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MJM Case Reports

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

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Case Reports

Adult onset urticaria pigmentosa: A case report

Nyoman Suryawati, PhD[1], Luh Nyoman Arya Wisma Ariani, MD[1], Ricky Setiawan, MD[1], Herman Saputra, MD[2]

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SUMMARY

Urticaria pigmentosa is the most common form of cutaneous mastocytosis, but the diagnosis is often missed due to the rarity. We report an adult-onset urticaria pigmentosa on a male with typical lesions, proven by Giemsa and CD117-immunocytochemistry staining. The patient responds well with appropriate oral H1 antihistamine and topical steroids.

INTRODUCTION

Urticaria pigmentosa (UP) is caused by abnormal mast cell accumulation in the skin, which might also accompany systemic symptoms such as flushing, itching, blisters, diarrhoea, abdominal pain, nausea, hypotension, headache and bone pain.[1] Systemic mastocytosis (SM) involves at least one extra-cutaneous organ, almost always involving bone marrow.[2] Urticaria pigmentosa is characterised by itchy hyperpigmented macules or papules usually found on the trunk but rarely on the scalp, palms of the hands and soles.[3] The incidence of UP is estimated at 3 to 7 per 1,000,000 population/year worldwide, and the prevalence in the population is difficult to determine because many cases are isolated and often undiagnosed.[1] Based on studies at the Karolinska Teaching Hospital and the Mayo Clinic, adult-onset cutaneous mastocytosis (CM) is an indolent variant of SM.[4] Based on patient visit data from the Allergy and Immunology Division of the Dermatology and Venereology Polyclinic, RSUP Prof. Dr. IGNG Ngoerah from January 2019 to January 2023 found only two cases of mastocytosis, all of which were CM.[5] The diagnosis of CM is made based on the clinical picture and histopathological examination.[4] Identification of SM needs to be done as early as possible to provide appropriate management and understanding of the risk of osteoporosis and anaphylactic reactions that may occur.[1,4]

CASE PRESENTATION

A 36-year-old man presented with red-brown patches on his face, chest, back and feet persisting for 6 months. The patches became itchy and thickened after being scratched or exposed to heat. There was no history of any systemic disease during childhood, and systemic symptoms were denied. Multiple well-defined, reddish-brown patches with varying sizes between 0.3 × 0.5 cm to 1 × 2 cm were found on the face, chest and back. A wheal develops after rubbing on an existing lesion (Darier's sign was positive) (Figure 1a). Dermoscopy examination (Figure 1b) shows a light-brownish blot (blue arrow) and pigment network (black arrow). We provisionally made a diagnosis of UP. We planned for a complete blood count, blood chemistry and skin biopsy. The complete blood count and blood chemistry are within normal limit. Histopathologic examination with hematoxylin and eosin (HE) stain revealed basketweave keratin pattern, an increased number of perivascular mast cells, and a preponderance of ovoid-spindle-round cells suggestive of mast cells (Figure 1c-f). Giemsa stain revealed positive granules (Figure 1g), and the CD117 stain revealed an increase of mast cells in perivascular at 400x magnification, shown as copper granules (Figure 1h).

He was treated with oral H1 antihistamine (cetirizine 10 mg daily) and topical steroid (0.25% desoximetasone cream twice daily) for 2 weeks, and he has achieved good control of his wheals and itch (Figure 2).

DISCUSSION

Mastocytosis is characterised by the expansion and accumulation of mast cells in one or more organ systems. The pathogenesis involved a c-kit mutation at codon 816 that causes amino acid substitution and excessive mast cell production.[6] Based on organ involvement, the World Health Organisation (WHO) differentiates mastocytosis into CM and SM. In CM, mast cell proliferation occurs in the skin, while SM involves at least one extra-cutaneous organ. It is typically observed that bone marrow involvement is strongly linked with SM.[4] Some triggering factors are food, exercise, heat, Hymenoptera and animal stings, skin trauma, alcohol and drugs.[7] In this case report, the exact trigger is unknown.

Diagnosis of UP is based on the clinical history, physical examination and supporting examination. Multiple macules and patches on the trunk and extremities with Darier's sign are the pathognomonic signs of this disease.3 Darier's sign is an urtication with erythematous halo that produced by rubbing on the lesions. A dermacoscopic examination shows light brown blots, a pigment network and a vascular pattern.[8] Light-brownish blot and pigment network seen with dermoscopy indicate hyperpigmentation of basal keratinocytes or papillary dermis caused by a high concentration of mast cell growth factor that stimulates melanocyte proliferation and melanogenesis. The classical histopathologic findings of UP are ovoid-spindle-round cells, indicating mast cells. In patients with cutaneous involvement, the only confirmatory diagnosis is skin biopsy, whereas SM is confirmed by bone marrow biopsy. Plasma

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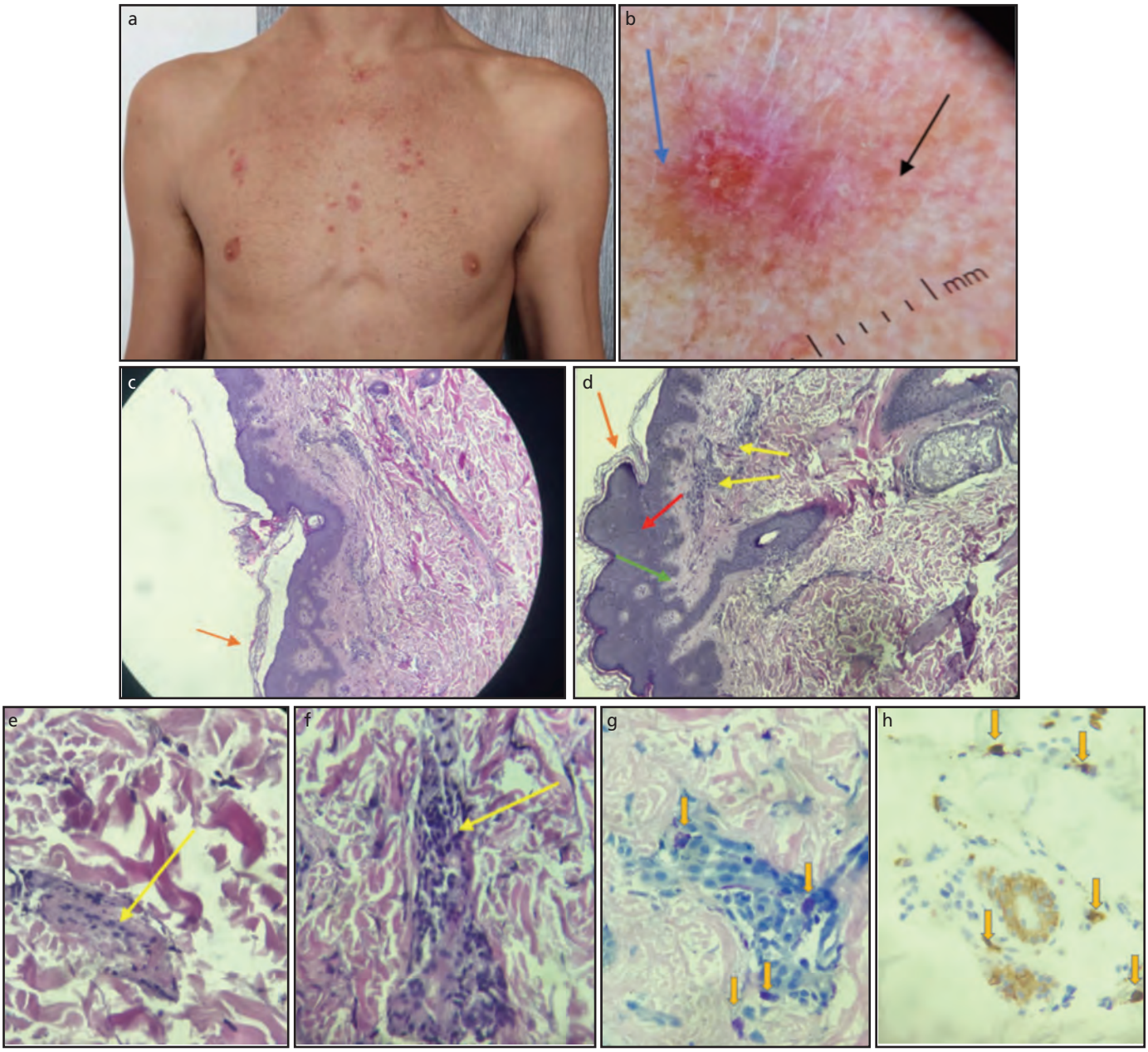

Fig. 1: a) Lesion on the chest. b) Dermoscopic finding. c-f) H & E stain indicates mast cell— g) Giemsa stain shows positive granules— h) CD117 stain shows copper granules.

tryptase examination is an alternative for those who reject bone marrow biopsy as it is a cell mast degranulation product. Total serum tryptase above >20 ng/mL becomes a minor criterion for SM. Skin biopsy followed with special stains such as Giemsa and CD 117 will reveal mast cells.[6] The diagnosis of UP in our case was based on the clinical picture and skin biopsy, however the possibility of SM could not be ruled out since tryptase examination is not available in Indonesia and bone marrow biopsy was not performed in this patient.

The main goal of CM management is to control symptoms related to mast cell mediators, which are based on histamine receptor antagonists.[3,6] The first-line treatment is the administration of first and second-generation H1 antihistamines.[2] If the patients have refractory symptoms, the H1 antihistamine dose may be increased, or other regimens such as H2 antihistamine, oral glucocorticoids, leukotriene inhibitors and monoclonal antibodies against immunoglobulin E can be used.[3,6] Oral disodium cromoglycate can also be given to treat gastrointestinal issues.[1,4] According to some studies, topical steroids can help improve skin lesions in UP. In this particular case, the patient was prescribed systemic AH-1 cetirizine 10 mg tablets, to be taken orally every 24 hours, along with topical anti-inflammatory 0.25% desoximetasone cream, to be applied topically every 12 hours. The treatment resulted in a good response.

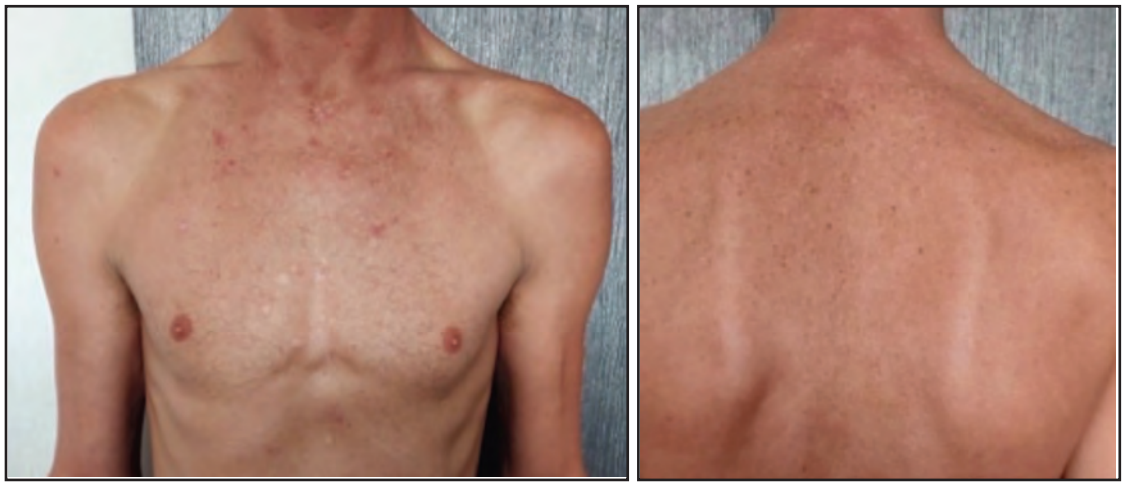

Fig. 2: The lesion showed improvement after receiving treatment.

From a dermatological perspective, no ideal classification system can correlate CM lesion type with prognosis.[3] The outcome of UP is influenced by age, severity and clinical subtype. There is a lack of extensive data on the long-term monitoring of CM. The previous studies on CM showed that children had a favourable prognosis, with 50 to 60% improvement observed in adolescents. However, if CM persists into adulthood, there is a 10% risk of developing SM with a poor prognosis.[9] Our patient responded well to treatment. However, we are uncertain about their prognosis as we cannot rule out the possibility of SM.

CONCLUSION

Adult onset urticaria pigmentosa was diagnosed through history taking, physical examination and skin biopsy. Even though the treatment with H1 antihistamine and topical steroids has shown improvement, long-term observation is still needed.

ACKNOWLEDGEMENT

The authors thank the patient for his cooperation and consent to this case report.

CONFLICT OF INTEREST

There is nothing to declare.

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CASE REPORT

A case report of large cervical oesophageal schwannoma: Importance of preoperative diagnosis in influencing surgical approach

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SUMMARY

We present two cases of cervical oesophageal submucosal polypoidal growth from oesophagogastroduodenoscopy. Tunnelled biopsy was performed and subsequent immunohistochemistry was confirmatory of benign oesophageal schwannoma. Endoscopic ultrasound and contrasted computed tomography (CT) neck and thorax further formed preoperative diagnostic workup. Tumour enucleation was performed via left cervical incision for the first case. The second patient underwent thoracoscopic mobilisation, laparotomy, stomach pull up and cervical oesophageal resection. Both of them remain well till date.

INTRODUCTION

Schwannomas are relatively rare, with many case reports arising in Asia. Different surgical modalities could be considered depending on disease pathology, of which, the malignant lesion would require a more radical surgery than a benign tumour. Knowing definite histology upfront can be challenging hence, therefore, it poses a daunting task for surgeons to outline the best management strategies.

CASE PRESENTATION

Case 1

A 31-year-old lady presented with dysphagia of 3 months duration. Upper endoscopy demonstrated a polypoidal tumour at 18 cm from upper incisor (Figure 1). Contrasted CT showed a well-circumscribed mildly enhancing homogenous tumour at the level between T2 to T3 thoracic spine measuring around 2.1 - 4.1 - 4.4 cm in diameter (Figure 2). A minor compressive effect was seen on the adjacent common carotid and brachiocephalic vessels. An endoscopic ultrasound further characterised the tumour being likely arising from the submucosal layer at the posterior wall. Initial biopsy showed spindle cell tumour of the oesophagus with occasional mitosis seen.

Subsequent immunohistochemistry confirmed benign oesophageal schwannoma with S-100 protein which was intense and diffusely positive. CD34 was weak and less intense. CD117, DOG1, smooth muscle actin, desmin, caldesmon, ALK1, STAT6, CKAE1/AE3 and LCA were all negative. The proliferative index estimation by Ki-67 was low; 1%.

Tumour enucleation was performed through 6 cm left anterolateral cervical incision. Oesophagotomy was closed in two layers with Vicryl 3/0 sutures. Nasogastric feeding was commenced on the next day until the oral gastrograffin study performed on the third post operative day. She was discharged on the next day.

Case 2: A 41-year-old man who had odynophagia of 3 days duration. He apparently had dysphagia to solid food in the last 2 years. Oesophagogastroduodenoscopy showed large oesophageal submucosal polypoidal growth with undigested food from 18 to 25 cm from upper incisor. PET-CT scan showed a well circumscribed supracarinal tumour from T1 to T5 vertebral body measured 4.0 cm (AP) -5.2 cm (W) - 6.8 cm (CC). There were also enlarged paraoesophageal and supraclavicular lymph nodes measured 19 mm and 15 mm respectively (with significant FDG tracer uptake). Immunohistochemistry confirmed the preoperative diagnosis of oesophageal schwannoma following a biopsy. Further management was discussed in regional Upper GI Surgery multidisciplinary teams to choose the appropriate surgical approach. Thoracoscopic mobilisation, laparotomy, gastric pull up, nodes dissection and cervical oesophageal resection were performed. Single layer hand sewn oesophagogastric anastomosis using Vicryl 3/0 sutures were done. He developed anastomotic leak and vocal cord palsy. No exploration done as he was not septic. Enteral feeding was prescribed using a nasojejunal tube at home along with vocal cord strengthening exercises. He recovered completely both for anastomotic leak and vocal cord palsy after 6 months. After 3 years of surgery, he is currently in good health.

DISCUSSION

Schwannomas of gastrointestinal tract commonly occur in the stomach followed by small bowel, rectum and rarely oesophagus. Gastrointestinal schwannomas are mostly benign, but there is only single-digit number of malignant oesophageal schwannoma cases reported. It commonly occurs in the upper thoracic segment of oesophagus and up to date, less than 50 cases of oesophageal schwannoma were reported in English literature.

Essentially, a definitive diagnosis can only be established through histology combined with immunohistochemistry,

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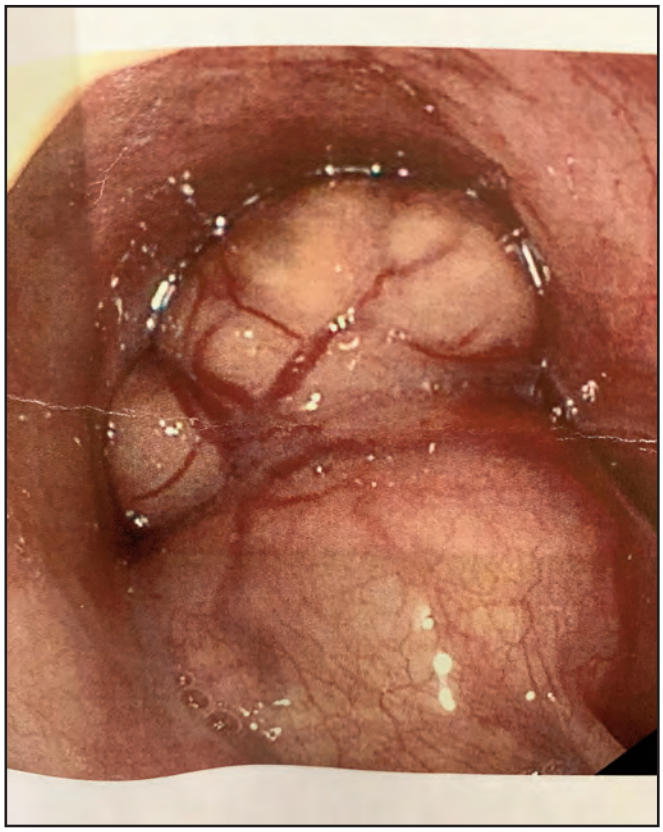

Fig. 1:

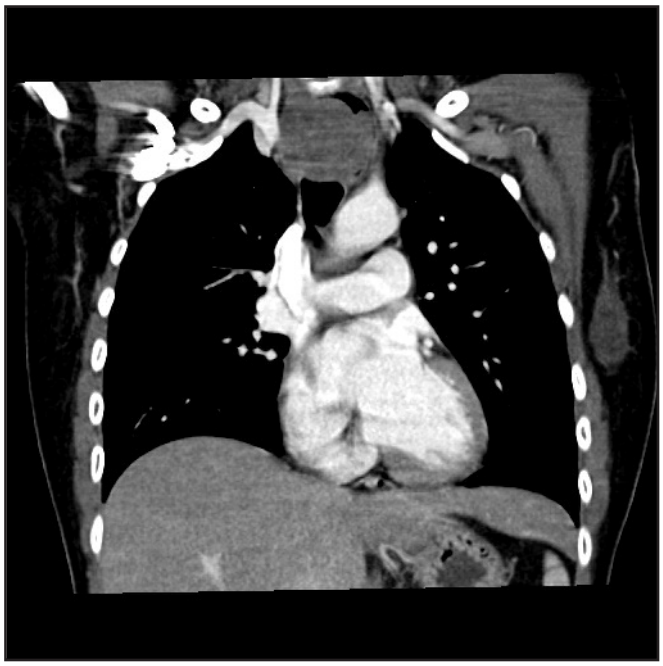

Fig. 2:

the latter being confirmatory. Dysphagia is the commonest presentation and rarely other symptoms like respiratory distress from airway compression, pneumonia and occasionally incidental finding from radiographs.

Oesophageal schwannoma is one of the differential diagnoses of oesophageal spindle cell tumours. In current practice, often an initial biopsy is done with immunohistochemistry being requested upon clinician's request. Hence, it is important not to assume all spindle cell tumours are malignant as this may influence surgical management. Furthermore, radiologically these tumours are indistinguishable. Establishing a diagnosis before resection is important as this may favour less invasive treatment.

Contrast-enhanced computed tomography scan (CECT) is the current imaging of choice and perhaps has replaced barium swallow in most centres. In contrast, positron emission tomography scan (PET) though widely used to stage oesophageal cancers, does not seem to provide any extra information to clinicians in any stage of the perioperative workup (1,4). Oesophageal schwannoma elicits high FDG uptake similar to malignant lesion despite being benign, hence making PET-CT, not a useful investigation to accurately distinguish between a benign or a malignant oesophageal lesion.

Flexible esophagogastroduodenoscopy allows the endoscopist to examine the oesophageal lumen particularly any mucosal involvement. One of the biopsy techniques for submucosal tumour as proposed by few authors is tunnelled biopsy. Commonly superficial bites lead to unsatisfactory reports. On the other hand, an imaging-guided biopsy is an alternative option if deemed feasible in terms of tumour size, location, relations to vascular structures and no other contraindications. We embarked on the former technique because more tumour tissue can be obtained under direct vision and haemostasis can be secured confidently.

Endoscopic ultrasound (EUS) is getting more popular especially to demonstrate and delineate the tumour origin, size and probability of its invasiveness[1,5]. Besides, it is also used as a part of the staging procedure to look for any lymph node enlargement and able to demonstrate layers of tumour involvement. In recent advances, tissue sampling can be obtained through EUS-fine needle aspiration (EUS-FNA), fine needle biopsy or trucut biopsy[3]. Diagnostic accuracy with EUS-FNA was reported at 85.2%. Tumour size of >2 cm , gastric tumour, large needle size, a high number of needle passes and the presence of onsite cytopathologist were favourable factors to obtain satisfactory tissue sampling.

Immunohistochemical (IHC) staining emerges as the utmost informative results in the histology report. S100 is positive in all cases of oesophageal schwannoma, suggesting nerve sheath origin. These stains characterise soft tissue tumour accurately with a huge impact on the preoperative plan. GIST is one of the main differentials of oesophageal schwannoma. CD117 and DOG1 which are confirmatory for GIST are negative for schwannoma. GIST patients with a massive or complex tumour where tyrosine kinase can be used to downsize GIST and minimise the extent of organs' resection

i.e. oesophagectomy for oesophagus or pancreaticoduodenectomy for duodenal tumour. Similarly, lymphoma of the oesophagus although it is rare, it responds well to chemotherapy which would preclude the patients from any major oesophageal resection. For oesophageal spindle cell sarcoma, radiotherapy would have a role as neoadjuvant or adjuvant even as a primary modality in selected cases, with durable long-term outcome, have been reported.

Complete surgical excision is the gold standard in treatment of oesophageal schwannomas and the prognosis of patients is excellent since these lesions are mostly benign. There have been various reports over the years discussing the optimal surgical treatments for oesophageal schwannoma from minimally invasive procedures to major resections. Several authors had reported a successful feasibility of endoscopic removal for small well-demarcated lesions. It can either be done by polypectomy, endoscopic mucosal resection (EMR) or endoscopic submucosal dissection (ESD) for lesions smaller than 15 mm in different parts of the oesophagus. On the other hand, a more aggressive approach through oesophagectomy has been proposed to get the adequate margins especially for bigger tumours or when anticipating some difficulty to close oesophagotomy securely.

Essentially, if the preoperative diagnosis has been confirmed, enucleation perhaps is the procedure of choice even for bigger tumour up to 87 mm[1,2]. The logic reason for this is because achieving clear margins and tumour recurrence are never a significant issue in benign tumours. Tumour enucleation is quite technically feasible because oesophageal schwannoma does not usually involve all layers of the oesophageal wall and is typically limited to the submucosa. Serious morbidities of oesophagectomy such as anastomotic leak, chylothorax and conduit necrosis are not worthy for small benign tumours. Nonetheless, when there is suspicion of malignancy, such as tumour larger than 10 cm, biopsy with mitotic figures, oesophageal muscle invasion or cellular atypia; oesophagectomy is worth to consider preventing recurrences or lymph node metastases.

Whilst cervical incision is the preferred approach for cervical oesophageal tumour, right thoracotomy or thoracoscopy is the procedure of choice for thoracic tumours. Tumour of the second case was bigger, adjacent to carina with significant enlarged nodes hence raised suspicion of malignancy. Since PET-CT scan is not always conclusive, we believe it was necessary to perform resection than enucleation to get clear margins with complete lymphadenectomy. Unfortunately, he developed anastomotic leak and likely traction nerve injury. Having more experienced-trained surgeons and with recent advances in minimally invasive surgery, has led to more cases being operated through video-assisted thoracoscopic surgery (VATS). A recent trend is to combine with endoscopic assistance to locate the tumour or with intraluminal dissection. Laterality (position) of the tumour is important for the surgeon to determine the side of thoracoscopic access. Generally left thoracoscopic approach is limited by the aortic arch and main bronchus. Nonetheless, Nakano et al from Japan had reported novel endoscopic assisted left thoracoscopic enucleation for large mid-thoracic schwannoma without any major morbidities[5]. More evidence with a better quality of trials are needed to determine whether minimally invasive procedures can be safely recommended as the standard procedure especially for benign thoracic tumours.

CONCLUSION

Establishing preoperative diagnosis in submucosal oesophageal tumours is imperative to outline subsequent management particularly in selecting surgical approach and anaesthetic preparation.

We embarked a comprehensive preoperative workup for both patients which include endoscopy with good tissue sampling technique, CT scan and endoscopic ultrasound. The role of immunohistochemistry is definitive in establishing a diagnosis for submucosal oesophageal spindle cell tumours preoperatively.

Enucleation can be considered in a small benign oesophageal schwannomas though larger tumours may require oesophagectomy.

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Progressive tubero-eruptive xanthoma in familial hyperlipidaemia: A case report

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SUMMARY

Xanthoma is a unique clinical presentation in primary care that requires prompt suspicion of familial hyperlipidaemia (FH), urging immediate lipid tests and comprehensive clinical evaluation for a confirmed FH diagnosis. In atypical cases, further investigation is necessary to differentiate xanthoma from malignant skin tumours, which require distinct management strategies. This case report details a 33-year-old man who presented with multiple subcutaneous nodules spreading over 5 years. Laboratory investigations confirmed tubero-eruptive xanthoma associated with FH. This report emphasises the importance of early recognition and comprehensive management of xanthomas to mitigate cardiovascular risks and highlights the need for strict treatment adherence in FH.

INTRODUCTION

Xanthoma, characteristic manifestations of lipid deposition in skin tissues, serve as clinical indicators of certain lipid metabolism disorders, particularly in the context of familial hyperlipidaemia (FH) that encompasses a group of genetic conditions leading to elevated levels of cholesterol and other lipids in the blood. Recognising and understanding xanthoma is pivotal in diagnosing and managing lipid disorders within the spectrum of FH.[1] Tubero-eruptive xanthoma is a specific type of xanthoma commonly associated with severe hypertriglyceridemia and hypercholesterolemia in the context of FH and strongly associated with systemic atherosclerotic diseases, significantly contributing to morbidity and mortality.[1]

CASE PRESENTATION

A 33-year-old Malay man with underlying diabetes mellitus (DM), hypertension and hyperlipidaemia presented with progressive development of subcutaneous nodules that initially appeared at the extensor surfaces of the bilateral knee and ankle, then subsequently spreading across multiple body regions over 5 years. While some nodules displayed eruption, they were not painful or itchy, but significantly impeded joint mobility, causing discomfort. He had a strong family history of DM and hyperlipidaemia. The patient was obese, with a BMI of 32 kg/m². Skin evaluation showed clustered, reddish nodules with a central yellowish hue distributed bilaterally on elbows, anterior thighs, knees, Achilles tendons and other extremities (Figure 1 and 2). Nodules varied in size, with the largest measuring 3 × 4 cm characterised by a firm consistency and fusiform nodules were also identified bilaterally on the Achilles tendons (Figure 2).

The plasma lipid profile showed markedly elevated triglycerides (TG) of 22.61mmol/L (normal range: 0.68-1.88 mmol/L) and total cholesterol (TC) of 8.7 mmol/L (normal range 3.6-6.3 mmol/L). The patient had uncontrolled diabetes, with a fasting plasma glucose levels of 20 mmol/L and an elevated HbA1c value of 11.7% (NGSP). Liver and kidney function and uric acid levels were normal. Other tests, including an electrocardiogram and chest radiograph, showed no notable abnormalities. The patient declined a carotid ultrasound and genetic testing. A skin biopsy revealed presence of extracellular lipid accumulation in subcutaneous tissue with numerous lipid-laden histiocytes with lymphoplasmacytic cell infiltrates, which were characteristics of xanthoma (Figure 3). Based on the distributions and characteristics of the nodules, the patient was diagnosed with tubero-eruptive xanthoma and familial hyperlipidaemia (FH), supported by clinical history and laboratory findings.

The patient initially was prescribed atorvastatin 80 mg and ezetimibe 10 mg for hyperlipidaemia, along with lifestyle modifications advocating a low-cholesterol and low-saturated fat diet. For diabetes, he was treated with subcutaneous premixed analogue 28 units twice daily, extended-release Metformin 2 g daily and gliclazide MR 60 mg in the morning. For hypertension, he took perindopril 4 mg daily. In a recent follow-up, atorvastatin was switched to rosuvastatin 40 mg, with ezetimibe 10 mg maintained. Repatha (evolocumab) was considered if his lipid levels remained poorly controlled. On subsequent follow-up, his TG levels decreased to 11.30 mmol/L with TC to 7.4 mmol/L. The appearance of xanthomas flattened, and no new lesions were detected.

DISCUSSION

Xanthomas are distinct cutaneous lesions resulting from lipid accumulation in the skin and subcutaneous tissues. They can manifest as plaques, nodules or papules and often serve as crucial clinical markers of FH. FH is a group of inherited disorders characterised by abnormally high levels of fats

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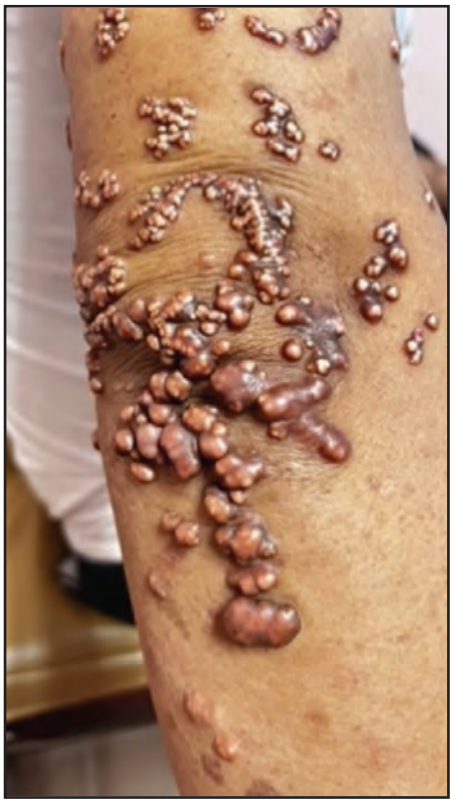

Fig. 1: Extensive clustering of tubero-eruptive xanthomas on the elbow, showing numerous reddish-brown nodules of varying sizes.

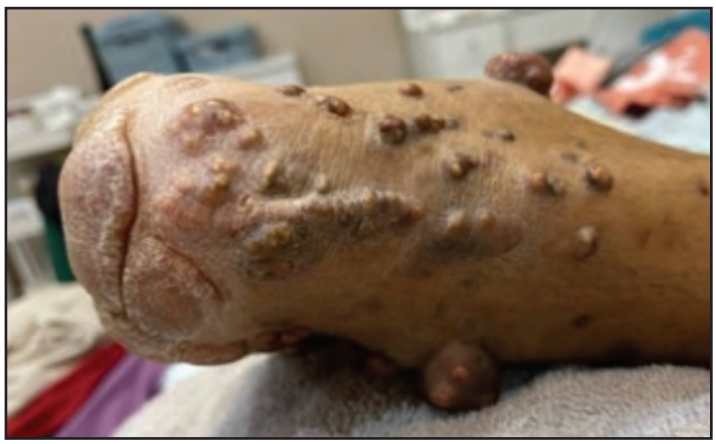

Fig. 2: Pronounced tubero-eruptive xanthomas on the Achilles tendon, characterised by fusiform nodules and large nodular formations.

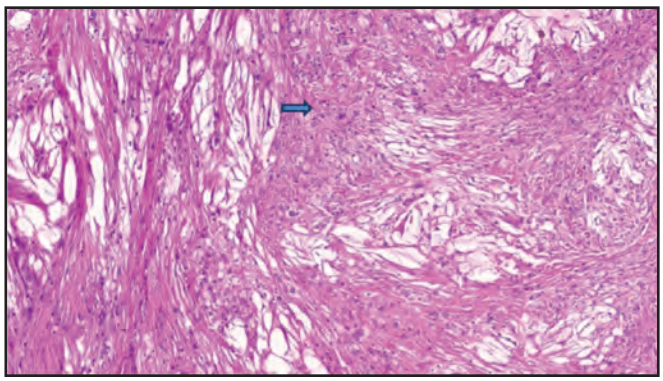

Fig. 3: Histopathological examination of biopsied xanthoma. Photomicrograph using hematoxylin and eosin (H&E) staining with arrow show numerous lipid-laden histiocytes which distinctive characteristic for xanthoma.

(lipids) in the blood, particularly cholesterol and triglycerides that result from genetic mutations affecting proteins involved in lipid metabolism, leading to impaired processing or clearance of lipids from the bloodstream. It is often hereditary and can manifest in various forms, including familial hypercholesterolemia and familial combined hyperlipidaemia. Genetic studies should be conducted when genetic cause-related hyperlipidaemia is suspected, however our patient was not keen for a genetic study due to financial issue.

Xanthomas are categorised as eruptive, tubero-eruptive, tuberous, tendinous and planar based on presentation and distribution. Eruptive xanthomas, characterised by multiple reddish-yellow papules arranged in crops, typically affect the extensor surfaces of limbs and buttocks. This manifestation is causally linked to severe hypertriglyceridaemia.[2] In contrast, tendon xanthomas appear as firm subcutaneous nodules localised over ligaments, fascia or extensor surface tendons of the hands, knees and elbows. Achilles tendons are commonly affected in this type of xanthoma, and these lesions are associated with conditions such as familial hypercholesterolaemia, familial dysbetalipoproteinaemia and phytosterolaemia.[3,4] Tuberous xanthomas manifest as nodules frequently found on the extensor surfaces of the elbows, knees, knuckles and buttocks, and they are linked to conditions such as familial hypercholesterolaemia, familial dysbetalipoproteinaemia, β-sitosterolaemia or cerebrotendinous xanthomatosis.[1] Other types of xanthomas include planar xanthomas, encompassing entities like xanthelasma palpebrarum/xanthelasma, xanthoma striatum palmare and intertriginous xanthoma. Xanthomas, while primarily known for their cutaneous manifestations, can also affect various organs and systems throughout the body, such as xanthomas that involve tendons and ligaments, oesophagus, orbit soft tissue, bone, oral and the brain.[5]

The unique appearance of xanthomas can sometimes resemble cutaneous tumours, leading to occasional diagnostic confusion with skin malignancies. We send this patient for a skin biopsy to rule out other skin malignancies. The reason is that xanthoma may be associated with malignancies of the reticuloendothelial system, such as myeloma, lymphoma and malignant histiocytosis that will change the treatment for the patient. Histopathological examination (HPE) findings of xanthoma typically reveal characteristic features, such as extracellular lipid accumulation, lipid-laden histiocytes, inflammatory infiltrate and fibrosis.[6] It is similar to the HPE findings of this patient that reported the presence of extracellular lipid accumulation within the subcutaneous tissue with numerous lipid-laden histiocytes were observed, often in association with lymphoplasmacytic cell infiltrates (Figure 3).

Tubero-eruptive xanthoma, a specific type of xanthomas characterised by the development of nodules with an eruption tendency, can lead to several complications, primarily due to their association with severe hyperlipidaemia and underlying metabolic disorders, specifically for this patient, he was diagnosed with FH. FH manifests as increased serum cholesterol level and/or increased TG, as shown by this patient. The abnormal increases in plasma lipids and TG present in patients with FH are prone to accelerated atherosclerosis formation, leading to a greater risk of cardiac events that eventually cause significant morbidity and mortality impacts.[7] Hypertriglyceridaemia associated with tubero-eruptive xanthoma in FH is associated with a higher incidence of acute pancreatitis and ocular complications such as lipemia retinalis that will impair vision.[8,9] The mortality risk is higher when associated with other comorbidities such as DM, obesity, hypothyroidism and liver disease.[10] Xanthomas in tendons and ligaments can impair joint function, and their rupture may lead to infection and pain. Tubero-eruptive xanthomas due to their size, distribution and tendency to erupt, can cause significant cosmetic concerns and affect self-esteem and quality of life. The visible appearance of these lesions may lead to social stigma and psychological distress.

Treatment aims to address lipid abnormalities and reduce xanthoma size and appearance. Statin therapy, the first-line treatment for FH, has been shown to effectively reduce xanthoma size.[11] Other options include fibric acid derivatives (fibrates), ezetimibe, bile acid sequestrants and PCSK-9 inhibitors. Intensive treatment combining statins, ezetimibe and PCSK-9 inhibitors has demonstrated significant xanthoma regression.[12] In cases resistant to medical treatment, plasma exchange has shown remarkable resolution of xanthomas and significant lipid profile improvement. While specific studies on exercise's direct impact on xanthoma reduction are lacking, incorporating regular physical activity into a comprehensive lifestyle approach for managing lipid abnormalities and cardiovascular health is widely recommended. This strategy includes exercise, dietary adjustments, medication and other lifestyle changes. The patient however, experiences limitations in engaging in aerobic exercise due to the inability to wear appropriate sports shoes. The size of the xanthomas on both feet hinders finding suitable footwear, leading to discomfort and pain when the xanthomas are compressed during exercise. For these reasons, this patient was planned to be referred for surgical excision to remove the larger lesions. Alternatively, laser therapy has been found to effectively treat xanthomas, though it may result in dyspigmentation and scarring. Other options such as chemical peeling, cryotherapy and electrosurgical techniques like radiofrequency ablation and plasma sublimation offer alternative approaches, each with its own considerations. Topical trichloroacetic acid (TCA) may be less invasive, but it still carries the risk of scarring and pigment changes. Careful consideration based on lesion characteristics and patient factors is essential, with discussions between patients and healthcare providers to determine the most suitable treatment approach.

Follow-up care is crucial to monitor complications and ensure optimal outcomes not only for the patient but also for his family members who require screening and long-term follow-up. In our patient, after intensifying lipid therapy with a high dose of statin and ezetimibe, along with suggested lifestyle modifications, the xanthomas flattened and no new lesions were observed during subsequent follow-ups, obviating the need for surgical or dermatologic intervention.

CONCLUSION

In conclusion, various types of xanthomas can serve as valuable indicators of underlying genetic disorders related to lipoprotein metabolism. Clinicians should remain vigilant regarding the cutaneous manifestations of metabolic disorders, as they necessitate prompt treatment due to the increased risk of cardiovascular events that contribute significantly to morbidity and mortality. The comprehensive evaluation and management of xanthomas are essential not only for cosmetic reasons but also for the prevention of severe systemic complications associated with underlying lipid metabolism disorders.

PATIENT CONSENT INFORMATION

The patient had given informed consent to publish his clinical details in this case report.

CONFLICT OF INTEREST

The authors declared that they have no conflict of interest.

FINANCIAL DISCLOSURE

The authors declared that this study has received no financial support.

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Artificially induced pneumothorax for diagnosis of pleural nodules

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SUMMARY

Obtaining biopsies of pleural nodules in suspected malignancy is crucial for prognosis and treatment planning. Diagnosing cases of dry pleural dissemination (nodules without associated effusion) presents a significant challenge, as the absence of fluid impedes accurate biopsy acquisition due to reduced visual field and potential lung parenchyma injury. Our case highlights a unique instance of artificially introducing a pneumothorax in a patient with dry pleural dissemination, to obtain accurate biopsies of multiple pleural nodules by enhancing surgical visibility and reducing complications.

INTRODUCTION

Pleural nodules are generally associated with a pleural effusion and are diagnosed via local anaesthetic thoracoscopy (LAT), utilising the fluid to facilitate trocar insertion and obtain multiple accurate biopsies. However, rare cases of pleural nodules without any associated effusion, known as dry pleural dissemination (DPD), present challenges due to the inability to safely obtain biopsies in the absence of fluid. In the past, these patients were subjected to open surgeries under general anaesthesia for biopsy acquisition, posing risks especially to patients with comorbidities.[1,2] Ultrasound-guided pneumothorax induction offers a solution to this problem, facilitating real-time visualisation and safe trocar insertion for biopsy acquisition. This case report highlights a rare case of a patient with dry pleural dissemination requiring biopsy of multiple pleural nodules, obtained by inducing a pneumothorax under local anaesthesia.

CASE PRESENTATION

A 73-year-old male with a history of type 2 diabetes, hypertension and a 30-pack year smoking history, presented to the clinic with complaints of chest pain for the last 1 month. He described the pain as “sharp and shooting” and had associated loss of weight (5 kg) and appetite over the last 1 month. He had no complaints of breathlessness, fever or cough with haemoptysis. Chest X-ray was normal, prompting further investigations with a computed tomography (CT) scan which showed multiple irregularly dispersed pleural nodules of various sizes in the costal pleura with no lesion in the lungs (Figure 1).

The decision was made to biopsy the nodule with the help of pleuroscopy for definitive diagnosis. Vitals on admission were within normal limits, and chest examination revealed normal vesicular breath sound. He was premedicated with IV fluids, IV antibiotics (ceftriaxone) and other supportive medications. The risks and benefits of the procedure were explained to the patient, and after consent was given, he was posted for pleuroscopy with biopsy.

The patient was kept under moderate sedation in the right lateral decubitus position, premedicated with 1 mg midazolam and 25 mcg of fentanyl. A bedside ultrasound was done to localise the point of entry along the mid axillary line in the safe triangle. The fully expanded lung was demonstrated by the presence of the sliding sign at the site of entry. The ultrasound probe was covered with a sterile cover for real time induction of pneumothorax. A 20 cc syringe filled with 2 % lignocaine was used to infiltrate the skin, followed by subcutaneous tissue and the deeper muscles. We gradually pushed the 21-gauge into the pleural space till we touched the lung and saw no more sliding sign, thereby inducing a pneumothorax.

The syringe was changed to a 50 cc bigger syringe prefilled with air with the same 21-gauge needle. The needle followed the same tract of entry and once the pleural line (where the sliding sign is absent) was reached, air was slowly pushed into the pleural space (Figure 2-A, B, C, D). The procedure was repeated 5 to 6 times, allowing for sufficient air to push the lung down to avoid injury during the blunt dissection. We then made a 2 cm incision with a scalpel at the site of entry followed by gentle blunt dissection. An 8 mm disposable trocar was gradually advanced through the dissected tract so that it entered the pleural space safely. An Olympus LTF 160 pleuravideoscope was then advanced in through the trocar and the parietal pleura with many tiny nodules was visualised (Figure 3-A, B). Biopsy forceps was introduced through the working channel of the pleuravideoscope and six to eight biopsies were collected for GeneXpert for tuberculosis and histopathological examination.

Once the biopsies were collected, a 24 Fr size intercostal drainage (ICD) tube was placed in the pleural space which allowed gradual evacuation of the pneumothorax. The ICD drain was removed after 24 hours after making sure that there is no bubbling in the ICD drain and no evidence of continuing air leak or residual pneumothorax on the chest X-

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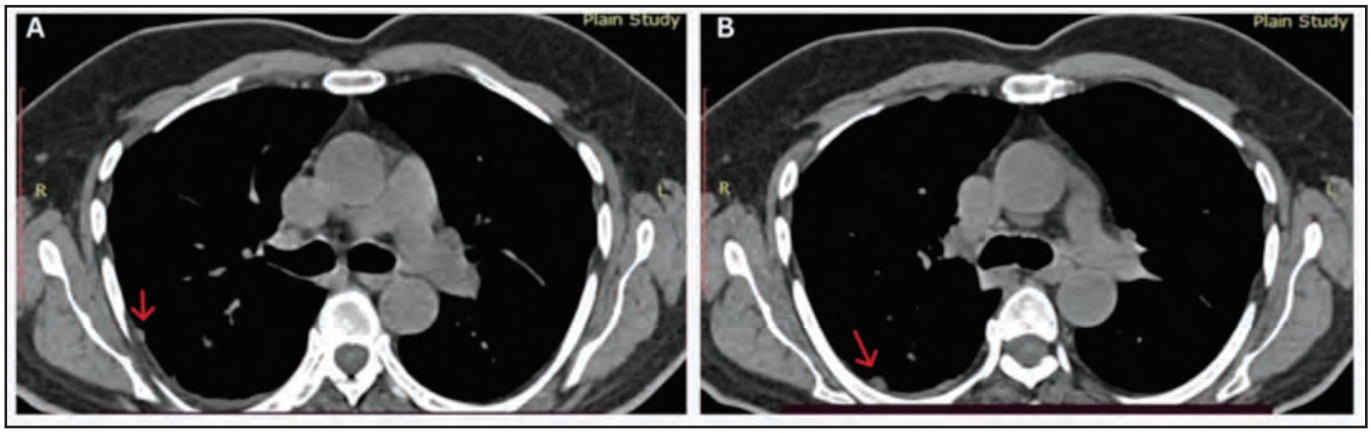

Fig. 1: Computed tomography showing multiple pleural nodules (arrow) without evidence of lesions in the lungs.

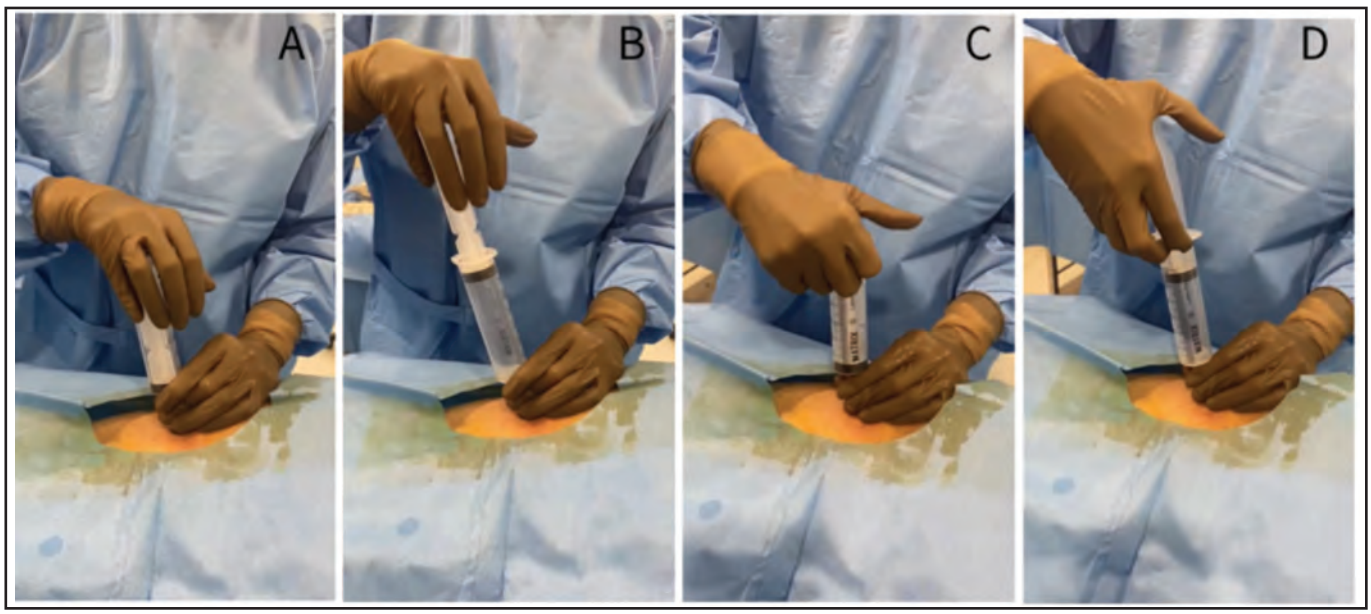

Fig. 2A-D : Demonstration of artificially inducing a pneumothorax by repeatedly pushing air into the pleural space using a 50 cc syringe and a 21-gauge needle.

ray. Histopathology showed fragments of pleural tissue lined by flattened mesothelial lining. The stroma showed infiltration by a malignant tumour composed of cells arranged in nests, sheets and focally in acinar pattern. Immunohistochemistry showed strong positive expression of CK7 (cytokeratin 7) and TTF-1 (thyroid transcription factor 1). The histology along with immunohistochemistry (IHC) markers favoured a diagnosis of moderately differentiated invasive adenocarcinoma of the lung. The patient was safely discharged the next day without any complications and was kept on regular follow-up. He was started on a chemotherapy regimen of cisplatin and vinorelbine and remained stable during treatment.

DISCUSSION

Pleural metastases are most commonly seen along with pleural effusions, a condition known as wet pleural dissemination (WPD) and are typically diagnosed using local anaesthetic thoracentesis (LAT), with the presence of pleural fluid facilitating safe access of the pleural space, enabling the collection of biopsies and cytological analysis of pleural fluid.[2,3]

However, in certain rare cases such as ours, pleural nodules may be seen in the absence of any effusion. This is known as dry pleural dissemination (DPD) and is characterised by CT findings revealing minimal (< 10 ml) or no effusion.[1,4] Obtaining an accurate biopsy via LAT in these patients is quite challenging, as without any fluid, there is a diminished field of vision and limited space to efficiently obtain biopsies, thereby increasing the risk of lung injuries during the procedure.[5] In the past, such cases were diagnosed by obtaining biopsies through open surgeries under general anaesthesia, however longer recovery times and comorbidities in patients have rendered these methods less effective.[3]

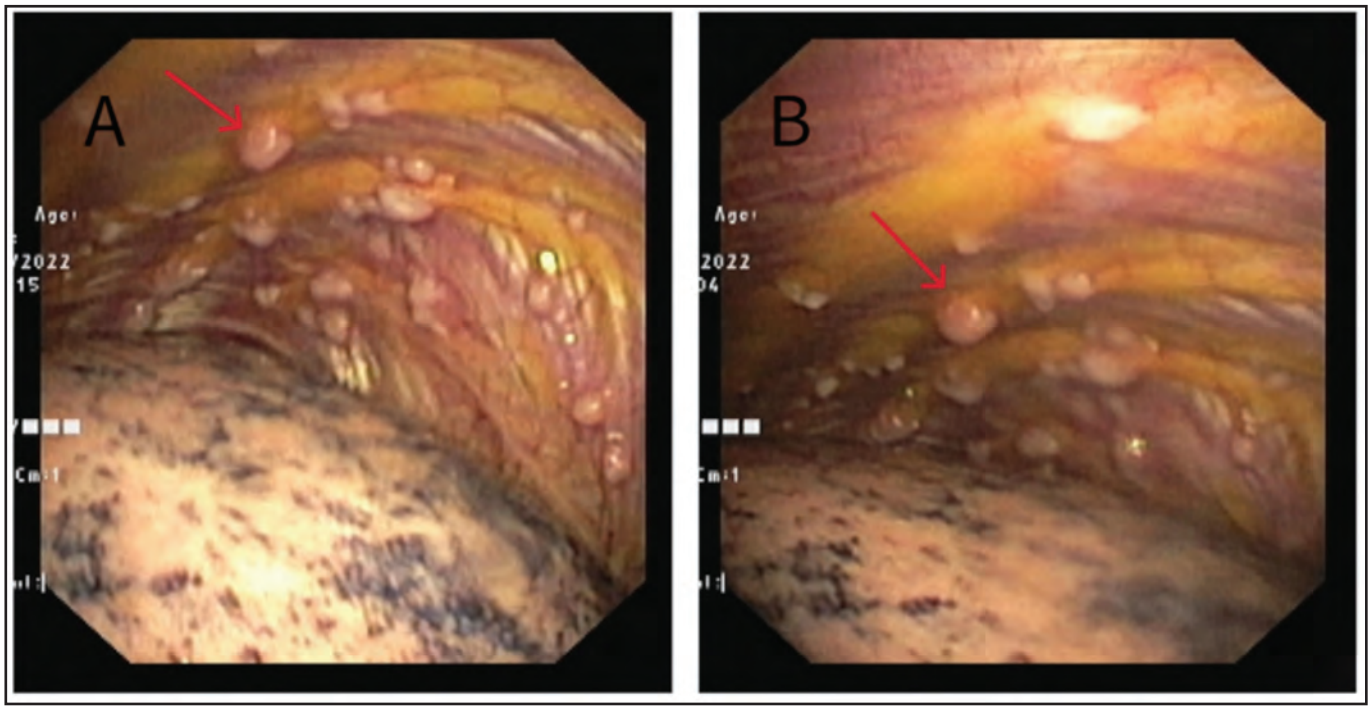

Fig. 3A-B : Pleurascopic view showing multiple irregular nodules on the surface of the parietal pleura (arrow) following pneumothorax induction.

We decided to proceed with LAT and overcame the above challenges by artificially inducing a pneumothorax, which improved visual field, provided adequate access to the pleural space, and created enough space for trocar insertion, thus enabling retrieval of multiple biopsies. A Boutin needle, used with the blunt end, or a Veress needle, with its spring-loaded blunt end and red-to-green visual cue, provides a safe and effective method for inducing pneumothorax in cases of dry pleural deposits. However, in our institute, lacking access to these instruments, we used a 21-gauge needle under ultrasound guidance to safely induce a pneumothorax. This method offers several advantages, including reduced anaesthetic requirements, smaller incision sites, the possibility of same-day discharge, and a higher safety profile when compared to open surgical methods.[4] Ultrasound plays a crucial role in identifying the safest entry point and avoiding potential adhesions (primary contraindication to pneumothorax induction).[2] By providing real-time visualisation, ultrasound confirms the successful introduction of pneumothorax, indicated by the absence of the lung sliding sign, thus obviating the need for confirmation through chest X-rays.[3]

Induction of a pneumothorax may be associated with certain complications such as desaturation, respiratory acidosis and hypercapnia, with partial aspiration remedying these complications. However, the procedure's benefits significantly outweigh potential complications, suggesting its potential application for similar cases in the future. More case reports on this topic are needed in the future to further establish the safety and validity of the procedure.

CONCLUSION

There have been very few studies highlighting the benefits of introducing a pneumothorax for diagnosis of pleural nodules and our case underscores its utility. It allows for a local anaesthetic thoracoscopy to be carried out without a pleural effusion and is particularly useful in elderly patients with several comorbidities. As a result, our case shows that introducing a pneumothorax proves highly effective in obtaining biopsies of pleural nodules with an increased safety profile and minimal complications.

DECLARATIONS

Theres is no conflict of interest between the authors. There was no funding received for this article. Patient consent was taken for publication.

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All authors have reviewed the final version to be published and agreed to be accountable for all aspects of the work. All authors were involved in the concept and design of the manuscript. Srivatsa Lokeshwaran and Sanjana Shanmukhappa supervised the drafting and critical review of the manuscript.

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Evaluation of haematological response to granulocyte colony-stimulating factor therapy in a patient with Chediak Higashi syndrome: A case report

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SUMMARY

Chediak-Higashi syndrome (CHS) is a congenital immunodeficiency disorder characterised by recurrent bacterial infections, oculocutaneous albinism and abnormal intracellular protein transport. One of the manifestations of the disease is severe neutropaenia. This case report presents the haematological effects of granulocyte colony-stimulating factor (G-CSF) therapy on a 16-month-old girl who was recently diagnosed with CHS. The patient exhibits classic features of CHS, including silver hair, albinism and recurrent infections. Initially, the patient was treated with antibiotics, but due to severe neutropaenia, G-CSF therapy was initiated. This resulted in an increase in absolute neutrophil count (ANC) with no adverse effects observed. This case highlights the effectiveness of G-CSF therapy and its rapid response in treating CHS-associated neutropaenia.

INTRODUCTION

Chediak-Higashi syndrome (CHS) is an autosomal recessive disorder, characterised by a range of symptoms, including partial oculocutaneous albinism, silver hair, severe immunodeficiency and the presence of abnormal large cytoplasmic granules in specific cells. The underlying cause of CHS is a mutation in the CHS1 gene, which is located on chromosome 1 and encodes the lysosomal trafficking regulator protein. This mutation disrupts protein synthesis and results in dysfunctional lysosomes.[2]

The immunological manifestations of CHS involve either a normal or reduced number of natural killer cells with impaired function, neutropaenia (low neutrophil count), and compromised neutrophil function.[3]

Around 85% of individuals with CHS progress to a fatal accelerated phase characterised by pancytopaenia (low blood cell counts), hemophagocytic lymph histiocytosis (HLH), and significant infiltration of organs by lymphocytes. These complications lead to multi-organ dysfunction and ultimately result in death.[4]

The management of CHS depends on the specific presentation of the individual and whether they have entered the accelerated phase (HLH). The severity of symptoms at the time of diagnosis also influences the appropriate management approach. In this study, we present a case involving a 16-month-old baby girl with severe neutropaenia and her response to granulocyte colony-stimulating factor (G-CSF) therapy. G-CSF is a therapeutic agent that stimulates the production and function of neutrophils.

By examining this case, we aim to contribute to the understanding of CHS management and highlight the potential benefits of G-CSF therapy in individuals with severe neutropaenia. This study underscores the importance of personalised treatment approaches in CHS and emphasises the need for further research to enhance our knowledge and improve the prognosis for individuals affected by this rare genetic disorder.

Consent form was obtained from the father of this patient and this study was ethically approved by IRB number (H-05-D-114).

CASE PRESENTATION

A 16-month-old Saudi girl was admitted to the paediatric medical ward with a 2 days history of fever accompanied by oral ulcers persisting for 1 week. The patient had a previous medical admission due to recurrent infections since the age of 6 months, which prompted an investigation into possible immunodeficiency. The lymphocyte subset (flow cytometry) showed normal results (Table I).

During the physical examination, the patient's silver hair caught the attention of the medical team (Photo 1). Notably, her hair had been darker at birth and gradually lightened, as she grew older. Additionally, abnormal pigmentation on her back “Café au lait” had been present since birth. The patient had positive consanguinity of the parents, and a family history of silver hair noted in her grandfather, who also had a low platelet count. Furthermore, two of her siblings exhibited the same hair colour.

The physical examination revealed light skin complexion, oral ulcers, thrush and Cafe au lait spots on her back were observed. Detailed ophthalmological examination was normal. Initial investigations (Table I) revealed severe

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Table I: Lab investigations

Investigation	Value before treatment	Value after treatment	Reference range
WBC	10.6 10^9/L	39.3 10^9/L	4.5 11.0 10^9/L
ANC	0.0	20.1 10^3/uL	0.6-5.1 10^3/uL
Haemoglobin	11.7 g/dl	11.7 g/dl	10.0 -14.0 g/dl
MCV	77.7 fL	77.5 fl	75.0 – 115 fL
MCH	24.7pg	24 pg	26.0 – 34.0 pg
Platelet	387 10^3/uL	647 10^3/uL	150 – 550 10^3/uL
CBC count before and after G-CSF			
Lymphocyte subset			
CD3	2787 (53%)	-	(1900 5900) (49 76%)
CD 4	2038 (39%)	-	(1400 4300) (31 56%)
CD 8	542 (10%)	-	(500 1700) (12 24%)
CD 19	1669 (32%)	-	(610 2600)(14 37%)
Natural killers cells	738 (14%)	-	(160950) (03 15%)

MCV: Mean corpuscular volume, MCH: Mean corpuscular haemoglobin, ANC: Absolute neutrophil count, WBC; White blood count

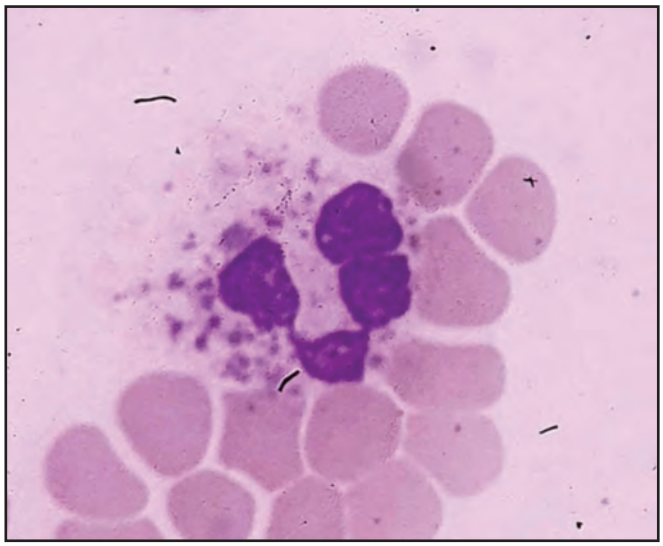

Fig. 1: Neutropaenia and giant granulocyte.

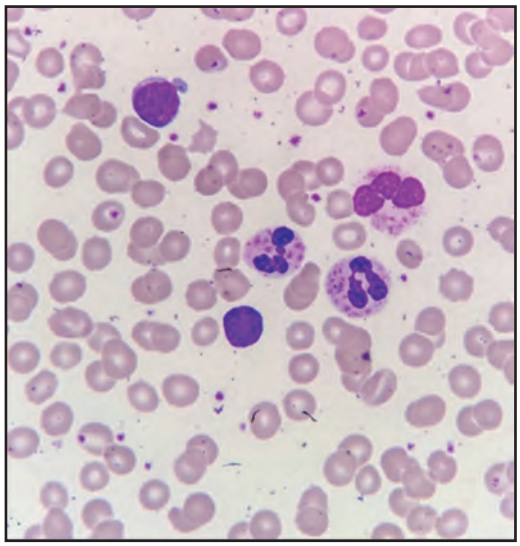

Fig. 2: Normalisation of neutrophil count after G-CSF.

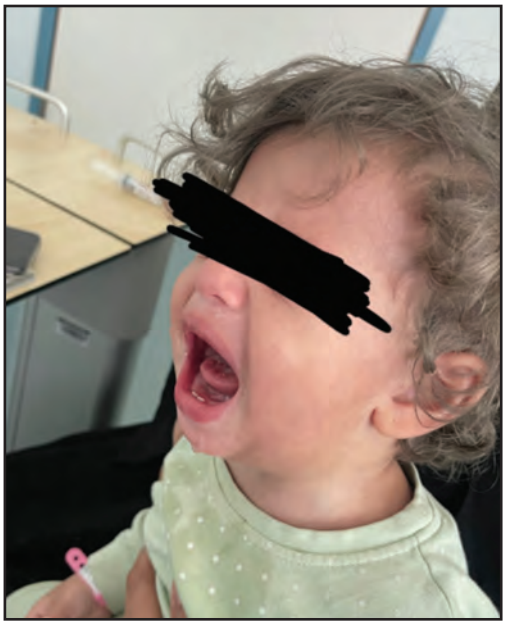

Photo 1: Fair skin and thin hair.

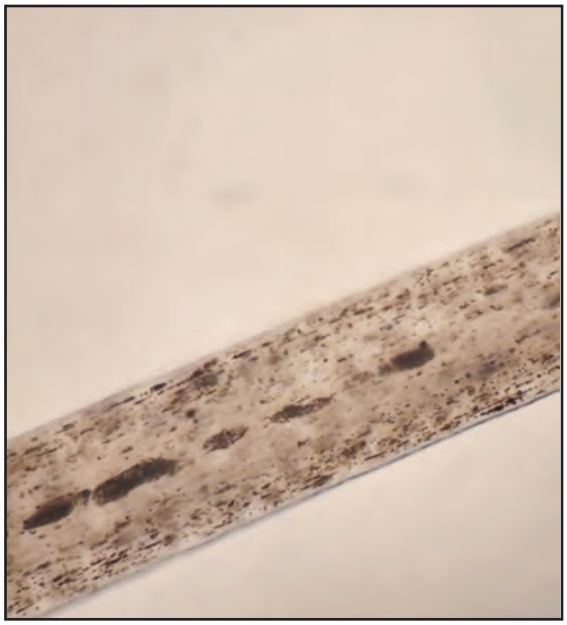

Photo 2: Thinning of hair shaft.

neutropaenia, with an absolute neutrophil count of zero. Upon closer examination of the peripheral blood film, rare neutrophils with giant granules were identified (Figure 1). Considering the severe neutropaenia and the presence of abnormal giant granules in neutrophils. The preliminary assessment indicated a suspicion of CHS as the potential diagnosis.

The hair shaft of the patient was examined under a light microscope, revealing an abnormal pattern of melanin clump distribution in the cortex of an irregular pattern and regular melanin granules larger than those seen in normal hair (Photo 2). Additionally, abdominal ultrasound was done, and it was normal. Subsequent ferritin testing showed a value of 112.59 µg/l (13 150), which further support that the patient was not exhibiting any signs of HLH.

The patient was prescribed piperacillin/tazobactam, next day of admission and continued for 7 days resulting in the resolution of fever within a few days. The absolute neutrophil count was still markedly low. After 5 days from admission, the treating physician decided to start the patient with granulocyte-colony stimulating factor (G-CSF) at a dose of 5 µ/kg/day for 3 days. There was dramatic increase in ANC from $0.2 \times 10^3/\mu L$ to $20.1 \times 10^3/\mu L$ (Table I) measured on the following day of G-CSF (Figure 2). Throughout the course of treatment, patient remained stable, a febrile and did not experience any side effects from the medication. Consequently, the patient was discharged with a follow-up plan in the outpatient department and was referred to a tertiary hospital for the purpose of undergoing genetic testing and further evaluation.

The results of the genetic test confirmed the diagnosis of CHS, revealing the presence of the pathogenic c.8869c>T p.(Arg2957*) variant in the "LYST" gene. Notably, this variant was detected in probable homozygosity. These findings provide valuable insights into the genetic basis of the patient's condition. Further analysis and interpretation of the results will be necessary to fully understand the implications of this specific variant in relation to the patient's clinical presentation.

DISCUSSION

CHS is a rare lysosomal disease characterised by abnormal fusion of primary lysosomes and the resulting enlargement of lysosomes in all tissues.[5] To date, approximately 500 cases of CHS have been reported.[1] The average age of onset is 5.85 years, with most patients succumbing to the disease before the age of 10 years. In those who do survive beyond childhood, neurological problems persist and may worsen over time.[4]

CHS is characterised by partial oculocutaneous manifestations, recurrent infections and presence of abnormal giant granules in neutrophils, lymphocytes and platelets, which are pathognomonic for the disease.3 Primary concern in this syndrome is the recurrent infections and the development of an accelerated phase of HLH.[1] In this reported case, the patient exhibited typical features of CHS, including light skin, silver hair and severe neutropaenia. The diagnosis of CHS is based on clinical manifestations, laboratory findings and confirmed through genetic testing.[5] In the laboratory investigation, the patient had a neutrophil count of zero and a history of recurrent infections, prompting suspicion of CHS. A hair shaft sample was examined under a microscope, revealing clumps of melanin, which are highly characteristic of the syndrome compared to normal hair.[1]

The management of CHS aims to prevent lethal complications such as HLH and recurrent infections.[1] In this case, G-CSF therapy established following the European guidelines for treatment of neutropaenia.[6] There was dramatic improvement of neutrophil count observed from the next day of starting the G-CSF therapy. G-CSF is a growth factor that promotes the maturation of neutrophil precursor cells, which are then released into the peripheral blood.[1] Throughout the course of treatment, the patient maintained a stable clinical condition. However, it is important to note that the use of G-CSF therapy can potentially lead to inflammatory responses.[1] Using G-CSF in stable patients with CHS requires careful consideration of its safety.

Of particular note, Mesfer et al.1 have used the same protocol for treating another patient with CHS. However, in that patient the effect of G-CSF takes more time to normalise the neutrophil count. This variation in time of response and the need to adjust the treatment highlight the fact that different people have different sensitivity to the treatment. This supports the idea of customised treatment according to the patient condition and response to treatment.

Other treatment options for CHS include chemotherapy, high-dose methylprednisolone, and IL-2 administration. Yet, allogenic hematopoietic stem cell transplantation (HSCT) is considered the most successful option in patients experiencing an accelerated phase of the disease.[5]

The researchers studied the genetic basis of CHS to better understand the disease mechanisms and be able to explore treatment options for this condition. CHS is caused by mutation in the LYST gene. LYST gene mutation result in abnormal lysosomal trafficking and impaired function of neutrophils and other immune cells.

The use of G-CSF in CHS aims to stimulate the production of neutrophils in the bone marrow and improve immune function, which subsequently reduce the recurrent infection. According to the literature, G-CSF does not address the underlying genetic defect or correct the abnormalities in neutrophil function in patients with CHS.

Moreover, it is important to acknowledge the limitations of this report, as it is based on a single case. Further evaluation of G-CSF therapy and its potential side effects would be more effective in larger studies involving a greater number of patients or in case series with similar clinical manifestations and the use of G-CSF in patients with severe neutropaenia. Additionally, follow-up of the patient is crucial, as they have been referred to a tertiary centre for further workup and possible bone marrow transplant. Research into the molecular genetics of CHS and the mechanisms of G-CSF therapy in this condition is mandatory.

CONCLUSION

This case report highlights the effectiveness and prompt response of granulocyte colony-stimulating factor (G-CSF) therapy in a patient with Chediak-Higashi syndrome (CHS). The administration of G-CSF not only improved the patient's immune function but also effectively controlled the infection. Importantly, the patient remained stable throughout the course of G-CSF therapy without experiencing any adverse effects.

Further studies should focus on investigating the efficacy of G-CSF therapy in a larger sample size of CHS patients who are not in the accelerated phase. This will provide more robust evidence of the potential benefits of G-CSF therapy in this patient population. We believe that such research endeavours will contribute to the development of more targeted and effective treatment modalities for patients with CHS.

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Placental chorioangioma: A rare cause of uterus larger than date

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SUMMARY

A placental chorioangioma is a relatively uncommon placental tumour with an estimated 1% incidence worldwide. As most placenta chorioangiomas are small in size, they are not diagnosed prenatally and are clinically insignificant. However, as tumour size increases, so does the risk of adverse outcomes. A 23-year-old woman, a primigravida, presented to a primary care clinic at 22 weeks of gestation with excessive weight gain and uterus fundal height larger than her gestational age. However, no abnormalities were detected. The placental chorioangioma diagnosis was made two weeks later via transabdominal ultrasonography. The pregnancy was subsequently complicated by an early foetal growth restriction and a spontaneous premature delivery, resulting in a poor outcome for the foetus. A histopathological examination confirmed the diagnosis of chorioangioma. Despite the fact that the outcome of chorioangioma varies depending on its size and other complications, early detection is important to ensure effective maternal and foetal surveillance. Early referral to a feto-maternal medicine unit and shared care management with primary care are crucial for developing an appropriate patient care plan.

INTRODUCTION

Placental chorioangioma is a type of placental tumour with an estimated 1% incidence worldwide.[1] This vascular tumour originates from the primitive chorionic mesenchymal tissue and is thought to be caused by abnormal vessel proliferation at various stages of differentiation in the fibrous stroma.[2] The majority of the chorioangioma placenta are small in size, therefore making them clinically not significant and not diagnosed prenatally. However, the risk of adverse outcomes increases as the tumour size increases.[1]

Large chorioangioma (> 5 cm) occurrences are rare, ranging from 0.11% to 0.29%.[3] The clinical presentations vary from asymptomatic to found incidentally from a routine antenatal sonography. The chorioangioma is typically a well-defined solid mass which protrudes into the amniotic cavity.[4] Placental chorioangioma can be differentiated from other placental tumour or masses by Colour Doppling Imaging (CDI)[3] which indicates the presence of a single blood vessel feeding the lesion or significant vascularity within the mass.[4] Complications that can arise from placental chorioangioma are polyhydramnion, pre-eclampsia, preterm delivery, foetal anaemia, cardiomegaly, hydrops fetalis, foetal growth restriction or foetal demise.[3] Management of this tumour is mainly tailored to the complications such as amnio reduction to reduce excessive liquor and intrauterine transfusions for foetal anaemia.[5] More interventions techniques are being explored to arrest the underlying pathophysiology of arterio-venous shunt within the chorioangioma.[5]

CASE PRESENTATION

A 23-year-old woman, with a background of primary subfertility and obesity, had a spontaneous conception. Her antenatal check-up was conducted at a health clinic. Her condition was uneventful until the early second trimester when she was found to have excessive weight gain ranging from 700 to 1500 g within 2 weeks, with gestational diabetes mellitus ruled out. At 22 weeks of gestation, her fundal height was 5 cm larger than her gestational age. However, no abnormality was found in the transabdominal sonography. The ultrasound finding showed a singleton foetus with growth corresponding to 22 weeks of gestation, normal liquor volume with no abnormality detected. Two weeks later, the fundal height was 30 cm, 6 cm larger than her actual gestation period. Repeated transabdominal ultrasound revealed a hypoechoic placental mass with the size of 8 cm x 5cm (Figure 1). The foetal growth was already restricted as evidenced by dropping a centile on the foetal growth chart. Subsequently, she was referred to the nearest tertiary hospital for an appointment with an obstetrician and for an ultrasound Doppler imaging.

However, at 26 weeks of gestation, 4 days prior to her hospital appointment, she had a premature contraction and was sent to hospital. Her transabdominal ultrasound finding showed a placental mass with the size of 12 cm x 7 cm and no vascular uptake. The doppler imaging of the umbilical artery revealed an absent end diastolic flow wave. She was admitted after receiving prematurity counselling and her delivery was expedited by 3 days. A baby boy was delivered with the birth weight of 495 g and poor respiratory effort. He succumbed to 1 hour of life. The placenta weighed 690 g. There was a solid mass with the size of 12 cm x 11 cm. The histopathological examination of the mass revealed chorioangioma, composed of capillary proliferation and surrounding stoma.

DISCUSSION

Placental chorioangioma, or more commonly known as chorioangioma, is the most common benign placenta

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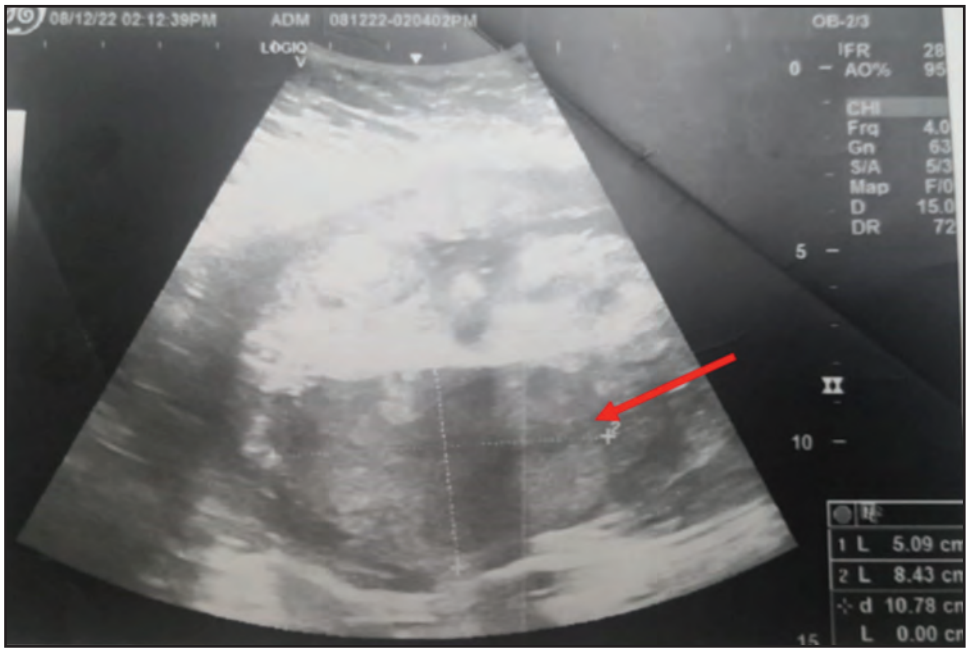

Fig. 1: A hypoechoic placental mass with the size of 8 cm x 5cm at 24 weeks period of gestation.

tumour.[3] Its incidence is 1% of all examined placenta but the exact incidence may be lower 1. A retrospective study involving 22,439 placentas found only 0.61% chorioangioma while in another study showed an even lower incidence of 0.16%.[3] Chorioangioma is thought to arise from the malformation of primitive angioblastic tissue of early placenta2 and has no malignant potential.[6] However, the tumour size plays an important role in determining the outcome of the pregnancy. Majority of the tumours are small in size, hence have no clinical significance. On the other hand, large chorioangioma incidences are rare and vary from one in 9000 to one in 50,000 pregnancies but have a higher association with maternal and foetal complications.[5]

Placental tumour is one of the causes of the uterus fundal height being larger than the gestational age. In this case, an early diagnosis of chorioangioma was undetected despite the presence of excessive weight gain and uterus being larger than date. Other causes of discrepancy of fundal height with gestational age were ruled out during the examination; however, the abnormality of the placenta was undetected due to its rare incidence. Furthermore, most chorioangioma are small and asymptomatic and may not be diagnosed prenatally. Chorioangioma can be found incidentally during routine prenatal sonography[3,4] or during maternal or foetal complications such as polyhydramnios or hydrops fetalis.[1,7]

Grayscale sonography is the primary tool used to detect chorioangioma.[3] The tumour could appear as either a hypoechoic or a hyperechoic placental mass. It may contain anechoic cystic area that may or may not contain fibrous septa. Colour Doppler imaging (CDI) is able to differentiate chorioangioma from other tumours such as partial hyatidiforme mole, placental haematoma, teratoma, degenerating fibroid and metastases with the confirmation of the presence of vascular channels in the tumour.[8] However, there are some avascular chorioangiomas where CDI dose is not able to demonstrate blood flow, similar to that seen with our patient.[3] Other than confirming chorioangioma, CDI is also important for prognosticating the pregnancy outcome and monitoring for foetal complications.[3] Magnetic resonance imaging (MRI) is useful for confirmation when the ultrasound findings are ambiguous.[8]

Polyhydramnios and foetal growth restriction are the most common complications of chorioangioma cases.[3,5] It was postulated that there is an increase in urine production associated with hyperdynamic circulation related to the arteriovenous shunting of blood and transudation of fluid from the tumour.[5] A retrospective study by Zanardini et al.[5] found that among 19 cases of chorioangioma, six cases resulted in foetal growth restriction, similar to our case. A reduction in the functional capacity of the placenta due to vascular shunting in the tumour causes inefficient nutrition and oxygen exchange within the placenta, resulting in foetal hypoxia and growth restriction. Besides that, foetal anaemia could also occur due to feto-maternal haemorrhage and microangiopathic haemolytic anaemia as a result of entrapment and destruction of foetal erythrocytes in the vascular network of chorioangioma.[5] Subsequently, foetal heart failure and hydrops fetalis may ensue.

Management of chorioangioma is based on tumour size, gestation period, foetal maturity and neonatal support, as well as the complications that occur.[5] Close prenatal surveillance is vital to constructing the plan of care and making timely decisions. For small and large-sized tumours, ultrasound surveillance can be done every six to eight weeks, and every 1 to 2 weeks, respectively.[8] If complications occur in late pregnancy, imminent delivery can be expedited. However, if it occurs during the second trimester, delivery is not an option due to foetal prematurity. The aim of the interventions is to relieve complications such as amnioreduction for polyhydramnios and intrauterine

transfusion for foetal anaemia.[5] New treatment techniques such as injection of absolute alcohol, endoscopic laser coagulation, endoscopic sutures with bipolar electrosurgery have been proposed to arrest the vascular supply in the tumour itself, as well as interstitial laser therapy to devascularise the tumour.[3,5] The success rate ranges from 50 to 65%.[5] These interventions have demonstrated good outcomes, as reported by Zanardini et al.[5] and Emilia et al.[9] However, these interventions require a well-equipped feto-maternal facility which is limited, at least in our local settings. Therefore, it is hoped that in the future, these interventions can be expanded to all tertiary hospitals, hence improving the outcome among pregnant women who have chorioangioma.

CONCLUSION

We reported a rare case of a large placental chorioangioma that was presented at primary care as excessive weight gain and uterus fundal height was larger than the gestational age. The patient had complications from chorioangioma, including foetal growth restriction and premature labour. As the outcome of chorioangioma varies and is dependent on the size and other complications, an early detection is vital to ensure that an effective maternal and foetal surveillance can be done accordingly. Early referral to the feto-maternal medicine unit is crucial to constructing a proper of plan of care for the patient.

CONFLICT OF INTEREST

The authors declare that there was no potential conflict of interest relevant to this article reported.

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CASE REPORT

Disseminated *Klebsiella Pneumoniae* infection: prostate, an easily overlooked source of infection

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SUMMARY

Intraabdominal and prostatic abscesses are usually caused by floras, which dominate the gastrointestinal (GI) and genitourinary (GU) tract. *Escherichia coli* and *Klebsiella spp* are some of the most commonly isolated organisms worldwide. In the context of tropical diseases in Southeast Asia, they are also caused by *Burkholderia pseudomallei*, known as melioidosis, occurring rather frequently among immunocompromised individuals especially diabetics. Interestingly, the scarcity of clinical signs and symptoms in these infections often leads to misdiagnosis and patients presenting late to hospitals with severe sepsis. This case came about when a gentleman in his 50s came to our healthcare facility with complaints of an unabating high fever for 1 -month, involuntary weight loss and 2 weeks of dysuria. His prostate was examined and was found to be unusually enlarged and boggy. Ultrasound (USG) abdomen and prostate revealed disseminated abscesses involving the liver and bilateral kidneys with prostatomegaly. The left renal abscess was drained, and a positive growth for *Klebsiella pneumoniae* was noted. In this case, the prostate was believed to be the likely source of disseminated *Klebsiella pneumoniae* infection based on his symptoms. He was treated with 6 weeks of antibiotics and had achieved good recovery with no ultrasonographic evidence of the progression of prostatomegaly to prostatic abscess.

INTRODUCTION

Pyogenic intraabdominal abscess occurs following a breach in the mucosal lining of a particular abdominal organ due to infection or inflammation leading to a sealed collection of cellular debris, enzymes and remains of an infectious source. Abscesses may be liquefied or partially liquefied, and its morphology determines feasibility for drainage to achieve proper source control. Isolated organisms from these abscesses comprise largely of intestinal floras including coliforms bacteria such as *Escherichia coli, Klebsiella spp., Proteus spp., Enterobacter spp., Streptococci spp., Enterococci spp.* and certain anaerobes.[1] On the other hand, based on meta-analysis, prostatic abscesses are largely caused by *Escherichia coli,* followed by *Klebsiella spp., Pseudomonas spp., Proteus spp., Enterobacter spp., Serratia spp.,* and *Enterococcus spp.* A large proportion of patients with prostatic abscess were found to be diabetic.[2-4] It is postulated that prostatic abscess is a sequel of refluxed infected urine causing acute prostatitis, which is not properly treated. Risk factors for development of prostatic abscess include poorly controlled diabetes, benign prostate hyperplasia, non-sterile urinary catheterization, prostate biopsy and other urological instrumentation procedures.[5] In Malaysia, *Escherichia coli, Klebsiella spp.* and *Burkholderia pseudomallei* remain the most commonly isolated pathogens in both intraabdominal and prostate abscesses.[6] The same organism can result in abscesses in both the intraabdominal organs and the prostate.

The prevalence of *Klebsiella pneumoniae* (KP) prostatic abscess varies geographically. Studies have shown that there is a higher incidence rate of prostatic abscess caused by the organism in Asian countries.[3-4] This is evidenced by a recent study in Taiwan which showed an astounding 58% of prostatic abscess cases related to Disseminated KP infection.[3] Likewise, in Korea, KP was the second most commonly isolated organism (17.3%) after *Escherichia coli* (40.4%) based on a 10-year retrospective study amongst fifty two (52) patients with prostatic abscess.[4] However, in the Western set-up, *Staphylococcus aureus* was noted to be the most common causative organism (56%), followed by *Klebsiella pneumoniae* (13%) and *Escherichia coli* (9%).[7] Untreated prostatic abscess can lead to severe urosepsis and septic shock and has been reported to cause metastatic endophthalmitis, septic arthritis and osteomyelitis.

While *Klebsiella pneumoniae* (KP) primarily affects those who are immunocompromised, the Malaysian populace, who generally have a high prevalence of diabetes, is at an alarming risk of acquiring such a disease and complications. As KP infection frequently presents with slow progression of fever and other non-specific clinical symptoms, the patient often presents late with disseminated infection involving multiple organs requiring surgical intervention, prolonged hospital stay and antibiotics treatment. Clinicians should thus be made aware of the nature of KP infection in order to identify the disease in its early phase for timely antibiotic treatment and prevention of disease-related complications mentioned above.

In the case report presented below, we detailed how our findings of an unusually enlarged and non-tender prostate in a diabetic patient with unexplained fever through clinical examination led to successful identification of disseminated KP infection involving the liver, bilateral kidneys and the prostate.

CASE PRESENTATION

A gentleman in his 50s with a background history of insulin-dependent type 2 diabetes mellitus and dyslipidaemia was readmitted from our specialist clinic for unresolved fever and new onset of dysuria. On admission, his fever had already

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Table I: Blood test results showed raised total white counts predominantly neutrophils suggestive of an on-going infection, further substantiated by an increment in C-reactive protein (an important infective marker). The unusual presentation of urinary leukocytes narrowed down urinary tract as the most possible site of infection.

Parameters	Result	Units	Reference Range
Full blood count			
Total White Count	21.2	10^9/L	4.0–11.0
Haemoglobin	11.6	g/dL	13.0–18.0
Platelet count	306	10^9/L	150–400
Haematocrit	32.3	%	40–52
MCV	83.9	FL	76.0–96.0
MCH	30.1	PG	27.0–32.0
Neutrophils	17.79	10^9/L	
Neutrophils %	83.8	%	40–75
Lymphocytes	1.69	10^9/L	
Lymphocytes %	8.00	%	20–45
Eosinophils	0.04	10^9/L	
Eosinophils %	0.20	%	1–6
Basophils	0.04	10^9/L	
Basophils %	0.20	%	0–1
Renal profiles			
Urea	3.2	mmol/L	1.7–8.3
Sodium	118	mmol/L	135–145
Potassium	4.2	mmol/L	3.5–5.5
Chloride	88	mmol/L	98–107
Creatinine	72	umol/L	62–106
eGFR	>90	ml/min/1.73m^2	
Liver function test			
Total protein	70	g/L	64–83
Albumin	22	g/L	35–50
Globulin	48	g/L	20–39
Alkaline Phosphatase	148	u/L	40–150
Aspartate Aminotransferase (AST)	36	u/L	5–34
Alanine Transaminase (ALT)	10.7	u/L	<56
Total bilirubin	8.4	umol/L	5.1–20.5
Full and microscopic examination of urine (Urine FEME)			
Glucose	3+		Negative
Ketone	Negative		Negative
Nitrite	Negative		Negative
Leukocytes	3+		Negative
Blood	Trace		Negative
Bilirubin	Negative		Negative
Protein	1+		Negative
Urobilinogen	Normal		Negative
Colour	Amber		
Clarity	Turbid		
PH	6.0		5–8
Specific gravity	1.009		1.003-1.030
Infective marker			
C- reactive protein	88	mg/L	<5.0
Other infective workup			
Leptospirosis IgM	Negative		
Dengue serology	Negative		
Blood film for malaria parasite	Negative		

lasted 1 month with significant loss of weight and appetite. He experienced dysuria for 2 weeks but had denied other urinary symptoms, including urinary frequency/urgency, poor stream or incomplete bladder emptying. He denied having prolonged cough, gastrointestinal losses, abdominal/perineal pain, sexual promiscuity or contacts with other sick persons. He works as a security guard and had also denied contact with rodents, sewage or contaminated soil. He is a married man with one child.

Two weeks earlier, this gentleman was admitted to the general medical ward for unexplained fever which lasted for 1 week. He was treated empirically for occult sepsis with IV Ceftriaxone 2g OD (Duopharma®) for 5 days. None of his blood and urine cultures demonstrated positive growth. He was discharged 5 days later and was given a date to follow-up in our specialist clinic.

On admission, his vitals were stable. Lungs and cardiovascular examinations were non-remarkable. The abdomen was soft and non-tender. His liver and spleen were not palpable. Prostate examination revealed a painless enlarged prostate measuring 4 finger-breadth, boggy with complete obliteration of the median sulcus.

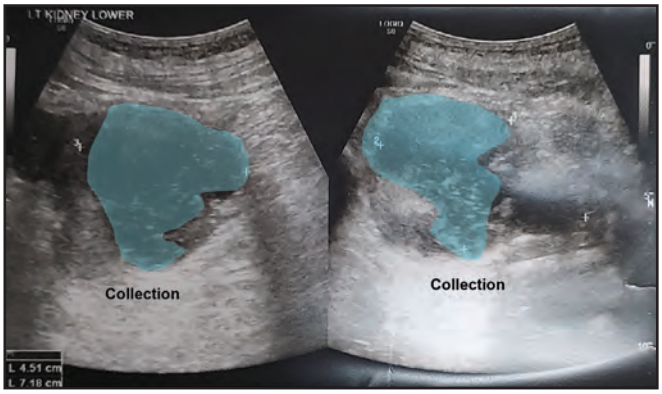

Fig. 1: Left kidney lower pole demonstrating heterogenous collection (Highlighted in Blue)

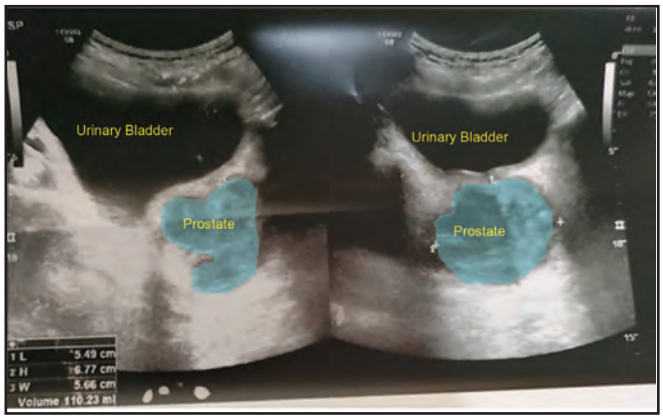

Fig. 2: An enlarged lobulated prostate (Highlighted in Blue)

His blood test results detailed in Table I showed raised total white counts, predominantly neutrophils suggestive of an active infection. Other important findings were the presence of leucocytes in his urine and a significantly raised C-reactive protein. Chest X-ray was grossly normal. Echocardiogram demonstrated no vegetation with a normal ejection fraction.

USG abdomen and prostate scans reported hypoechoic lesion in segment VI of the liver measuring 2.4cm x 1.8cm x 2.2cm, a small hypoechoic lesion with septation in the right upper pole kidney measuring 1.1cm x 1.4cm and heterogenous collection left lower pole kidney measuring 4.9cm x 5.7cm x 5.9 cm (Figure 1). The prostate was enlarged and lobulated, measuring 5.5cm x 6.8cm x 5.7cm (Volume 110cc) (Figure 2) Overall impression was consistent with focal abscesses involving the left kidney lower pole, right kidney upper pole and liver. (Note: Echogenicity of the prostate was inconclusive to be commented as an abscess)

Preliminary diagnosis of melioidosis was made in view of high prevalence of melioidosis in the country, and patient was started on IV Ceftazidime 2g TDS (Duopharma®) pending confirmation of organism from blood and urine culture. Urology opinion was sought, and an agreement was made to reassess the intraabdominal collection and prostate 2 weeks post antibiotics.

Five days after the commencement of IV Ceftazidime 2g TDS (Duopharma®), the patient developed a spiking fever up to 39^0C. We escalated antibiotics to IV Meropenem 1g TDS (Fresenius Kabi®). Following a joint discussion with urology and radiology teams, a decision for USG guided drainage of the left lower pole kidney abscess was made in order to achieve proper source control and to identify the organism for antibiotics selection. Approximately 50ml of purulent collection was drained and sent for culture and gram stain. Collection at segment VI of the liver and the right lower pole kidney was deemed too small for drainage.

Aspirate culture grew mucoid lactose fermenter colonies on MacConkey agar, which was later confirmed by our microbiologist to be *Klebsiella pneumoniae*. Kirby-Bauer testing confirmed sensitivity to Amoxicillin/Clavulanate, cefuroxime and Ampicillin/Sulbactam. The other blood and urine cultures were concluded as no growth.

Final diagnosis was concluded as disseminated *Klebsiella pneumoniae* infection confirmed radiologically and microbiological testing. Infectious disease team opinion was sought. Antibiotics were deescalated to IV Amoxicillin/Clavulanate 1.2g TDS (Mylan®)

Following the identification of Klebsiella pneumoniae, slit lamp assessment was carried out by our ophthalmology team to rule out endophthalmitis. It was confirmed that our patient did not have the condition.

USG abdomen, after 20 days of antibiotics, reported hypoechoic lesion in segment VI of the liver measuring 2.6cm x 1.5cm x 2.1cm, small hypoechoic lesion with septation in upper pole right kidney measuring 1.1cm x 1.8cm, and heterogenous hypoechoic collection lower pole left kidney measuring 3.3 cm x 3.7cm x 4.3cm. Prostate size 2.8cm x 3.6cm x 2.8cm (Volume 15ml). There was no splenic lesion. In all, repeated scan showed unchanged focal abscesses of the right kidney and liver; residual focal abscess of the left kidney and complete resolution of the prostate lesion.

Our patient was allowed to be discharged with another three more weeks of oral Amoxicillin/Clavulanate 625mg TDS (Pharmaniaga ®). Followed-up USG abdomen 1 month after completion of antibiotics showed residual multiple sub-centimeter hypoechoic nodules scattered throughout the liver measuring 0.5cm each (Differential diagnoses include liver micro abscesses or liver cirrhosis with nodular appearance). Previously seen hypoechoic lesion at segment VI of the liver and bilateral kidneys were no longer apparent in this study. At the point of writing this case report, our patient remains well and is still under-going follow-up in our specialist clinic.

DISCUSSION

Untreated *Klebsiella pneumoniae* (KP) prostatic infection risks dissemination to distant organs, causing abscesses. The initial signs and symptoms of KP prostatitis and prostatic abscess are usually non-specific and misleading and thus

have resulted in delayed identification of the disease and administration of treatment. To complicate the matter further, diabetic polyneuropathy involving the genital nerves may even mask the symptoms of prostatic abscess or prostatitis at its early phase of the disease. Routine practices initiating broad-spectrum antibiotics for patients with occult sepsis have also lowered bacterial density, resulting in poor yield and negative cultures. It is uncertain whether our patient was prescribed antibiotics prior to culture sampling during the first admission, which had led to a falsely negative blood and urinary culture results.

Contrary to popular belief that KP grows readily in routine culture bottles and agar media, an observational study led by Ter et al. also reported significant false negative results after 5 days of incubation. Amongst the 195 day-5 negative blood culture samples tested, 8 of them were positive for *Klebsiella Pneumoniae* using PCR technique. It is postulated that organism death, inappropriate sampling technique and long storage time in culture bottle prior to sampling invariably led to false negative results. In our healthcare setting where PCR testing remains largely limited to tertiary hospitals, the timely identification of KP may be hampered by this factor.[8]

It is important to take note that several published case reports on *Klebsiella pneumoniae* related prostatic abscess were largely incidental findings by imaging, leading to clinical suspicion and successful diagnosis of the disease.[9] Such sophisticated imaging modalities may not be available in resource-stricken countries; thus, clinical assessment and high clinical suspicion serve as the only way to hasten referral to appropriate tertiary healthcare centres. In our patient, the finding of an enlarged prostate was not identified during his first admission. It should be an invaluable learning point to all clinicians to consider a prostate examination in patients with prolonged fever to exclude a potential pathology of the prostate.

If an enlarged prostate is identified, USG and/or CT abdomen should be utilised to visualise the presence of prostatic abscess and to identify other location of intraabdominal abscesses. Serial imaging should be done to track evolution into prostatic abscess so that urological intervention can be undertaken earlier. As the Latin medical term "Ubi pus, ibi evacua" which translates directly to "where [there is] pus, evacuate [it]". All prostatic abscesses should be considered for drainage where feasible for proper source control.

Another important point in the context of tropical diseases in Southeast-Asia (SEA), symptomatology and complications for both *Burkholderia pseudomallei* and *Klebsiella pneumoniae* are surprisingly similar. They affect primarily the immunocompromised patients particularly diabetics, and result in disseminated abscess formations. In 2009, Ng et al. reported 5 cases of prostatic abscesses caused by *Burkholderia pseudomallei* in Pahang, Malaysia, among which four of five patients were asymptomatic, and 60% of them were noted to have an enlarged and non-tender prostate during examinations.[6] Gold standard for diagnosis of *Burkholderia pseudomallei* remains routine blood culture. Serologic testing is not reliable.

In conclusion, the authors recommend that for all male patients with unknown sources of fever, a prostate examination should be considered in the clinical process after thorough exclusion of other common sites of infection. An enlarged prostate which is tender or boggy especially in younger males should raise suspicion of an early infection caused by *Escherichia coli, Burkholderia pseudomallei* or *Klebsiella pneumoniae*.

CONFLICT OF INTEREST

None.

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CASE REPORT

Primary biliary cholangitis-autoimmune hepatitis overlap syndrome: an overlapping condition that responded to overlapping treatment

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SUMMARY

Primary biliary cholangitis (PBC) is an autoimmune liver disease, characterised by inflammation and destruction of small bile ducts, leading to cholestasis and eventually biliary cirrhosis. Up to 9.2% of patients demonstrated moderate to severe interface hepatitis, a feature characteristic of autoimmune hepatitis (AIH), hence referred to as PBC-AIH overlap syndrome (PBC-AIH-OS). Here we report a woman in her 50s, presented with severe hepatocellular injury, with alanine aminotransferase (ALT) and aspartate aminotransferase (AST) > 20x upper limit of normal (ULN). Laboratory tests revealed positive anti-mitochondrial antibodies (AMA), anti gp210 and Sp_100 antibodies; raised serum IgG and IgM level, favouring the diagnosis of PBC. However, PBC is more commonly associated with cholestasis rather than hepatocellular injury, hence liver biopsy was performed to look for AIH features which revealed moderate interface hepatitis and confirmed our suspicion of overlap syndrome. Based on the widely used Paris Criteria, she was diagnosed with PBC-AIH-OS and started on treatment promptly. Treatment of PBC-AIH-OS remains controversial with weak recommendation and no clear consensus from the recent guidelines due to the paucity of data. As for our patient, we took a liberal approach and started her on corticosteroids, ursodeoxycholic acid (UDCA) and azathioprine (AZA), a combination of treatments for both PBC and AIH, and she responded well with normalisation of liver enzymes.

INTRODUCTION

Primary biliary cholangitis (PBC) is an autoimmune cholestatic liver disease, characterised by inflammation and destruction of small intralobular bile ducts which leads to cholestasis and eventually biliary cirrhosis. This condition is more prevalent among women in fourth and fifth decades of life with the estimated worldwide incidence and prevalence of 1.76 and 14.6 per 100,000, respectively.[1] The aetiology is not well understood but studies have suggested that environmental and immunogenetic interaction may trigger the pathogenesis of the condition.[2]

Most PBC presents with hepatic inflammation but up to 9.2% of patients demonstrate moderate to severe interface hepatitis, a feature characteristic of autoimmune hepatitis (AIH), hence refer to as PBC-AIH overlap syndrome (PBC-AIH-OS).[3] There is paucity of data on the treatment for PBC-AIH-OS with weak recommendation and no clear consensus based on the recent European Association for the Study of the Liver (EASL) 2017 and Asian Pacific Association for the Study of the Liver (APASL) 2022 guidelines.[4,5] Here we report a case of PBC-AIH-OS which the patient presented with severe hepatocellular injury and responded well to corticosteroids, ursodeoxycholic acid (UDCA) and azathioprine (AZA) combination therapy.

CASE PRESENTATION

A woman in her 50s presented with malaise for 1 month, associated with right hypochondriac pain and jaundice for 4 days. There were no other complaints upon systemic review. She is a social drinker and non-smoker. She denied any use of traditional medications. On physical examination, she was jaundiced, but otherwise unremarkable with normal findings on the abdomen and no stigmata of chronic liver disease.

Initial laboratory tests revealed severe hepatocellular injury with elevated alanine aminotransferase (ALT) 2183 U/L, aspartate aminotransferase (AST) 729 U/L, alkaline phosphatase (ALP) 264 U/L, total bilirubin (TB) 352 umol/L, direct bilirubin (DB) 250 umol/L, of which other possible causes such as viral infection, drug induced and ischaemic hepatitis had been excluded. Iron, serum ceruloplasmin/urinary copper, alpha 1 antitrypsin were normal. Serologic markers showed positive anti-mitochondrial antibody (AMA); negative anti-nuclear antibody (ANA), anti-liver kidney microsome antibody (anti LKM) and anti-smooth muscle antibody (ASMA). Serum IgG and IgM were elevated (Table I). Abdominal ultrasound and magnetic resonance cholangiopancreatography (MRCP) were done with both reported unremarkable findings of calculous cholecystitis and normal biliary ducts. While positive AMA and elevated serum IgM level favour the diagnosis of PBC, it is not commonly associated with severe hepatocellular injury, hence liver biopsy was performed to look for overlapping AIH features. Meanwhile, her liver function continued to deteriorate in ward as evident by the gradual increase in serum bilirubin level, up to 702 umol/L

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Table I: Initial laboratory test and liver antibodies panel.

Test	Result	RR	Test	Result
Haemoglobin (g/dL)	11.1	11 – 15.2	Anti-HAV IgM	-
White blood cells (10^3/uL)	7.3	4.69 – 12.01	Anti-HAV IgG	+
Platelet (10^3/uL)	328	184 – 432	HbsAg	-
ALT (U/L)	2183	0 – 55	Anti-HbC (Total)	-
AST (U/L)	729	5 – 34	Anti-HCV	-
ALP (U/L)	264	40 – 150	Anti-HIV	-
GGT (U/L)	261	5 – 40	ANA	-
TB (umol/L)	352	3.4 – 20.5	Anti-dsDNA	-
DB (umol/L)	250	0 – 8.6	AMA	+
Albumin (g/L)	31	35 – 50	ASMA	-
INR	1.22		Anti-LKM	-
A1AT (g/L)	2.12	0.9 – 2.0	Anti-gp210	+
Ceruloplasmin (g/L)	0.33	0.16 – 0.45	Anti-Sp100	+
24H urinary copper (umol/24H)	2.56	< 0.9	Anti-Ro-52	-
Ferritin	1043	14 – 233	Anti-SLA/LP	-
IgA (g/L)	2.51	0.65 – 4.21	Anti-LC-1	-
IgG (g/L)	21.76	5.52 – 16.31	Anti-LKM-1	-
IgM (g/L)	4.39	0.33 – 2.93	Anti-PML	-
			Anti-M2-3E	-
			Anti-AMA-M2	-

Initial laboratory results showed markedly elevated transaminases, raised serum bilirubin and negative viral serologies. Raised serum IgG and IgM; positive AMA, anti-gp210 and Sp100 are typically associated with PBC. ALT: alanine aminotransferase; AST: aspartate aminotransferase, ALP: alkaline phosphatase, GGT: gamma-glutamyl transferase, TB: total bilirubin, DB: direct bilirubin, INR: international normalized ratio, A1AT: alpha-1 antitrypsin, HAV: hepatitis A virus, HbsAg: hepatitis B virus surface antigen, anti-HbC (Total): hepatitis B virus core total antibody, HCV: hepatitis C virus, ANA: antinuclear antibody, Anti-dsDNA: anti-double stranded deoxyribonucleic acid antibody, AMA: anti-mitochondrial antibody, ASMA: anti-smooth muscle antibody, Anti-LKM: anti-liver kidney microsome antibody, Anti-gp210: anti-glycoprotein-210 antibody, Anti-SLA/LP: anti-soluble liver antigen/liver-pancreas antibody, Anti LC-1: anti-liver cytosol antibody, Anti-LKM-1: anti-liver kidney microsome 1 antibody, anti-PML: anti-promyelocytic leukemia protein, Anti-AMA-M2: anti-mitochondrial M2 antibody.

and decrease in serum albumin level, down to 23 g/L, both of which are commonly used predictors for short term prognosis of PBC or AIH. Otherwise, her international normalised ratio (INR) was normal and there were no features to suggest hepatic encephalopathy.

Liver biopsy revealed both AIH features with moderate interface hepatitis and portal inflammation with lymphocytes, plasma cells and occasionally eosinophils infiltrates, and PBC features with chronic cholestasis and bile duct paucity (Figure 2A-2F). In addition, she was also noted positive for anti gp210 and Sp_100 antibodies, which are specific for PBC. Based on Paris Criteria, she was diagnosed with PBC-AIH-OS and started on IV hydrocortisone 100 mg BD and UDCA 500 mg/250 mg BD. She responded well to treatment with improvement of liver function and was discharged home with oral prednisolone 1 mg/kg OD, UDCA and outpatient follow up. AZA was added during clinic review, and she was in remission with normalisation of liver function (Figure 1).

DISCUSSION

PBC and AIH are separate clinical entities among autoimmune liver diseases with different biochemical, histological and serological characteristics. Overlapping features between autoimmune liver diseases may present in some patients, which both conditions may occur simultaneously or later in the course of the disease. PBC-AIH is the most common overlap syndrome in this spectrum of diseases.

PBC-AIH-OS is widely defined using the Paris Criteria by fulfilling the following:

At least two out of three features of PBC:

i. ALP > 2x ULN or GGT > 5x ULN.*
ii. AMA positive.*
iii. Florid bile duct lesion on histology.

And at least two of out three features of AIH:

i. ALT > 5x ULN.*
ii. IgG serum levels > 2x ULN or ASMA positive.
iii. Moderate or severe interface hepatitis on histology.*

**Criteria met in our patient*

As per Paris criteria, our patient fulfilled two out of three features of PBC and AIH respectively, establishing the diagnosis of PBC-AIH-OS. It was noted that her serum IgG level was 1.3x ULN which did not meet the Paris Criteria of AIH (> 2x ULN). Studies have debated that serum IgG level seldom raise above 2x ULN which limit the diagnosis of PBC-AIH-OS using Paris Criteria.[6] A study by Wang Q et al in 2013 reported serum IgG levels ≥1.3x ULN has 60% sensitivity and 97% specificity for PBC-AIH-OS, which is more sensitive than Paris Criteria, and also endorsed by the latest APASL guideline.[5,7] At present, there are no clear consensus in regard to the treatment of PBC-AIH-OS due to the paucity of data. EASL 2017 PBC guidelines recommend immunosuppression in patients with severe interface hepatitis and to consider in patients with moderate interface hepatitis.4 Similarly, APASL 2022 PBC guidelines also mentioned that immunosuppression could be used as add-on or de novo combination therapy with UDCA.[5] However, both these guidelines were based on grade III evidence and grade 2

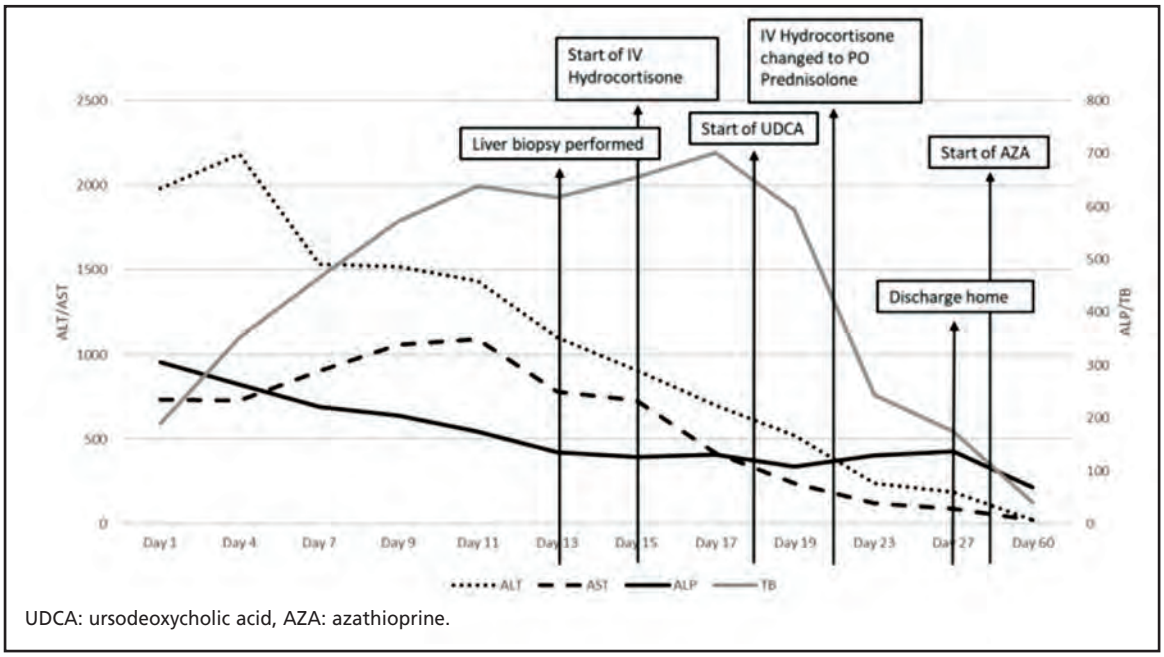

Fig. 1: Liver enzymes (ALT, AST, ALP) and serum bilirubin level over time.

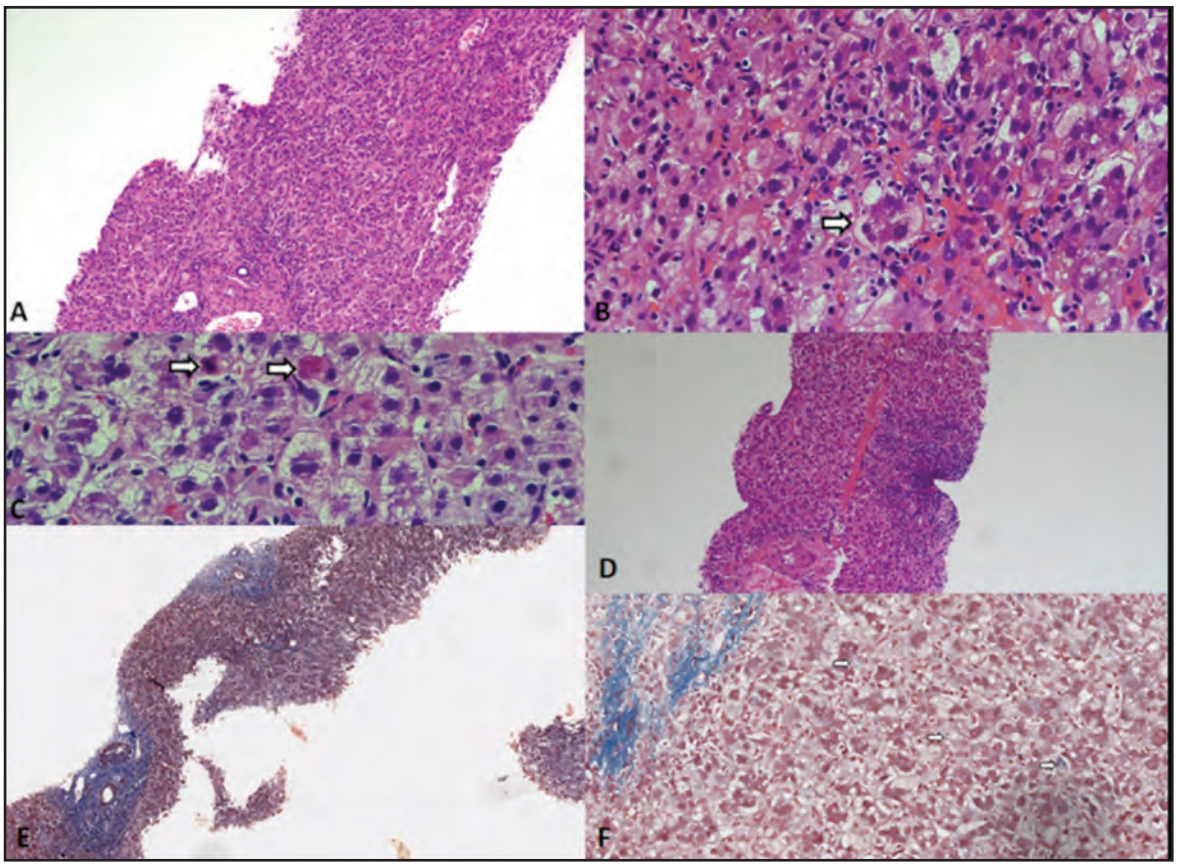

Fig. 2: Photomicrographs of liver biopsy.
A - The liver biopsy shows large portal tract with intact bile duct and mild ductular reaction, interface hepatitis with lymphoplasmacytic infiltrates. The lobules contain scattered foci of spotty necrosis with dropout of hepatocytes. Hepatocanalicular cholestasis is also present. (x10). B - Syncytial giant cell formation in high power view (shown by arrow, x40). C - Scattered acidophil bodies in high power view (shown by arrows, x40). D - Two portal tracts with loss of bile ducts. (x10). E - The figure shows portal fibrosis as highlighted by Masson Trichrome stain (x10). F - The figure shows periportal copper-associated protein as demonstrable by Victoria blue stain (shown by arrows, x40)

recommendation. Meanwhile, American Association for the Study of Liver Diseases (AASLD) 2018 PBC guidelines did not provide recommendation in PBC-AIH-OS, citing no clear consensus on optimal therapy and treatment should be targeted at the predominant histological pattern of injury.[8]

Furthermore, there are conflicting opinions regarding the efficacy of combination therapy (UDCA & immunosuppressive agents). Several studies reported better outcome with combination therapy (UDCA and corticosteroids with or without AZA), as compared to monotherapy alone[9] while the recent meta-analysis by Freedman et al showed no clear differences in clinical outcomes between these treatment regimens.[10]

CONCLUSION

PBC-AIH overlap syndrome (PBC-AIH-OS) is a rare disease but not uncommon among patients with primary biliary cholangitis (PBC). Liver biopsy should be considered if patient with PBC demonstrates autoimmune hepatitis (AIH) features (disproportionately elevated serum transaminases or raised serum IgG level as per PARIS criteria). Treatment of PBC-AIH-OS remains controversial with limited data notwithstanding, we had great result with combination therapy of corticosteroids, ursodeoxycholic acid (UDCA) and azathioprine (AZA) in our patient. Nevertheless, more evidence is still required to provide stronger recommendation and guide the management of such rare disease.

ACKNOWLEDGEMENT

We would like to acknowledge the healthcare workers of our hospital who were involved in the management of this patient.

CONFLICT OF INTEREST

None to declare.

ETHICAL STATEMENT

Verbal consent was obtained from patient for publication of this case report and accompanying images.

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CASE REPORT

Obturator hernia: What to do with the other side?

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SUMMARY

Obturator hernia is a rare variant of abdominal hernia that occurs in thin elderly women, invariably causing intestinal obstruction requiring surgical intervention. A contrast-enhanced computerised tomography (CECT) scan of the abdomen and pelvis is an invaluable tool in the diagnosis and surgical planning. Rarely, an incidental contralateral obturator hernia can be found intraoperatively, but there is limited evidence available to guide as to repair simultaneously or treat conservatively. We present a case of a 90-year-old woman with intestinal obstruction. Preoperative CECT scan of the abdomen and pelvis was suggestive of small bowel obstruction due to strangulated obturator hernia. Intraoperative findings were a Richter right obturator hernia with a loop of viable distal ileum and an incidental left obturator hernia with empty content present. Primary repair was done on both obturator hernias with a prolene® 2/0 suture. Due to the diagnostic challenge and high mortality rate, we advocate for the keen exploration for a possible asymptomatic contralateral obturator hernia in cases with symptomatic unilateral obturator hernia and both to be repaired at the same sitting.

INTRODUCTION

Obturator hernias are rare and known to affect thin elderly multiparous women, attributed to a wider pelvis, enlargement of the obturator canal after pregnancy, loss of fat pad around the obturator canal and increased tissue laxity with aging. They are thought to occur more often on the right side due to the presence of the sigmoid colon.[1] Patients often present with acute small bowel obstruction. The Howship-Romberg sign may be demonstrated by the patient noting pain radiating along the medial thigh when the ipsilateral leg is extended or abducted and is due to irritation of the obturator nerve by the hernia sac causing obturator neuralgia. A high index of clinical suspicion is required as the lack of specific symptoms poses a clinical challenge in early diagnosis. Obturator hernias present bilaterally only in a small percentage of cases and are associated with significant mortality and morbidity often due to delayed diagnosis and management.

CASE PRESENTATION

A 90-year-old, para five woman, independent in activities of daily living (ADL), presented with severe generalised colicky abdominal pain with bloating for 4 days with right medial thigh pain radiating to the right buttock and down the right lower limb. She had no bowel output for 1 week, had not passed flatus and had a poor appetite. She also had non-bilious vomiting, mainly food content and no blood. She had been seen and treated symptomatically 2 days before admission. She has hypertension and a right hip replacement done 2 years ago. She was frail, underweight and in severe pain on admission. She exhibited severe distention of the abdomen with visible bowel peristalsis which was tender on palpation. No peritoneal signs. Inguinal and femoral hernias were not found on palpation. Rectal examination revealed no frank blood or palpable masses with an empty rectum noted.

A CECT scan of the abdomen and pelvis showed small bowel obstruction with a transition point at the distal ileum of the right side of pelvis with no evidence of abdominal malignancy. Fluid-filled loops were seen between pectineus and obturator muscles bilaterally containing short segment non-dilated small bowel loops (Figure 1). She underwent an emergency exploratory laparotomy. Intraoperatively, a Richter right obturator hernia with incarcerated but viable distal ileum was found. A contralateral obturator hernia was noted. Bilateral obturator hernia was repaired with a prolene® 2/0 suture. The patient was discharged on postoperative day 5.

She was followed up on day 17 post-operation to remove her staples. The lower midline laparotomy wound has healed well. The patient had no major complaints, is tolerating orally, and has her usual bowel habits, but is yet to ambulate.

DISCUSSION

Not to operate was not an option for our patient when the diagnosis was evident on CECT imaging. Despite her age, ADL independence was a promising pre-operative feature in her case. Operating on the contralateral hernia did not add significant metabolic stress to her recovery. Her good recovery, returning to active life validated the surgery.

The rare incidence of obturator hernia appears to be increasing with growing awareness, better understanding, and improved documentation among healthcare professionals. Advancements in diagnostic techniques such as the CECT scan or diagnostic laparoscopy have led to more accurate identification of obturator hernias. The Danish Hernia Database from 1998 to 2023, presented a prevalence of obturator hernias in hernia surgery as 0.084% (95% CI: 0.071-0.098%), with an incidence of one per 400,000 inhabitants annually.[2] Obturator hernias carry a high

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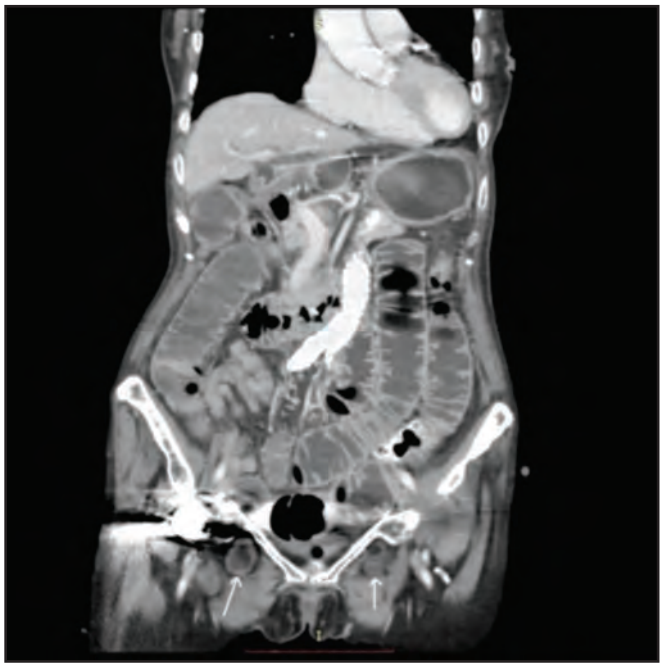

Fig. 1: CT abdomen and pelvis with contrast coronal view shows right and left obturator hernia containing fluid-filled short segment non-dilated small intestines (white arrows), with small intestine dilatation and artifact from right hip implant seen.

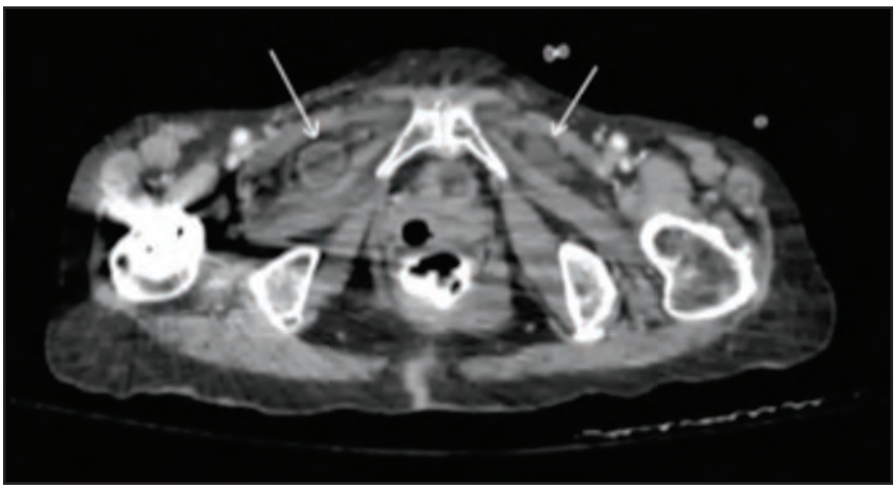

Fig. 2: CT abdomen axial view shows right and left fluid-filled loop seen between right and left pectineus and obturator muscles respectively, representing bilateral obturator hernia (white arrows).

mortality rate ranging from 12 to 70% as they are often diagnosed late and have an operative mortality rate of 11%.[3] A retrospective study done by Chan et al, reported an overall mortality rate of 47.6%.[4] This highlights the need for prompt diagnosis and timely surgical intervention.

Obturator hernias, unlike most hernias, have no specific clinical signs, but the Howship-Romberg sign is noteworthy. CT scan has been reported to improve the preoperative diagnosis of obturator hernias to 78%. A non-invasive pre-operative diagnosis is favoured to avoid misdiagnosis and surgical complications of an exploratory laparotomy.[3] Obturator hernias can be seen on the CT scan as a peritoneal sac or bowel loop passing through the obturator foramen and extending between the pectineus and obturator muscles.[5]

A retrospective analysis by Zhengzheng et al[6] reported that 100% of their patients had been diagnosed with obturator hernia based on preoperative CT findings. This shows that such details on CT scan can almost always be picked up with confidence, especially in patients with high clinical suspicion. An accurate preoperative diagnosis is also needed to facilitate the planning of a minimally invasive surgical approach, either open or laparoscopic.

To Fix or not to Fix the Asymptomatic Contralateral Side?

Contrary to the challenges faced in diagnosis, an obturator hernia is easy to repair. When an obturator hernia presents unilaterally, the contralateral side must be investigated for an asymptomatic obturator hernia. The decision whether to repair the asymptomatic contralateral side requires clinical judgment involving several factors such as the fitness of the

patient, comorbidities, difficulty of the repair on the affected side as well as complications such as bowel gangrene the hernia may have caused. In our patient who is 90-years old, there was little hesitation to repair the contralateral asymptomatic obturator hernia as her morbidity and mortality risk was expected to be increased should she need to undergo a second repair at a later date. We advocate for the timely prophylactic repair of the incidental finding of an asymptomatic obturator hernia during abdominal surgery to avoid a future diagnostic challenge and the need for another surgical intervention.

Primary Tissue vs Mesh Repair

The choice of an open laparotomy or laparoscopic approach depends on the surgeon. The argument for primary tissue repair or mesh repair depends on factors such as the age of the patient, probability of recurrence and potential post-operative complications. Although the primary repair is quick and a common method as reported by Holm et al in a scoping review, it is associated with a recurrence rate of 10%. On the other hand, no recurrences were reported with the mesh repair,[7] suggesting that the mesh repair may be better. In a systematic review and meta-analysis by Burla et al,[8] they similarly reported a significantly higher recurrence in patients who underwent primary tissue repair, however noted that there were no differences in mortality or complication rates between both groups. In our patient, however, a primary tissue repair was preferred considering her age (90 years) and the average life expectancy of Chinese women in Malaysia being 80.2 years.[9] The risk of recurrence can be arguably negligible and primary repair also avoids mesh-related complications. Looking retrospectively, we would like to advocate for a laparoscopic approach should a confident preoperative diagnosis have been made on the CECT scan of our patient, as less manipulation of the intestines and a smaller surgical wound would probably have drastically improved her post-operative outcomes.

CONCLUSION

There is no consensus on the best surgical approach in the repair of an obturator hernia, thus we recommend a national retrospective audit of obturator hernias to identify their prevalence in the past decade in relation to the advancements of imaging techniques, to report on the latest data of the demographic characteristics, the accuracy of CT scan in pre-operative diagnosis, common surgical approaches and the associated postoperative outcomes. CT scan has proven to be an invaluable tool in the diagnosis and surgical planning of the patient with an obturator hernia, hence detailed attention should be given to identifying obturator hernias in patients with high clinical suspicion. Considering the challenges in diagnosis and high mortality rate, we advocate for the keen exploration for an asymptomatic contralateral obturator hernia when a patient presents with a symptomatic unilateral obturator hernia, and both to be repaired in the same sitting to prevent a future diagnostic challenge and the need for another surgical intervention in the same patient.

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DECLARATION

Written consent for publication was obtained from the patient's caretaker. All authors have no conflict of interest to declare. This manuscript has not received any funding.

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The Blunt Abdominal Aortic Disruption experience in Hospital Kuala Lumpur: An aortic injury case report

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SUMMARY

Blunt abdominal aortic disruption (BAAD) is an extremely rare and highly lethal diagnosis. It is rarely diagnosed in the adult population as mortality rates are extremely high. Most individuals with these injuries almost never make it to the hospital and those who do unfortunately are seldom diagnosed in time for any intervention. We present a case of a 44-year-old gentleman who presented with cardiopulmonary arrest requiring two cycles of cardiopulmonary resuscitation and successfully underwent an exploratory laparotomy which found a transected infrarenal aorta. He underwent open repair with a tube graft and was discharged home well after 2 weeks. The aim of this publication is to highlight the possibility of such a diagnosis which should be considered during first contact with the patient, along with the urgency in management, complexity involved with the intraoperative management without appropriate radiological investigation and post operative care.

INTRODUCTION

Blunt abdominal aortic injury (BAAI) or blunt abdominal aortic disruption is a rare injury with a literature review showing only case reports published over the last 10 years. Majority of patients do not make it to hospital, and those who do, almost one third of them do not survive the initial 24 hours.[1] Injury to the aorta is based on the direct and indirect mechanism, as the aorta is tethered to the spinal column, peritoneum and abdominal viscera. Due to these mechanisms, and according to the severity of the force, this can lead to aortic disruption. The level of the IMA (33%), renal arteries (24%) and between the IMA and aortic bifurcation (19%) are the most common sites for blunt aortic disruption.[2]

Majority of literature available with regards to this injury is from the paediatric age group, however the consensus is that there needs to be a high index of suspicion with prompt diagnosis and intervention for patient survival.[3] The aim of this report is to present the successful management of a middle age gentleman with a blunt abdominal aortic disruption along with a systematic literature review. The patient survived without any neuro-vascular related complications and remains well at 6 months follow up.

CASE PRESENTATION

A 44-year-old gentleman, with no medical illness, presented to the emergency department of a private hospital with severe abdominal pain and hypotension. Prior to presentation to hospital, he claimed to have gone to two local theme parks and went on their rides the day before, which involved a pendulum ride. He denied any other history of trauma preceding his admission. On presentation to the emergency department at a private hospital his GCS was full, and however due to severe abdominal pain he was planned for a contrast enhanced computed tomography (CT) abdomen and pelvis. However, while on the CT gantry he developed hypotension owing to which the procedure was abandoned, with only a plain CT being done (Figure 1). He was immediately transferred to the emergency department at Hospital Kuala Lumpur. On arrival to our centre, he was hypotensive with a blood pressure (BP) of 86/40, requiring high flow mask to maintain his oxygenation. In the emergency department his abdominal pain worsened, and due to respiratory distress was intubated for airway protection. Immediately following this, he had an episode of asystole, requiring CPR and initiation of inotropes. Bedside FAST scan showed generalised free fluid. His baseline haemoglobin was 4.1 g/dL with platelets of 71 × 10^9/L. Renal profile, liver function and coagulation profile were unremarkable. After discussion with the surgical team and family members, consent was obtained to proceed with an exploratory laparotomy. His BP crashed following induction, requiring another 5 mins of CPR and initiation of triple inotropes.

With a BP of 52/25, we proceeded with an exploratory laparotomy which showed a large hematoma over the left retroperitoneal region which subsequently ruptured during manipulation and required four quadrant abdominal packing. The massive transfusion protocol was initiated by the anaesthesia team along with the use of Level 1 rapid infuser, a device used for rapid infusion of fluids at a temperature close to 37°C. Intraoperatively it was noted that there was arterial bleeding from the left flank. A cross clamp was applied on the infrarenal aorta, and the aorta was skeletonised, which showed > 50% circumference of the aorta was transected between the IMA and the aortic bifurcation (Figure 2). He underwent an interposition Dacron tube graft placement (Figure 3) with successful return of bilateral femoral pulses and inotropes was tapered to low dose single inotropes. There was no laceration, rupture or perforation to the mesentery or bowel and his solid organs showed no evidence of blunt trauma. This further justifies that the mechanism of injury to the aorta was from blunt injury shearing stress due to the acceleration and deceleration

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Table I: Mechanism of abdominal aortic injury

Mechanism of injury	Examples	Pathophysiology
Direct impact	Seat belt compression, motorcycle handlebars, blunt weapons, steering wheel in MVA	Compression of aorta against the vertebrae
Shearing stress	MVA, acceleration – deceleration injury,	Intimal Injury, Dissection or Laceration
Increased intraluminal pressure (rare)	Blunt force against abdominal wall	1000 mmHg luminal pressure

Table II: Classification of traumatic aortic injury

Grade I	Intimal tear
Grade II	Intramural hematoma
Grade III	Pseudoaneurysm
Grade IV	Rupture

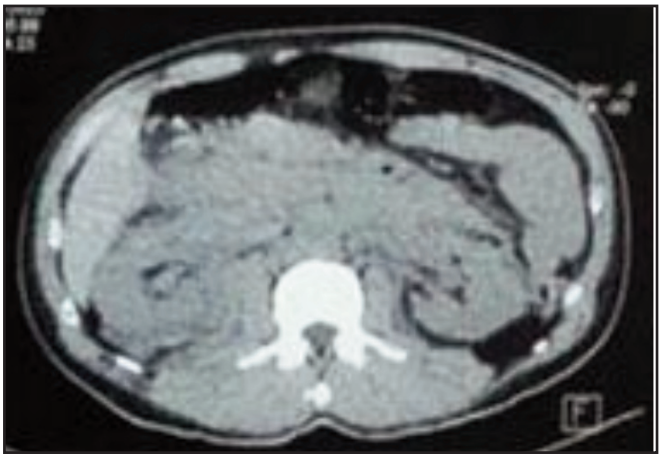

Fig. 1: Plain axial CT scan with presence of hematoma in retroperitoneum.

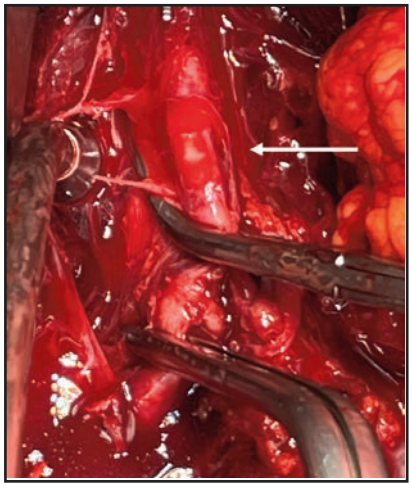

Fig. 2: Infrarenal abdominal aorta with transection (arrow).

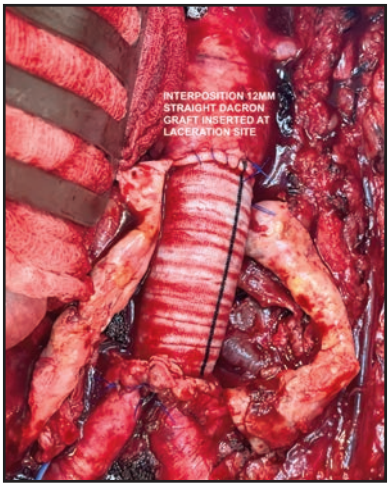

Fig. 3: Post Interposition Dacron tube graft placement at transacted site.

nature of the pendulum ride. His EBL was 10 litres, requiring three DIVC cycles and 14 pints packed cell transfusion. He was monitored in the intensive care unit after surgery.

Post operatively he was extubated on day 4, but on day 8 he complained of abdominal pain, fever and diarrhoea. Due to the high risk of ischemic bowel, he underwent a relaparotomy, which showed that his bowel was viable, but had residual hematoma approximately 2 litres. The abdomen was irrigated with copious amounts of saline and closed. He was successfully extubated immediately post op, and on day 12 was tolerating normal diet, passing motion and had no renal impairment. He was discharged home day 14 after abdominal sutures was removed. On follow up 2 weeks after discharge he was doing well, with no further complications.

DISCUSSION

BAAD is a major cause of mortality after blunt trauma and is rarely diagnosed as most patients do not survive till diagnosis or intervention. The individuals who survive till presentation in hospital require rapid and urgent diagnosis which is crucial for prompt treatment.

In an analysis of the National Trauma Databank in 2009, the authors demonstrated over a 5-year period the incidence of blunt aortic injury was 0.3%. From this, 23% of the patients died on arrival or during triage.[4] Unsurprisingly the majority of patients, 72%, were males with a mean age of 41 (± 20) years.[4] This should be remembered when dealing with relatively young, fit patients, who present, as our patient did, in severe shock and hemodynamic instability after trivial preceding activities.

Teixeira et al. based on autopsy reports, reported that the sites affected in blunt aortic injury were the isthmus/descending thoracic aorta (66%), arch (11%), ascending (3%), root (2%) and multiple (18%).[5] Abdominal aorta injury is rare due to the retroperitoneal position which is covered anteriorly by the abdominal wall and visceral organs and posteriorly and laterally by the vertebrae and paravertebral muscles.[6] When injury of the abdominal aorta is present in blunt trauma, the mechanism of injury is mainly due to direct impact, shearing stress or increased intraluminal pressure (Table I).[7] As seen in our patient, the nature of injury to the aorta could possibly be due to the shearing stress he sustained while on the theme park pendulum rides, leading to only injury to the aorta and not the other intraperitoneal organs.

Traumatic aortic injury is classified into four grades based on the nature of injury[8] and is tabulated below in Table II.

The importance of having a universal classification for aortic injury is that it allows for diagnosis, uniformed management, and dictates the urgency for intervention. Stable grade I and II aortic injuries can undergo conservative management and allow for appropriate imaging. However, grade III and IV may require emergent intervention.

Computed tomography angiography (CTA) is commonly used as a screening tool due to the availability in most hospitals and the high sensitivity (95%) and high negative predictive value (99%). However, CTA can have a low specificity (40%).[8] Patients with an equivocal CTA often require additional imaging such as IVUS, aortography or transoesophageal echocardiography. IVUS provides real time circumferential images of the vessel, does not require contrast or radiation and can be performed from the same femoral puncture for angiography. The downside currently with IVUS is the high cost, limited availability and increased operating time.

If a CTA was successfully performed in this patient, it would have been able to identify the aortic injury and also determine the grade of the injury. This would have permitted a focussed approach in the management, meaning immediate control intraoperatively of the infrarenal aorta thus preventing further haemorrhage. Additionally, taking into account the hemodynamic instability of the patient, with a CTA of the aorta, the option for endovascular aortic repair (EVAR) would have been a viable and potentially less morbid approach in the management for this patient. In established endovascular centres equipped with hybrid operating theatres or angiography suites and with availability of stent grafts of the shelf, this procedure can be done via a minimally invasive approach. Unfortunately, due to financial constraints and limited infrastructure, this option currently is limited to elective or semi elective cases in our centre.

In patients who undergo surgery for BAAI, the common complications seen in this group of patients are acute kidney injury (AKI), ARDS, deep vein thrombosis, pulmonary embolism, pneumonia or ventilator associated pneumonia and mortality in up to 28% of patients.[9] Our patient developed AKI which resolved with hydration and did not require dialysis. The prognosis for patients who develop such injuries is very much dependent on the rapid diagnosis and intervention. However, one must be familiar with the dissection of the aorta if there is no vascular surgeon around. Although the incidence of such cases is rare, the morbidity and mortality of undiagnosed cases particularly grade III to IV is exponentially high. The limitation encountered by the authors in this case was the inadequate preoperative imaging, a plain CT abdomen, due to the hemodynamic instability which prevented the patient from having adequate imaging done. In a more stable patient, a complete contrast enhanced CT scan would have allowed the involved surgeons and anaesthesia team to anticipate the severity and take proactive measures prior to the patient undergoing surgery.

CONCLUSION

The aim of this report is to highlight the possibility of blunt abdominal aortic disruption in trivial injuries, without involvement of other intraabdominal organ injury. The case presented here underwent intervention based on the clinical presentation and diagnosis. However, although sparse, literature shows there is an established classification and recommended intervention for such cases. The authors acknowledge that the availability of vascular trained surgeons played a role in the positive outcome for this patient, however prompt diagnosis and referral to a vascular centre may also provide similar outcomes.

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Beyond stertor: A rare case report on nasopharyngeal mature teratoma in an infant

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SUMMARY

Teratomas are the most frequent congenital tumours in children, originating from two or three germ layers. Since the sacrococcygeal region is the most prevalent site for this tumour, the nasopharyngeal region is uncommon in its localisation. Teratomas are generally benign and have a well-recognised clinical and histopathological entity. This case report describes a 4-month-old boy who had stertor since day 10 of life and presented to the emergency department with worsening noisy breathing and rapid breathing for two weeks prior to the admission. During the admission, he experienced many desaturation episodes necessitating non-invasive ventilation. Imaging supported the endoscopy's discovery of a solitary cystic lesion obstructing the left posterior choanae. The patient underwent a successful surgical excision of the mass, and a histological examination revealed a mature teratoma free of any indications of cancer. He had a smooth recovery following surgery, and regular check-ups revealed no signs of a tumour recurrence. This report addresses the need for a thorough assessment and evaluation of the stertor to rule out additional serious upper airway issues, such as the one in this instance. As a result, we can prevent severe morbidity and mortality.

INTRODUCTION

Teratomas represent one of the most common extragonadal germ cell tumours of childhood. It is a benign tumour composed of cells from ectodermal, mesodermal and endodermal layers.[1] They can be found in any body site, but most are in a midline or paraxial location from the brain to the sacral area. The most common locations for teratomas are the sacrococcygeal site, anterior mediastinum, ovaries, testicles and retroperitoneal area. The head and neck are rarely involved, 2 to 9% of all teratomas, and the incidence is only one in every 40,000 births.[1,2] Although nasopharyngeal teratomas are rare, they can lead to severe airway obstruction. The presentation will be stertor, respiratory distress, feeding problems and cosmetic deformity. Neonates who present with stertor, a low-pitched breathing sound, should be alerted to the possibility of obstruction along the nasal cavity, nasopharynx or oral cavity. Congenital mass obstruction in those mentioned areas should be considered. Stertor in neonates signifies a critical airway blockage demanding urgent attention from clinicians familiar with the intricacies of neonatal physiology. Managing this condition requires a multidisciplinary approach, emphasising effective communication among healthcare providers and caregivers. This collaborative effort is paramount for ensuring favourable outcomes for these vulnerable infants.

CASE PRESENTATION

A 4-month-old boy was brought to the emergency department (ED) with worsening noisy breathing and rapid breathing. The noisy breathing had been presented since he was 10 days old but was not associated with rapid breathing or issues with feeding and sleep. However, over the past 2 weeks, his breathing has worsened, becoming more rapid and disturbing his sleep. He has no fever, cough, runny nose, bluish discolouration or seizure. He also has no previous history of hospital admission. Antenatal history was uneventful. He was born full-term with a birth weight of 3 kg and good Apgar scores. During the neonatal period, he has no other issues and has been followed up regularly at the nearest health clinic. His growth and development have been appropriate for his age, and his immunisation is up to age.

Upon examination on the day of admission, he had a low-pitched inspiratory stertor and was in respiratory distress, as evidenced by the tachypnoeic and subcostal recession. Lung auscultation was equal, and air entry was clear. Other systemic examinations were unremarkable.

He was referred to the paediatrics team and admitted to the intensive care unit, where he required continuous positive airway pressure (CPAP) with positive end-expiratory pressure (PEEP) of six due to three episodes of oxygen desaturation down to 85% while on room air. Despite this intervention, he continued to experience multiple desaturation episodes, with the oxygen level dropping to 85% and associated with tachycardia while on CPAP. Consequently, he was referred to the otorhinolaryngology (ORL) team for an upper airway assessment.

Surprisingly, flexible nasopharynx-laryngoscopy showed a single cystic lesion at the posterior nasal space, completely obstructing the left choanae and likely originating from the left side and crossing midline toward the right posterior nasal

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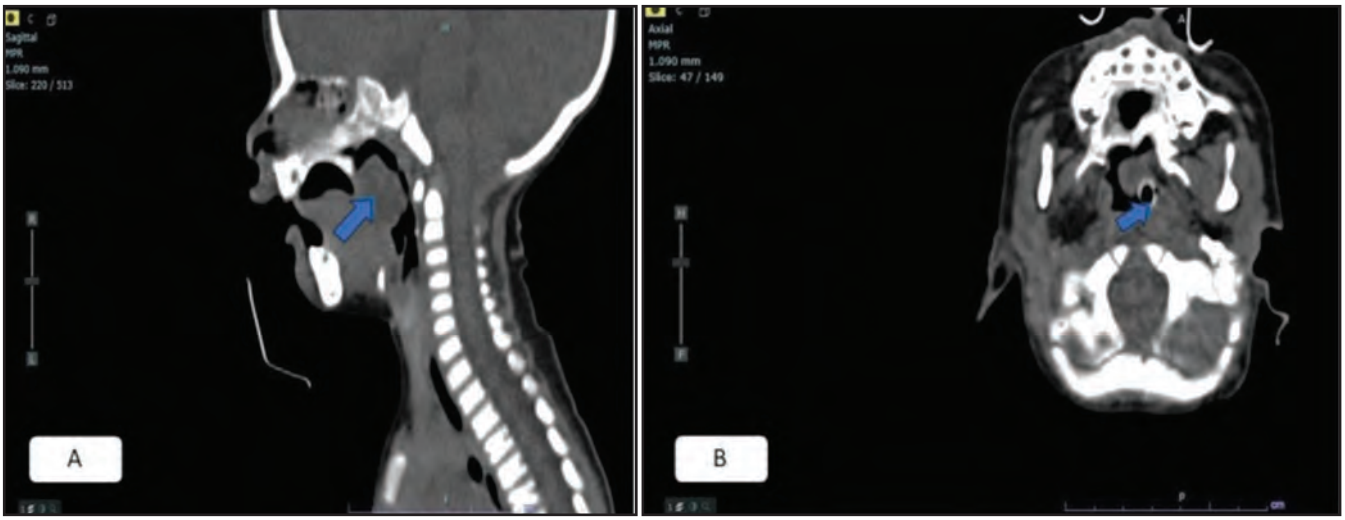

Fig. 1: A&B. Blue arrow; CECT brain showing a round non-enhancing cystic lesion likely arising from the left posterior nasal space protruding onto the nasopharynx measuring approximately 1.7 × 1.7 × 2.2 mm (AP × W × CC). There is thin enhancing septation at the inferior part of the lesion. No calcification, solid or fatty component within. There is no abnormal enhancement to suggest infiltration—the features of benign nasopharyngeal cysts.

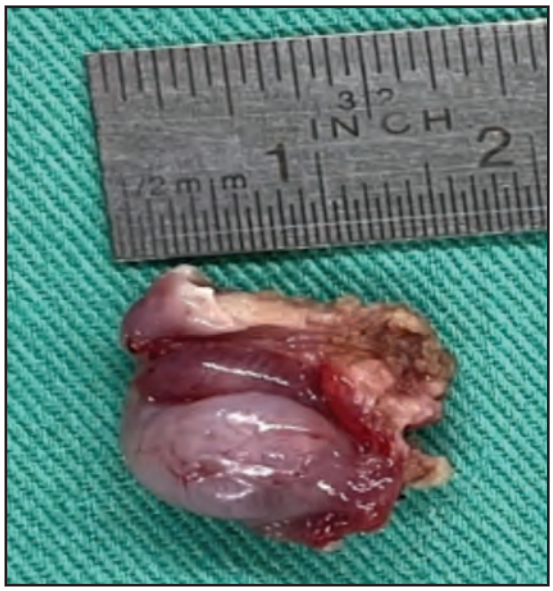

Fig. 2: Intact cyst measuring 13 × 10 × 8 mm. The cyst is surrounded by fatty tissue measuring 8 × 3 × 3 mm. The cyst wall is 2 to 3 mm in thickness.

space. There were no features to suggest laryngomalacia. An urgent contrast-enhance computed tomography (CECT) scan of the neck and base of the skull was arranged. The CECT result indicated a benign nasopharyngeal cyst from the left posterior nasal space protruding onto the nasopharynx, measuring approximately 1.7 × 1.7 × 2.2 mm (AP × W × CC) (Figure 1).

After 6 weeks of admission and undergoing the CECT scan, he was discharged home with CPAP for use during sleep and was well at home. There was no respiratory distress, sleep or feeding issues. He was then re-admitted again 2 weeks after the discharge for excision and biopsy surgery under elective general anaesthesia (GA). During the surgery, a nasopharyngeal cyst and base (Figure 2) were removed and sent for biopsy. The surgery was successful without any complications, and he was able to wean off the CPAP postoperatively. A few days after the surgery, he was discharged on room air. Histopathological findings were consistent with features of mature cystic teratoma (Figure 3). Subsequent follow-ups at the outpatient ORL clinic showed no further noise or fast breathing, and he was clinically well. The ORL team will continue the surveillance by monitoring the symptoms like stertor and regular flexible scope during scheduled follow-ups. Paediatrics teams closely follow up with him to observe for any recurrence of teratomas elsewhere. At the same time, he continues the follow-up at the nearest health clinic for developmental and vaccinations.

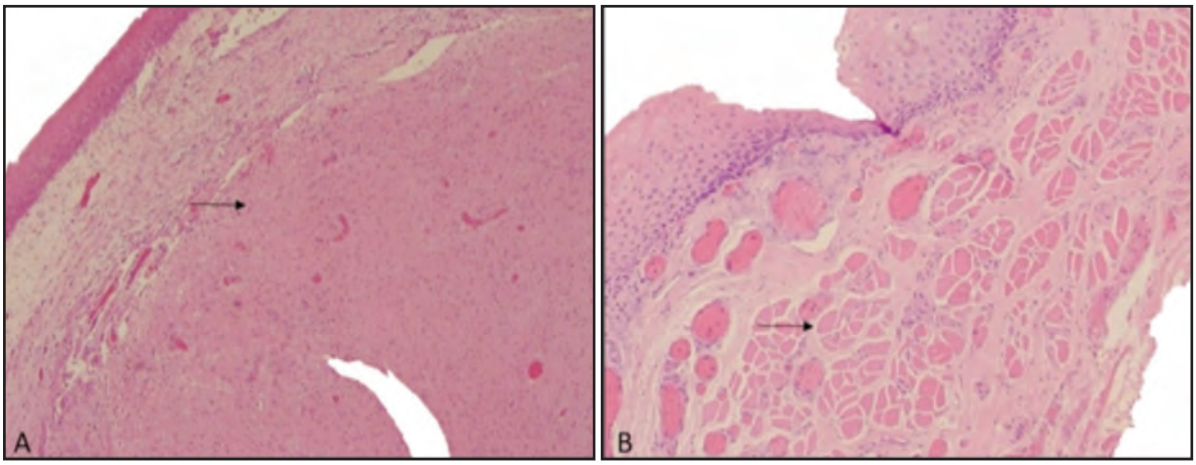

Fig. 3: A. Histopathology showing glial tissue within the subepithelial layer (arrow) (H and E stain, x 100). B. Histopathology showing smooth muscle bundles (arrow) with overlying pseudostratified squamous epithelium and congested vascular channels (H and E stain, x 200).

DISCUSSION

Noisy breathing can be described by its quality, location of obstruction, and underlying pathology. Stertor is a low-pitch sound from the base of the tongue and hypopharynx, often heard during sleep due to decreased pharyngeal muscle tone and gravity during inspiration. Stridor is a high-pitched sound resulting larynx and trachea obstruction, heard during inspiration, expiration or both.[3]

Neonates are obligate nasal breathers, meaning they exclusively breathe through their nose until six months, allowing them to breathe and eat simultaneously.[3] Obstruction from the nasal cavity downward is crucial for them. Most literature reports respiratory distress and feeding problems appearing in the neonatal period.[1,2,4,5] However, in this case, the patient had stertor since day ten of life, but he had no alarming issues like feeding, poor weight gain or respiratory distress until at four months old. Subtle symptoms led to missed recognition by the physician until signs and symptoms of upper airway obstruction developed.

That is why an early diagnosis of potential airway obstruction in neonates will improve outcomes. This can be obtained with a comprehensive history and physical examination, encompassing familial genetic factors, prenatal diagnoses, and birth-related details such as prematurity, labour duration, presentation, and delivery trauma. Recognising signs suggestive of nasal obstruction, including tachypnoea, nasal flaring, cyclical cyanosis, epistaxis, sternal retraction, and episodic apnoea, is crucial.

In the primary health clinic, airway obstruction can be assessed using a cold spatula test for nasal/nasopharynx patency or Ryle's tube insertion test. Consulting the ORL team is recommended before proceeding with Ryle's tube test to avoid complications. Referral to the ORL team for an endoscopic examination is essential to identify any possible obstruction from the nasal cavity, posterior choana and nasopharynx. This holistic approach at the primary care level significantly influencing outcomes, even though the most common causes of neonatal stertor do not cause immediate harm to the neonate.

Nasopharyngeal teratoma is a rare benign entity. During antenatal, ultrasonography can help detect pharyngeal teratoma early, often polyhydramnios and increase alpha-fetoprotein levels.[6] Differential diagnoses include other oropharyngeal masses like encephalocele, meningocele, nasal glioma, congenital rhabdomyosarcoma, haemangiomas, neurofibromatosis, congenital epulis, congenital epignathus, and lymphatic malformation. Nasopharyngeal causes of airway obstruction to consider are choanal atresia, choanal stenosis, mid-nasal stenosis, piriform aperture stenosis and craniofacial abnormalities.[2]

A CT scan was chosen for our case due to its immediate availability and the no need for general anaesthesia (GA). It effectively provided information on the mass's vascularity and extension. While magnetic resonance imaging (MRI) is ideal for evaluating soft tissue mass, it has a long waiting time and requires GA. The treatment for this case is complete surgical removal, and the timing is as early as possible. In our case, the surgery occurred eight weeks after admission and alpha-fetoprotein was not measured as it is not a sensitive marker.[2]

The prognosis depends on the patient's age, tumour resectability, and metastasis. Early resection, pathological evaluation for premalignant or malignant changes, and long-term follow-up are critical for positive outcomes.[7] The case series reveal that the survival and morbidity of head and neck teratoma is excellent following surgery, with rare recurrence.[2] Therefore, the primary care team play a crucial role in coordinating follow-up care, monitoring for recurrence or complications, and supporting appropriate growth and development.

CONCLUSION

Mature nasopharyngeal teratoma is a rare disease in neonates. However, proper assessment is warranted when a newborn presents with marked noisy breathing because it can lead to a life-threatening event that is high in morbidity and mortality. Even though nasopharyngeal teratoma in otorhinolaryngology is urgent in localisation, other

disciplinary teams, such as primary physicians, obstetricians, and paediatricians, should collaborate closely for a successful early diagnosis and treatment.

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DECLARATIONS

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Paediatric Spontaneous Pneumomediastinum 'Ruptured Alveoli for Observation': A Case Report

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SUMMARY

Children rarely experience spontaneous pneumomediastinum (SPM), 2 Because these cases are typically self-limiting, most patients will be admitted for observation. Regarding the treatment of paediatric patients who present to the emergency department (ED) with spontaneous pneumomediastinum, whether primary or secondary SPM, there is currently no agreement regarding their management. This case study describes a patient who had asthma-like symptoms for one day before being brought to the emergency room of Hospital Raja Perempuan Zainab II on January 15, 2024. Otherwise, the child was well before this event. Interestingly, chest X-ray after multiple nebuliser administration revealed pneumomediastinum. This case report highlights the overall management of spontaneous pneumomediastinum in paediatric patients.

INTRODUCTION

The pneumomediastinum is the accumulation of air or gas in the mediastinum. It is also referred to as mediastinal emphysema. It can be classified as either spontaneous or traumatic pneumomediastinum. Spontaneous pneumomediastinum (SPM) refers to the occurrence of air in the mediastinum that is not caused by trauma or medical procedures. Traumatic pneumomediastinum is secondary to blunt or piercing chest trauma, iatrogenic damage or complications from thoracic surgery or mechanical breathing.

Incidence of SPM was documented ranging from 1 in 800 to 1 in 42,000 hospitalised adult and paediatric patients.[1,2] The prevalence of SPM among children seeking emergency care for asthma varies between 0.3 to 5%.[3]

Paediatric SPM resolves on its own and is considered a reasonably harmless condition. Therefore, paediatric patients with SPM, whether primary or secondary, are typically admitted for observation in the emergency department and undergo further diagnostic tests due to the lack of consensus on definitive care.

CASE PRESENTATION

A 9-year-old girl with underlying bronchial asthma who did not receive proper medical supervision presented with fast breathing for 1 day. It is associated with fever, productive cough and post tussive vomiting. She denied any recent history of illness, interaction with sick individuals, falls, or trauma. No recent travel or aquatic activities. Upon arrival at the emergency department, normal blood pressure with pulse rate of 86, mild tachypnoea was noted with a respiratory rate of 26 breaths per minute, oxygen saturation of 97% on room air, and low-grade temperature of 37.5°C. She was triaged to the asthma bay and received nebulised salbutamol due to widespread rhonchi with equal air entry detected during lung auscultation. She received an additional two nebulised doses of salbutamol and Combivent due to persistent rhonchi in the lungs and reported no improvement in symptoms before undergoing a chest X-ray.

The X-ray of the patient revealed pneumomediastinum and soft tissue emphysema (Figure 1 A). Bedside ultrasonography did not find any features suggestive for pneumomediastinum in this case. The patient's septic condition was indicated by a total white blood cell count of 16.24 (predominantly neutrophils at 83% and lymphocytes at 8.7%), haemoglobin of 12, haematocrit of 34 and platelet count of 694. C-reactive protein level is 12.2. The patient was referred to the paediatric team for admission because of persistent tachypnoea despite resolution of bronchospasm and for further pneumomediastinum management.

The patient was initially assessed in the asthma bay due to a known case of bronchial asthma and stable condition. She received two doses of nebulised salbutamol and one dose of nebulised Combivent due to lack of improvement and persistent bronchospasm during each cycle of complete nebulised inhaler. She later conducted a Chest X-ray and administered Intravenous Hydrocortisone at a dosage of 4 mg/kg due to the patient's persistent tachypnoea despite improvement in bronchospasm. The patient was moved to the yellow zone for nasal prong oxygen at a rate of 3 L/min due to tachypnoea and the need for proper monitoring.

She was admitted to the ward for treatment of moderate acute exacerbation of bronchial asthma caused by atypical pneumonia, along with mild persistent asthma worsened by pneumomediastinum.

The patient in the ward received nebulised salbutamol every 2 hours, alternating with nebulised Combivent every 4 hours before transitioning to Metered Dose Inhaler (MDI) salbutamol 10 puffs every 3 hours then every 4 hours, in addition to MDI beclomethasone two puffs twice a day. The patient was administered intravenous hydrocortisone 120 mg four times a day for 1 day before switching to oral prednisolone 30 mg once a day for 3 days. She was initially

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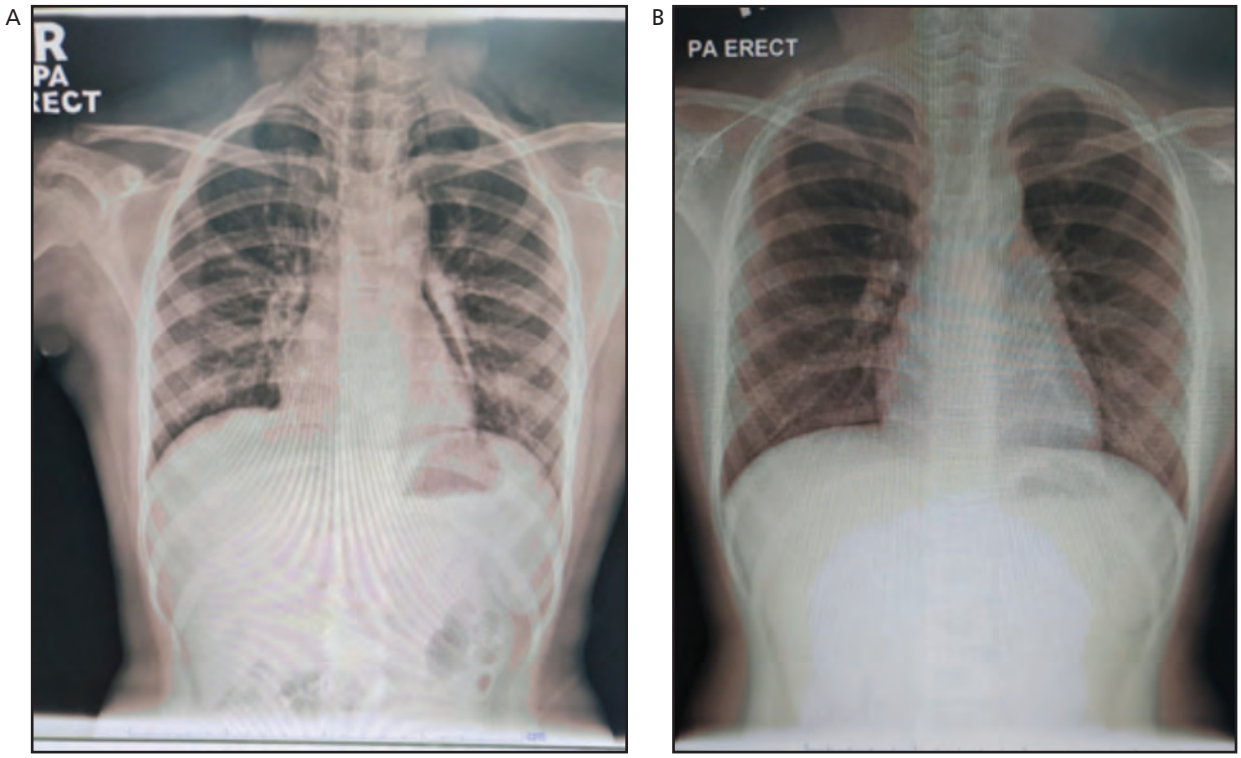

Fig. 1: Sequential chest Xray (A) on admission day and (B)discharge day showed improvement of pneumomediastinum and subcutaneous emphysema (red arrow).

administered intravenous C-Penicillin 1.5 million units four times a day for one day before transitioning to oral azithromycin 300 mg once daily for 2 days, followed by switching to oral azithromycin 250 mg once daily for 1 day. The case was reviewed with a respiratory paediatrician regarding the patient's health and X-ray results. The diagnosis was pneumopericardium along with concurrent pneumonia. Because the patient was clinically stable, conservative therapy was selected, with vigilant monitoring for signs of respiratory distress or desaturation and septic parameters.

The patient was discharged from the ward after 4 days because they were not experiencing rapid breathing and were able to maintain good oxygen saturation without the need for supplemental oxygen besides improving septic parameters. Chest X-ray results indicate resolving pneumonia and pneumomediastinum (Figure 1 B). She was scheduled for an appointment at the pulmonary clinic within 2 weeks to repeat the X-ray and reassess her symptoms.

DISCUSSION

Forced exhalation against a closed glottis is the main cause of spontaneous pneumomediastinum.[4,5] It is further classified as primary or secondary SPM. Primary SPM occurs in healthy children without pulmonary diseases, whereas secondary SPM is associated with underlying pulmonary pathologies, such as asthma, viral respiratory infections and pneumonia[4,5] where can be seen in my case report.

Individuals with primary SPM often experience symptoms such as chest pain, coughing and difficulty swallowing.[5,6] Most patients do not have a specific triggering event, such as vomiting, choking, coughing, athletic effort or puffing, that may be identified.

Pneumomediastinum is hypothesised to result from alveolar rupture due to inhalation against a closed glottis and can occur in individuals who are coughing, vomiting or engaging in intense activities.[3,4] The highest incidence of SPM in paediatric patients occurs during the neonatal period, followed by late infancy and early childhood, likely because of the high prevalence of respiratory infections in this age range. SPM's connection to respiratory infections may be influenced by elevated pressure in blocked airways or by tissue death resulting from parenchymal infection.

The examinations involved numerous repeated chest radiographs, as well as radiographs of the neck and abdomen. In a previous study, more than one-third of patients underwent Computed Tomography (CT) scan of the neck, chest and/or abdomen. However, CT imaging in patients with pneumomediastinum did not affect clinical care or outcomes. Routine CT imaging is not indicated for juvenile patients with SPM who appear healthy because radiation exposure is a particular concern in this population. Point of care ultrasonography is a quick evaluation tool for pneumomediastinum that minimises radiation exposure and aids in the early detection of mediastinal or free peritoneal air or subcutaneous emphysema. In Küng et als report, they characterise the typical appearance of pneumomediastinum

on ultrasonography as the 'angel-wing' or 'spinnaker sail' pattern, which is caused by air trapped in the front part of the mediastinum.[9] In the parasternal view of a lung ultrasound, a pattern of horizontal hyperechogenic reflections resembling a stairway may be observed when air becomes trapped behind the thymus.

Possible follow-up procedures include esophagogastroscopy, direct laryngoscopy, bronchoscopy, echocardiography and upper extremity Doppler scan, depending on the patient's symptoms. No specific therapeutic measures were identified, and no problems were noted in any patient with primary SPM who was admitted to the hospital, as reported in a previous study.[7,8] A study including 28 individuals with asthma and pneumomediastinum found that children with pneumomediastinum had comparable clinical outcomes during asthma exacerbations to children without pneumomediastinum suffering asthma attacks.[3] Most participants in this trial showed improvement on successive chest X-rays. A few individuals had deteriorating pneumomediastinum on chest X-rays, but none advanced to pneumothorax.[3]

Previous research indicates that patients without a history of trauma, respiratory infection, asthma exacerbation or vomiting and in whom the cause of pneumomediastinum is believed to be genuinely primary spontaneous should have a comprehensive history and examination.[7] Patients without respiratory distress, with normal vital signs, normal oxygen saturation and adequate pain control should be observed in the emergency department for 2 to 4 hours. If patients remain stable, they can be discharged with a follow-up appointment with their primary care physician on the next day to assess their general condition.

Typically, additional imaging does not offer more information than secondary spontaneous respiratory-associated pneumomediastinum. Therefore, clinical care should consider symptoms and clinical appearance. Chest X-ray is advised based on the specific respiratory disease. CT scan of the chest can be performed to assess respiratory conditions; however, it is not advisable for further examination of pneumomediastinum.

CONCLUSION

Spontaneous pneumomediastinum (SPM) is a rare, self-limiting illness that often leads to benign progression in children and healthy teenagers. Precise analysis of the initial chest X-ray findings is crucial to prevent needless investigations such as CT scans.

Patients with SPM who are clinically stable can be managed conservatively via clinical surveillance without the need for radiation exposure or invasive procedures. Patients with primary SPM should receive symptomatic therapy and be observed in the emergency department with close follow-up in an outpatient setting.

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DECLARATION

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