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KLIPPEL-TRENAUNAY SYNDROME: A RARE CASE NOT TO BE MISSED

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ABSTRACT

Klippel-Trenaunay syndrome (KTS) is a rare congenital disorder characterised by malformation of capillary-venous vascular. In most reported cases, KTS was diagnosed clinically. However, this syndrome's clinical manifestations range from modest asymptomatic illness to life-threatening haemorrhage and embolism. Here we presented a case of a middle-aged woman who had experienced recurrent chronic thromboembolism events. She presented with middle cerebral artery infarction complicated with lower limb popliteal vein thrombosis. Subsequently, she was admitted to our centre and diagnosed with pulmonary embolism. The unilateral hypertrophic limb and cutaneous lesion over the right lower limb were mistakenly assumed as a birthmark. We reported this case due to its rare occurrence and to increase awareness of this condition.

Keywords: Klippel-Trenaunay syndrome (KTS); pulmonary embolism; limb hypertrophy; port-wine stain

1.0 INTRODUCTION

Klippel-Trenaunay syndrome (KTS) is a rare congenital disorder beginning in early childhood. It is characterised by a cutaneous port-wine stain. As the sufferer grows and spends more time in an upright position, clinical characteristics such as vein varicosities and limb oedema eventually develop [1]. The disease is an eponym to Klippel and Trenaunay, two French researchers who originally described the condition in 1900. Since then, a wide spectrum of this disease, including various vascular malformation, limb hypertrophy with different localisation, lymphatic involvement, and complication due to thromboembolism, have been reported [2]. Due to the low-flow vascular malformation of KTS, venous thromboembolism is the most prevalent consequence.

Evaluation of the severity of the malformation and confirmation of the lack of clinically significant arteriovenous shunting should be the emphasis of investigations in KTS. Although imaging or laboratory/genetic testing is not required to diagnose KTS, somatic mutations of the PIK3CA (phosphoinositide 3-kinases) gene may be associated with KTS [3]. Therefore, unless problems develop, KTS is treated conservatively.

2.0 CASE REPORT

Here we reported a case of a Malay lady aged 53 years old with a history of left middle cerebral artery infarction in January 2019 complicated with haemorrhagic transformation, in which she required a decompressive craniectomy. Within the same period of hospitalisation, she developed right lower limb popliteal vein thrombosis for which she completed a 3-month course of rivaroxaban. She had no comorbidities prior January 2019.

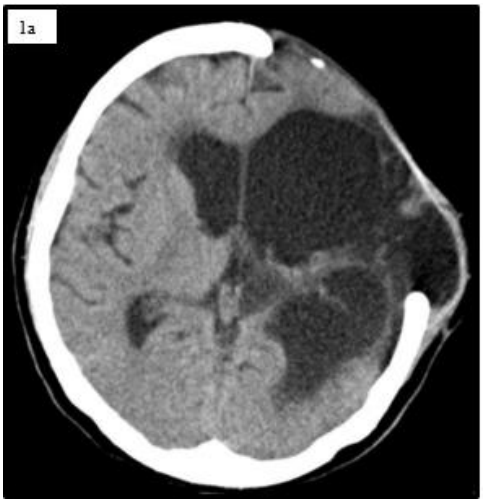

Figure 1 CT brain showed a large old infarct.

She presented to our emergency department with one episode of generalised tonic clonic seizure at home associated with hypotension and hypoxia. CT brain on arrival (Figure 1) showed a large old infarct.

Upon examination, there was noticeable oedema on the right lower limb compared to the left side. The right mid-femoral circumference was larger (58 cm) than the left mid-femoral circumference (46 cm). The oedema was non-pitting. There was presence of large hyperpigmented lesion with a raised margin that covered almost the upper half of the right thigh. The non-blanching and non-tender lesion extended medially towards the posterior aspect of the knee, calf, anterior part of the sole, and heel. There was, however, no visible superficial varicose vein. Both upper limb measurements were equal. The abdomen was soft, not distended, and the liver was marginally palpable. According to her daughter, the patient has had hypertrophic limbs and cutaneous lesions since childhood, but she thought they were part of her birthmark.

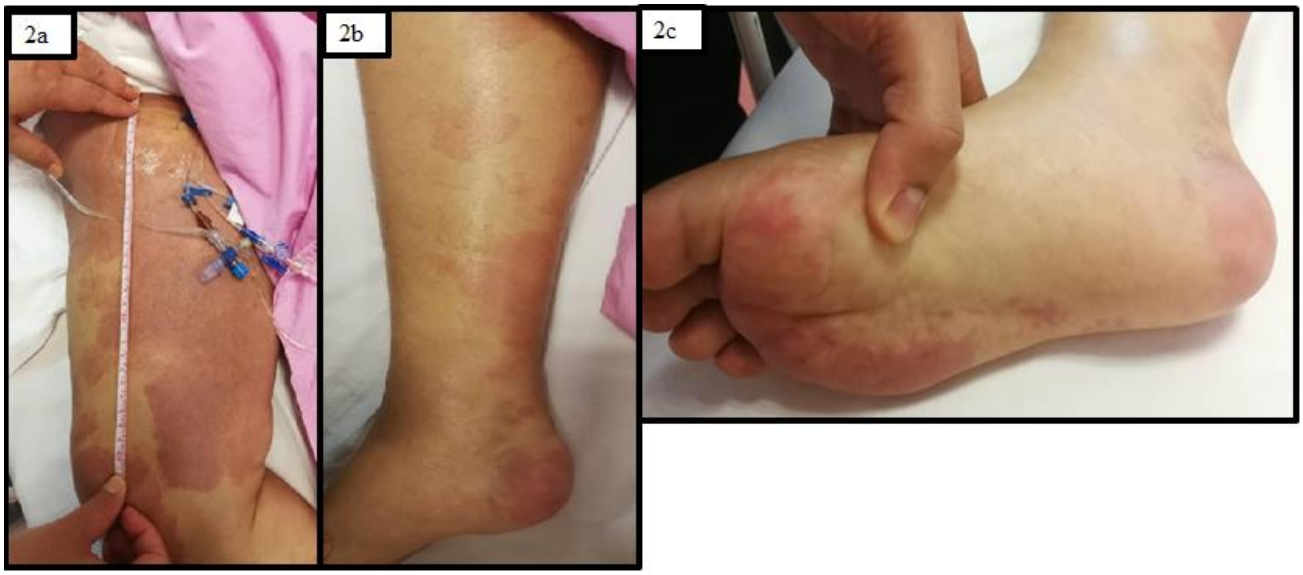

Figure 2 Right limb hypertrophy and oedema with port-wine stain lesion.

Her electrocardiogram showed ventricular tachycardia. She was resuscitated and subsequently started on an inotrope for blood pressure support. Once her condition stabilised, an urgent Doppler sonography of the right lower limb was performed. In contrast to a previous ultrasound Doppler, we observed a normal blood flow during the colour flow Doppler. Deep major veins were patent and compressible. Echocardiography was also performed on the patient. The echocardiogram showed paradoxical motion with D-shaped right ventricle, suggesting right ventricular pressure overload. We also noted severe mitral and tricuspid valve regurgitations. The ejection fraction was 65%, and no abnormality in the regional wall motion was detected.

Computed tomography (CT) pulmonary angiography was performed urgently to rule out a massive pulmonary embolism. Although the main pulmonary trunks were patent, we noted a few small filling defects at the segmental branch of the right upper lobe pulmonary artery. The pulmonary trunk also appeared dilated.

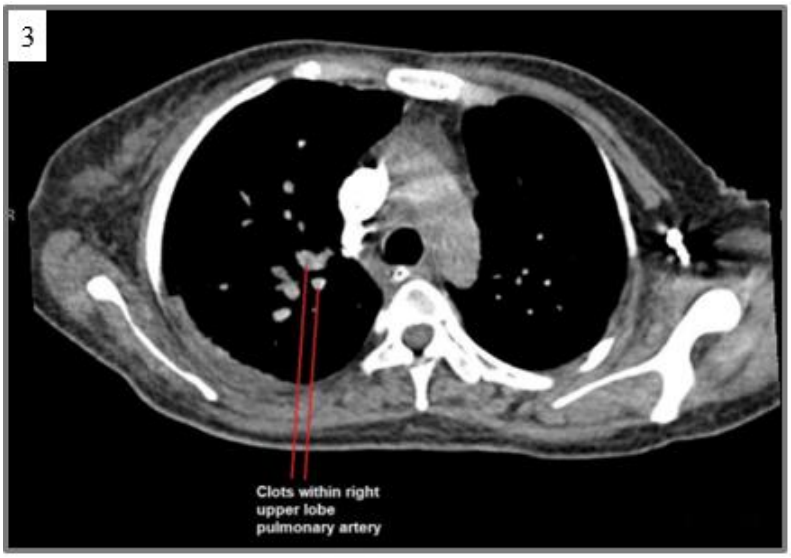

Figure 3 Clots seen within right upper lobe pulmonary artery

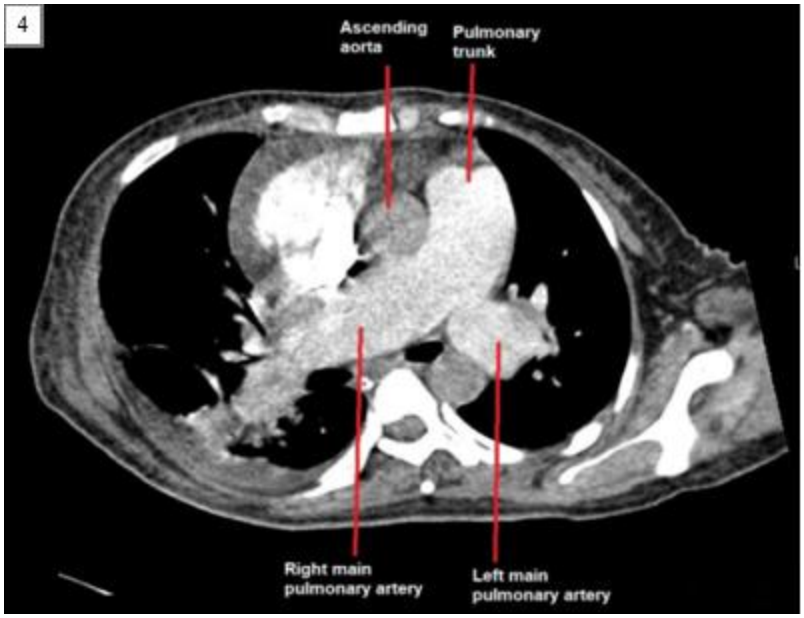

Figure 4 The main right and left pulmonary arteries appear dilated in the pulmonary trunk.

A repeated CT brain scan showed no new infarction or any intracranial bleed. Upon further investigation, we traced the contrasted CT abdomen, which was done in another hospital while the patient was being examined for a purported gynaecological problem. Interestingly, a dilated tortuous ovarian vein was seen bilaterally in the study. No other significant abnormalities were found.

We also sent the patient for antiphospholipid syndrome (APLS) screening. The results of lupus anticoagulant, anti-cardiolipin, and anti B2 glycoprotein antibodies were negative. The KTS was then diagnosed based on the above triad of port-wine stains, varicosities of veins, and soft tissue hypertrophy of a limb. In addition, she also didn't have any other risk factor prior for recurrent thromboembolism.

The patient started her medication on subcutaneous low-molecular-weight heparin before it was later converted to oral rivaroxaban prior to discharge from our centre. She was also required to wear compression stockings to improve venous circulation. As the primary caretaker, her family was advised to keep her lower limb elevated at home.

3.0 DISCUSSION

From the triad of capillary malformation (port-wine stain) vascular malformation (deep vein thrombosis) and lymphatic malformation (hypertrophic, swollen limb), we, therefore, diagnosed this patient with KTS. To date, the exact cause of KTS is unknown. However, a few theories in the literature postulate the cause of KTS. Among these theories, one postulates that mesodermal growth abnormality during fetal development causes persistent communication between arteries and veins in the limb bud. The persistent communication between the blood vessels promotes continuous growth and later gives rise to the classic triad [4]. Berry *et al.* 1998 postulated that changes in vascular remodelling, possibly at the level of altered angiopoietin-2 antagonism, may be the underlying cause of KTS [5]. An observational study by Aelvoet *et al.* suggests a hereditary pattern with multifactorial involvement [6].

The thromboembolism events described in this case report, such as deep vein thrombosis (DVT) or pulmonary embolism, are relatively common among KTS patients. For example, a Dutch study has shown that 8% of otherwise healthy KTS patients have DVT confirmed with duplex sonography studies. This percentage is higher than the average national incidence rate of 1.9 per 10,000 person-years in individuals ranging from 30 to 34 years [7]. A different study by Baskerville *et al.*, they found that as high as 22% of 49 KTS patients examined in a single-centre had radiologically proven DVT or pulmonary embolism [8].

The exact mechanism of thromboembolism has not been proven yet. However, Mazoyer *et al.* proposed that reduced blood flow in venous malformation and activation of the coagulation cascade may play a role in promoting what he termed as "local intravascular coagulopathy" [9]. As opposed to disseminated intravascular coagulopathy, the depletion of coagulation factors was confined locally within the malformed vessel. This finding was supported by demonstrating a reduced level of coagulation factors from the blood withdrawn from the malformed vessel compared to the peripheral blood sample of the same patient [9]. In another study, Baskerville *et al.* found that the procoagulant state of the patient with KTS may be contributed by a higher level of fibrinopeptide A and abnormal thrombin activity that is stimulated by the turbulence flow inside the malformed vessel [8].

Currently, there is no definitive cure for KTS. Most patients are treated with compression garments to improve venous circulation. Surgical interventions, including excision of the angioma, sclerotherapy of the nevus, vein ligation, and vein stripping, are usually reserved when conservative management is inadequate to control the symptoms or patients develop complications [8]. If a patient develops a thromboembolic episode, an anticoagulant is indicated with a therapeutic approach utilising low-molecular-weight heparin. This treatment

option appears highly effective compared to Vitamin K antagonist or unfractionated heparin [9].

4.0 CONCLUSION

KTS is a rare congenital disorder characterised by a triad of capillary malformation, vascular malformation, and lymphatic malformation. Early recognition of the disease is imperative as patients require lifelong monitoring and appropriate management due to being at a higher risk of developing thrombotic events such as pulmonary embolism or DVT.

5.0 ACKNOWLEDGEMENTS

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6.0 CONFLICT OF INTEREST

The authors declare no conflict of interest.

7.0 FUNDING STATEMENT

This case report did not receive any specific funding.

8.0 ETHICAL APPROVAL ISSUE

Not applicable

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