microscopy like hematuria, pyuria and albuminuria.[4]

GUTB is caused by the infectious Mycobacterium tuberculosis bacilli which is acquired through inhalation of aerosolised droplet containing the microorganism.[5] The mycobacteria will replicate in alveolar macrophages of the lung, and subsequently metastatically spread hematogenously reaching the genitourinary organ.[1]

GUTB can involve kidneys, ureters, bladder, adrenal gland, male genital, female genitourinary organs and the retroperitoneum.[6] Kidneys can be part of the disseminated infection or localised genitourinary infection which may be present as unilateral or bilateral.[4] The healing process during the course of the infection will result in calcification and fibrosis.[3] This process will result in obstructive uropathy as seen in this patient. Tuberculous infection involving ureters is caused by the spread from kidneys with the ureterovesical junction being the most common site. From the ureteral orifice, this tuberculous infection can extend to the bladder. Further inflammation can cause stricture, rigidity and dilated golf hole-like appearance.[7]

In order to detect M. tuberculosis infection, several diagnostic investigations should be performed. For this patient, the diagnosis was confirmed with urine acid fast bacilli. However, urine acid-fast bacillus smear is often negative, hence might not be reliable as it may be positive for Mycobacterium smegmatis.[4] The diagnosis of GUTB should be made with at least three consecutive early morning urine specimen cultures.[4] Between 10 to 90% of tuberculosis patients have positive urine culture.[3] Polymerase chain reaction (PCR) is also a sensitive and specific diagnostic method for detection of GUTB. Between 25 to 30% of GUTB diagnosis were made from positive culture or histology specimen in combination with M. tuberculosis PCR.[4] A positive tuberculin test supports the diagnosis of tuberculosis, but a negative tuberculin test does not exclude extrapulmonary manifestations.[8]

In GUTB, plain radiograph may show calcifications which occurred in more than 50% of patients.[9] Ultrasound of the urinary tract commonly show involvement of multiple areas in the urinary tract with multiple stages of the disease.[10] For example, the granuloma can be seen as masses and causes distortion of calyces. Cavitations, calcification of kidney and nephrocutaneous fistula can also be seen.[10] CT scan can detect calcifications, distortion of anatomy such as hydronephrosis, renal parenchymal lesions and scars, and the extent of extrarenal infection.[10] Retrograde pyelography may be used to determine the length of the stricture and the severity of the obstruction and dilatation above the stricture.[4] Cystoscopy should be performed to look for cystitis changes and to exclude tumours. Bladder biopsy can be done in patients with tubercles or ulcers distance from a normal ureteral orifice as is needed to exclude carcinoma.[4] Histopathology is also very useful to assist in diagnosing GUTB. In a recent study conducted in Sabah, Malaysia, 52.9% of GUTB cases were confirmed via histopathological assessments.[11] Admittedly, the limitations found in this case is that mycobacterium urine culture and bladder biopsy were not performed. Both assessments are of paramount importance and should be performed in future cases to improve investigation and management for similar conditions.

The treatment for GUTB using anti-tuberculous drugs is generally for 6 months.[1,12] In complicated cases, the treatment may take 9 to 12 months, such as in recurrences of tuberculosis and in immunosuppressive patients. For multidrug resistance tuberculosis (MDR TB) which is defined as resistant to rifampicin and isoniazid, it requires the use of at least four drugs that are selected based on drug susceptibility test. The duration for MDR TB also depends on the susceptibility of the drugs.[12]

Surgical management in GUTB accounts to about 0.5% of urological procedures.[13] Ablative surgery is also one of the treatment available especially in complicated GUTB with abscess and non-functioning kidneys. Examples of ablative surgery are nephrectomy and partial nephrectomy.[4] Reconstructive surgery such as repair of strictures at the lower end of ureter and bladder augmentation are usually performed after at least four weeks of anti-tuberculosis medications.[7] Early ureteral stenting or percutaneous nephrostomy (PCN) in tuberculous ureteral strictures decreases the chance for renal loss and increase the chance for later reconstructive surgery.[14]

CONCLUSION

There should be high suspicion for patient presenting with chronic urinary symptoms and not responding to antibiotics treatment. Early diagnosis is essential to prevent further destruction of the urinary system as multiple modalities of treatments are available nowadays.

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DECLARATION

The authors declare no conflict of interest.

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CASE REPORT

A young lady with massive black pleural effusion and a yellow pleura

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SUMMARY

A young lady presented to the out-patient department with a massive right pleural effusion. The cause remained unknown despite initial investigations and pleural fluid evaluation. She underwent a medical thoracoscopy which revealed black pleural fluid and dull thickened pleura with diffuse yellow plaques. The biopsy was suggestive of xanthomatous pleuritis, but the cause remained elusive. On further evaluation, pleural fluid amylase was found to be very high and magnetic resonance cholangio-pancreaticography (MRCP) demonstrated a pancreatic pseudocyst with a pancreatico-pleural fistula (PPF). Black coloured pleural fluid and xanthomatous pleuritis are rare features seen in pleural effusion secondary to PPF. Such patients generally have no abdominal complaints at presentation and hence a high index of suspicion is essential for diagnosis.

INTRODUCTION

The cause of a pleural effusion can remain unclear in many cases despite a detailed clinical history, physical examination, and pleural fluid analysis. Invasive procedures such as medical thoracoscopy or video assisted thoracoscopic surgery (VATS) should be considered in such patients. No diagnosis is ever established for approximately 15 percent of patients despite invasive procedures.[1] Black pleural effusions are rare with only 32 cases being reported to date. The cause of such effusions include malignancy, pleuro-pancreatic fistula, fungal infection, crack cocaine induced pleural effusion, Boerhaave hydropneumothorax, bronchopulmonary fistula and thoracic endometriosis.[2] Here we present an interesting case of a young female patient with a massive right sided black pleural effusion.

CASE REPORT

A female patient in her twenties presented to our out-patient department with a one-month history of dull, non-radiating right sided chest pain, dry cough, and progressively worsening dyspnea, which was now limiting her from walking up a slope or climbing stairs. She also had loss of appetite and generalised weakness. She denied history of fever, weight loss, or hemoptysis. There was no history of trauma or history of lifting heavy weights. She denied history of tuberculosis or recent contact with a tuberculosis patient. She had no history of recurrent respiratory tract infections, bronchial asthma, diabetes mellitus or cardiac disease. She denied smoking or consuming alcohol.

She was on regular thyroxine supplementation for hypothyroidism. She was diagnosed to have an ovarian cyst two months ago when she presented with abdominal pain and for which she underwent a laparoscopic cyst excision, which was confirmed to be a simple ovarian cyst.

She was initially evaluated at a local medical center where blood investigations revealed mildly elevated leucocyte count of 12450/ mm^3 and an elevated erythrocyte sedimentation rate (ESR) of 106mm/hr. Renal and liver function tests were normal. Chest radiograph revealed a white out right hemithorax (Figure 1A) which was confirmed to be a massive right pleural effusion by ultrasonography.

She underwent a diagnostic thoracentesis and 200 ml of dark coloured fluid was aspirated (Figure 1B). Results of pleural fluid aspiration were as follows: protein of 3.4 g/dl (total serum protein: 6.0 g/dl); sugar of 138mg/dl; total white blood cell count of 160/mm^3 (80% neutrophils) and adenosine deaminase (ADA): 28 U/L (normal: 0–40 U/L). Pleural fluid cytology was negative for malignant cells. Pleural fluid bacterial culture, fungal smear and geneXpert MTB/Rif were negative. She was referred to our centre for medical thoracoscopy as she had an undiagnosed, exudative pleural effusion.

On initial examination, her vital parameters were as follows: temperature 37.2^{0}C; pulse rate 96 beats/minute; respiratory rate: 20 breaths/minute; blood pressure 108/64 mmHg; oxygen saturation 97% on room air. She had no pallor, cyanosis, icterus, or lymphadenopathy. She did not have pedal oedema or signs of increased jugular venous pressure. On respiratory system examination, percussion revealed a dull note over the entire right hemithorax. Breath sounds and vocal resonance were decreased in the entire right hemithorax. Other systems examination was normal.

Computed tomography scan (CT scan) of the chest revealed a massive right pleural effusion with collapse of the underlying lung. No evidence of pleural thickening, parenchymal lesions or mediastinal lymphadenopathy was seen.

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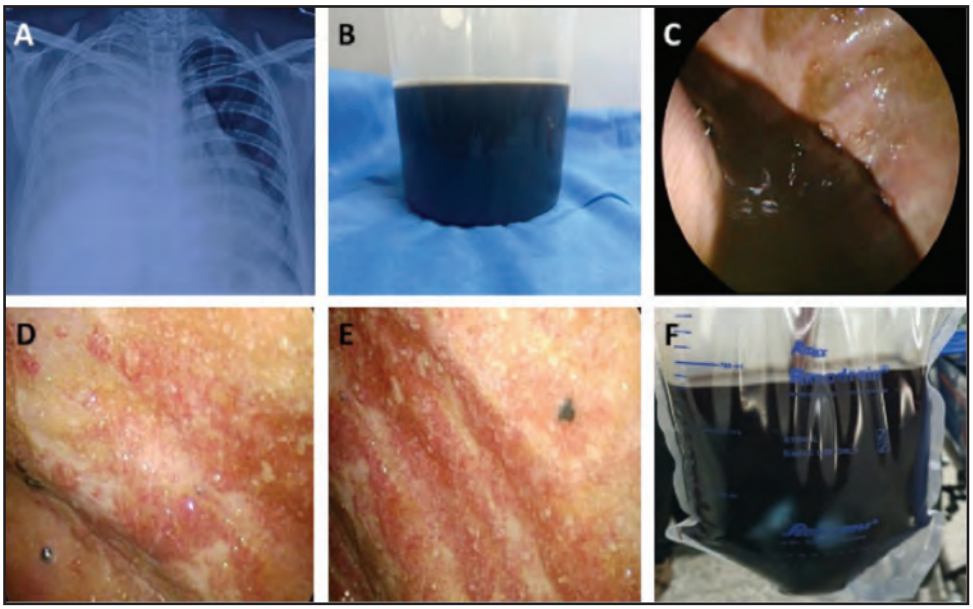

Fig. 1: A) Chest x-ray (PA view) showing complete white out right hemithorax with contralateral mediastinal shift. B) Black coloured pleural fluid obtained during diagnostic thoracocentesis. C) Black coloured pleural fluid visualised within the pleural cavity during medical thoracoscopy. D), E) Dull, thickened pleura with diffuse, yellow-coloured plaques and multiple small nodules seen on medical thoracoscopy. F) Black coloured pleural fluid collected in under water seal bag, connected to intercostal drain.

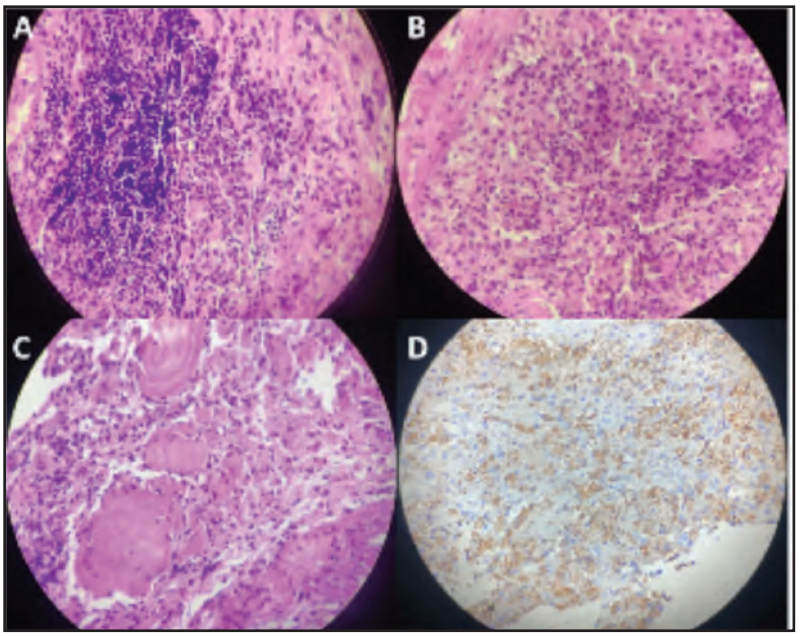

Fig. 2: A) Photomicrograph showing markedly inflamed pleural tissue with lymphocytes and plasma cells, original magnification 40X (H&E stain). B) Photomicrograph showing aggregates of foamy macrophages with lymphoplasmacytic cells, original magnification 40 X (H&E stain). C) Photomicrograph showing fibrinoid necrosis and inflammatory infiltrate within the pleural tissue, original magnification 40X (H&E stain). D) Photomicrograph shows aggregates of foamy macrophages diffusely positive for CD 68, original magnification 40 X (H&E stain).

After taking informed consent, medical thoracoscopy was performed. Procedure was performed under sedation and intercostal nerve block using a Karl Storz mini-rigid thoracoscope. Thoracoscopy revealed black coloured fluid in the pleural space (Figure 1C) and dull, thickened pleural with diffuse yellow plaques and small nodules (Figure 1D,1E). During the procedure, 1800 ml of black coloured pleural fluid was drained (Figure 1F), and ten parietal pleural biopsies obtained from abnormal areas. Microscopic examination of the pleural biopsy showed markedly inflamed pleural tissue with aggregates of foamy macrophages and lympho-plasmacytic cells with few scattered eosinophils (Figure 2A, 2B). Capillaritis, microthrombi, hemosiderin laden macrophages and fibrinoid necrosis were also seen (Figure

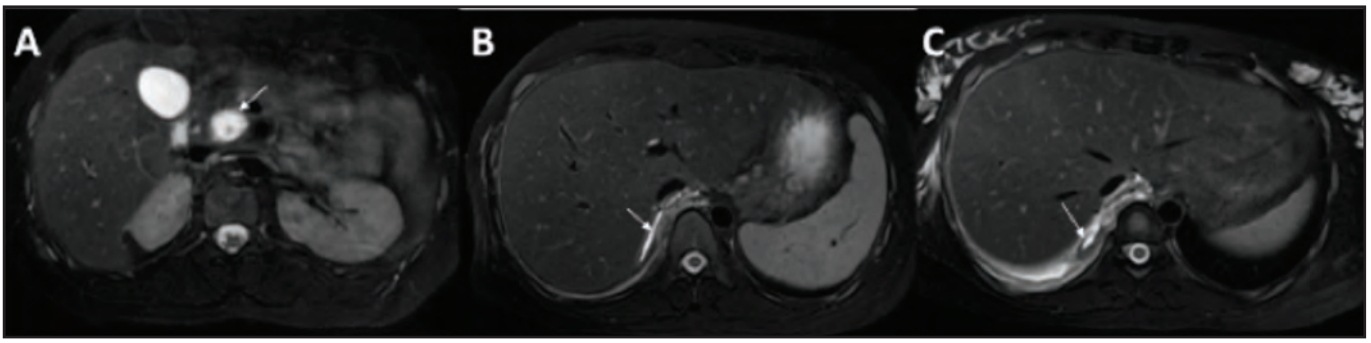

Fig. 3: A) Image of magnetic resonance cholangio-pancreaticography (MRCP) showing a pseudocyst (white arrow) in the region of uncinate process. B) Image of MRCP showing a fistulous tract (white arrow) along the crus of the diaphragm in the midline. C) Image of MRCP showing a fistulous tract opening into the right pleural cavity (white arrow).

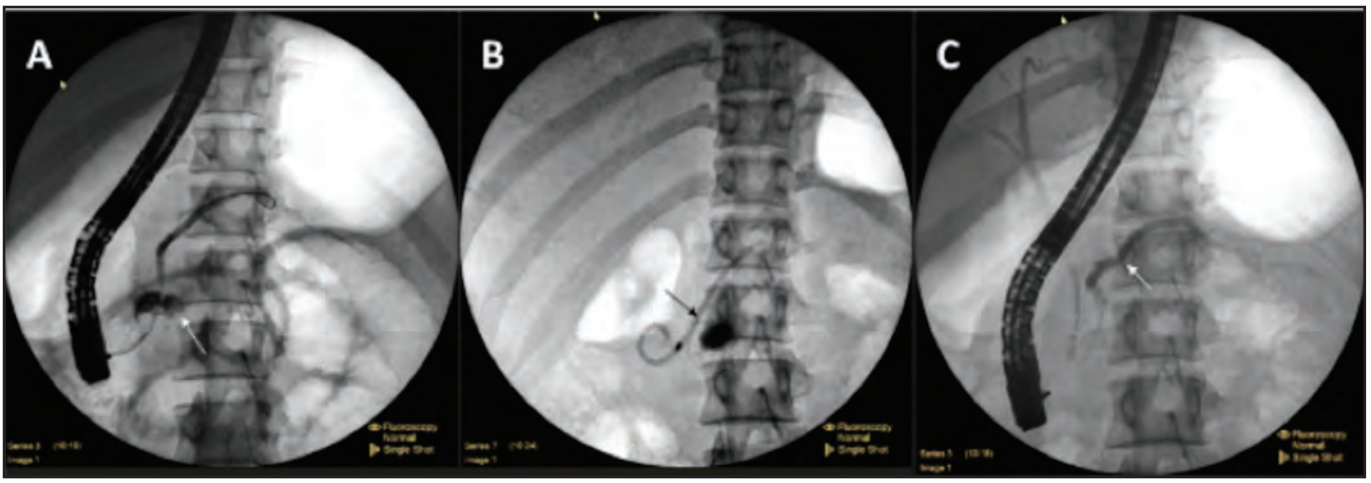

Fig. 4: A) Fluoroscopy image of endoscopic retrograde cholangio-pancreaticography (ERCP) showing a pancreatic duct communicating with the pseudocyst (white arrow). B) Fluoroscopy image of ERCP showing the stent in situ in the pancreatic duct (Black arrow). C) Fluoroscopy image of ERCP showing normal pancreatic duct (white arrow) and resolution of the pseudocyst.

2C). There were no granulomas or atypical cells. Immunohistochemistry revealed CD68 positive foamy macrophages (Figure 2D). A histopathological diagnosis of xanthomatous pleuritis was made. Post-procedure a 24 Fr intercostal chest was placed, and her daily pleural fluid drain output ranged from 500 ml to 700 ml. The cause of her pleural effusion remained unclear.

In view of the history of abdominal pain and black coloured pleural effusion, the possibility of pleural effusion secondary to pancreatitis was entertained. Pleural fluid amylase was performed and found to be very high (103420 U/L). Serum amylase and lipase were mildly elevated at 157 U/L and 511 U/L, respectively. Serum calcium and serum triglycerides levels were within normal limits. In view of her very high pleural fluid amylase levels (>50,000 U/L), a possibility of pancreatico-pleural fistula (PPF) was considered.

To confirm PPF, magnetic resonance cholangio-pancreaticography (MRCP) was performed. It demonstrated a well-defined collection measuring 3.6 x 2.1 cm with internal debris in the region of the uncinate process, which was likely to be a pseudocyst (Figure 3A). A linear tract was seen extending posteriorly from this pseudocyst and coursing along the crus of the diaphragm in the midline and communicating with the right pleural cavity (Figure 3B, 3C). There was no evidence of calculi or sludge in the gall bladder and biliary tree. In view of the above findings a diagnosis of xanthomatous pleuritis secondary to a pancreatico-pleural fistula caused by idiopathic pancreatitis was made.

Patient underwent an endoscopic retrograde cholangio-pancreaticography (ERCP) which showed the pancreatic duct communicating with the pseudocyst (Figure 4A). Sphincterotomy was performed and a 5fr, 7cm pigtail stent was placed in the pancreatic duct (Figure 4B). Soon after the pancreatic duct stenting the daily quantity of pleural fluid drained, started to decrease. Intercostal drain was removed after 10 days when pleural fluid drain decreased to less than 50ml/day for 3 consecutive days and after ultrasonography of the chest showed no residual pleural effusion.

Patient is currently under regular follow up with no recurrence of abdominal pain or pleural effusion. The pancreatic duct stent was removed after 3 months when repeat pancreaticogram showed resolution of the pseudocyst (Figure 4C).

Table I: Clinical details of published cases with black pleural effusion due to pancreatico-pleural fistula

	Author/Year	Age/Sex	Symptoms at presentation	Side of effusion	Pleural fluid Amylase	Mode of Diagnosis	Treatment
1	Koide *et al*/2012	54/M	Dyspnoea	Left	5292 IU/L	CT scan	Conservative
2	Huang *et al*/2013	47/F	Dyspnoea	Left	53600 IU/L	CT Scan	Conservative
3	Kaur *et al*/2014	37/F	Dyspnoea/Chest Pain	Right	23000 U/L	CT Scan	ERCP-Pancreatic Duct Stenting
4	Mookherjee *et al*/ 2014	37/F	Right Chest pain/ Dyspnoea	Right	26673 IU/L	MRCP	ERCP-Pancreatic Duct Stenting
5	Hirosawa *et al*-2016	58/M	Left Chest pain/ Dyspnoea	Left	10649 IU/L	CT Scan/ERCP	ERCP-Pancreatic duct stenting
6	Guo e*et al*/2017	14/F	Cough, Right Chest Pain	Bilateral Right>Left	NA	MRCP	Surgery
7	Ishigaki *et al*/2018	54/M	Asymptomatic	Right	4752U/L	CT Scan/ERCP	NA
8	Index case	26/F	Dyspnea, dry cough and dull chest pain	Right	103420 U/L	MRCP	ERCP-Pancreatic duct stenting

CT: Computed tomography; ERCP: Endoscopic retrograde cholangio-pancreaticography; IU/L : International units per litre; MRCP: Magnetic resonance cholangio-pancreaticography; NA: Not available.

Table II: Clinicoradiologic details, diagnosis and outcomes of reported cases of xanthomatous pleuritis.

Sl. No	Author/year	Age (Years)/ Sex	Symptoms at presentation	Radiology	Pleuroscopic appearance	Final Diagnosis	Treatment received/ Recurrence at follow up
1	McGuire et al/ 2009	69/Female	Pleuritic chest pain, dyspnea	Massive Left PE	Two plaques with petechial hemorrhage	Unclear	Steroids/ No recurrence at 18 months
2	Singh et al/ 2018	21/Male	Dyspnea, chest pain	Moderate Left PE	Greyish pigmented pleura	Unclear Unclear	Oral amoxicillin 6 weeks/ No recurrence at 3 months
3	Bateman et al/ 2020	54/Male	Dry cough, dyspnea, joint pains	Moderate Left PE	Diaphragmatic mass with yellow pleural plaques	Unclear	Oral steroids/ Recurrence at 10 months
4	Nakashima et al/ 2022	62/Male	Dyspnea	Left PE	Diffuse yellow plaques	Pancreatico-Pleural Fistula	Distal pancreatectomy/ Follow up details NA
5	Augustine et al/ 2022	27/Female	Dyspnea, Chest Pain, Fever	Moderate Left PE	Xanthomatous Pleuritis	Tubercular Pleural Effusion	Anti-Tubercular Treatment/ No recurrence at 1 year
6	Present report	24/Female	Dyspnea, dry cough and dull chest pain	Massive Right PE	Diffuse yellow plaques	Pancreatico-Pleural Fistula	ERCP pancreatic duct stenting/ No recurrence at 6 months

ERCP: Endoscopic retrograde cholangio-pancreatiography; NA: Not available

DISCUSSION

Pleural effusions are a common complication of pancreatic disease with the latest reports suggesting that they occur in nearly 50% of the patients with acute pancreatitis. Various mechanisms have been described for the development of pleural effusion which includes transdiaphragmatic lymphatic blockage, exudation of fluid into the pleural cavity from the subpleural diaphragmatic vessels and formation of pleuro-pancreatic fistula.[3]

Black pleural effusion or soy sauce pleural effusion has been reported in only 32 cases to date. The causes of black pleural effusion range from malignancy (14 patients), pleuro-pancreatic fistula (8 patients), acute pancreatitis (1 patient), fungal infections (3 patients), crack cocaine induced pleural effusion (2 patients) Boerhaave hydropneumothorax, bronchopulmonary fistula and thoracic endometriosis (1 patient each).[2] Clinical details of cases of PPF leading to black pleural effusion are shown in Table I.

In patients with pancreatico-pleural fistula, necrotic pancreatic and ascitic fluid traverse the fistulous connection to reach the pleural cavity resulting in a black coloured pleural effusion.[4,5] The most common presenting symptom in these patients was dyspnoea followed by chest pain, cough, fever, and abdominal pain. Seven patients had exudative effusion while one had transudative effusion. Recurrence was seen in four patients and one patient died.[2]

Pancreatic fistulas are rare and usually seen as a complication of alcoholic pancreatitis.[6] They are seen in 0.4% to 7% of chronic pancreatitis patients and in 6% to 14% of patients with pancreatic pseudocyst.[7] Pancreatico-pleural fistulas develop either as a consequence of pseudocyst rupture or disruption of posterior wall of the pancreatic duct.[8] It is usually seen in middle aged men, and they present with pulmonary symptoms. Up to half of them have no history of pancreatitis. Our patient was a young female with no addictions. While she had a history of abdominal pain

attributed to an ovarian cyst previously, she had no abdominal complaints at presentation.

Pancreatico-pleural fistulae related pleural effusions are usually moderate to massive and predominantly left sided. Right and bilateral pleural effusions are seen in 19% and 14% of the patients, respectively. Pleural fluid analysis usually reveals an exudative pleural effusion with extremely elevated pleural fluid amylase levels.[9] While high amylase can be seen in many conditions such as acute pancreatitis, oesophageal rupture, lymphoma and other malignancies, levels above 50,000U/L are seen only in PPF. MRCP is the diagnostic modality of choice as it is non-invasive and demonstrates the fistulous connection, pancreatic parenchymal and ductal structural changes, and the presence of intra or extra pancreatic pseudocysts.[10]

Xanthomatous inflammation is a rare, benign type of chronic inflammation which has generally been reported from organs such as the kidney, gall bladder, appendix, prostrate etc. It is characterised by the presence of foamy macrophages admixed with lymphocytes, plasma cells, neutrophils, and multinucleated giant cells.[11] Xanthomatous inflammation of the pleura is extremely rare with only five cases[12-15] being reported till date (Table II) of which only one was secondary to PPF. Like in the previous case report, our patient had diffuse yellow plaques over the pleural surface.[15] Chronic inflammation secondary to presence of pancreatic enzymes in the pleural cavity and the overwhelming of the lysosomal system of the macrophages due to the ingestion of erythrocytes and platelets from the haemorrhagic effusion causing deposition of phospholipids, are likely to be the mechanisms of xanthomatous inflammation of the pleura secondary to PPF.[18 -23] Ours is the first case to be reported of a black pleural effusion with xanthomatous pleuritis, secondary to PPF.

PPF can be managed medically, endoscopically, and surgically. Medical management consists of pleural fluid drainage and reducing pancreatic exocrine secretions using a combination of octreotide and total parenteral nutrition. The success rate of medical management is moderate, and failure leads to higher rate of complications and prolonged treatment. ERCP with pancreatic duct stenting is the current treatment of choice and can be combined with octreotide administration. It aims to restore the anatomic continuity of the pancreatic duct to provide a path of lower resistance for the pancreatic secretions to flow into the duodenum allowing time for the fistulous connection to heal. Surgery is used as a last resort, only if medical and endoscopic management fails.[9,10] Our patient was successfully managed with pleural fluid drainage using intercostal drain and pancreatic duct stenting.

CONCLUSION

Black pleural effusion is a rare presentation of PPF. It can present as a right sided pleural effusion with no abdominal complaints. Having a high index of suspicion is essential. Presence of black coloured pleural effusion, a very high amylase level (>50,000 U/L) and/or yellow plaques on pleura should raise the suspicion of a PPF, and it should be evaluated accordingly. MRCP is the diagnostic modality of choice, and PPF can be successfully managed with minimally invasive endoscopic techniques.

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DECLARATION

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Asymptomatic fasting hyperglycaemia, a case of Glucokinase maturity onset diabetes of the young with a novel mutation

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SUMMARY

Maturity onset diabetes of the young (MODY) is not commonly encountered in clinical practice. It is rare and can be difficult to differentiate from type 1 and type 2 diabetes. To confirm the diagnosis, genetic testing must be done which is not readily available and is expensive. This patient presented with asymptomatic fasting hyperglycaemia and was previously diagnosed to have type 2 diabetes. Further investigations showed that she had normal β−cell function and normal insulin resistance. Diabetic autoantibodies were all negative. Confirmatory genetic testing was done and she was found to have a genetic variant at the glucokinase gene at Exon 7, c.830T>G (p.Val277Gly). Screening of the patient's father also revealed the same genetic variant, showing an autosomal dominant pattern of inheritance. This clinical case illustrates a patient that was misdiagnosed to have type 2 diabetes and confirmed with genetic testing to have glucokinase MODY. This changes the clinical management of the patient as no further treatment and investigation is required as there are no lifelong consequences of developing complications of diabetes.

INTRODUCTION

Maturity onset diabetes of the young (MODY) is a rather rare form of diabetes which is a separate entity from type 1 and type 2 diabetes. It is inherited in an autosomal dominant fashion and typically presents before the age of 25.[1] Genetic mutations result in diabetes due to their effects on β–cell dysfunction.[2]

To date there have been at least 13 genes identified that cause MODY and additional genes exist that are yet to be identified.[3] Mutations in the glucokinase (GCK), hepatocyte nuclear factor 1 alpha (HNF1A), hepatocyte nuclear factor 4 alpha (HNF4A) and hepatocyte nuclear factor 1 beta (HNF1B) genes are the most common causes of MODY, and they account for 32%, 52%, 10%, and 6%, respectively, of cases in the United Kingdom (UK).[3] The prevalence of these causes varies in different countries. In countries where glucose testing is done more frequently to screen for diabetes, GCK mutations predominates in these countries, such as France, Germany, Italy and Spain.[2]

Patients with GCK MODY mutation also known as MODY 2, usually present with asymptomatic fasting hyperglycaemia, which is present from birth and remains stable throughout life. One of the challenges in diagnosing MODY is distinguishing it from type 1 and type 2 diabetes as clinical features are similar and features may overlap.[2] Presentation of patients with GCK MODY are usually incidental as the mild hyperglycaemia does not lead to any overt symptoms and findings of a raised fasting glucose are usually incidental during a health check-up.[5]

This clinical case illustrates a young patient who was misdiagnosed as type 2 diabetes mellitus and was confirmed to have GCK MODY.

CASE REPORT

A 31-years-old lady was referred to the general medical clinic for further management of young type 2 diabetes. She was previously diagnosed to have type 2 diabetes and started on Metformin 500 mg twice daily by a private health clinic. Further questioning revealed that she had known to have abnormal fasting glucose since the age of 20 when she went for a general health screening. Over the past 10 years, she has monitored her fasting glucose and reported it to range from 6.8 to 7.1 mmol/L. However, as she felt well with no symptoms she did not think to investigate further. She has a strong family history of diabetes, with both her parents diagnosed to have type 2 diabetes on treatment. All her maternal relatives were also diagnosed to have type 2 diabetes. Her paternal family history was not known as her father was adopted.

Physical examination showed that she was a slim lady with a BMI of 17. Her waist circumference measured was 64 cm. Other systemic examinations were unremarkable.

Blood investigations were ordered as summarised in Table I. Elevated fasting glucose at 7.4 mmol/L with a HbA1c reading of 6.4% were diagnostic of type 2 diabetes. Diabetic autoantibodies were not detected. As she did not fit the clinical phenotype of a patient with type 2 diabetes, further testing was done.

A glucagon stimulation test (GST) was done to assess the pancreatic β–cell function. Glucagon 1 mg was given, and glucose, C-peptide and insulin levels were taken at 0 min and 6 min after administration. The results of the C-peptide and insulin are as summarised in Table II. The GST showed that she had normal β–cell function.

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Table I: Summary of investigations

Investigations	Results
Fasting glucose	7.4 mmol/L
HbA1c	6.4%
Anti-islet cells	0.34 IU/ml (Negative)
Anti-glutamic acid decarboxylase (GAD)	0.99 IU/ml (Negative)
Anti-insulinoma-associated antigen 2(IA2)	0.94 IU/ml (Negative)

Table II: Glucagon stimulation test results

	0 min	6 min
Glucose	7.0 mmol/L	8.4
C-peptide	331 pmol/L	1252 pmol/L
Insulin	22.4 pmol/L	

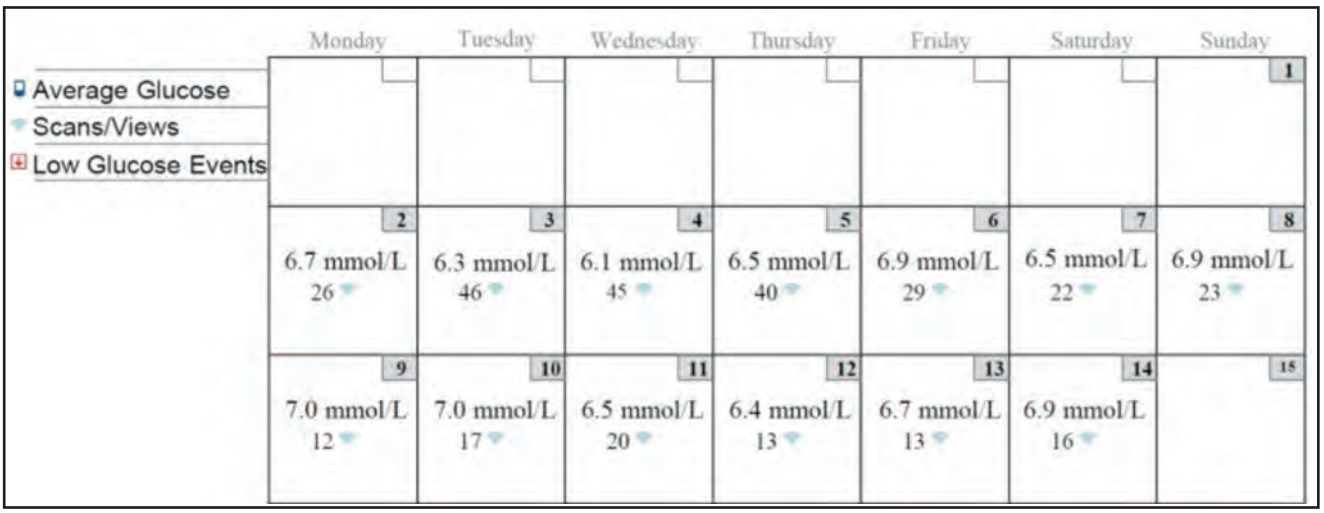

Fig. 1: Average blood glucose over 2 weeks duration

Assessment for insulin resistance was measured using the homeostasis model assessment of insulin resistance (HOMA-IR). By using the values of her fasting insulin and glucose, her calculated index was 0.9 which shows normal insulin resistance.

Medications were withheld and she was offered continuous glucose monitoring for 2 weeks to monitor her glucose trend (Figure 1). Average glucose trends ranged from 6.1 to 7.0 mmol/L.

She was informed on genetic testing for MODY as her clinical presentation did not fit type 1 or type 2 diabetes. Genetic testing would be done at a private lab in the United States and would have to be self-funded by the patient. She agreed for genetic testing to assess for MODY.

Results from the genetic testing showed that the patient was found to have a heterozygous mutation of the GCK gene at Exon 7, c.830T>G (p.Val277Gly). Further genetic screening of both her parents revealed that her father carried the same genetic variant. This genetic variant has not been reported in literature in individuals affected with GCK MODY and is not present in population databases such as the gnomAD database.

She was then confirmed to have GCK MODY and thus did not require any treatment. She continued to be asymptomatic and was told to inform if she planned to get pregnant, as she may require treatment during pregnancy.

DISCUSSION

GCK was the first gene to be identified to cause MODY in French and UK populations in 1992.[6] GCK MODY is characterised by persistent mild asymptomatic fasting hyperglycaemia, absence of autoimmune antibodies for type 1 diabetes, good β–cell function and an autosomal dominant mode of inheritance.[6] Among cases in the UK, GCK MODY was the second most common form of MODY.[3] In Japan, a study showed that among paediatric onset MODY, GCK mutation was the most common form of MODY detected.8 To date, there are no studies in Malaysia that analysed the prevalence of MODY in our population.

Clinical suspicion of MODY is usually characterised by non-obesity, onset before 25 years of age and positive family history suggestive of dominant inheritance.[7] This patient was underweight, known to have mild hyperglycaemia since the age of 20 and had a strong family history of diabetes, therefore genetic testing was considered in her case. Genetic testing confirmed that she inherited the GCK variant from

her father, however further details on her paternal family were unknown as her father was adopted. Although the gene is inherited from an affected parent, there may be no positive family history of diabetes if no prior screening of the parents were done to diagnose diabetes.[5] Therefore, when suspecting MODY as a diagnosis for a patient, screening of the parents with fasting glucose or HbA1c readings would be helpful.

Patients who are diagnosed to have diabetes at a young age, strong family history of diabetes, have negative diabetic autoantibodies and do not fit a diagnosis of type 1 or type 2 diabetes should be considered for genetic testing for MODY. In China, a study in a single centre was conducted which showed that from 587 children with newly diagnosed diabetes mellitus, only 11 children fit the clinical criteria for a diagnosis of MODY and genetic testing showed GCK mutations in 9 out of the 11 children tested.[4] However, in Malaysia, genetic testing is not readily available and is expensive. Furthermore, type 2 diabetes is very common in Asian populations causing difficulty in differentiating it from MODY. Therefore, genetic testing should be considered on a case-to-case basis.

Patients with GCK MODY generally do not require treatment and the mild hyperglycaemic does not lead to long term microvascular complications.[3] The only exception is during pregnancy where treatment with insulin may be required. If the foetus does not inherit the GCK mutation, it will produce more insulin in response to the maternal hyperglycaemia which will cause excess foetal growth.[2] Patients with GCK MODY are at the same risk as the general population in developing type 1 or type 2 diabetes and if this occurs, achieving glycaemic levels below their normal hyperglycaemic levels is very difficult.[5]

Although GCK MODY is rare, the diagnosis would have important implications towards treatment modalities, prognosis and follow up of those affected by it.[3] Many clinicians in the primary health care are unfamiliar with this condition and may diagnose a patient as either type 1 or type 2 diabetes if they presented to their clinics. Making a diagnosis of GCK MODY is essential to avoid unnecessary treatment and investigations.[5]

Confirmatory testing to diagnose MODY is through genetic testing. If an individual is diagnosed to have GCK MODY, family screening is recommended in those who are diagnosed to have diabetes.[5] Family members who were previously thought to have type 1 or type 2 diabetes may be able to stop treatment if the GCK mutation is detected.

The patient was able to afford genetic testing and was found to have a mutation at the GCK gene at Exon 7, c.830T>G (p.Val277Gly). More than 600 abnormal GCK gene mutations have been documented.[4] This variant was not previously reported in literature in patients affected with GCK MODY. However, in this case, it is likely a pathogenic variant as the patient exhibits typical features of GCK MODY. Further testing of her siblings should be done to determine if they carry the same genetic variant.

CONCLUSION

In a young patient aged less than 25 who presents with hyperglycaemia, is not obese, and has a positive family history of diabetes, a clinical suspicion of Maturity onset diabetes of the young (MODY) should be considered. A detailed history especially family history should be obtained, and further investigations should be considered, such as genetic testing. The diagnosis of MODY is very important to the patient and their family as it changes their clinical course and long-term prognosis.

CONFLICT OF INTEREST

None

DECLARATION

Informed consent was taken from the patient for publication of this case report. There are no competing interests.

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CASE REPORT

Molluscum contagiosum associated immune reconstitution inflammatory syndrome in human immunodeficiency virus infection treated with trichloroacetic acid 80% and imiquimod 5% cream

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SUMMARY

Urgency in treating molluscum contagiosum (MC) is still controversial due to its efficacy, especially when MC is associated with either human immunodeficiency virus (HIV) or immune reconstitution inflammatory syndrome (IRIS). Despite its manifestation as a benign skin disease that is mostly transmitted sexually, it has a negative impact on quality of life for the patient that is infected due to its cosmetical aspect. We reported a case of MC with HIV on highly active antiretroviral therapy (HAART) that was treated with trichloroacetic acid (TCA) 80% on body and imiquimod 5% cream on the face. In four weeks, improvement was more visible on TCA 80%. HIV on HAART may interfere the improvement of the lesion.

INTRODUCTION

It is estimated that 5 to 18% of human immunodeficiency virus (HIV) patients experienced molluscum contagiosum (MC) when $CD4^+$ levels are below 100 cells/µL. MC has been a predictor of weak immunity in HIV patients and is associated with immune reconstitution inflammatory syndrome (IRIS).[1,2] In cases of serious disease and aesthetic complaints, there are several therapeutic options for MC, including physical destruction, topical keratolytic agents, and topical immunomodulators. Trichloroacetic acid is a keratolytic agent that is often used in the treatment of MC. Meanwhile, another option is imiquimod, a topical immunomodulatory agent that stimulates local innate and adaptive immunity in lesions. The choice of therapeutic modality in MC with HIV has its own challenges regarding the therapeutic efficacy and side effects that differ from immunocompetent patients.[3,4]

CASE REPORT

A female, age 22 years old, complained of skin-coloured bumps since July 2021. Initially, only one lesion appeared on the face, and over time, the lesion increased accompanied by itch, sore or painful at the same time. The patient reported that when the lesion was pressed by hand, white patches such as rice came out of the lesions. But no medication was taken regarding to the bumps. She suffered prolonged fever and weight loss in December 2021. She was diagnosed with HIV and had a two-cell/UL CD4 count in January 2022. Highly active antiretroviral therapy (HAART) consisted of tenofovir 300 mg, lamivudine 300 mg and dolutegravir 50 mg were given daily. Due to the bumps still persisting, she consulted a dermatologist and was given 20% potassium hydroxide topically on the lesion every night for two weeks, but there was no improvement.

On the face, right breast, right infra mammary, inguinal, right and left labia, inferior abdominal, right and left femoral, right and left gluteus, were multiple papules, skin coloured, firm borders, round to oval, diameter 0.3 to 0.8 cm, shiny smooth surface with central umbilication, with discrete configuration. The treatment was 80% trichloroacetic acid (TCA) solution topically on MC lesions regularly every week on majority of the lesions (except face) and 5% imiquimod cream every two days on facial lesions.

During the sixth week of treatment, the patient still complained of several new lesions appearing on the face. In May 2022, the CD4 count was 115 cells/µL. On the face, right breast, right infra mammary, inguinal, right and left labia, inferior abdominal, right and left femoral, right and left gluteus, there were multiple papules, skin coloured, firm borders, shaped round to oval, diameter 0.3 to 0.8 cm, shiny smooth surface with central umbilication, and discrete configuration. On the right infra mammary, posterior abdomen, right and left femoral were multiple hyperpigmented macules, well defined round to oval in shape, 0.3 to 0.8 cm in diameter, with discrete configuration. The treatment was continued until all lesions disappeared.

DISCUSSION

Before starting treatment, it is important to discuss the risk and benefit to the patient because MC is a naturally benign condition and resolves without complications in immunocompetent patients. Treatment may be required for

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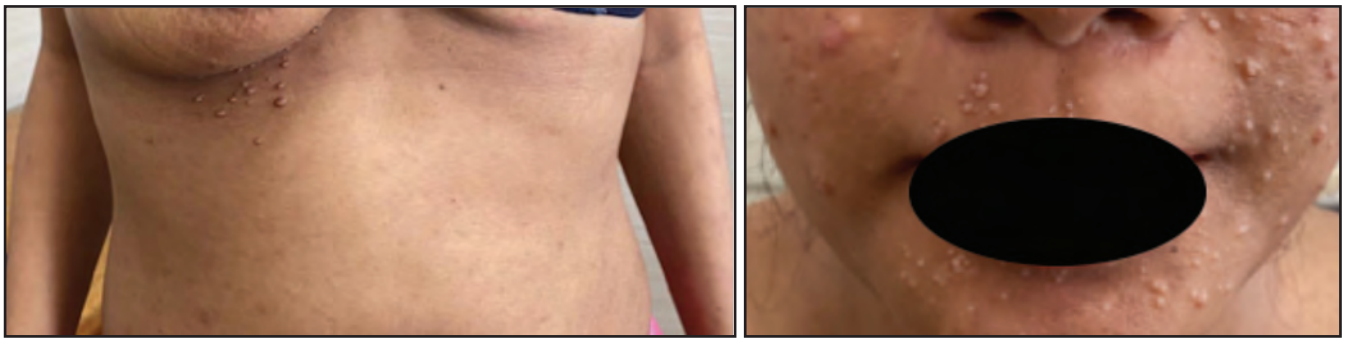

Fig. 1: Lesions before treatment

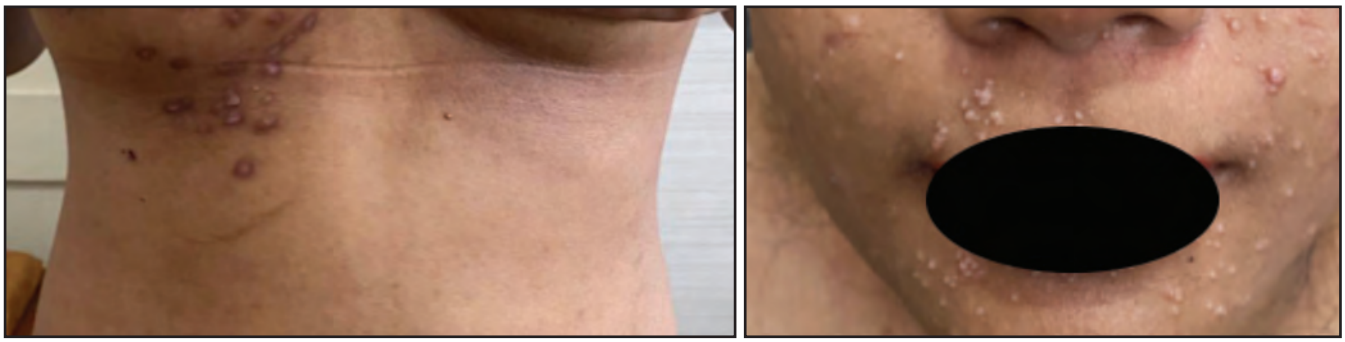

Fig. 2: Lesions after 4 weeks of treatment

persistent, pruritic, diffuse, or cosmetically undesirable lesions, and to prevent autoinoculation or transmission to others.[1,5]

In the immunocompetent population, 30% of cases resolved spontaneously due to strong cellular immunity. However, spontaneous regression usually does not occur in MC patients with HIV/AIDS.[1] Patients with HIV/AIDS tend to have more extensive MC lesions and are less responsive to conventional therapy. HIV infection lowers the immunity in the skin, so it is unable to suppress MCV replication and this results in the growth of lesions in large numbers and sizes. Factors that influence the responsiveness of the lesion to therapy include CD4 cell count, viral load and HAART consumption. HIV patients with CD4 counts <200 cells/uL and viral loads >100,000 copies/mL had more persistent lesions.[6] In this case, the patient was infected with HIV with CD4 count only 2 cells/uL, leading to more extensive MC lesions.

Various studies have shown that the management of the underlying disease, HIV with HAART, is the most important first step in the eradication of MC lesions. However, it should be noted that at the time of initiation of HAART, there may be impaired immune function, known as IRIS.[7] This condition is an improvement of the immune system in patients with severe immunosuppression. At the beginning of the reconstitution phase, CD4 lymphocytes will increase and viral load decreases, so that IRIS will occur as a result of an inflammatory reaction against microbes and autoimmune antigens, which mistaken seen as a decrease in clinical condition. This incidence occurs in 25% of patients starting HAART, 52 to 78% of cases of IRIS involve dermatological manifestations, such as herpes zoster, condyloma acuminata, and MC. In a cohort study of 199 patients, 2% of patients developed MC within six months of HAART initiation. The lesion will then spontaneously resolve once the reconstruction phase is complete.[5,8] Patients already taking HAART daily within 4 months, there was an improvement, but a new lesion still appeared continuously.

On the breast, abdomen, and thighs patient were given 80% TCA. TCA is an acidic caustic agent. It has a mechanism of action in the form of protein denaturation and coagulation that causes necrosis of the superficial tissues. According to the Centers for Disease Control and Prevention (CDC) therapeutic guidelines, the TCA concentration used is between 80% and 90%.[6] The TCA treatment can be applied carefully directly to the surface of the lesion using a cotton swab until it forms a white clot (frosting) every week. The advantages of TCA is that it is relatively inexpensive, easy to perform, safe if used with caution, rarely causes systemic toxicity, very effective for small lesions, as well as large and extensive lesions. Side effects include pain and burning for 5 to 10 minutes after application, erosion and hyperpigmentation. Excessive use of TCAs can cause scarring which can be minimised with petroleum jelly to protect normal skin around the lesion and washing with sodium bicarbonate or liquid soap immediately after excessive application.[6,9] After 80% TCA therapy, an improvement was seen in the form of lesions that were destroyed in only one treatment. The crushed lesions leave scars which then become hyperpigmented. After application, the patient complains of a burning sensation but still tolerable.

Patient also got 5% imiquimod cream every two days on facial lesions. Imiquimod, is a synthetic compound of the

imidazoquinoline group. It has strong antiviral and antiproliferative properties that can induce the production of various proinflammatory and antiviral cytokines such as interferon-α, IL-12, TNF-α and interferon-γ, followed by activation of innate and acquired immunity.[10] There will be Langerhans cell activation with increased antigen presentation and increased migration to lymph nodes. In addition, imiquimod directly induces a death receptor-independent apoptosis by the mitochondrial route. These observations underlie the use of imiquimod in viral infections. Its strong effectiveness has been demonstrated in various trials in condyloma acuminata (HPV). However, in several double-blind, or controlled trials[11] comparing the use of imiquimod with other topical treatments in molluscum contagiosum, imiquimod has shown good results. Imiquimod has also shown good results in immunocompromised patients, although it is primarily used as monotherapy. Compared with other destructive agents, imiquimod has been shown to be non-traumatising and has no side effects of scarring.[6,10] Based on a Cochrane systematic review, it was found that in a 2015 study by Chatra,[11] the use of imiquimod 5% cream daily gave a better clearance rate than KOH 20% which was also applied daily for 12 weeks. The use of 80% TCA and 5% imiquimod in several studies gave similar results and the majority of studies were carried out in combination. The difference in side effects that are less favourable is the use of 80% TCA.[4] In this case, facial lesions with imiquimod 5% found gradual changes in the form of thinning of the lesion. After application, the patient complained of minimal itching which was tolerable.

CONCLUSION

After four weeks of therapy, there was an improvement in the lesion in the form of a reduction in the size of the lesion and the destruction that is more visible on trichloroacetic acid (TCA) 80% application. It was suspected that the progression interferes by several comorbidities, such as human immunodeficiency virus (HIV) infection, (immune reconstitution inflammatory syndrome (IRIS) condition. Increase of CD4 count was found in patient which contribute as a good prognostic factor. To evaluate the skin improvement, a longer observation is needed until the IRIS phase completed.

ACKNOWLEDGEMENT

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CONFLICT OF INTEREST

None to declare.

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Life-threatening ascariasis complication in 4-year-old indigenous child: Prevention is better than cure

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SUMMARY

Soil-transmitted helminths account for a major burden of parasitic disease worldwide. It is particularly endemic in tropical and underdeveloped countries and mainly infects children who live in poor sanitary conditions, poverty, and poor education. We present a case of a 4-year-old Orang Asli (OA) girl who presented to the emergency department (ED) with vomiting, abdominal pain, and abdominal distension. On examination, she was dehydrated and had generalized abdominal tenderness and rigidity with reduced bowel sounds. A plain abdominal radiograph (AXR) and ultrasonography suspected the diagnosis of appendicitis with perforation and revealed roaming intestinal worms possibly causing an intestinal obstruction (IO). Emergency exploratory laparotomy, appendicectomy, and bowel decompression were performed. She was treated with intravenous antibiotics and oral albendazole post-operatively and was discharged on the sixth day of admission. In Malaysia, ascariasis remains highly prevalent in the OA community, which is attributed to inadequate hygiene care and poor sanitary conditions. Prevention of worm infestation is essential in reducing the risk of complications. It can be achieved by scheduled deworming programs. Clinical consultations and home visits from primary care providers are essential in educating, monitoring, and ensuring periodic deworming to this community, hence preventing life-threatening worm infestation complications. It also helps improve OA children's nutrition status and good-condition growth.

INTRODUCTION

Ascariasis is the most common parasitic worm infestation in the world, mainly prevalent in developing countries with tropical climates, primarily affecting children from low socioeconomic status with poor hygiene care and lack of access to basic sanitation.[1,2,3] While most ascariasis are asymptomatic, it can cause serious long-term health issues such as undernourishment, which may impede growth and lead to poor academic performance.[2,3] Furthermore, acute ascariasis complications can be life-threatening, for instance, occlusion of the appendiceal lumen by adult worms or secondary infection of Ascaris eggs, which may result in acute appendicitis and leads to perforation.[4] Hence, we reported a case of acute complication of Ascaris infestation in a four-year-old OA girl when she presented with acute abdominal pain and vomiting. Acute perforated appendicitis with possible intestinal obstruction (IO) was diagnosed by abdominal imaging. Exploratory laparotomy, appendicectomy, and bowel decompression, followed by post-operative treatment with antibiotics and anti-helminthic drugs, cleared the infestation.

CASE REPORT

A 4-year-old OA girl was brought by her parents and presented to the emergency department (ED) with severe abdominal pain and distension for two days associated with nausea and persistent vomiting. The vomitus consisted of food and saliva, with no blood, bile stain, or worm seen. The stool consistency had changed to watery for seven days, and she developed intermittent fever for two days.

On examination, the girl was thin, in pain, and dehydrated. Her temperature was 38.3℃, pulse rate was 124 beats per minute, and blood pressure was 101/58 mmHg. Examination of the abdomen revealed abdominal distension with generalized tenderness and rigidity, and auscultation of the abdomen revealed sluggish bowel sounds. Other systemic examinations were unremarkable. The growth chart plotted fell on the borderline range.

Laboratory tests were done during the initial assessment, and the results as shown in Table I. She was shown to have electrolyte imbalance and hyperlactatemia, indicating dehydration. Blood gas showed no acidosis. She had mild anaemia, and her other blood parameters were normal.

Urgent imaging tests such as abdominal x-ray (AXR) and abdominal ultrasonography were performed in ED. Air-filled loops of dilated bowels were seen in the abdominal radiograph (Figure 1). Dilated bowels with thickened walls throughout the abdomen and blind-ended dilated tubular structures at the right iliac fossa were visualized via ultrasonography of the abdomen. In real-time, multiple mobile echogenic tubular structures were observed within the dilated bowels (Figure 2). Intraabdominal fluid collections were visualized in the right iliac fossa, pelvic and perihepatic regions. These findings suggested acute appendicitis with possible perforation, IO, and worm infestation.

The patient was transferred to a tertiary hospital with an in-house pediatric surgeon for emergency exploratory laparotomy, appendicectomy and bowel decompression. Intraoperatively, contaminated fluid and pus collections were seen within the peritoneal cavity. Bowels appeared dilated

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Table I: Blood investigation results on presentation

Investigations	Result	Unit Type	Reference Range
Haemoglobin	11.8	g/dL	12 – 18
White cell count	7.7	109/L	4 – 10.5
Neutrophils	50.7	%	40 – 75
Lymphocytes	36.2	%	20 – 45
Monocytes	12.8	%	1 – 11
Eosinophils	0.0	%	0 – 6
Basophils	0.3	%	0 - 2
Platelet	261	109/L	150 – 450
Haematocrit	33.6	g/dL	41 – 53
PT	13.8	seconds	11.7 – 15.3
APTT	31	Seconds	30 – 44.4
INR	1.06		1.0 – 1.1

Investigations	Result	Unit Type	Reference Range
Urea	2.8	mmol/L	2.8 – 8.0
Sodium	127	mmol/L	136 – 145
Potassium	3.17	mmol/L	3.5 – 5.1
Chloride	90	mmol/L	98 – 107
Uric acid	434	µmol/L	143 – 359
Calcium	1.9	mmol/L	2.15 – 2.55
Magnesium	0.96	mmol/L	0.66 – 1.07
Phosphate	0.63	mmol/L	0.81 – 1.45
pH	7.418	-	7.35 – 7.45
pCO2	37.3	mmHg	32 – 48
Lactate	2.4	mmol/L	0.5 – 1.6
HCO3	23.4	mmol/L	21.8 – 26.9

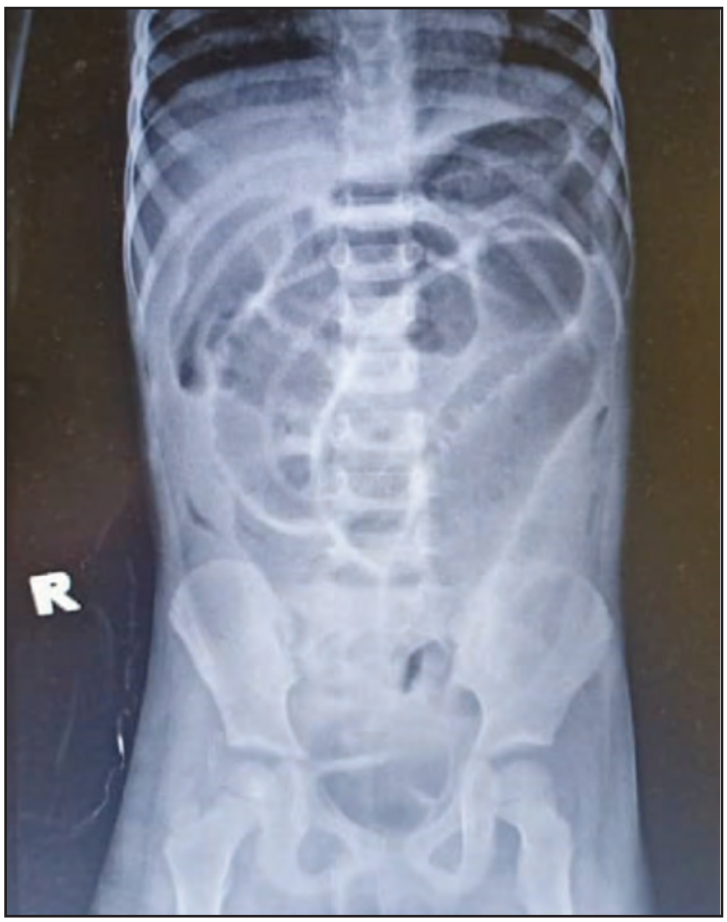

Fig. 1: Multiple loops of dilated bowel can be seen on abdominal x-ray

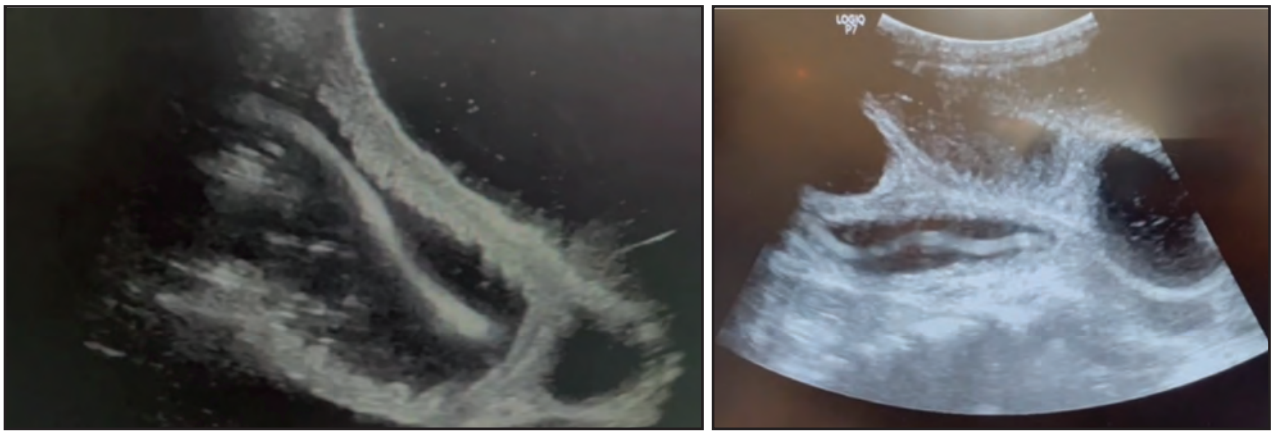

Fig. 2: Several mobile hypoechoic tubular structures with well-defined echogenic walls were seen within the intestines on abdominal ultrasonography. In real-time, the 'structures' were freely moving

and oedematous indicating intestinal obstruction. The appendix was perforated at the body with faecolith within. The base of the appendix and caecum appeared healthy. No parasitic worm was extracted during bowel decompression.

Post-operatively the child stayed in the ward for six days for post-operative care. She received intravenous (IV) antibiotics (cefuroxime 210 mg three times a day and metronidazole 105 mg three times a day) before being converted into the oral formulation for seven days and oral albendazole 400 mg daily for three days.

Upon discharge, she was referred to the nearest health clinic for growth monitoring, periodic deworming and deworming of the entire household. Ascaris infestation awareness counselling was given to the parents, educating them regarding ascaris transmission, improving hygiene care, proper use of sanitation facilities, good dietary habits, and the importance of biannual prophylaxis deworming in the at-risk community, including adults.

DISCUSSION

Roundworms *(Ascaris lumbricoides)*, whipworms *(Trichuris trichiura)* and hookworms *(Ancylostoma duodenale* and *Necator americanus)* are classified as soil-transmitted helminthiasis (STH), and STH is the most common parasitic illness in humans affecting an estimated 2 billion people worldwide with ascariasis infects 1.5 billion individuals.[1,5] It is transmitted by the faecal-oral route via contaminated food, water sources, and soil which another individual then ingests.[3,5] Ascariasis is often associated with poverty, inadequate hygiene, and poor sanitation.[1,2,3]

In Malaysia, the prevalence of STH over the past 40 years saw a dramatic decline nationwide, attributed to the rapid socioeconomic and infrastructural development.[6,7] However, the STH prevalence decline among the OA community, the Indigenous people of Malaysia was much slower, from over 90% in the 1970s to fluctuating between 40% to 80% in recent 2010s studies.[7,8] A review paper by Sinniah, B. et al., a comparison study from 1970 to 2013, stated that among 24.6% of children infected with STH, OA children (44.3%) were the majority.[7] One study in 2014 even showed that as high as 98.4% of OA school children in the Lipis district of Pahang state were found to be infected by at least one intestinal parasite species.[9]

This case report presents a case of ascariasis with perforated appendicitis in an OA child. It also provides vital information on common, inadequate hygiene practices in low socioeconomic areas with low education levels among the OA community that contribute to the spread of STH.

Our patient, a 4-year-old OA girl, lives with her parents in a government-developed OA housing complex with complete basic amenities. The children in the area are usually barefooted when playing outside the house, with poor awareness regarding self-cleanliness before eating their meals, likely exposing them to contaminated soil. The parent reported that the patient had never taken deworming medication since birth. On direct questioning, the parent did not know how STH spreads and the importance of hand washing before meals, regular fingernail cutting, and periodic deworming in preventing STH transmission.

The World Health Organization (WHO) acknowledges that the total elimination of STH from endemic areas is not plausible; thus, efforts should be focused on reducing the prevalence and burden of infection.[3] WHO recommends frequent, large-scale deworming to reduce STH infection and to improve at-risk children's health.[3] Periodic deworming reduces intestinal worm burden to prevent life-threatening complications.[2,3,10] It also improves the long-term health sequelae of undernourished and undergrown children.[2,3] Although prophylaxis chemotherapy only proved to be beneficial for infected individuals, treating the entire at-risk population is more cost-effective and logistically viable, especially in remote OA communities.[3]

Managing and educating at-risk groups regarding the harms of STH can be very challenging to primary healthcare medical personnel. Our patient's parents have defaulted her six-monthly government health clinic appointments and periodic deworming. She lives in a housing complex with appropriate basic amenities, so her ascariasis was likely

attributed to poor personal hygiene practices. The evidence shows that hand hygiene, food preparation techniques, barefooting, suboptimal use of sanitation facilities, and open defecation are risk factors for STH in the OA community, apart from infrastructural factors.[7,8,9,10] Efforts should be directed toward improving the OA community's health literacy and hygiene practices during every encounter either in a clinical setting or home visit. The importance of hygienic practices such as hand washing before eating, wearing footwear, boiling water before drinking, washing and cooking raw food before consumption, discouraging using human faeces for fertilizer, avoiding open defecation, and periodic deworming should be emphasized to prevent STH infestation.[7,9,10]

Symptoms of ascariasis vary heavily and are dependent on intestinal worm burden, thus stressing the importance of regular deworming.[2] Ascariasis could present acutely as pneumonitis, cholecystitis, cholangitis, pancreatitis, intestinal volvulus, appendicitis, and IO, whereas chronic infestation could lead to malnutrition, growth retardation, and impaired cognition.[1,2] Ascariasis-related perforated appendicitis is a rare, life-threatening condition.[3] As in this case, perforated appendicitis likely occurred due to a secondary infection of Ascaris eggs in the appendiceal lumen, leading to inflammation and perforation.[3,5] Although no worm was extracted during bowel decompression, occlusion due to the Ascaris worm was very likely, as evidenced shown by the ultrasonography findings.

Any individuals from the at-risk community presenting with symptoms of acute abdominal pain and IO should warrant high suspicion of ascariasis. AXR only detected intestinal worms when they formed a tangled mass of thick cords, which was absent in this girl.[5] Ultrasonography, initially done to assess the appendix, identified multiple moving tubular structures in real-time, confirming ascariasis. Ultrasonography is an excellent modality to detect the presence of intestinal worms; however, the findings are influenced by many factors, including the worm's orientation relative to the probe, the transducer's resolution, the presence of fluid around the worm, the segment of the worm being examined, and whether the worm is dead or alive during the examination.[5] Ultrasonography could exclude the presence of intestinal worms. In addition, computed tomography (CT) is the alternative to facilitate the detection of parasitic intestinal worms and to identify the etiology of those presenting with acute abdomen.[4,5]

Depending on the concurrent symptoms and the patient's condition, treatment options for ascariasis can be either conservative or surgery. Conservative management with IV fluids, broad-spectrum antibiotics, anti-helminthics, and nasogastric drainage is effective initial therapy.[5] Surgery is necessary if conservative management fails or the patient has complete IO or perforation.[1,5] In her case, she was treated surgically due to the clinical and imaging findings of perforated appendicitis and complete IO.

CONCLUSION

Ascariasis is prevalent in tropical countries and associated with low socioeconomic status, lack of hygiene, and lacking appropriate basic sanitation. At-risk groups, such as the OA community, are susceptible to ascariasis and its complications, warranting a high index of suspicion when presenting with acute abdominal pain and IO symptoms. Initial tests of AXR and ultrasonography are helpful in detecting and diagnosing ascariasis infestation, especially in cases with complications such as appendicitis. These modalities provide vital information on the aetiology, which could guide the management course. Oral albendazole, the drug of choice for treatment and prophylaxis, should be periodically taken by children in the at-risk community to prevent ascariasis and its related morbidity. Primary care providers are essential in educating, monitoring, and delivering periodic deworming and emphasizing good hygiene practices to the community, especially at-risk groups.

CONFLICT OF INTEREST

There was no conflict of interest.

CONSENT

Informed consent was obtained from the patient's mother before the preparation of this case report.

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CASE REPORT

Hepatic angiomyolipoma masquerading as hepatocellular carcinoma

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SUMMARY

We reported a relatively unusual case of hepatic angiomyolipoma (HAML), which originated from a progenitor mesenchymal cell with pluripotent potential. It commonly affects middle-aged women and imitates various liver tumours radiologically. This case report aims to emphasise the value of histopathology and immunohistochemistry in diagnosing HAML and for further prognostication. Herein, we describe a case of HAML in a 54-year-old woman with its radiological manifestations, immunochemistry findings and management.

INTRODUCTION

Hepatic angiomyolipoma (HAML) is an unusual triphasic mesenchymal tumour that consists of dysmorphic blood vessels, smooth muscle, adipose tissue and occasional foci of extramedullary haemopoiesis. It belongs to part of perivascular epithelioid cell tumours. The most common extrarenal site is the liver. Renal angiomyolipoma (AML) is associated with tuberous sclerosis in 20% of cases; on the contrary, only 6% of cases of HAML are related to tuberous sclerosis.[1] Multiple HAMLs are usually seen in tuberous sclerosis, especially in cases with bilateral diffuse renal AML.[2]

CASE REPORT

A 54-year-old Malay woman with underlying multiple uterine fibroids, bronchial asthma, acute gastritis and hypertension, presented with deranged liver function test in March 2020, which was associated with weight loss of approximately 10 kg in 2 months. Per abdominal examination was unremarkable. Biochemical investigations showed normal serum albumin and alkaline phosphatase. Alanine transaminase and aspartate transaminase were slightly above the upper normal limit. Her hepatitis B surface antigen and hepatitis C virus antibody were non-reactive. Tumour markers levels such as alpha-fetoprotein (AFP) and cancer antigen 19-9 were within the normal range. Abdominal computed tomography (CT) demonstrated a segment V/VIII mixed density mass, measuring 4.6 cm × 3.4 cm × 4.5 cm (AP × W × CC). This lesion appeared to be of mixed soft tissue-fat density on the plain, heterogenous progressive enhancement on the arterial and porto-venous and hypodense on the delayed phase, which was initially suspicions of hepatocellular carcinoma (Figure 1). Magnetic resonance imaging (MRI) of the liver revealed a heterogeneously hyperintense mass on T2WI and hypointense mass on T1 fat-saturated image. There is identifiable fat within the tumour evidenced by the significant signal drop in the opposed phase, rim enhancement in the early arterial phase, progressive enhancement from the late arterial till equilibrium phase and hypointense in the 10-minute and 20-minute images (Figure 2). The intra-operative findings demonstrated a generalised fatty liver with a palpable tumour at the anterior surface of segment VII which extended to segment VIII. There were no peritoneal nodules or ascites. The patient underwent non-anatomical liver resection of segments VII and VIII. The diagnosis of hepatic AML was confirmed by histopathology examination (Figure 3).

DISCUSSION

The primary hepatic tumour may emanate from different elements, including hepatocytes, bile ducts, mesenchymal cells, epithelial and neuroendocrine cells. The mesenchymal cell is a progenitor and pluripotent cell, which shows multilineage differentiation. Therefore, a mesenchymal tumour comprises mixed components of vascular, adipose tissue, fibrous and smooth muscle. Owing to the varying difference in proportions of these three histological components in each HAML, this poses a diagnostic challenge in radiology. HAML is rarely diagnosed pre-operatively and is commonly misdiagnosed as hepatocellular carcinoma (HCC), adenoma or focal nodular hyperplasia. Here, we discuss the clinical, radiological, histopathological, and immunohistochemical examinations; although it is not fully pathognomy, they can be used as guidance in diagnosing HAML.

HCC can be distinguished from HAML by several clinical features. HAML predominantly occurs in middle-aged women (83.3%) without underlying liver disease, whereas HCCs are commonly found in men (75%) with either chronic Hepatitis B, Hepatitis C, or alcoholic liver disease.[3] Only 68.8% of HCC demonstrated elevated AFP and none of HAML showed abnormal AFP, which makes HCC another possible differential diagnosis in this AFP normal patient. Patients with either HAML or HCC usually present with non-specific symptoms such as abdominal distension, abdominal pain, and weakness. Some are asymptomatic and diagnosed incidentally during clinical screening.[4]

Differentiating HAML from HCC is notoriously difficult by imaging. However, there are several radiological

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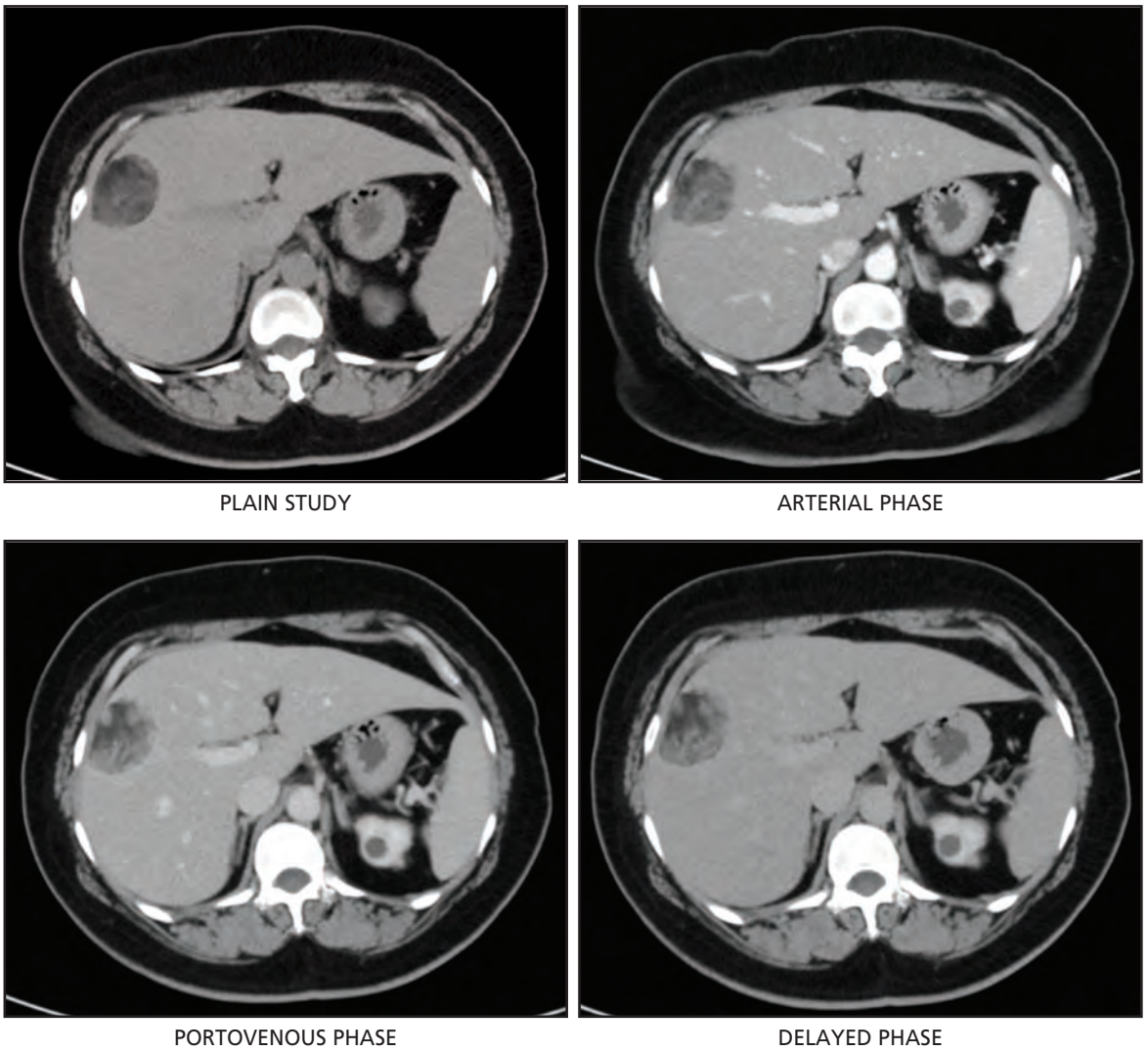
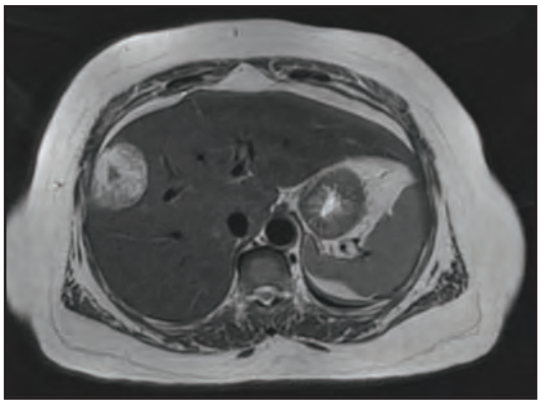


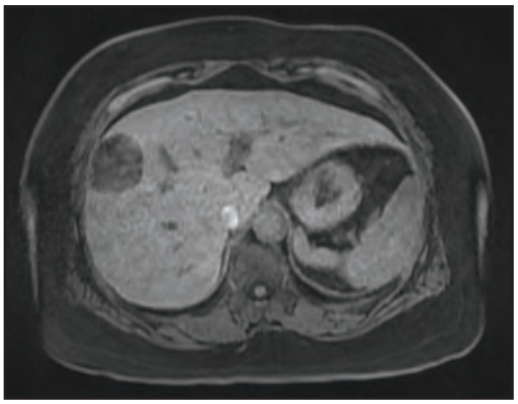
Fig. 1: Multiphasic computed tomography (CT) imaging findings of HAML: A segment VIII mixed soft tissue-fat density mass, with heterogenous progressive enhancement on the arterial and porto-venous and hypodense on the delayed phase

characteristic features that can help to differentiate it. The characteristic imaging features of HAML include visible intralesional fat, prominent draining vessel, and absence of capsule.[3,5] The typical HAML is regarded as a benign tumour, which shows the characteristic features of a large amount of fat content within a plain study. The other possible differential diagnosis of the fat-containing benign liver lesion with soft tissue component comprises adenoma, hepatic adrenal rest tumour and teratoma; however, the malignant liver lesion encompasses HCC, primary liposarcoma and metastatic deposit. Furthermore, another typical radiological feature is the presence of a prominent central vessel, but in fact, the HAML and HCC are also hypervascular tumours, some showing similar enhancement patterns. The radiological enhancement pattern solely depends on the number of intralesional blood vessels, and no specific enhancement pattern is seen in HAML. The lesion with ample central vessels will show rapid enhancement and washout in the subsequent phase; besides, the lesion with a tiny or devoid vessel will show prolonged enhancement in portal venous/ delayed phases. But Lee et al[3] also mentioned that only portovenous phase is significantly different between these two entities, where hypointensity on portovenous phase is depicted in 61.1% of HAML versus 88.9% of HCC. In this case, the lesion showed continued enhancement on portovenous and equilibrium phases in MRI images, which should be the salient characteristics to differentiate HAML from HCC and cavernous haemangioma. Nonetheless, the presence of enhancing capsule in the portal or delayed phase is near pathognomonic for HCC.[6]

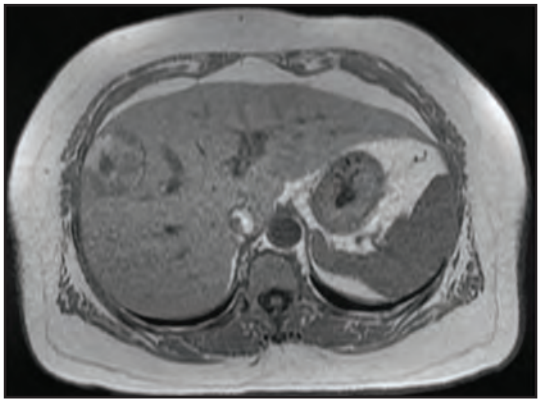
The radiologist must be aware of the spectrum of morphologic features of HAML, which have been subcategorised as classic, fat-poor, HAML with the epithelial cyst, and lastly, epithelioid HAML (Epi-HAML). Epi-HAML was regarded as a tumour of unpredictable malignant potential. It will appear as a well-defined, unencapsulated lesion with a paucity of adipose tissue, which engenders more than 50% of the fat-poor HAML cases to be misdiagnosed as HCC.[5] MRI is more sensitive in detecting small amounts of



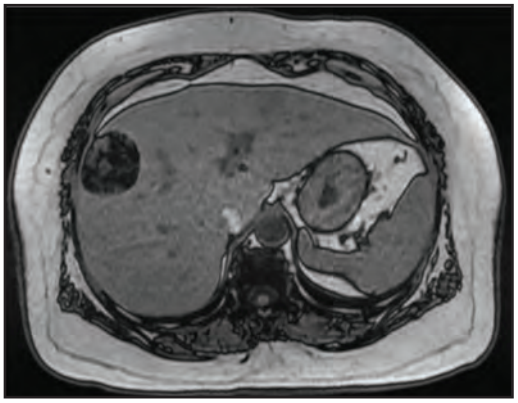
T2-WEIGHTED IMAGE



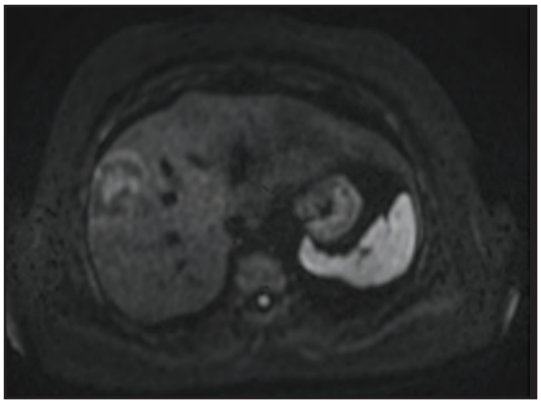
PRE-LAVA T1-WEIGHTED



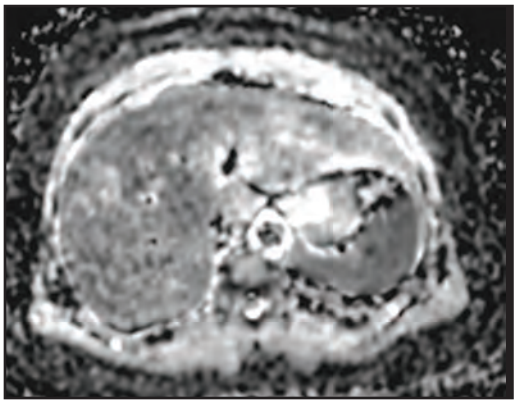
IN-PHASE



OUT-PHASE



DWI



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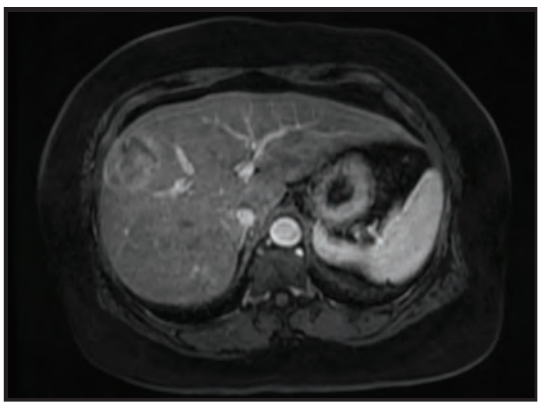
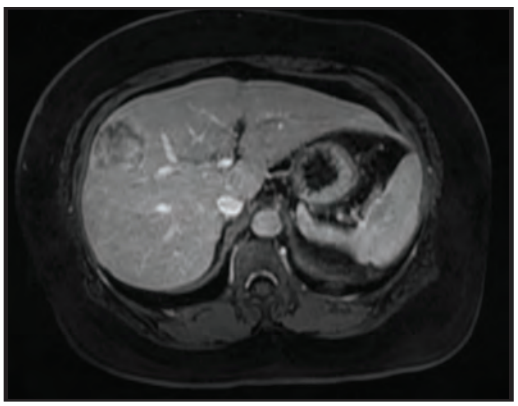


EARLY ARTERIAL



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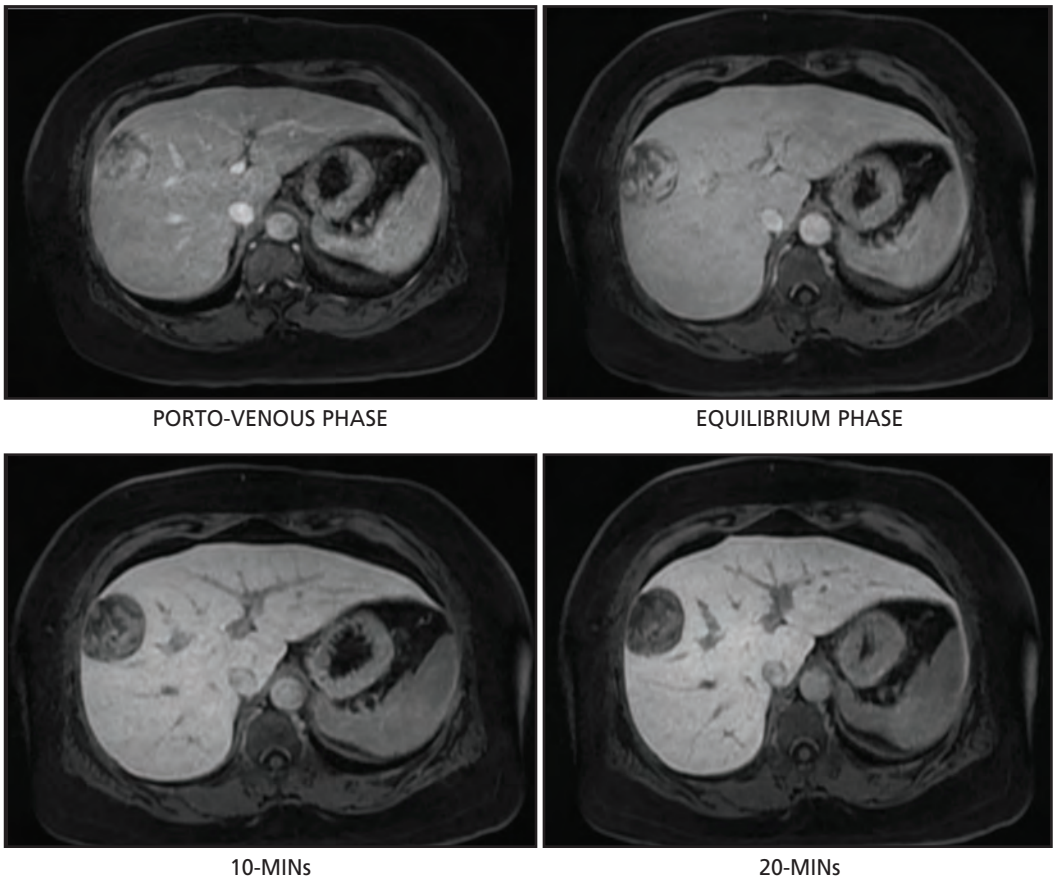

Fig. 2: Magnetic resonance imaging (MRI) features of HAML: The mass is heterogeneously hyperintense on T2WI and hypointense on T1 fat-saturated image. The presence of significant signal drop on the opposed phase indicates fat content, with rim enhancement in the early arterial phase, progressive enhancement from the late arterial till equilibrium phases and hypointense in the 10-minute and 20-minute images

intra-tumoral fat by relying on the different precession frequencies of water and fat proton. Conversely, the conspicuousness of microscopic fat on CT might be affected by volume averaging. On high b-value DWI, the epi-HAML mainly manifests mild hyperintense, while HCC manifests as a marked hyperintense lesion. Indeed, another distinctive feature of epi-HAML is rich intra-tumoral blood vessels at different phases, draining hepatic vein during the arterial phase and prolonged enhancement pattern. It is worth noting that the enhancement intensity of the sectional area within the tumour is higher than surrounding liver parenchyma during the delayed phase, which should not be interpreted as a wash-out pattern. It is imperative for radiologists accustomed to the classifications of HAML to avert improper treatment such as transhepatic arterial chemoembolisation and liver transplantation in HCC cases.[4]

Histologically, HAML displays variable and deviant features, which can be further subclassified into mixed, lipomatous (≥70 % fat), myomatous (≤10%) and angiomatous types. This reported case belongs to the mixed type. The diagnosis of AML can be confirmed by using histopathologic and immunohistochemical features as in this reported case, whereby more than 90% expressing melanocytic antigens, i.e. human melanoma black (HMB)– 45 and Melan-A staining; as well as smooth muscle cell markers i.e. actin and/or desmin. However, the uncertain malignant potential of HAML should not be disregarded. The prognostication of HAML can be further evaluated by using the mitotic marker, i.e. Ki-67 or P53 immunoreactivity or mutation,[7,8] which was not performed for this patient.

Although almost all the HAMLs are benign, the possibility of malignant transformation needs to be taken into consideration. Invasive/infiltrated growth in HAML is hitherto not indicative of malignancy. Indeed, actual malignant HAML is rare, and only a few cases have been reported. Delle et al.[9] reported the first case of malignant HAML in 2000, in a 70-year-old female patient with a right liver lobe hypervascular mass and HPE-proven HAML, which showed positivity in HBM-45/NKIC-3. In view of recurrent abscess formation, the mass was resected 5 years later. Histologically, it showed epithelioid AML with prominent vascular invasion. Unfortunately, the patient passed away due to recurrent disease. Nguyen et al[10] also described a case of recurrent localised HAML after 6 months post-operation, followed by second-look surgery showed local recurrence and extensive intraabdominal metastases. Furthermore, HAML also has the potential risk of enlargement, imposing the mass-compression effect, and the patient has a high

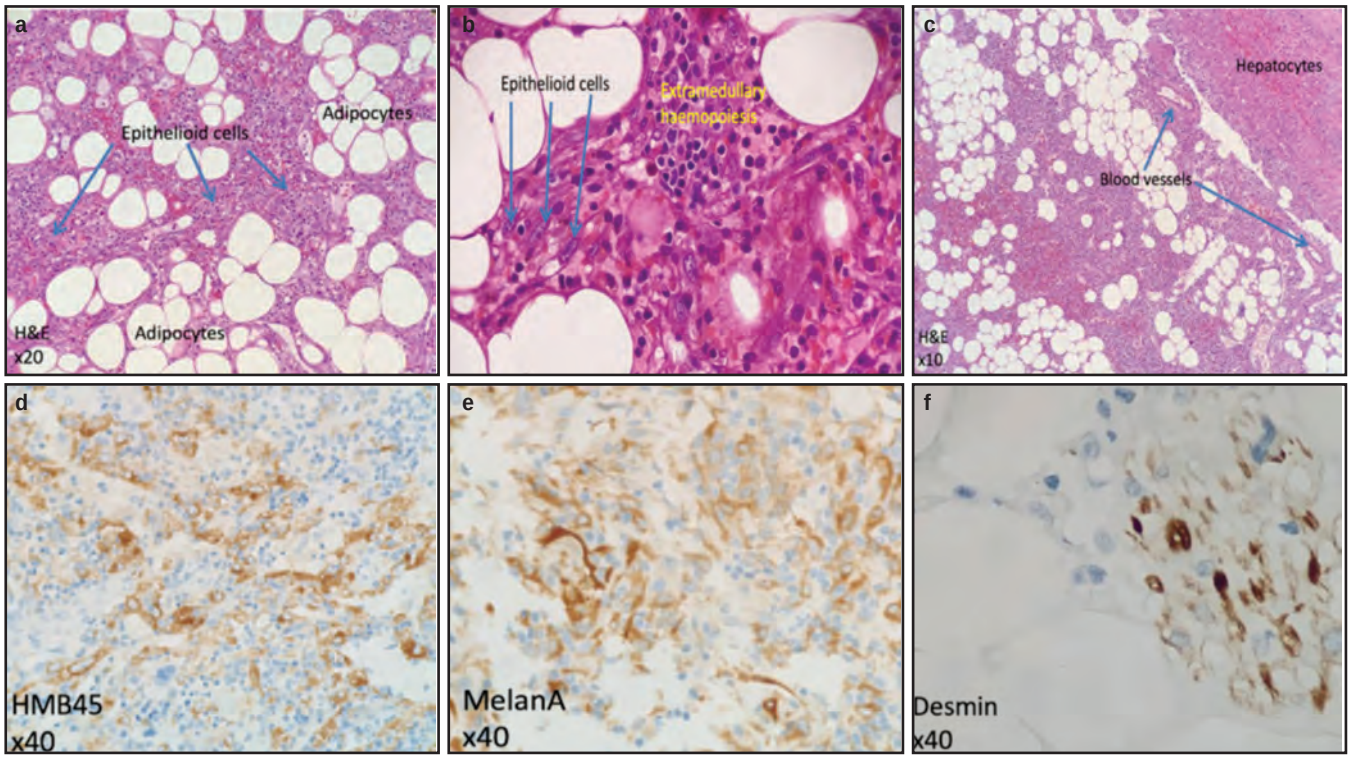

Fig. 3: Histopathological findings—the liver nodule is formed by an admixture of adipocytes (a), epithelioid tumour cells (a, b) and scattered thick-walled blood vessels (c). Extramedullary haematopoiesis is also observed (b). The epithelioid tumour cells show positivity for HMB45 (d) and Melan A (e) with focal positivity for desmin (f). No overt features of malignancy were seen

propensity of being symptomatic. Enlarging tumours will also make the surgery become more complicated, thus early operation is recommended once diagnosed with large HAML.

Malignant transformation features of HAML can be supported by using either radiology or immunohistochemistry. The common features of benign and malignant HAML encompass three basic histology components (mature adipose tissue, blood vessels, spindle and epithelioid cells), immunochemistry (immunoreactivity in melanocytes markers (ie. S100, HMB-45, Melan-A), and smooth muscle antigens (ie. SMA, Desmin)), sinusoidal spaces and circumjacent portal blood vessels invasion and cytology atypia, which are not a definitive benchmark for predicting malignancy in HAML. Notwithstanding, large (>10 cm), coagulative necrosis and metastases are radiological manifestations of malignancy. Loss of CD-117 (c-kit) expression, which is tyrosine kinase growth factor receptor is a feature of malignancy.[10] Borderline cases should be categorised as AML of uncertain malignant potential, and further close follow-up is warranted. Other than the loss of CD-117 expression, Ki-67 and P53, which were not performed in our centre, none of the features were found in our cases, suggesting that this is probably a benign lesion and she is still under surveillance imaging.

CONCLUSION

This case report is helpful to increase awareness among managing teams of HAML with diverse prognoses. Concordance imaging correlation with pathology results is important in making the diagnosis explicitly. Resection is advisable for the symptomatic, large HAML (>5 cm), non-compliance patient or hepatitis B virus carrier who endures the risk of hepatoma. Close imaging follow-up is suggested for patients under conservative management. Eventually, curative resection is an ideal choice for this patient because the tumour size is borderline big, and the patient defaulted to all the follow-ups for many reasons, but the latest ultrasound was done 1 year after resection, which revealed a normal study with no focal liver lesion.

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CONFLICT OF INTERESTS

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Carina resection and reconstruction: Our experience and challenges

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SUMMARY

Carina resection is a technically challenging and uncommon procedure in thoracic surgery. This is in part due to the deep and narrow space of dissection to achieve complete resection that is confined by the various major mediastinal vessels, as well as the challenge of maintaining ventilation continuity pre- and post-carina resection. Meanwhile, primary carina neoplasm be it malignant or benign, is uncommon, rendering limited experience even in high-volume thoracic surgery centres. Here, we present a case of an inflammatory myofibroblastic tumour of carina, which has undergone successful carinal resection and reconstruction and discusses some of the operative challenges faced. The patient is currently disease-free and doing well 21 months post-surgery.

INTRODUCTION

Carina resection is a technically challenging and uncommon procedure in thoracic surgery. This is in part due to the deep and narrow space of dissection to achieve complete resection that is confined by the various major mediastinal vessels, as well as the challenge of maintaining ventilation continuity pre- and post-carinal resection. Meanwhile, primary carina neoplasm, be it malignant or benign, is uncommon, rendering limited experience even in high-volume thoracic surgery centres.

Therefore, the important tenets of thorough patient selection, pre-operative evaluation and optimisation, experienced anaesthetist management, sound surgical technique and prompt post-operative management in a multidisciplinary manner are paramount to a positive outcome when embarking on carinal resection.

Here, we present a case of inflammatory myofibroblastic tumour of carina which has undergone successful carinal resection and reconstruction. Discussions mainly focus on the surgical aspects of carinal resection and reconstruction and the challenges faced in our local setting.

CASE REPORT

A 29-year-old woman was referred from a private medical centre for a partially obstructive carina tumour. She presented with chronic cough, wheezing in right lateral position and recurrent episodes of dyspnoea. There was no haemoptysis. In view of the positional-related wheezing, a contrast-enhanced computed tomography (CECT) was performed and showed a lobulated soft tissue lesion at the distal end of trachea arising from the carina, with near total luminal occlusion (Figure 1a). Bronchoscopy revealed a lobulated mass at the lower trachea (Figure 1b), and a biopsy was done. She was referred on the same day to our unit for consideration of surgical intervention.

After multidisciplinary meeting and family counselling, a right video-assisted thoracoscopic surgery (VATS) carinal resection and reconstruction was performed. The airway control was by using a direct intubation of the left main bronchus using a 7-mm single lumen endotracheal tube. Two ports access was used. In the left lateral position, the working port was placed at the fifth intercostal space, 4 cm length just lateral to the anterior axillary line and the second port was placed at the 7th intercostal space, mid axillary line. A 30-degree 10 mm telescope was used.

Dissection was started by mobilising the azygos vein and dividing it with a vascular stapler. The vagus nerve was dissected and anchored to the posterior chest wall. A lobulated and friable carinal tumour extending into the distal tracheal was noted. The trachea, carina, right and left main bronchus were mobilised, looped and divided. Upon division of the left main bronchus, a flexo-metallic tube was inserted through third intercostal space, mid clavicular line to establish cross-field ventilation into the divided left main bronchus. Margins from the proximal trachea, distal right and left main bronchus edges were sent for a frozen section to determine a clear margin before reconstruction (Figure 2a).

The reconstruction was performed by using polydioxanone suture sized 3-0. The lateral wall of the left main bronchus was sutured to the corresponding wall of the trachea. Subsequently, the right main bronchus was sutured to the remnant opening of the left main bronchus-tracheal anastomosis (Figure 2b). In view of the friable membranous portion of the tracheal wall that was tearingduring the suturing, decision was made to convert to thoracotomy to complete the carinal reconstruction. The surrounding pericardial fat was used to cover the anastomosis. There was no air leak seen, and chest drain was inserted prior to closure. She was extubated immediately after surgery.

Chest physiotherapy and incentive spirometry were started early once returned to ward, and nasogastric feeding as well as deep vein thrombosis prophylaxis were commenced on post-op day one. Bronchoscopy assessment was done on post-op day five, and anastomosis was found to be intact, with

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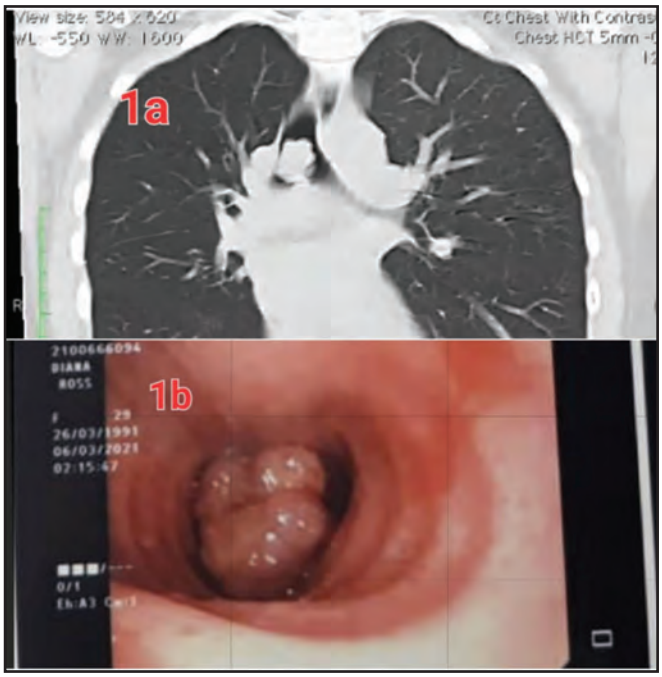

Fig. 1: (a) CECT thorax in coronal view showing the location of the carinal tumour. (b) Pre-operative bronchoscopy showing the carinal tumour.

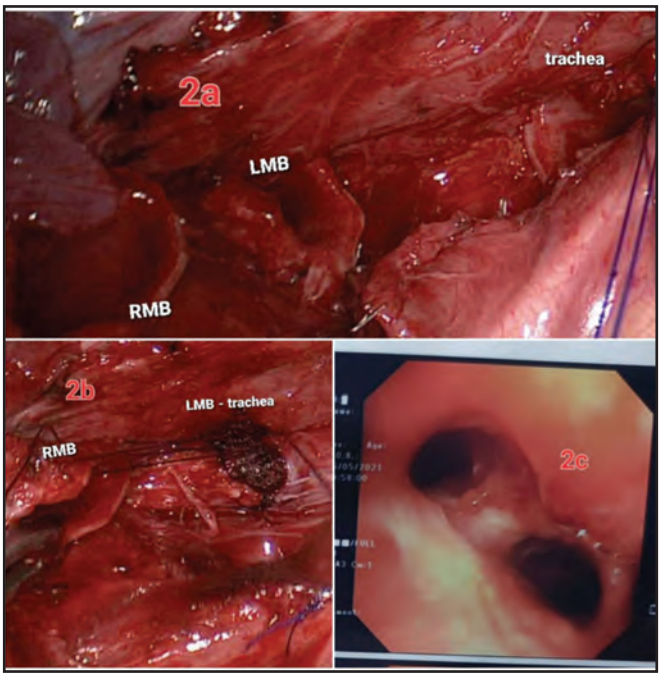

Fig. 2: (a) CECT thorax in coronal view showing the location of the carinal tumour. (b) Pre-operative bronchoscopy showing the carinal tumour.

some mucous plugging seen at the left lower lobe bronchus. Her chest drain was removed, and she was put on soft cervical collar for six weeks. She was discharged home the same day.

Histopathological examination result showed an inflammatory myofibroblastic tumour, and all the lymph nodes were spared. The immunohistochemistry staining was positive for ALK1 and negative for S100, Desmin and PanCK. She was subsequently planned for surveillance by oncology. She was followed up with serial bronchoscopic assessments by us. After a year of surgery, the neocarina looks healthy, with no evidence of recurrence in both the CECT and bronchoscopy (Figure 2c).

DISCUSSION

Benign neoplasm of the carina is rare and can be considered for resection with reconstruction. Although the technicality has been well documented, the complication rate post-op remains high.[1] Detailed preparations with clear communication with anaesthetist and thorough patient selection, pre-operative evaluation and optimisation, sound surgical technique and prompt post-operative management in a multidisciplinary manner are paramount to a positive outcome when embarking on carinal resection.

CECT thorax is the prerequisite that often reveals the presence of a distal trachea/carina lesion. It helps in determining primary tumour extent, mediastinal lymph nodes or lung involvement, and the presence of pleural or pericardial effusion. Magnetic resonance imaging (MRI) is helpful both in delineating the extent of the tracheal tumours into peritracheal tissues and also shows the mediastinal vessel involvement to a better extent, but it is not widely available.

Pre-operative bronchoscopy by the operating surgeon is also very important as it enables a direct visual assessment of the tumour extent, tissue biopsy and potentially therapeutic intervention like debulking to temporarily re-establish airway patency. This is especially important in allowing time for completion of necessary staging, optimisation of patient before surgery and drainage of distal bronchial infection and antimicrobial therapy when warranted. We prefer to perform the bronchoscopy in the operating theatre prior to surgery. This allows a more controlled and safer environment, and airway control could be achieved better if any complications were to arise during the scope. For this patient, there were a few reasons we did not attempt a repeat biopsy or endobronchial intervention. Firstly, the referring pulmonologist found the lesion to be causing significant luminal obstruction and highly vascular, with attempted biopsy resulting in bleeding and airway compromisation. Despite that, the histopathology examination result was inconclusive (spindle cell lesion). More importantly, when pre-operative imaging assessment showed this lesion to be resectable, surgical resection with clear margins was the definitive treatment for this patient who came with a central airway obstruction.

Securing the airway, ventilation and maintaining oxygenation is the ultimate anaesthetic challenge in tracheal or carinal surgery. The double lumen endotracheal tube, a prominent feature in pulmonary surgery, is bulky and not helpful during carinal resection. It hinders tracheobronchial anastomosis compared to smaller lumen catheter like those used in jet ventilation. Cross-field ventilation is often used to help in temporary distal bronchial ventilation.[2] For our patient, a single lumen endobronchial tube was inserted into the left main bronchus directly to achieve single lung ventilation during the initial right video-assisted

thoracoscopic surgery approach. Under bronchoscopy guidance, successful navigation of the tip of the endobronchial tube past the side of the lobulated carinal tumour extension into the left main bronchus was achieved.

The extent of airway resection is determined, on one hand, by the extent of tumour involvement, and limited on the other, by the lack of feasible replacement conduit. A longer extent of airway resection can sometimes be safely compensated by various release manoeuvres to mobilise and advance the resected airway edges in order to achieve a tension-free anastomosis. However, one critical aspect during airway release is that care must be taken to preserve its lateral blood supply. This will prevent devascularisation of the tracheal proximally during pretracheal plane dissection and the bronchial airway distally during peribronchial dissection. Circumferential peribronchial release should be limited to a few millimetres adjacent to the level of transection. The resected carinal length for our patient was about 3 cm.

In this case, a U-shape pericardiotomy around the right inferior pulmonary vein was carried out to provide 1–2 cm of hilar release length to achieve cranial advancement of the right main bronchus. Circumferential pericardiotomy around both pulmonary veins has been described in complete hilar release to achieve greater distal mobilisation. Left hilar release was not performed as tension was not an issue on that side and aortic arch usually prevents significant left main bronchial advancement. Neck flexion also helps descend the larynx and facilitates caudal advancement of the resected distal tracheal edge. This manoeuvre can provide a further 1–2 cm length to help relieve anastomotic tension.[3] For our patient, neck flexion was carried out just prior to anastomosis.

In the case of more extensive involvement of carina resection, different anastomotic configurations have been described in order to achieve additional length and minimise anastomotic tension. One such configuration is an end-to-side anastomosis of the left main bronchus to the cartilaginous wall of the right bronchus intermedius after an initial end-to-end anastomosis of the right main bronchus to the trachea.[4]

Tracheobronchial anastomosis was achieved using synthetic monofilament absorbable (Polydioxanone) sutures. Non-absorbable sutures were found to cause granuloma formation by Grillo et al.[5] Usage of both 3/0 and 4/0 sutures was described in literatures, and we preferred a 3/0 suture for the bigger central airways. Anastomosis was initially performed under video-assisted thoracoscopic approach, where sutures were applied in a continuous manner. During the final stage of anastomosis, the membranous wall of the distal trachea was noted to be flimsy and torn easily due to oedema, which prompted the decision to convert to right anterolateral mini-thoracotomy to gain better traction of both ends of the airway in order to achieve tension free and healthier anastomosis.

Some surgeons advocate wrapping the anastomosis with a pedicled intercostal muscle flap, mediastinal fat, pericardial or pleural flap, while another school of thought practices leaving the anastomosis as it is.[6] It is still debatable if wrapping of the anastomosis helps in reducing the rate of dehiscence and post-op complications such as stenosis, bronchopleural or bronchovascular fistula. In fact, complications like increased thoracotomy pain with intercostal muscle pedicled flap and reossification have been shown with wrapping. There are no strong evidence to date that favour one over another, and we did not place any wrap around our tracheobronchial anastomosis post-carina resection.

Tracheobronchial anastomosis can take up to six weeks to heal. It is crucial to ensure the patient does not extend her neck post-op to keep the anastomosis in a tension-free environment. This can be aided by means of guardian stitches, although some authors found this not mandatory as long as the neck is kept in a neutral position.[7] Grillo stitches were used to maintain the neck in a neutral position after surgery for this patient. The submental crease to presternal skin stitches was removed on fifth day post-surgery after bronchoscopic assessment, and the patient was advised to apply a soft cervical collar to keep the neck in a neutral position without extension for a period of six weeks. Some centres avoid the use of these guardian stitches in compliant patients and reported decreased length of stay.[8]

CONCLUSION

Carina resection and reconstruction is a complex procedure and needs to be undertaken by a team of experienced and skilled thoracic surgeons and anaesthetists. Thorough multidisciplinary discussions and sound perioperative planning hold the key for a successful surgical outcome. Improvements in airway management, intravenous anaesthetic agents and intensive care management have also helped to reduce operative mortality over the past half a century.

DECLARATION

We certify that there is no actual or potential conflict of interest in relation to this article.

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Trials and tribulations of childhood type 2 diabetes mellitus

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SUMMARY

Type 2 Diabetes Mellitus (T2DM) is a common condition among adults. However, increasing rates of childhood obesity has led to a rise in this condition among children worldwide. Children with T2DM develop comorbidities and complications similar to adults, resulting in increased morbidity. Managing T2DM among children requires good family support along with the involvement of a multidisciplinary team to ensure optimal glycaemic control and minimal complications. This case describes the diagnosis and management of a 12-year-old girl with T2DM using Family-Centred Care (FCC) approach, pharmacological treatment and supportive care from a multidisciplinary team consisting of a family physician, dietician, pharmacist and physiotherapist. Key elements of care in managing this lifelong condition in a child is by using a coordinated approach of lifestyle modification, family support and medication based on the latest evidence. A summary of the recent management guideline for T2DM in children is also provided.

INTRODUCTION

More than 41 thousand children and adolescents under the age of 20 years are estimated to have T2DM worldwide.[1] In Malaysia, the prevalence of T2DM among children and adolescents under the age of 20 years is about 17.5%.[2] It usually occurs in obese children at puberty, when they may be asymptomatic or present with metabolic symptoms.[3] T2DM among children is aggressive and associated with rapidly progressive pancreatic beta cell destruction and early development of complications.[4,5] Hence identification of this condition and its appropriate management is essential to ensure that these children reach adulthood with minimal complications. This case illustrates how an obese child was diagnosed with T2DM and the challenges faced by the medical team and her family in her management. Recent update on the management and follow-up care of T2DM among children and adolescents is also summarised.

CASE REPORT

A 12-year-old girl was noted to have a body mass index (BMI) of 44.3 by the school health team and was referred for further evaluation at the nearest health clinic. She had symptoms of polyphagia, polydipsia and polyuria for two months. Both her parents were healthy, and her mother did not have gestational diabetes during pregnancy. Her birth weight was 3.7 kg, she had normal developmental milestones and average academic performance. She had a sedentary lifestyle as she was not involved in any co-curricular activities or sports at school and spent about two hours a day on digital devices and television. She attained menarche at the age of ten and her menstrual cycle was regular. Her four younger siblings were all healthy and had normal BMIs.

Clinically, she did not have any dysmorphic features. Her weight was 107.7 kg, height was 156 cm and BMI was 44.3, which was more than the 95th centile for her age. Her blood pressure was 135/80 mm Hg. Physical examination showed the presence of acanthosis nigricans on her neck. Secondary sexual characteristics development was at Tanner stage V. No other abnormalities were noted. She was diagnosed to have obesity, and baseline blood investigations were done. Blood investigations showed a high fasting blood sugar of 15.1 mmol/L and HbA1c of 11.5%. She had dyslipidemia with a triglyceride (TG) level of 2.2 mmol/L, low density lipoprotein (LDL) of 3.2 mmol/L, high density lipoprotein (HDL) of 1.1 mmol/L and total cholesterol (TC) of 7.0 mmol/L. Liver, renal and thyroid function tests were all normal.

Both parents and the patient were were informed of the diagnosis of T2DM and that she needed medication. At first, they could not accept the diagnosis as they perceived that T2DM was a disease of older people and could not occur in children. Hence, the initial management was to educate them regarding diabetes. However, even after receiving relevant information, they refused medication mainly because of the misperception that their daughter would become dependent on the medication for life. Although they were given explanation that the drug does not cause dependence but that it will be required for a long time as it helps to normalise blood sugar level and prevent complications but, they were not keen for any medication. Exploring the patient's perception of her diagnosis revealed that she too felt that she did not have any disease as she felt well and refused medication. It took many encounters with the multidisciplinary team members and after much

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explanation regarding T2DM and counselling to help them understand the nature of this condition, both the patient and her parents were open for the first step of intervention. After understanding about the relationship between obesity and diabetes, they were keen to try lifestyle modification but still refused medication. After a few months of trial of lifestyle modification with diet, active lifestyle and exercise, her blood glucose level remained high. Parents were still not keen to start medication but agreed to meet a paediatrician for a second opinion and further assessment. She was referred to a paediatrician at the nearest tertiary hospital where she was assessed and was advised to start Metformin 500 mg twice daily. The patient and her parents agreed for metformin trial. After a few months of treatment with metformin while continuing lifestyle changes, her HbA1c level reduced to 9.5%. Since her glycaemic control was not optimal, she was advised for basal insulin, but her parents refused insulin and requested to be referred back to primary care.

At primary care, her medication and follow up care plan was continued using the Family Centred Care (FCC) approach by a multidisciplinary team consisting of a family physician, dietician, pharmacist and physiotherapist. FCC is a partnership approach between the family and the health care provider for a collaborative health care related decision making to provide optimal health and wellbeing of children. The multidisciplinary team members meet the patient with her mother, who was her main caregiver, once a month. Initially the dietician assessed the diet history, previous measures used to prevent weight gain and their obstacles. Her current food intake was noted to be high in portion and in calories. She liked to snack on junk food such as potato chips and sweet cakes which were bought either from the stores by her parents or self-purchased by the patient from the school canteen. They were also assessed on their understanding of the concept of calorie content of food, their motivation and readiness to prevent weight gain and to lose weight. On the subsequent monthly visits, they were given simple methods to count calories for common food items. They were also given advice, which was tailored to the patients' needs. For example, to be able to reduce junk food consumption, parents were advised to stop buying snacks and replace it with fresh fruits of her choice like apples, grapes or carrot bites. Her mother was encouraged to pack simple homemade healthy food for school and given simple advice on how to prepare meals so that the whole family consumed healthy food. The family was suggested to eat the same healthy food together during mealtimes so that the patient did not feel alone in facing her disease and knew that the family supports her.

During the same monthly sessions, the pharmacist and the family physician would check on her glycaemic control. Since her blood sugar level remained high, counselling sessions were given, and parents were requested to consider insulin. Initially the patient and her parents refused insulin but when there was no further improvement of the serial HbA1c levels after eight months, they agreed to try insulin. She was started with subcutaneous Insulatard 10U injections at night before bedtime and gradually titrated up based on the Self-Monitoring of Blood Glucose (SMBG) levels. The patient and her mother were taught how to use the insulin injection (Novopen) and to monitor blood glucose levels using a glucometer. Glucometer was lent to them by the pharmacy and only the needle and test strips were purchased by the family. Initially, her mother administered the insulin injections. A few months later, the patient became more confident and wanted a more active role in her treatment and started taking the insulin injections herself.

The patient and her mother also met the physiotherapist on these visits where they were taught to do simple sets of exercises which could be done at home twice a week. The family was encouraged to do physical activities together for example walking or cycling a few times a week. Patient liked cycling, so she started cycling in a field near her house two or three times a week. Mother and daughter also were motivated to attend the group aerobic exercise sessions organised by the physiotherapy team on every Thursday evening, at the open space in front of the clinic.

Although the multidisciplinary team managed to achieve some of the targets of treatment through a holistic approach, they faced multiple challenges. Initial challenge for the team was to convince the parents and the patient that metformin was required and later insulin. Achieving glycaemic targets was also difficult as blood sugar levels were constantly fluctuating due to multiple issues especially related to compliance to dietary restrictions and medications. Other challenges faced by the team was the frequent non-attendance which was because the appointments overlapped with school activities and the patient was not keen to miss school. Non-adherence to dietary advice and medication was also an issue. This was addressed by using the reward method where the patient was allowed small food rewards when a milestone in weight management was achieved to encourage and motivate her to continue adherence to a healthy diet. Motivational interview sessions also brought about some changes in the patient's attitude. From the parent's perspective, one of the main challenges they faced was that they found it difficult to cope with the multiple appointments at the clinic and the amount of dedication required to manage their child's health. Sometimes the patient's mother had other commitments and could not accompany her daughter for the scheduled appointments. In these situations, her appointment was rescheduled to a different date which was convenient for parents and the team members.

DISCUSSION

The rising number of children and adolescents with T2DM over the years has been attributed to the increase in obesity, sedentary lifestyle and intrauterine exposure to hyperglycemia. The onset of T2DM among children usually occurs at puberty and tends to be more common among females, those with a family history of diabetes and the low socioeconomic group.[4] T2DM among children is of concern as it progresses quickly due to more severe insulin resistance and rapid deterioration of pancreatic beta cells. T2DM complications such as retinopathy, nephropathy and neuropathy also tend to occur earlier, and progress more rapidly compared to type 1 diabetes (T1D).[4] Hence it is important to detect T2DM early, as diagnosis may be missed or delayed as children may not be perceived as being at risk. The first step is to make the diagnosis of T2DM among children. Most guidelines suggest that for children, a fasting

blood glucose of ≥ 7.0 mmol/L or a random blood glucose of ≥ 11.1 mmol/L with symptoms such as polyuria, polydipsia and unintentional weight loss, in the absence of islet autoantibodies, can be used to diagnose T2DM. Other parameters such as HbA1C level ≥ 6.5% or a 2-hour post-oral glucose tolerance test (OGTT) of ≥11.1 mmol/L (1.75 g of glucose per kg body weight) may also be used. T2DM in adolescents may be misdiagnosed as T1D, especially if the child is not obese or when ketoacidosis is detected at presentation, suggesting caution in interpreting these results.[3,4] Once T2DM is suspected, pancreatic autoantibodies should be done to exclude autoimmune T1D. Differentiating these two conditions is important as the management approach, treatment and outcome is different for each condition.[5] As for our patient, the diagnosis of T2DM was straight forward as she had symptoms of polyphagia, polydipsia, polyuria and hyperglycemia with fasting blood sugar of 15.1 mmol/L and HbA1c of 11.5%. To facilitate early detection, the American Diabetes Association (ADA) recommends that overweight (BMI > 85th percentile) or obese (BMI > 95th percentile) Asian children and adolescents at the age of 10 years and above or at puberty presenting with one or more of the following risk factors should be screened for T2DM:[3,5]

- 1st or 2nd degree family history of diabetes
- Maternal diabetes or gestational diabetes during the pregnancy with the child
- Signs of insulin resistance (e.g., acanthosis nigricans, hypertension, dyslipidemia, polycystic ovarian syndrome or small for gestational age birth weight)
- If the child is currently on atypical antipsychotic agents which can cause weight gain

Our patient fulfilled the criteria for screening as she was above 10 years of age, obese with BMI more than 95th centile for her age and had acanthosis nigricans on her neck. ADA also recommends that if the initial screening of high-risk children is normal, it should be repeated every three years. High risk patients with increasing BMI and a strong family history of T2DM should be screened annually.[5]

Management of adolescents with T2DM requires a comprehensive multidisciplinary approach including the family, paediatric endocrinologist, family medicine specialist, dietician, diabetic nurse educator and psychologist. The management triad includes lifestyle modification, pharmacological intervention and management of comorbidities.[5] This can be done by using the FCC approach as demonstrated in the management of our patient. The rationale for involving the family is based on the fact that children will not be able to manage their disease independently and they will need their family as they can provide the best support and care for them. This approach also facilitates bonding between the child and their family to foster a positive outcome. This approach involves sharing of information and involving the family in the care of the child by providing knowledge and skills to empower them to incorporate these skills in managing their child at home. Involving the family in the child's care is also important for decision-making processes regarding medication, implementing lifestyle changes and to ensure that the child received adequate support for this chronic condition.[6] For our patient, the FCC was established based on the partnership between the family, the patient and a multidisciplinary team of health care providers consisting of a family physician, dietician, pharmacist and physiotherapist. The objectives of this approach were to manage her holistically to achieve good glycaemic control, prevent further weight gain and to prevent diabetic related complications. This was achieved through multiple meetings with the patient and her mother who was the main caregiver.

An important aspect of T2DM management in obese children is to strike a balance between achieving and maintaining ideal body weight without compromising on linear growth and development as these children are still growing.[3] In general, obese children with T2DM are encouraged to reduce about 7 to 10% of the excess body weight.[5] Diet and weight related intervention should involve the family as they greatly influence children's food intake. Healthy eating habits include limiting portion size, eating low sugar and calories. For our patient, she managed to lose 8 kgs over 18 months by gradual change in dietary intake and increasing physical activity. She also managed to reduce screen time which gave her more time to have good quality sleep. Achieving regular and good quality sleep of about 8 to 11 hours a day, regular physical activities and reducing screen time entertainment of less than two hours a day plays an important role in lifestyle modification.[3,5]

Although there was a strong indication for starting pharmacological management for our patient at presentation as she had high blood sugar levels, parents had refused medical management. Hence the team had to tailor plans to the needs of the patient using a shared care approach with lifestyle modification as a first step in management. Current guidelines recommend that oral metformin, which is the drug of choice for children with T2DM, should be initiated at the point of diagnosis with concomitant lifestyle modifications. Metformin 500 mg daily can be initiated and titrated over 3 to 4 weeks to a maximum of 1 g twice daily.[3,4,5] Short-term basal insulin (intermediate or long acting) may be required if:

- Random blood sugar is ≥ 13.9 mmol/ L
- HbA1C level is >8.5%
- Glycaemic control is poor with 3 to 4 months of metformin monotherapy

Basal insulin dosage of 0.25 to up to 0.5 U/kg/day dose can be given and increased every two to three days guided by self-monitoring of blood glucose (SMBG). If target HbA1C of < 7% is not achieved with metformin and maximum basal insulin of 1.5 U/kg/day, then fast-acting prandial insulin may be added. Once target blood sugars are achieved, insulin may be reduced by 10 to 30% every few days over 2 to 6 weeks and stopped but maintenance therapy with lifestyle modification and metformin must be continued. The aim is to achieve fasting blood glucose levels between 4 to 6 mmol/L, post-meal between 4 to 8 mmol/L and three monthly HbA1C between < 6.5 to < 7% without inducing hypoglycemia. [3,5] However this is an uphill task to achieve and may take a long time with much commitment from the patient, the family and the multidisciplinary team members. This is compounded by the fact that puberty itself can affect blood

glucose control due to hormonal changes. For example, the increase in cortisol and catecholamines raises blood glucose levels. Rapid weight gain during puberty of both lean body mass and adipose tissue increases insulin demand and deteriorates blood glucose level further.[7] For our patient, intermediate acting insulin was started at 10 units and gradually increased by two units every two weeks and monitored closely. The patient and her mother attended diabetes self-management education (DSME) sessions conducted by the diabetic nurse educator at primary care for tips on selfcare. Each time the insulin dose was adjusted, the patient was seen on two weekly basis by the diabetic nurse educator to evaluate the glycaemic control and assess for hypoglycemia.

New diabetic medication, such as the Glucagon-Like Peptide-1 (GLP-1) receptor agonists (e.g., liraglutide) is now approved for children between 12 to 17 years with a body weight of ≥ 60 kg.[3] However, the use of this drug is best done in collaboration with the paediatric endocrinologist at a tertiary facility for close monitoring and dose adjustment.

Other aspects of the management of children with T2DM include screening and managing comorbidities in such as hypertension and dyslipidemia. [3,4,5] Our patient had mildly elevated blood pressure and lipid levels hence, we proceeded with non-pharmacological management to lose weight, in anticipation that these parameters would normalise with this intervention. Initial blood pressure management should be advocated by salt restriction and weight loss, failing which, an angiotensin-converting enzyme inhibitor (ACEI) or an angiotensin receptor blocker (ARB) may be used. The targeted blood pressure is <90th percentile or blood pressure < 130/80 mm Hg.[3,5] Statins should be considered when the LDL levels are persistently > 3.4 mmol/L after 6 months of lifestyle modification, while fibrates may be considered if triglyceride levels are > 4.6 mmol/L. The aim of treatment is to optimise LDL level to <2.6 mmol/L, HDL to >0.9 mmol/L and triglycerides to <1.7 mmol/L. Our patient's lipid and blood pressure gradually improved with weight loss, hence, did not require any medications.

Management of T2DM in this child was a long and challenging journey with multiple obstacles and issues with adherence. But, with perseverance and patience of the medical team, the patient and her mother, small achievements were made gradually. Although the patient was not able to achieve her ideal body weight and to normalise glycaemic control rapidly, some changes were observed over time. One of the main challenges in managing diabetes in this child was the resistance from parents towards medication, poor adherence to treatment and inconsistent adherence to dietary and lifestyle modification intervention. Although the patient has made some progress towards achieving the treatment targets for now, there will be other challenges in the near future especially during transition to adulthood when the patient becomes independent and takes full responsibility for her diabetes self-care. Hence the multidisciplinary team must be vigilant to anticipate challenges and be prepared as comorbidities and risk of complications are higher as the child grows.

CONCLUSION

Early identification and management of children with T2DM is important, as it is a lifelong condition with severe complications and consequences. Managing this condition among children is a long and challenging journey which requires much perseverance and patience from healthcare personnel, family and the patient themselves. Furthermore, the onset of T2DM at puberty, which is a crucial stage of physical and emotional upheaval, acts as an additional burden for these children. Early management using the family centred care involving a multidisciplinary team is essential as these children need regular follow-up, good family and health care support. Comprehensive lifestyle modification and medication can help these children to achieve a healthier life with minimal complications as they grow into adults.

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DECLARATION

The authors declare no actual or potential conflict of interest in relation to this article.

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Rotavirus outbreak in hospital: A lesson learnt

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SUMMARY

This case report presents an outbreak of rotavirus infection in a hospital paediatric ward, with five laboratory-confirmed cases identified among paediatric patients. The sixth case had an epidemiological link with the affected patients. This report highlights the importance of prompt identification, appropriate management, and adherence to infection control measures to prevent the spread of rotavirus in healthcare settings.

INTRODUCTION

Rotavirus is a highly contagious viral infection primarily affecting infants and young children, characterised by severe diarrhoea and vomiting. Rotavirus is common, accounting for 35 to 60% of acute severe diarrhoea in children < 5 years of age in countries without rotavirus vaccine, with the highest attributable percentage in infants.[1,2] Rotavirus has a case-fatality rate (CFR) of approximately 2.5% among children in developing countries who present to health facilities[2]. This CFR is higher in areas without good access to health care. In 2013, rotavirus caused an estimated 215 000 deaths worldwide[3-5]. It imposes a significant burden of disease globally, with substantial morbidity and mortality, particularly in developing nations.[6] The transmission of rotavirus commonly occurs through the faecal-oral route, and outbreaks can rapidly propagate in settings where individuals, especially young children, are in close proximity.[7] Although outbreaks in healthcare facilities have been reported, limited literature exists documenting the spread of rotavirus within healthcare staff in paediatric wards.

Studies published during the past 20 years have documented that in Malaysia, the range of the proportion of hospitalisations due to rotavirus-associated acute gastroenteritis was 28 to 43%,[8] and, in the only community-based rotavirus study in Malaysia, rotavirus was detected in 12% of children seen for acute gastroenteritis.[9,10] Paediatric wards in healthcare settings play a critical role in managing and treating various illnesses, including rotavirus gastroenteritis, among children. The transmission of rotavirus among healthcare staff in these wards not only pose a risk to the affected staff members but also increases the likelihood of secondary infections among vulnerable patients. Understanding the dynamics of rotavirus spread within healthcare staff is crucial for implementing appropriate preventive measures and controlling outbreaks.

This case report aims to describe a cluster of rotavirus infections among paediatric patients in a paediatric ward and to highlight potential risk factors contributing to its spread. The report underscores the significance of adherence to infection control practices, including hand hygiene and appropriate personal protective equipment (PPE) usage, to prevent rotavirus transmission within healthcare settings.

To the best of our knowledge, limited published data exists on similar outbreaks involving rotavirus transmission among healthcare staff in paediatric wards. By documenting this case and sharing our findings, we seek to raise awareness regarding the importance of implementing preventive strategies and reinforcing infection control measures to mitigate the spread of rotavirus within healthcare facilities.

CASE REPORT

Larut Matang & Selama District Health Office had received few rotavirus case notifications on 25th July 2022 where four cases were notified from paediatric ward in a hospital. All the cases experienced clinical signs and symptoms of acute gastroenteritis (AGE). On 27th July 2022 at 1715H, we received another rotavirus case notification involving a 5-month child from same ward. On 1st August, another case was notified from the same ward, resulting in a total of six cases of the AGE cluster (Figure 1). Further history taking, noted that the sixth case had no history of recent admission in the ward but the son to the staff nurse who worked in the same ward and had dealt with all the previous five rotavirus positive cases.

A retrospective analysis was conducted to investigate the rotavirus outbreak in the paediatric ward. Data were collected from medical records, laboratory reports and infection control logs. The demographic information, clinical presentation and laboratory confirmation of rotavirus infection was recorded for each case. In addition, the staff nurse's involvement and potential exposure to the infected patients were examined.

Surrounding swab (baby weighing scale) was done on 26th July 2022. Water sampling activities were also carried out on 1st August 2022 from baby room tap water, patient pantry tap water and nurse counter tap water. All water samples were sent to the National Public Health Laboratory Sungai Buloh (MKAK) on 2nd August 2022 for analysis purpose. Active Case Detection (ACD) activities were carried out from 2nd August 2022 onwards involving all patients, caretakers and staffs in the paediatric ward. Caretakers and staffs refused to provide sample as they had been asymptomatic during ACD activities. Further investigation revealed that the mother of the sixth case was a staff nurse who had directly handled the previous five rotavirus cases. She did not reveal to have had symptoms of AGE but recorded as asymptomatic at the time of ACD. Thus, no sample was taken from her for testing.

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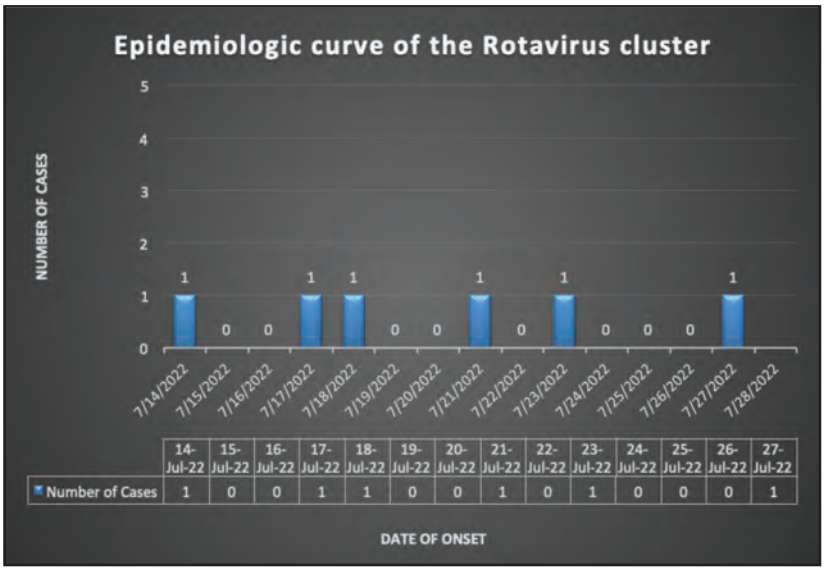

Fig. 1: Epidemiologic curve of the rotavirus cluster

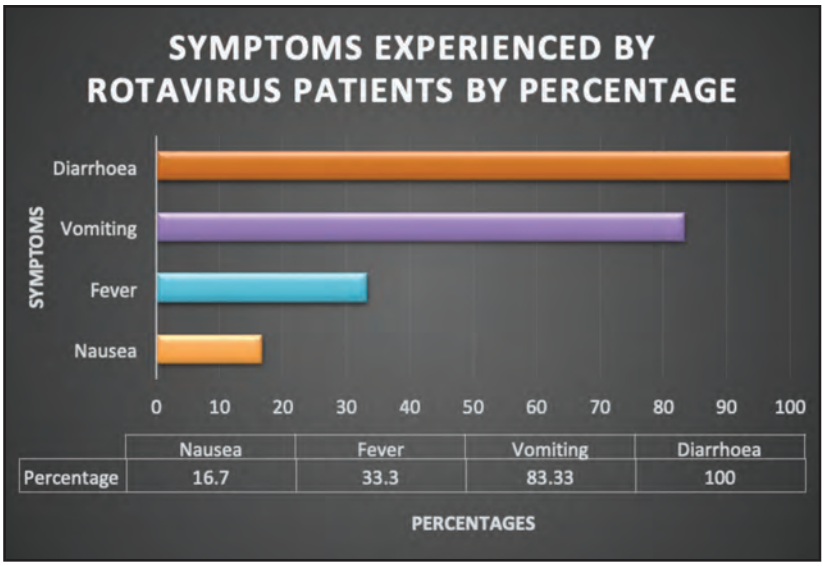

Fig. 2: Symptoms experienced by rotavirus patients by percentage

This paediatric ward consists of three zones, which were red, yellow and green zones. There is a high dependency unit (HDU) situated in the red zone of this ward with maximum capacity of four beds at a time. There was a total of 127 people in this ward at the time of investigation, namely seven doctors, 35 nurses, seven attendants, 39 patients and 39 caretakers.

The symptoms, which were experienced by AGE cases, included diarrhoea (100%), vomiting (83.33%), fever (33.3%) and nausea (16.67%) as shown in Figure 2. Results from water samples (baby room tap water, patient pantry tap water, nurse station tap) were negative (rotavirus A not detected). Result from surrounding swab (baby weighing scale) taken on 26th July 2022 was also negative (rotavirus A not detected).

DISCUSSION

The ACD activity in the ward found that no staff had symptoms of AGE throughout the incubation period. However, a nurse had symptoms of AGE staring from 27th July 2022 but did not seek any treatment and was not screened for rotavirus. The nurse had contacted with five rotavirus cases on rotation basis. Furthermore, this nurse's son started showing symptoms of AGE on 31st July 2022 and was admitted to the same ward and confirmed to be infected with rotavirus on the same day. The sixth case was likely to have been infected by his mother.

The analysis of environmental swab samples (the baby weighing machine, and water samples) did not detect the presence of rotavirus A. It might be due to the hospital regularly carrying out disinfection activities and the water supply is treated water from *Lembaga Air Perak* (LAP).

This cluster incident is probably caused by poor hand washing practice by staffs in the ward concerned. However, no hand swab samples, or other environmental samples were taken. Therefore, the cause of this infection was not identified. According to records, health education and monitoring of hand hygiene skills and practices by all members in the paediatric ward were done periodically. All positive cases had also been isolated to special wards or cubicles to isolate cases from other patients in the ward. All caregivers and staffs were reminded not to share toys among patients. In addition, sanitation and disinfection activities would be monitored by ward supervisors to ensure that they were carried out regularly and according to the schedule. All visitors were also reminded to wash their hands first before visiting patients in the ward.

The spread of rotavirus infections in healthcare facilities, including paediatric wards, poses a significant risk to vulnerable populations, particularly young children. This case report highlights the importance of implementing preventive measures to control the transmission of rotavirus, emphasising the need for rotavirus vaccination among children in Malaysia.[11] Rotavirus vaccines have demonstrated efficacy in reducing the incidence and severity of rotavirus gastroenteritis worldwide.[7,12] However, despite the availability of safe and effective vaccines, rotavirus vaccination coverage in Malaysia remains suboptimal. Increasing vaccine uptake among children is crucial to prevent the spread of rotavirus diseases, not only in the community but also within healthcare facilities.

In healthcare settings, where children may be more susceptible to infections due to underlying conditions or weakened immune systems, the introduction of rotavirus vaccines can help mitigate the risk of outbreaks and protect both patients and healthcare providers. By reducing the number of rotavirus cases among children, the overall burden of disease can be decreased, leading to a decrease in hospital admissions, healthcare costs and the potential for nosocomial transmission.

Hand swab/rectal swab from caretakers/staffs were not sampled to prove the link or cause of the cluster due to the period of asymptomatic and poor cooperation from them.

CONCLUSION

The outbreak of rotavirus infections in the hospital paediatric ward emphasises the need for stringent infection control measures. Early identification of cases, prompt testing, proper isolation precautions and adherence to hand hygiene protocols are vital to prevent the spread of rotavirus in healthcare facilities. Staff education and awareness programs should be implemented to reinforce the importance of disclosing symptoms and following appropriate infection control practices.

The implementation of routine rotavirus vaccination programs in Malaysia should be a priority, targeting all the eligible children. This should include educating healthcare providers, parents and caregivers about the benefits and safety of rotavirus vaccines, addressing any concerns or misconceptions they may have. By promoting rotavirus vaccination among children, particularly in healthcare settings, Malaysia can significantly reduce the burden of rotavirus infections, minimise the risk of outbreaks and protect the health and well-being of the population.

CONFLICTS OF INTEREST

This research has no conflicts of interests.

ETHICAL CLEARANCE

Ethical clearance has been obtained from NMRR Secretariat. (NMRR ID-22-02692-BYR). Parent's consent were gained for the publication of this case report.

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CASE REPORT

Case of emphysematous splenic abscess in *Burkholderia pseudomallei* infection

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SUMMARY

Emphysematous splenic abscess is a rare occurrence, and there have been no known reported cases associated with *Burkholderia pseudomallei* infection. Melioidosis, commonly found in Southeast Asia, can lead to abscess formation in various organs such as the lungs, liver, spleen, skeletal muscle and prostate. It is important to maintain a high level of suspicion in high-risk populations and consider relevant epidemiological factors. Timely and appropriate administration of antimicrobial treatment has shown positive clinical outcomes in managing splenic abscesses and minimising the need for invasive surgical intervention.

INTRODUCTION

Emphysematous abdominal infections typically occur after trauma or abdominal surgeries. There have been documented cases of emphysematous splenic abscess following surgical intervention for disseminated *Klebsiella pneumoniae* infection, necessitating splenectomy. However, our case is the first to report a rare and insidious occurrence of emphysematous splenic abscess associated with *Burkholderia pseudomallei* infection that was successfully treated without requiring invasive surgical intervention.

CASE REPORT

A 61-years-old male farmer with no pre-existing medical condition presented with a one week history of generalised weakness, along with right hypochondriac and epigastric pain, left pleuritic chest pain, yellowing of the eyes, loss of appetite, weight loss and fever. The patient was icteric upon examination but hemodynamically stable and not tachypnoeic. Lung examination revealed reduced breath sounds in the left hemithorax, while the cardiovascular examination was unremarkable. Abdominal examination revealed tenderness in the right hypochondrium and epigastric region. Laboratory investigations demonstrated markedly elevated inflammatory markers (C-reactive protein 366.8 mg/L), leukocytosis (WBC 35.8 x 10^9 /L), impaired liver function tests (total bilirubin 50.7 g/L, direct bilirubin 44.1 g/L, ALP 907 U/L, ALT 38.3U/L, AST 36 U/L) and renal impairment (Na 134 mmol/L, K 3.2 mmol/L, urea 13.8 mmol/L, creatinine 245 µmol/L). Blood glucose monitoring during the inpatient stay indicated that the patient did not have diabetes. Chest x-ray showed a blunted left costophrenic angle, while ultrasound thorax examination revealed a left pleural effusion. Ultrasound abdomen showed a distended gallbladder with sludge with several enlarged porta hepatis lymph nodes but no biliary tree dilatation and ill-defined hypoechoic liver lesions with echogenic focus with reverberation artifacts (Figure 1A and 1B). Computed tomography (CT) scan of the abdomen and pelvis displayed multiple ill-defined hypodense splenic lesions with air focus within while the biliary system appeared normal in the imaging (Figure 2).

The patient initially received intravenous ceftriaxone 2 g once daily and metronidazole 500 mg three times daily for suspected biliary sepsis but later developed worsening symptoms and dyspnoea, requiring non-invasive mechanical ventilation. The antibiotic treatment was changed to intravenous meropenem 1 g three times a day for broader pathogen coverage, and a pigtail catheter was inserted for drainage of the left pleural effusion. Additional blood and sputum cultures were performed to rule out hospital acquired pneumonia, and pleural fluid analysis indicated an exudative effusion. Despite negative findings for pleural fluid and sputum culture, blood cultures taken during admission and repeated during deterioration revealed the presence *Burkholderia pseudomallei*, which was found to be sensitive to trimethoprim-sulfamethoxazole, meropenem, ceftazidime and amoxicillin-clavulanic.

The patient's antibiotics were switched to intravenous ceftazidime 2 g four times daily and oral trimethoprim-sulfamethoxazole, as per local guidelines for treating melioidosis. Over time, the patient's condition gradually improved, with positive changes in inflammatory markers and other blood parameters. A follow-up ultrasound assessment after 14 days of receiving intravenous antimicrobial therapy showed a decrease in the size of the splenic lesion (1.7 × 1.4 cm). The patient spent one week in the high-dependency ward and an additional three weeks in the general ward, receiving intravenous antibiotics. After completing a 4-week course of antibiotics (1 week of meropenem and 3 weeks of ceftazidime), the patient was discharged home in stable condition. He was prescribed a 3-month course of oral trimethoprim-sulfamethoxazole for eradication therapy. Serial ultrasound examinations demonstrated an improvement in the size of the splenic abscess prior to stopping treatment (Figures 1C and 1D). He completed the total three months duration of oral trimethoprim-sulfamethoxazole.

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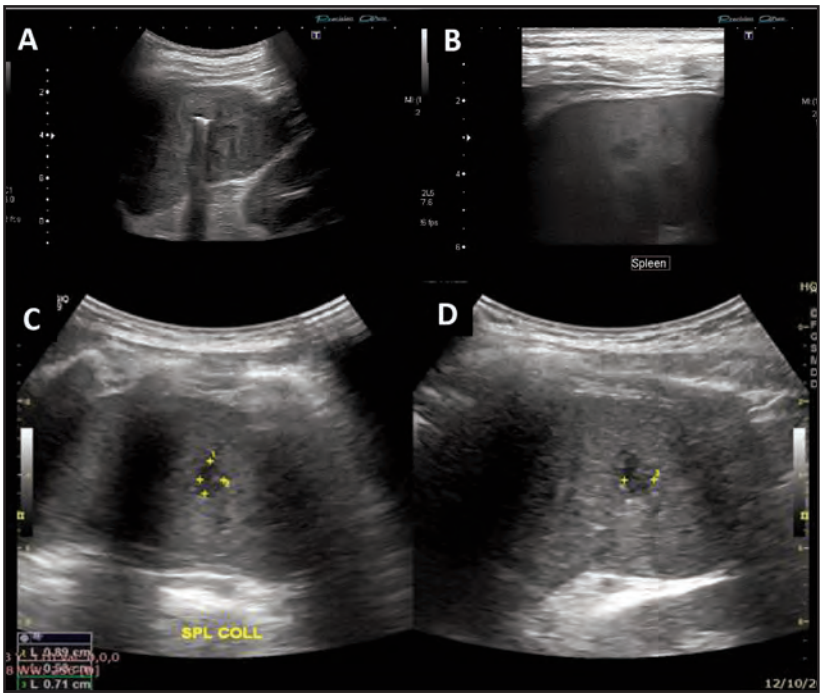

Fig. 1: 1A (on curvilinear probe), 1B (linear probe)-Ultrasound images upon initial presentation showing ill-defined hypoechoic liver lesions with echogenic focus with reverberation artifacts. 1C, 1D - Ultrasound reassessment 1 month post treatment showing smaller splenic lesion measuring less than 1cm with no obvious air focus noted within.

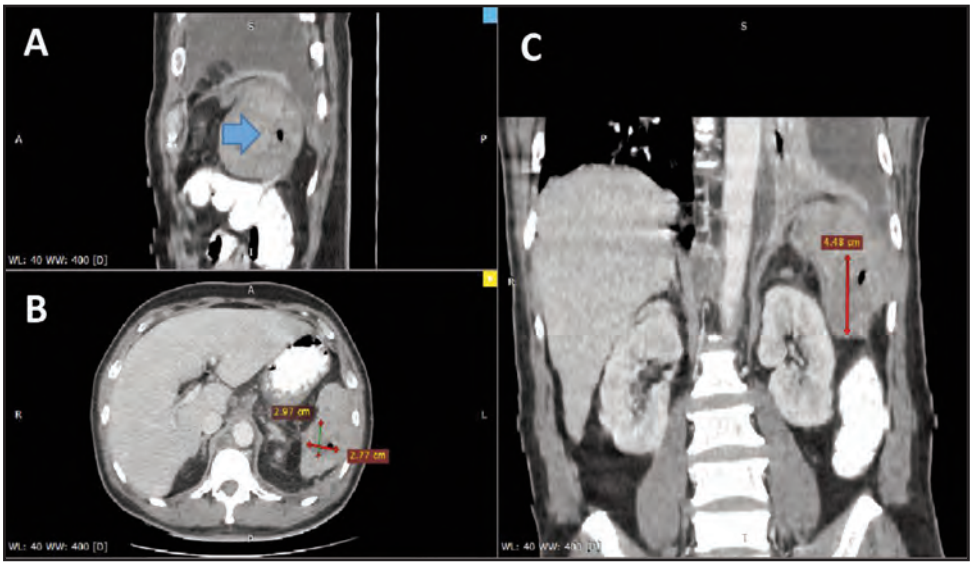

Fig. 2: Computer tomography (CT) of abdomen done on the day 1 of presentation. This is the Multiplane Reconstruction (MPR) view showing a multiple ill-defined hypodense splenic lesions with air focus within. 2A – sagittal view, 2B – axial view, 2C – Coronal view. The largest lesion (thin arrow) measuring apporximately 3.0 x 2.8 x 4.5 cm (AP x W x CC). Thick arrow showing an air focus.

DISCUSSION

Splenic infections can generally be attributed to primary infections, recent traumatic injury, haematologic or metastatic spread of infection, and certain medical conditions like sickle cell anaemia.[3] Splenic abscesses are primarily caused by disseminated bacterial infections, which can be either mono or polymicrobial.[1] Gram-negative bacteria such as *Escherichia coli, Klebsiella pneumoniae* and *Proteus mirabilis*, as well as gram-positive bacteria like *Staphylococcus aureus* and group D Streptococcus, are commonly implicated.[3] Polymicrobial flora is responsible for at least 10 to 15% of patients with splenic abscesses.[5] Splenic infections can also originate from endocarditis. Additionally, intra-abdominal conditions like appendicitis, diverticulitis, bowel infarction or genitourinary tract infections (particularly caused by *E. coli*) can lead to splenic infections. In rare cases, direct invasion of the spleen may occur through fistulisation of gastric ulcers, colonic adenocarcinoma or

distal pancreatic malignant disease, resulting in gas-forming necrosis of the spleen.[3] In emphysematous infections, the presence of gas is a result of glucose fermentation, leading to the production of carbon dioxide and nitrogen. Studies have shown that *Burkholderia pseudomallei*, the causative agent of melioidosis, does not ferment lactose.[2,4] In this case, the emphysematous splenic infection is possibly a result of unidentified polymicrobial infection, possibly involving fastidious bacteria, in addition to *Burkholderia pseudomallei*. It is also possible that a microperforation of an adjacent visceral organ, which was not detected in this study, contributed to the infection. The exact mechanism by which *Burkholderia pseudomallei* forms gas in a specific environment remains unknown. However, in this specific case, the patient presented with emphysematous splenic infection and Burkholderia pseudomallei bacteraemia. Interestingly, conservative treatment using antimicrobial agents was successful, and surgical intervention was avoided.

Despite the presence of fever, right hypochondriac pain and a cholestatic liver function test suggests a biliary sepsis, there was no sonographic evidence of biliary tree dilatation, bile duct thickening, cholelithiasis or cholecystitis. The cholestatic jaundice observed, along with normal biliary structure and abnormal renal profile, was likely a result of the ongoing sepsis.

From a therapeutic perspective, splenectomy was previously considered the gold standard.[1] However, the need for splenectomy as a primary modality has been questioned by several recent studies showing that conservative management (i.e., antibiotics with or without percutaneous drainage) is possible. In a case series done in India by Divyashree and Gupta,[5] only about 18 to 22% of patients required therapeutic splenectomy. Approximately 80% of the patients were managed conservatively. In the series, no patient needed a therapeutic splenectomy.[5] For those who do not respond to conventional therapy and have abscesses larger than 10 cm, splenectomy is still considered the treatment of choice.[1] To the best of our knowledge, reported cases of emphysematous splenic abscess required surgical drainage with or without splenectomy. This case highlights that not all emphysematous infections necessitate surgical intervention. Prompt initiation of suitable intravenous antibiotics, along with a high level of suspicion regarding the likely organism based on epidemiological and social factors, is crucial for successful treatment. This approach reduces the risk of disease progression, thereby minimising the need for invasive management.

CONCLUSION

Hospitals equipped with ultrasound services and trained sonographers can reasonably detect abdominal emphysematous infections. To ensure proper management of intra-abdominal abscesses, it is crucial to promptly send blood cultures for all patients. Additionally, it is important to consider the possibility of *Burkholderia pseudomallei* infection in high-risk patients. Since emphysematous infections can be associated with non-gas-producing organisms as well it may be wise to start administering a broad-spectrum antibiotic before receiving the blood culture and sensitivity report. This aggressive approach could potentially save lives and reduce the need for invasive interventions.

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CONFLICT OF INTEREST

Author declares no conflict of interest.

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A young man with atrioventricular dissociation: something to worry about or just a false alarm?

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SUMMARY

Atrioventricular dissociation is an abnormality of the cardiac electrical conduction when the atria and ventricles beat independently. It often manifests as a life-threatening bradycardia in complete atrioventricular heart block where the atria and ventricles beat asynchronously. This is usually caused by acute coronary events in the older population with cardiovascular risk factors and requires a prompt treatment to stabilize the hemodynamics by cardiac pacing. In rare cases, the atria and ventricles can beat synchronously despite atrioventricular dissociation. This type of atrioventricular dissociation occurs in younger population without cardiovascular risk factors especially in athletes. It is not life-threatening and usually does not require treatment or monitoring. We report a young man who presented with a syncopal attack due to a heat stroke after a marathon run, with an incidentally found atrioventricular dissociation in his electrocardiogram, which resolved by physical exertion.

INTRODUCTION

Syncope is a common presentation to the Emergency Department (ED) with a wide spectrum of possible aetiologies. The main aim of the initial approach to syncope is to distinguish it between life-threatening and benign causes of syncope.[1] Important aetiologies of syncope include cardiogenic causes such as cardiac arrhythmia and structural abnormality leading to cardiac outflow obstruction, and neurological causes such as seizure and vertebrobasilar vascular insufficiency, while vasovagal attack is one of the benign causes. Apart from history taking and physical examination, initial investigations for a syncopal attack consist of an electrocardiogram and a brain computed tomography to rule out cardiogenic and neurological causes respectively.

About 90% of patients with cardiogenic syncope have abnormal electrocardiogram findings, thus an electrocardiogram gives a good diagnostic value as an initial assessment tool for syncope.[2] Nevertheless, patients with non-cardiogenic syncope can have incidental abnormal electrocardiogram findings. It is important to rule out cardiogenic syncope as it is associated with an increase in all-cause mortality and morbidity. Further investigations with echocardiogram to look at structural abnormality, functional stress tests with electrocardiogram or echocardiogram to look at inducible ischemia, and Holter monitoring are crucial to confirm or rule out cardiogenic causes to guide the management of syncope.

CASE REPORT

A 17-years-old man presented with a syncopal attack after a marathon run. During the syncopal attack, he fell and landed with outstretched arms without any witnessed tonic-clonic movement of limbs or significant injury. He regained consciousness within a few minutes but could not recall any incident prior to the syncope. He was active in track and field for the past 3 years, with no medical illness and previous hospitalisation. He did not have any family history of heart diseases or seizures.

He had a brief period of confusion upon presentation to the ED, which resolved subsequently with a full Glasgow Coma Scale. His physical examination revealed that he was febrile with a body temperature of 38.5°C and tachycardic with a heart rate of 130 beats per minute, evidenced by sinus tachycardia on cardiac monitoring. His haemodynamic status was otherwise stable with a blood pressure of 132/56 mmHg and other systemic examination was unremarkable. His blood investigations showed myositis and acute kidney injury with elevated serum creatinine kinase, alanine transaminase, aspartate transaminase, and creatinine at 2107 U/L, 942 U/L, 500 U/L, and 180 µmol/L respectively. Other laboratory investigations, particularly his electrolytes and urinalysis were unremarkable.

He was treated for heat stroke with myositis and dehydration after a marathon run. With adequate intravenous hydration, his clinical condition improved with resolution of fever and tachycardia. His electrocardiogram revealed an isorhythmic atrioventricular dissociation with a heart rate of 50 beats per minute (Figure 1). Otherwise, he was asymptomatic, and an echocardiogram confirmed no cardiac structural abnormality with normal sized all cardiac chambers and a good left ventricular systolic function with an ejection fraction of more than 55%. A functional stress test with a 6-minute-walk-test revealed that he had no issue completing more than 700 m in 6 minutes, with a resolution of atrioventricular dissociation to sinus bradycardia in electrocardiogram with a heart rate of 56 beats per minute (Figure 2). He was discharged well after a 3-day-duration of hospital stay when his blood investigations normalised.

DISCUSSION

The sinoatrial node is the major pacemaker in the heart. It initiates a propagation of electrical impulses in the heart from the atria to the ventricles via the atrioventricular node and His-Purkinje system, results in a synchronous

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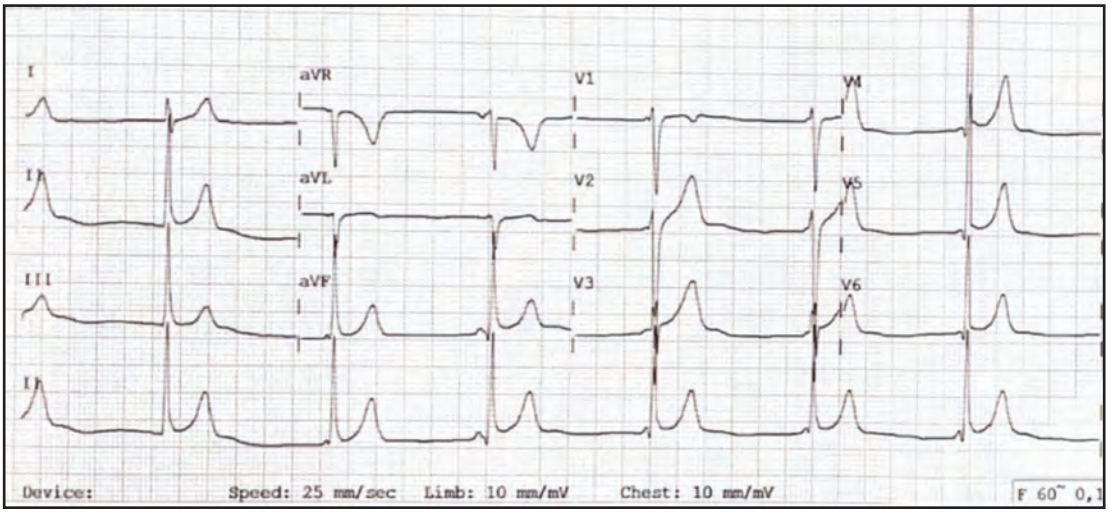

Fig. 1: A 12-lead electrocardiogram showed an isorhythmic atrioventricular dissociation, evidenced by a regular R-R interval with P waves "wander" from left to the QRS complex to "hide" within the QRS complex.

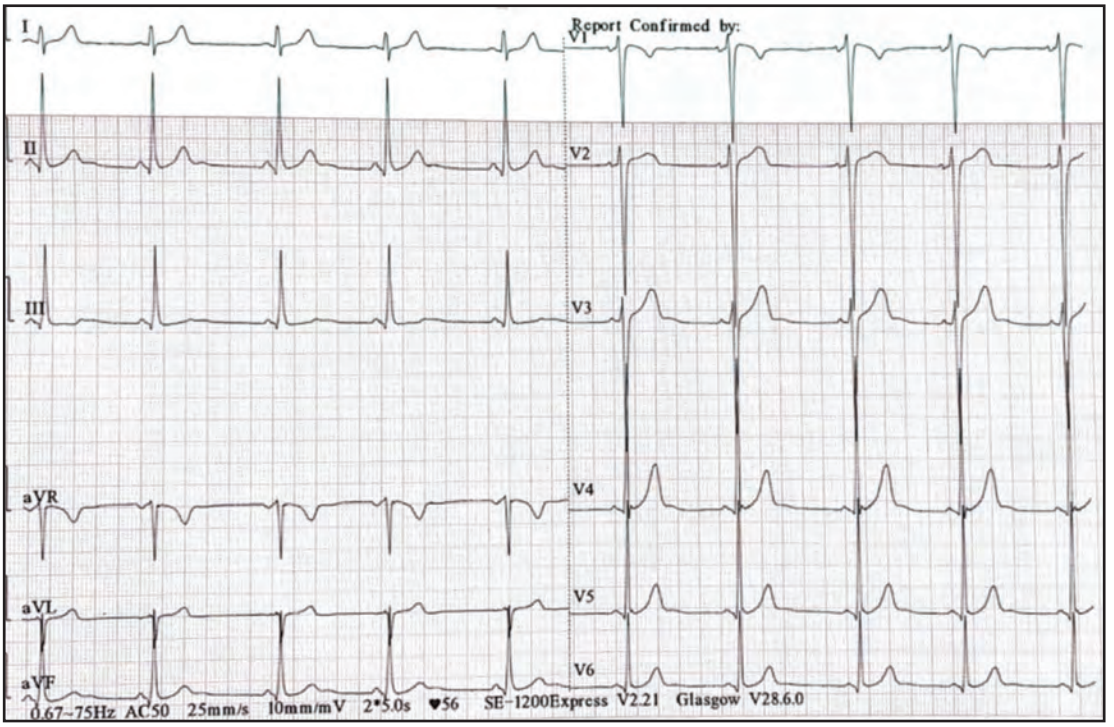

Fig. 2: A 12-lead electrocardiogram showed sinus bradycardia with short PR intervals of 104 milliseconds, evidenced by a regular R-R interval with fixed PR intervals.

depolarisation of the atria and ventricles to ensure an effective cardiac contraction. In cases when the pacing rate of sinoatrial node is low or any conduction disturbance of impulses from sinoatrial node to the atrioventricular node, the intrinsic pacemaker cells located at the atrioventricular junction will be the major pacemaker to pace the ventricles at a rate of 40 to 60 beats per minute. This rhythm is known as a junctional rhythm.

An atrioventricular dissociation occurs when the atria and ventricles are paced by different pacemakers, hence beat independently. Three theories of atrioventricular dissociation were described in the literature, which are atrioventricular dissociation by default, atrioventricular dissociation by usurpation, and a complete heart block. In atrioventricular dissociation by default, a slowing of sinoatrial node as the dominant pacemaker leads to the dominance of an independent ventricular pacemaker. Atrioventricular dissociation by usurpation describes an acceleration of the ventricular pacemaker which surpasses the intrinsic atrial rate of the sinoatrial node. A pathological blockage of the atrioventricular node occurs in complete heart block, which prevents the conduction between the atria and ventricles, and results in independent rhythms.[3]

In cases of atrioventricular dissociation with bradycardia, it is crucial to rule out complete heart block and drug toxicity such as digitalis toxicity as urgent treatment is required to prevent fatal complications.[4] However, in our present case, the young man was an athlete who was active in track and field for 3 years without previous hospitalisation. His incidental abnormal electrocardiogram findings did not fit into the clinical conditions to suggest a cardiogenic syncope. A normal echocardiogram and a reversion of atrioventricular dissociation to sinus bradycardia after a 6-minute-walk-test confirmed his bradycardic atrioventricular dissociation was physiological. Bradycardia is common amongst athletes with sinus arrhythmias, junctional rhythms, atrioventricular conduction delays, as well as isorhythmic atrioventricular dissociation such as present case reported in the literature.[5]

Isorhythmic atrioventricular dissociation happens when the sinus rate and the junctional rate are nearly similar, but they are beating independently. It is a physiological condition for those with low resting heart rate, especially young athletes, whereby a low sinus rate that falls within the range of the intrinsic junctional rate will lead to co-dominance of both sinus and junctional pacemaker. In physiological conditions where the atrioventricular node is not diseased, any simple activities which can increase the sinus rate will reverse the condition back to sinus rhythm.

CONCLUSION

The young man in our present case had an "abnormal" electrocardiogram which is completely normal. It is an incidental physiological finding that does not warrant any further investigation and he should be allowed to continue his activities in sports without restriction. Abnormal electrocardiogram findings in patients presented with cardiac associated symptoms such as syncope often result in difficulties in decision-making and diagnosis by the attending medical personnel. Good clinical acumen and appropriate investigations are crucial to ensure a proper diagnosis and management.

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Malignant cutaneous horn: a case report

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SUMMARY

Cutaneous horn (cornu cutaneum) is rare lesions consisting of keratotic material resembling a horn. It comes in variable size and shape. The lesions typically occur in sun exposed areas particularly the face, nose, ear and dorsal of hands. Cutaneous horn usually is benign in nature, but the possibility of skin cancer should always be considered. Most common premalignant condition is actinic keratosis with squamous cell carcinoma (SCC) being the most common cause of malignancy. Herewith, we are reporting a case of cutaneous horn over the pinna with underlying malignancy at its base for around five years duration. Surgical removal of the lesion had been done and currently he is under routine surveillance. Awareness of such lesions should be made to detect and manage early.

INTRODUCTION

Cutaneous horn *(cornu cutaneum)* are relatively uncommon lesions consisting of hyperkeratotic epithelial lesion resembling that of an animal horn. It is defined as having a height that is more than half of the diameter of its base.[1] Cutaneous horn was first officially documented in an older Welsh woman by the name of Mrs. Margeret Gryffith in 1588 which was displayed in circuses worldwide as magical beasts.[2] The lesions typically occur in sun exposed areas, particularly the face, ear, nose and hands. Cutaneous horns are now widely accepted as a reactive cutaneous growth caused by a variety of benign, premalignant or malignant primary processes. Most common cause of benign cutaneous horn is seborrheic keratosis whereas actinic keratosis is the most common premalignant cause. Squamous cell carcinoma (SCC) is the most frequent malignant type seen in cutaneous horn. Therefore, for appropriate histopathological diagnosis such lesion should undergo biopsy at the base of the horn and for smaller lesions excision should be considered.

CASE REPORT

An 83-year-old man residing in a nursing home was referred to our clinic with persistent discomfort over his right ear. He has hypertension and Parkinson's disease with regular follow up at the local clinic. He has no previous surgical history. The primary caregiver at the nursing home had noticed a horny projection from his ear for the past five years. The growth had been slowly increasing in length. Otherwise, there are no complains of ear discharge, ringing, reduced hearing or facial asymmetry.

On examination, there was a hyperkeratotic growth arising from the medial side of the right helix of his pinna measuring 6 x 3 cm from base to tip (Figure 1). It has a broad base with evidence of hyperkeratosis circumferentially. It caused slight discomfort upon manipulation. Otherwise, it was non-tender and non-warm to touch. Other regions of the right external ear appeared normal. Left ear examination was unremarkable. Otoscopy examination showed a healthy external auditory meatus with an intact tympanic membrane. There was no regional lymphadenopathy. The examination was completed with a full examination of the branches of the facial nerve which were normal. Cardiovascular and respiratory evaluations had been normal. An echocardiography showed normal cardiac functions. Other systematic reviews were unremarkable.

Wedge excision of the cutaneous horn and primary closure of the defect had been done under general anaesthesia (Figure 2). The wound recovered within two weeks without any complications. Histopathological examination revealed malignant keratinocytes with moderately pleomorphic, hyperchromatic and prominent nucleoli suggesting of SCC. The epidermis adjacent the tumour show evidence of actinic keratosis. Lesion appears to be completely excised with more than 5 mm margins. Computed tomography showed no involvement of regional lymph nodes and no distant metastasis.

DISCUSSION

Cutaneous horn *(cornu cutaneum)* is a conical shaped excessive hyperkeratosis of variable size ranging from few millimeters to several centimeters. Giant horns are horns having the length of more than one centimeter. Unlike animal horns that usually contain an osseous cast, cutaneous horns consist solely of cornified proliferative keratinocytes without a bony component. Histologically, the cutaneous horn shows an abundance of compact keratin protruding from the epidermis.[3] Cutaneous horn are commonly found in the older population between 60 to 80 years of age. The sex distribution of benign lesions is equal among males and females. However there is a greater incidence of premalignant and malignant cutaneous horns in males.[4] Most commonly they are located in areas most vulnerable to ultraviolet radiation such as nose, ears and upper extremities.

Cutaneous horns can be divided into benign, premalignant and malignant lesions. The most common cause of benign

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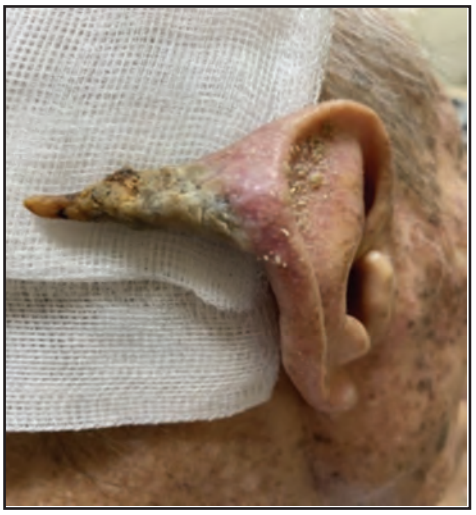

Fig. 1: Hyperkeratotic growth arising from the medial side of the right helix of ear.

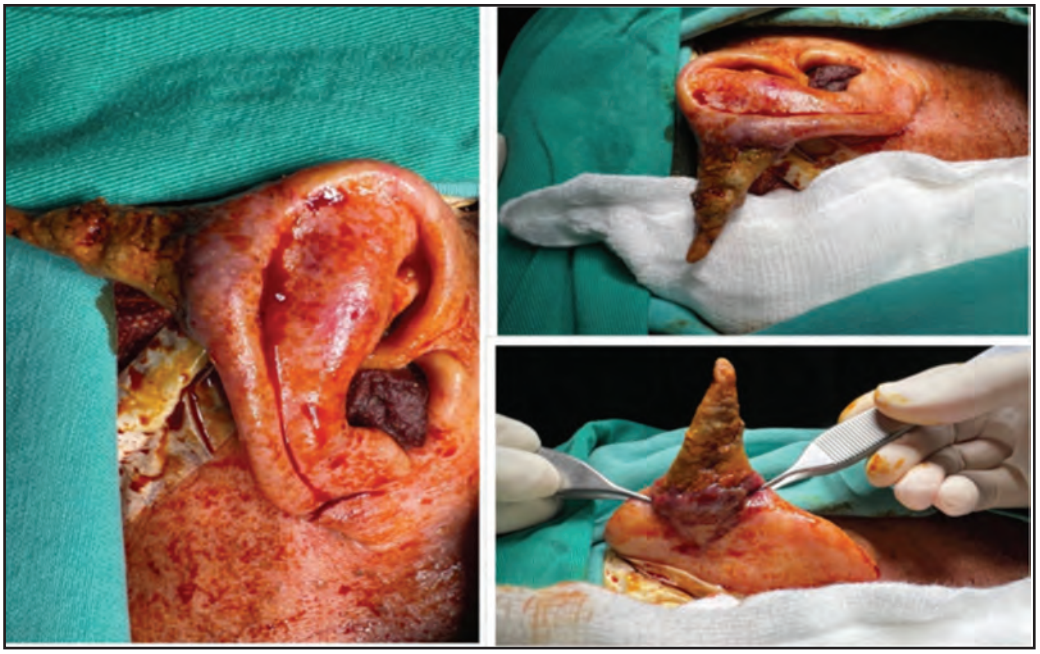

Fig. 2: Pre-operative preparation before the excision of the cutaneous horn over the right ear.

cutaneous horn is seborrheic or lichenoid keratoses. Other benign causes are infections from human papillomavirus and molluscipoxvirus. Benign cutaneous horns make up around 85% of all cutaneous horns.[5] Actinic keratosis are the most common premalignant cause of cutaneous horn, while squamous cell carcinoma is the most common malignant cause as reflected in our index patient.

Excision biopsy of the lesion and formal histopathological examination to rule out malignancy is recommended for large and broad base cutaneous horns. Malignancies should be excised with appropriate margins and evaluated for metastasis. Treatment options include wide surgical excision and laser ablation such as carbon dioxide or neodymium-doped yttrium aluminium garnet laser is preferred for aesthetic considerations. Despite these alternatives, total surgical excision remains the gold standard of treatment of choice, ensuring that the base of the horn is preserved for histological examination. For our index patient, he embarked on wide surgical excision to remove the cutaneous horn completely. Subsequently, primary closure of the wound had been made. The patient was seen two weeks later for follow up which showed good healing of the wound. No gapping or keloid formation was seen. In view of adequate margins, and no involvement of regional lymph nodes or metastasis he is currently under active surveillance.

CONCLUSION

Cutaneous horns are predominantly benign lesions. However, the possibility of nearly 16-20% of the lesions which might be harbouring premalignant or malignant lesions should always be considered. Full thickness excision with adequate margins is the gold standard of treatment of choice to enable detailed pathological examination of the underlying tissue of cutaneous horns.

DECLARATION OF PATIENT CONSENT

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient has given his/her consent for his/her images and other clinical information to be reported in the journal. The patient understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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