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CASE REPORT

A rare presentation of Klipple Trenaunay Weber Syndrome

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ABSTRACT
Klippel Trenaunay Weber Syndrome (KTWS) is a rare, sporadic, complex manifestation characterised by micro arteriovenous and capillary malformation, along with varicose veins and bony and/or soft tissue hypertrophy. The vascular malformation are usually limited to single extremity and affected limb has cutaneous flush involving skin and is increased in length and girth. Patients can have visceral organ complications that are very dreadful complications of the syndrome. Treatment is normally cautious, regular follow-up for progression is advised. There are very limited case reports available on this rare syndrome.

Key words: Klipple Trenaunay Weber Syndrome

INTRODUCTION

Klippel-Trenaunay syndrome (KTS) is a vascular malformation disorder characterized by a heterogeneous involvement of cutaneous capillaries, veins, and lymphatic structures, accompanied by hypertrophy of the soft tissues and bones in the affected limb. This condition is also known as capillary-lymphatic-venous malformation (CLVM), which highlights the alterations observed in these vascular components. The syndrome was initially documented in 1900 by French physicians Maurice Klippel and Paul Trenaunay. Diagnosis of KTS is primarily clinical, requiring the identification of at least two of the three hallmark features: localized cutaneous capillary malformations, venous irregularities, and limb hypertrophy. It is important to note that the presence of arteriovenous malformations is now classified as a distinct condition known as Parkes-Weber syndrome, separate from KTS.[1-3]

Recent research has established a connection between the etiology of Klippel-Trenaunay syndrome and somatic mutations in the phosphatidylinositol-4-5-bisphosphate 3 kinase, catalytic subunit (PIK3CA) gene. These mutations result in the activation of the phosphatidylinositol-3-kinase (PI3K)/protein kinase pathway, leading to cellular overgrowth through the dysregulation of the mTORC2 pathway. Such mutations typically arise during the embryonic phase of development, particularly during angiogenesis, which aligns with the clinical manifestations of the syndrome. Currently, KTS is categorized within a broader classification of similar overgrowth syndromes known as the PIK3CA-related overgrowth spectrum (PROS). Several overgrowth syndromes exhibiting overlapping clinical features associated with various mutations in the PIK3CA gene have been identified, with rare cases also reporting translocations involving chromosomes 5-11 and 8-14.[4-6]

CASE REPORT

A 14-year-old male patient came with complaints of pain and dark coloured patches and worm like swellings on lateral side of the left thigh since 3 years of age which bleeds on minor trauma.(Figure 1). On examination, he had multiple discrete & grouped red to bluish black papules present over the pink coloured patch. Localised muscle atrophy of left leg was present along with dilated & tortuous superficial veins up to the level of iliac spine with local rise of temperature. Saphenofemoral valve was competent. Perforator incompetence was detected at mid-calf and above ankle region. Soft tissue ultrasonography of the left thigh showed prominent dilated vein which shows mixed waveform(monophasic and high flow biphasic/triphasic wave form). This dilated vein is noted predominantly in subcutaneous plane and appears to drain into superficial femoral artery. No abnormal dilated bunch of focal vascular channels.

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Underlying bone is normal. Arterial doppler study of both lower limbs shows triphasic flow pattern from bilateral lower limb arteries from common femoral artery to dorsalis pedis artery. Venous doppler study showed an enlarged lymph node in the right inguinal region measuring 25x7 mm. No thrombus noted within the lumen. And no e/o acute DVT. Dermoscopy shows capillary haemorrhages and telangiectasia.(Figure 2) laser treatment was offered for the port wine stain. No other systemic symptoms were found. Patient was referred to vascular surgeon for further management.

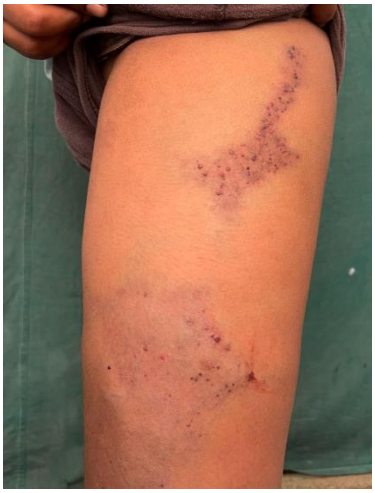

Fig 1: Port wine stain on left thigh with worm like swellings

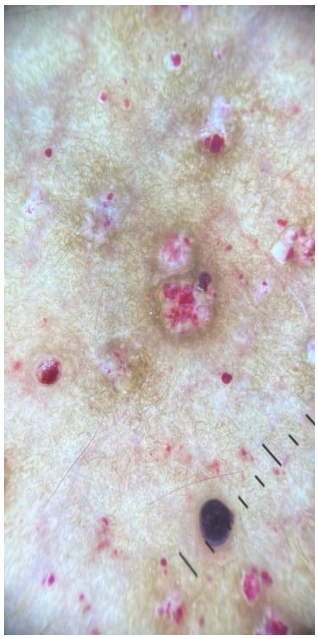

Fig 2: Dermoscopy of port wine stain showing capillary hemorrhage and telangiectasia.

DISCUSSION

The molecular basis for many vascular malformations is now much better understood and provides a genetic framework for many well-recognised Vascular Anomaly phenotypes. It is now known that KTS belongs to the so-called PIK3CA-related overgrowth spectrum (PROS).1 The phosphatidylinositol-3-kinase (PI3K)/AKT/mammalian Target of Rapamycin (mTOR) pathway is an intracellular signalling pathway important in regulating cell cycles ensuring normal cellular growth and differentiation. These cellular functions involve PI3Ks (phosphoinositide 3-kinases, otherwise known as phosphatidylinositol 3-kinases) which are an enzyme family of 4 classes. When somatic gain-of-function PIK3CA gene mutations occur (i.e. the so-called PROS-causing PIK3CA mutations) there is activation of class 1 PI3K enzyme activity, resulting in dysregulated cellular growth and malformed vascular channels. KTS is one of a number of recognised segmental overgrowth phenotypes with vascular malformations occurring as a result of somatic mutations in the PIK3CA gene.[7-9]

In the present case report, a 14-year-old male patient came with complaints of pain and dark coloured patches and worm like swellings on lateral side of the left thigh since 3 years of age which bleeds on minor trauma. On examination, he had multiple discrete & grouped red to bluish black papules present over the pink coloured patch. Dermoscopy shows capillary haemorrhages and telangiectasia. laser treatment was offered for the port wine stain. No other systemic symptoms were found. Patient was referred to vascular surgeon for further management.

KTS is a multifaceted disorder characterized by the presence of capillary, lymphatic, and venous malformations, accompanied by an overgrowth of the affected limb. The capillary malformations, commonly referred to as "port-wine stains," represent the most prevalent type of vascular cutaneous anomaly associated with KTS, occurring in 98% of cases. These malformations consist of abnormal ectatic capillaries located within the papillary dermis, which exhibit notably thin walls. Varicose veins are observed in 72% of individuals with KTS, with a particularly notable feature being the persistent (embryonic) lateral vein, identified in 56% of patients, which may serve as a pathognomonic indicator. Additionally, there are significantly enlarged valveless truncal veins that manifest as substantial varicosities, alongside a range of other potential anomalies, including compressive fibrous bands, aneurysmal dilatation, duplication, hypoplasia, atresia, and aplasia. The presence of venous stasis in these large valveless veins predisposes patients to complications such as deep vein thrombosis (DVT) and associated pulmonary embolism.[10-12]

A conservative strategy is recommended for the symptomatic management of Klippel-Trenaunay Syndrome (KTS) through non-invasive interventions. In most instances, patients are advised to utilize either elastic or non-elastic compression stockings. The combination of elastic stockings with psychological support has demonstrated the highest efficacy in managing individuals with KTS. These stockings are often used alongside additional conservative

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strategies, including regular leg elevation, physiotherapy, lifestyle adjustments, and rigorous hygiene practices. Analgesics, antibiotics, and corticosteroids are frequently prescribed to address cellulitis and thrombophlebitis. Anticoagulants may be administered either as a preventive measure prior to surgical procedures or in response to acute thrombosis. While conventional sclerotherapy is a viable option for smaller malformations, it proves ineffective for larger ones. Pain management is a prevalent concern in KTS, impacting up to 88% of affected individuals. Consequently, effective pain management is essential for these patients. The management approach is guided by the underlying cause of the pain, leading to targeted treatment strategies. Surgical intervention is typically reserved for cases exhibiting significant symptoms. The success of surgical procedures is contingent upon thorough pre-operative assessments of the deep venous system, utilizing imaging techniques such as computed tomography (CT) arteriography and duplex scanning contrast geography to evaluate the extent of vascular involvement and identify any arteriovenous fistulae. Numerous studies have indicated that symptoms may worsen following interventions such as multiple ligations and stripping.[13- 15]

CONCLUSION

Klipple Trenaunay Weber Syndrome is a rare syndrome involving multiple organ systems. Patients can have visceral organ complications that are very dreadful complications of the syndrome. Treatment is normally cautious, regular follow-up for progression is advised.

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