

Klippel-Trenaunay Syndrome: Insights into Vascular Malformation

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1. Abstract

1.1. Background and Clinical Significance

Klippel-Trenaunay Syndrome (KTS) is a rare congenital vascular disorder characterized by capillary malformations, venous varicosities, and limb overgrowth. Patients with KTS are prone to complications such as thrombosis, bleeding, and chronic venous insufficiency, making early recognition and management crucial.

1.2. Case Presentation

We present the case of a 23-year-old male with Klippel-Trenaunay Syndrome, who initially sought care for varicosity on the left medial aspect of his leg. Upon thorough examination, additional signs consistent with the syndrome were identified. The patient was placed under follow-up to monitor any changes or complications.

1.3. Conclusions

Although Klippel-Trenaunay Syndrome patients commonly present with complications, this case underscores the need for timely intervention in instances of acute issues such as bleeding. The patient initially sought emergency care due to sudden bleeding from a varicosity, highlighting the importance of recognizing potential life-threatening complications and managing them promptly in affected individuals.

2. Introduction and Clinical Significance

Klippel-Trenaunay Syndrome (KTS) is a rare congenital condition marked by a combination of three primary features: port-wine stains consistent with capillary malformations on the skin, venous varicosities that lead to abnormal vein dilation and impaired circulation; and limb overgrowth, where one limb is notably larger than the other due to excessive bone and soft tissue development [1]. The exact cause of KTS remains uncertain, although recent studies have suggested that mutations in the *PIK3CA* gene play a crucial role in abnormal blood vessel formation during embryonic development [2]. Individuals with KTS may suffer from pain, swelling, functional limitations, and increased risk of complications such as bleeding or infection from the vascular lesions. Diagnosis typically involves clinical evaluation, supported by imaging techniques like ultrasound or MRI, with genetic testing considered when needed [3]. Treatment is largely aimed at symptom management, with options including compression garments, sclerotherapy, laser therapy, and, in severe cases, surgical intervention. Although KTS is not usually fatal, it can severely affect a person's quality of life. Ongoing surveillance is necessary to detect complications like thrombosis [1]. We are presenting a case of uncomplicated KTS.

3. Case Report

A 23-year-old male patient presented to the emergency room in Juan Jose Arevalo Bermejo Hospital in Guatemala during the month of December 2024. His main complaint was a dilated vein that started an acute episode of bleeding on his left lower limb. He has reported this issue since birth; however, it was consistently treated as a varicose vein. He had no history of ulceration, trauma, difficulty walking, paraesthesia or cellulitis. On further examination multiple varicose veins were present over the dorso-medial part of the left lower limb over a cutaneous

hyperpigmentation with raised margins (port-wine stain) extending from the knee crease to the groin (Figure 1). Predominant varicose vein measured 2 cm of length and 2 cm of width with a blood scab, which shows no signs of infection, discharge, or active bleeding (Figure 2).

4. Review of Literature

4.1. Epidemiology

Klippel-Trenaunay Syndrome is an extremely rare vascular disorder, with its precise incidence and prevalence still unknown. Unlike many genetic conditions, KTS does not appear to show any preference for a specific ethnic group or sex, suggesting that its occurrence is largely sporadic and unrelated to demographic factors.

4.2. Etiology

The International Society for the Study of Vascular Abnormalities (ISSVA), established in 2018 that KTS is characterized by the presence of capillary and venous malformations which may or may not be associated with lymphatic malformations. Advancements in genomic studies and analysis have led to reconsideration of KTS as part of a broader category known as *PIK3CA* - Related Overgrowth Spectrum (PROS). This reclassification came on the discovery that many cases of KTS are caused by mosaic activating variants in the *PIK3CA* gene. Therefore, PROS encompasses a variety of conditions with segmental overgrowth and vascular abnormalities including: fibroadipose hyperplasia, hemi hyperplasia multiple lipomatosis, CLOVES syndrome, macrodactyly, fibroadipose infiltrating lipomatosis, dysplastic megalencephalic, and Megalencephaly-capillary malformation-polymicrogyria (MCAP) syndrome.



Figure 1: Cutaneous hyperpigmentation (port wine stain).



Figure2: Main Varicose Vein.

4.3. Pathogenesis

KTS is a sporadic disease in the majority of cases, although rare familial cases have been reported. It is now evident that most patients with this syndrome carry a postzygotic somatic variant in the phosphatidylinositol [4,5] biphosphate 3 - kinase, catalytic subunit alpha (PIK3CA) gene. Gain-of-function mutations in pIK3CA trigger the activation of protein kinase B (AKT), which ultimately stimulates the mammalian target of rapamycin (mTOR) pathway, leading to increased cell proliferation and angiogenesis.

5. Clinical Manifestations

5.1. Vascular Malformations

Venous malformations are a defining characteristic of Klippel-Trenaunay Syndrome (KTS), commonly affecting both superficial and deep veins. These abnormalities can be confined to the affected limb or extend to other regions, such as the abdominal, pelvic, and genitourinary systems. A key feature is the lateral marginal vein, which lacks valves, leading to significant venous stasis and impaired drainage. This contributes to the overall clinical presentation of KTS. In some cases, venous malformations may result in serious complications, including bleeding and thrombosis.

5.2. Limb Abnormalities

Limb hypertrophy is often one of the most prominent signs of KTS. The affected limb may be enlarged in both length and circumference due to excessive growth of soft tissue and bone. This overgrowth can be localized to specific areas or spread throughout the limb, impacting its overall structure. Some individuals may also develop skeletal deformities, such as joint contractures, limb asymmetry, or reduced bone density (osteopenia/osteoporosis), which can contribute to functional limitations.

5.3. Lymphatic Malformations

Lymphatic abnormalities are frequently observed in KTS and may manifest as lymphangiomas or localized swelling, primarily in the limbs. These issues arise due to defects in the lymphatic system that disrupt normal drainage, leading to persistent lymphedema. Over time, this can cause chronic swelling, discomfort, and a higher susceptibility to infections like cellulitis. In more severe cases, lymphatic malformations may extend to internal organs, potentially causing systemic complications.

5.4. Cutaneous and Soft Tissue Manifestations

Skin changes are common in KTS, often presenting as extensive, irregular vascular lesions known as port-wine stains. These lesions can vary in size and distribution and may be associated with deeper vascular anomalies, resulting in soft tissue overgrowth or disfigurement.

Additionally, some individuals develop prominent soft tissue masses that can be firm or nodular. If these growths interfere with limb function or cause significant discomfort, surgical intervention may be necessary.

5.5. Systemic Involvement and Severity

The clinical presentation of KTS varies widely, ranging from mild cosmetic differences to severe functional impairments and life-threatening complications. Many individuals experience chronic pain, particularly in the affected limb, which may stem from vascular congestion, nerve compression, or inflammation associated with tissue overgrowth. Extensive venous or lymphatic involvement can lead to chronic venous insufficiency, increasing the risk of ulcers, recurrent infections, and long-term disability.

6. Diagnosis

The diagnosis of KTS is largely clinical, based on the presence of the characteristic triad: capillary malformations (commonly presenting as port-wine stains), venous varicosities, and soft tissue and/or bony overgrowth affecting one or more limbs. A detailed clinical history and physical examination are essential, but imaging and, in some cases, genetic testing play a crucial role in confirming the diagnosis and guiding management. Doppler ultrasound is often the first imaging modality used, particularly for assessing superficial and deep venous insufficiency or identifying thrombosis. MRI, with or without contrast, is considered the most informative imaging technique, as it can clearly delineate vascular malformations and associated soft tissue or skeletal involvement. In cases where deep venous involvement is suspected especially in the pelvis or abdomen magnetic resonance venography (MRV) is useful for detecting ectatic or incompetent pelvic veins. Genetic testing may be indicated in ambiguous or complex presentations. Mosaic mutations in the PIK3CA gene have been identified in a significant number of KTS cases, situating the condition within the broader spectrum of PIK3CA-related overgrowth syndromes (PROS).

7. Management

Management of KTS is individualized and typically requires a multidisciplinary approach. While the condition is not curable, a range of treatments can significantly improve symptoms and reduce the risk of complications. Conservative management remains the cornerstone of treatment for most patients. Compression garments are commonly used to manage chronic venous insufficiency and reduce edema. Good skin care and hygiene are essential to prevent secondary infections and manage occasional bleeding from fragile superficial veins. For patients with mobility issues or functional impairments due to limb overgrowth, physical therapy can provide meaningful support. In selected cases, minimally invasive procedures like sclerotherapy may be indicated. This technique involves injecting a sclerosing agent into abnormal veins to induce closure, and is particularly useful for managing localized venous malformations. Surgical intervention is typically reserved for patients with severe symptoms or complications that do not respond to conservative therapy. Options may include debulking surgery to remove excessive tissue, or orthopaedic procedures to address limb length discrepancies. Surgery, however, carries risks including recurrence and potential damage to surrounding structures, and should be carefully considered. In very rare and extreme cases, where complications such as severe infection or uncontrollable bleeding are present, amputation may be discussed as a last resort.

8. Conclusions

1. Early recognition and management of Klippel-Trenaunay Syndrome (KTS) are crucial for preventing complications, such as bleeding from varicosities.
2. Conservative treatments, including compression stockings and pharmacological therapy can effectively manage symptoms and improve the patient's quality of life.
3. Regular follow-up and monitoring are essential to detect and address potential complications, such as thrombosis and infection.
4. Timely intervention can help avoid severe complications and ensure better outcomes for patients with KTS.
5. The case emphasizes the importance of accurate diagnosis through clinical evaluation and imaging techniques.

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