Case Report

Klippel-Trenaunay syndrome (KTS): A case report in an infant

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Author's Contribution

[1,2] Conception of study
[2,3,4] Experimentation/Study conduction
[1,2,3,4] Analysis/Interpretation/Discussion
[3,4] Manuscript Writing
[1,2] Critical Review

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Article Processing

Received: 08/08/2020
Accepted: 31/10/2020

Cite this Article: *Surani, M.K., Noureen, A., Khizar, U., Tabasum, S. Klippel-Trenaunay syndrome (KTS): A case report in an infant. Journal of Rawalpindi Medical College. 30 Dec. 2020; 24(4): 434-438.*
DOI: https://doi.org/10.37939/jrmc.v24i4.1448

Conflict of Interest: *Nil*
Funding Source: *Nil*

Access Online:

Abstract

Background: Klippel-Trenaunay syndrome (KTS) is a rare and congenital disease having a prevalence of 1/20-40,000, live births. KTS is a vascular malformation affecting generally one or rarely more than one limb. It is a combination of port-wine stain, hemihypertrophy of limb, and additional vascular anomalies. The diagnosis of KTS is made clinically by the appearance of any two of the signs. The syndrome is named after two French physicians, Klippel and Trenaunay. Klippel first described the possible features of KTS in the nineteenth century.
The etiology is unclear but many believe that it is a developmental disorder of embryogenesis involving mesoderm that affects different phases of angiogenesis. Vascular malformations can affect many internal organs such as the gastrointestinal tract (GIT), spleen, liver, and heart. The features of the disorder grow progressively.
If AVM is present, the syndrome is named as Klippel–Trénaunay–Weber syndrome and is considered a different syndrome. The complication of vascular lesions of the skin involves infection, cellulitis, profuse bleeding, and non-healing wounds. The diagnosis is confirmed by ultrasonography, Doppler study, multi-detector CT scan, conventional Angiography, and Magnetic Resonance Angiography (MRA) which show the types of vascular malformations that may not be seen on conventional radiology. X-rays show hypertrophy of bones with delayed epiphyseal closure. PWS may result in a reduction in size by laser therapy. Surgical team involvement may be necessary for de-bulking the hypertrophied tissue and to excise extra veins or hemangiomas. Surgery can correct uneven tissue growth.
Case presentation: We present a rare case of Klippel-Trenaunay syndrome in an infant who presented at an early stage of this disorder. The index case presented to us with a port-wine stain and edema of the right lower limb due to soft tissue swelling. The Doppler scan showed venous malformation of the right leg. The clinical and radiological criteria were used to make the final diagnosis of KTS.
Conclusion: The case is being reported to increase awareness among medical professionals.
Keywords: Klippel-Trenaunay Syndrome, Port-Wine Stain, Vascular Malformations, Capillary Malformations, Capillary Malformation-Arteriovenous Malformation.

Introduction

Klippel-Trenaunay Syndrome (KTS) is one of the rare congenital syndromes involving the vascular system and is diagnosed clinically at birth. It generally involves one limb of the lower extremities. It characterizes a clinical triad involving:

1. Capillary malformations (port-wine stain PWS)
2. Venous malformations (varicose veins)
3. Hypertrophy of bone and soft tissue

The syndrome is diagnosed clinically by the presence of at least two of the above-mentioned signs.[1]

The syndrome is named after two French physicians, Klippel and Trenaunay. They first described the possible clinical features of KTS in the 1990s. The etiology is unclear and has been postulated to be the result of an embryonic developmental disorder involving mesoderm that affects different stages of angiogenesis, possibly resulting from intra-uterine insult. Many researchers have proposed that malformations of deep veins such as obstruction and/or atresia can cause chronic venous hypertension, eventually resulting in abnormalities such as port-wine stains, varicose veins, and hypertrophy of limb. The lesions usually involve the lower limb but can affect the upper limb and rarely the trunk.[2]

Vascular malformations have been reported to affect many internal organs such as the gastrointestinal (GI) tract, liver, spleen, and heart. The disorder follows a progressive course. Vascular malformations may also affect the genitourinary tract (kidney, bladder, penis, scrotum, vagina, and vulva) and can present as intra-abdominal and intra-pelvic vascular masses.[3] Sometimes, patients with KTS can also present with symptoms of involved organs such as hematuria and/or hematochezia when an internal organ is affected.[2]

KTS is sometimes known as capillary-lymphatic-venous malformation (CLVM) or Capillary Malformation-Arteriovenous Malformation(Cm-AVM). This is a low-flow malformation of the vascular system and is not an arteriovenous malformation (AVM), which is a disorder of high flow. In the case of AVM, the syndrome is termed as Klippel–Trénaunay–Weber syndrome and is considered a separate syndrome. The vascular abnormality is typically seen in one limb, but rarely, more than one limb can be involved.[4]The complication of vascular lesions of the skin involves infection, cellulitis, profuse bleeding, and non-healing wounds.[1]

The prevalence of KTS is approximately 1 per 20,000-40,000 live births. The disorder can affect any ethnic group and it equally affects both genders. Usually, the diagnosis of KTS is clinically visible at birth, often the only visible sign in newborn babies is a port-wine stain and the diagnosis is further confirmed with the appearance of varicose veins or when limb hypertrophy becomes noticeable.[5]

We present a typical case of KTS at the Children hospital & the institute of child health, Multan Pakistan who presented to us with a typical Port-wine stain and limb hypertrophy of the right lower limb.

Case Report

The index case is a three months old male child who was delivered at home. He is the third sib among the three sibs with two elder sisters. Pregnancy and the perinatal period was uneventful except that the family noticed a large pinkish colored spot extending from the great toe of the right foot to the right lumbar region and involving both the right and the left hips. At birth, there was no difference in lengths and circumferences of both lower limbs and the same was true in the case of upper limbs.

At age of two months, the circumference of the right lower limb started increasing with the development of lymphedema which was more marked in the right foot and leg. His other two sisters are healthy and there is no family history of such lesions. The patient was referred to the children's hospital and the institute of child health, Multan for diagnosis and management of increasing right leg swelling. In our hospital, the patient underwent X-ray and Doppler studies of the involved limb. The diagnosis of KTS was made based on clinical and radiological findings which included that:

Skin: A port-wine stain extending from right foot to right lumbar region involving the whole length of the right limb was noted (Figure 1).

Musculoskeletal: There were soft tissue swelling and edema of the right lower limb (Figure 2). There was also a significant difference in the circumference of both lower limbs (Table 1). Both upper limbs were equal in circumference (MUAC of the right arm was 13 cm and MUAC of the left arm was 13 cm).

Systemic Examination: All other systems were normal on examination.

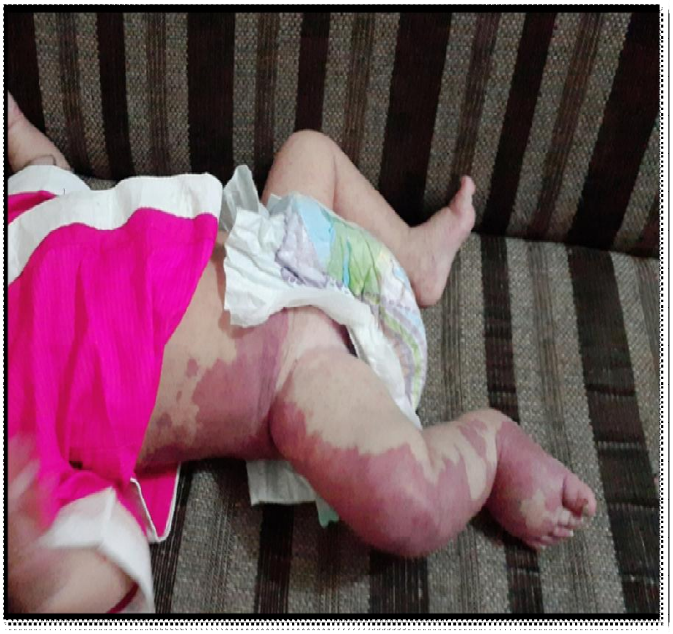

Figure 1: Port wine stain noted on right lower limb

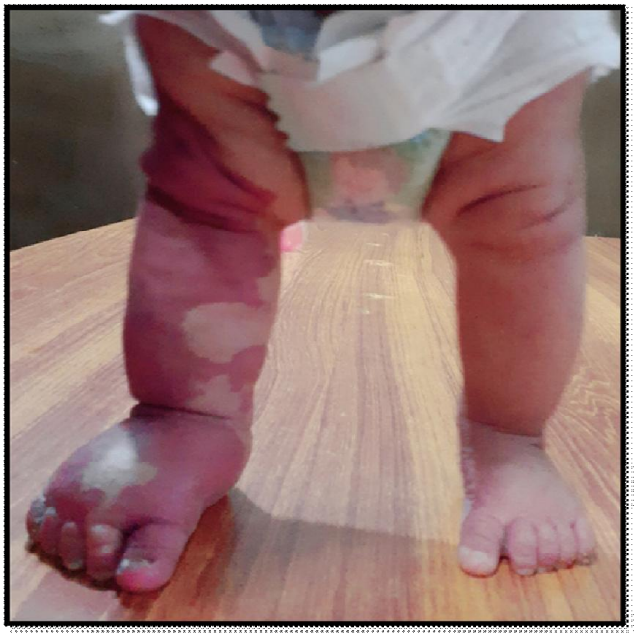

Figure 2: Hemihypertrophy of right lower limb due to soft tissue edema

Table 1: Circumferential measurements of both lower limbs

	Landmark	Right lower limb	Left lower limb
Thigh circumference	8cm from ASIS	19cm	17cm
Leg circumference	5cm from knee joint	14.5cm	13cm
Foot circumference	4cm from ankle joint	13.5cm	11cm

Radiological Findings: The Doppler study of the lower limbs showed a slow flow venous malformation most likely hemangiomas involving the right lower limb extending from the dorsum of the foot up to the right thigh (Figure 3). Arteriography (MRA) and Venography (MRV) of the lower limbs were advised for patients to rule out arterio-venous malformation.

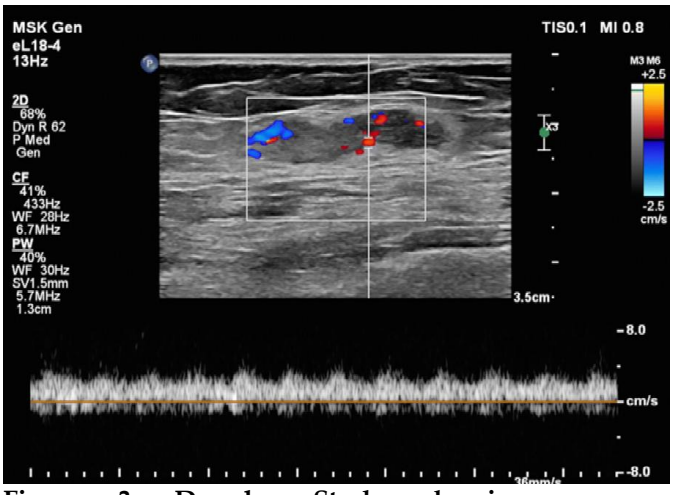

Figure 3: Doppler Study showing venous malformation

Discussion

Klippel-Trénaunay syndrome (KTS) is a rare congenital condition and is characterized by a triad of:

1. Capillary malformations resulting in a "port-wine stain"
2. Limb hypertrophy
3. Varicose veins

This congenital malformation was first described by the French physicians Klippel and Trénaunay in 1900. Klippel-Trénaunay syndrome typically presents unilaterally and involves the lower limbs. It is distinguished from Parkes-Weber syndrome by the absence of substantial arterio-venous malformation or fistulas. Due to the clinical outcomes and complications of an arteriovenous fistula, differentiation between the two syndromes is of prime importance, as the prognosis and treatment for the above-mentioned conditions are entirely different.[6] In our index case, the infant had one-sided pinkish port-wine stain and limb hypertrophy, and the Doppler study further confirmed the diagnosis of KTS.

The exact cause of Klippel-Trenaunay syndrome (KTS) is unclear, though many theories exist. Bliznak and Staple recommended intrauterine damage to the sympathetic ganglia resulting in dilated microscopic arteriovenous connections as the main cause. Baskerville et al suggested that a defect in the mesoderm during intrauterine life causes maintenance of microscopic arteriovenous anastomoses. Most cases of KTS are sporadic, although a few cases in the literature report an autosomal dominant pattern of inheritance. The disease manifests in individuals who demonstrate loss of heterozygosity from a somatic mutation during embryogenesis. The relationship between the angiogenic factor *AGGF1* gene and KTS appears to be significant. Kihiczak et al published that KTS can result from a pathological gene for vascular and tissue malformations.[7]

A series of 252 patients with KTS was studied at a Clinic, Rochester from January 1956 to January 1995. The results showed the presence of port-wine stains in 246 patients (98%), venous varicosities in 182 (72%), and hypertrophy of limb in 170 (67%). All of the three manifestations of KTS were present in 159 patients (63%), and two of the three features were present in 93 (37%). The less common features of KTS include thromboembolic phenomena, hematuria, hematochezia, Kasabach-Merritt syndrome, vaginal, vulval, or penile bleeding in patients with visceral and pelvic vascular anomalies.[8]

Diagnosis is made by ultrasonography, Doppler study, multi-detector CT scan, conventional Arteriography, and Magnetic Resonance Angiographic (MRA) studies which show the types of vascular malformations that may not be seen on conventional radiology. X-rays show hypertrophy of bones with delayed epiphyseal closure.[9]

The differential diagnosis of KTS includes Proteus syndrome, a rare hypertrophy syndrome, and is only diagnosed if there is cutaneous nevus, adipose tissue deposition, tumors, and vascular abnormalities. . Others include CLOVE syndrome; also overgrowth of body tissues as well as lymphatic and capillary anomalies. But port wine stain is absent in the above-mentioned conditions which the index patient had. Maffucci's and Sturge Webber's syndrome also presents with port-wine stain but hypertrophy of body tissues is absent.[4]

The differential diagnosis of a hypervascular limb may include Paget's disease, osteomyelitis, primary bone malignancy, and other vascular anomalies e.g. hemangiomas giving a comparable look in the three-phase bone scan but the clinical features would be different.[10]

The usual agents used for the treatment of hemangiomas, Such as steroids and interferon-alpha are usually of no benefit in KTS. PWS may result in a reduction in size by laser therapy. KTP (532 nm) laser is efficacious and safe in the management of capillary malformations of PWS type. Surgical intervention may be necessary to de-bulk the hypertrophied tissue, to excise extra veins or hemangiomas, Surgery can correct uneven tissue growth.[11]

Conclusion

Klippel-Trenaunay syndrome is one of the rare syndromes of congenital vascular malformation. It mostly involves only one limb. The malformations include port-wine stain or hemangiomas, hemihypertrophy, and venous varicosity. Diagnosis can be made by clinical and/or radiological studies such as Ultrasonography, Doppler study, or Conventional CT Arteriography. The knowledge of this rare disease is important as the complications such as varicose veins may pose difficult decision making for the treating physician and surgeon.

List of Abbreviations

Klippel-Trenaunay syndrome	KTS
Port-wine stain	PWS
Capillary-lymphatic-venous malformation	CLVM
Arteriovenous malformation	AVM
Mid-upper arm circumference	MUAC
Anterior superior iliac spine	ASIS
Magnetic Resonance Arteriography	MRA
Magnetic Resonance Venography	MRV
Computed Tomography	CT

Acknowledgements

I cannot express enough thanks and sincere gratitude to my senior and advisor Dr. Asim Khurshid (Associate professor, The Children Hospital, and the Institute of Child Health, Multan) for his continuous support, encouragement, and immense knowledge. I could not have imagined having a better advisor for my case report.

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