Recurrent Cellulitis in the Intergluteal Area in a Pediatric Patient with Klippel-Trenaunay Syndrome

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ABSTRACT

Klippel-Trenaunay syndrome (KTS) is a rare congenital vascular disorder associated with somatic mutations in the PIK3CA gene, characterized classically by a triad of capillary malformations, venous malformations, and soft tissue and bone hypertrophy. While KTS commonly involves a single lower extremity, we present an atypical pediatric case featuring extensive venolymphatic malformation of the intergluteal region. This uncommon anatomical localization predisposed the patient to recurrent episodes of cellulitis, significantly complicating clinical management. This case underscores the importance of recognizing atypical presentations of KTS and the heightened susceptibility to recurrent infections, such as cellulitis, which may significantly impact morbidity and patient care.

KEYWORDS: Klippel-Trenaunay-Weber syndrome; venous malformation; cellulitis

INTRODUCTION

Klippel-Trenaunay syndrome (KTS) is a rare congenital vascular disorder characterized by a classic triad of capillary malformations (port-wine stains), venous malformations (including varicose veins), and hypertrophy of bones and soft tissues. These clinical features typically affect a single limb, most commonly a lower extremity; however, involvement of the upper extremities, gluteal region, or torso has also been reported, albeit rarely.[1,2]

Venous malformations in KTS include abnormalities of both the superficial and deep venous systems, increasing the risk of thrombosis.[2] Additionally, KTS is associated with an increased risk of soft tissue infections, including cellulitis that may induce subsequent ulceration, due to abnormal lymphatic drainage.[3] Although less common, KTS may also affect other organ systems including the gastrointestinal and genitourinary systems.[3]

Epidemiological data suggest that KTS occurs in approximately one in 100,000 people globally.[3] The true incidence is difficult to determine due to the rarity of the condition, although some studies suggest it ranges from two to five cases per 100,000 people. KTS typically presents at birth, during early infancy, or in childhood, and current evidence indicates a slightly higher prevalence in males than in females.[4] Given its low prevalence and incidence, the number of new cases each year remains limited, consistent with the rare nature of the syndrome. Herein, we present the case of a 12-year-old female with KTS involving the intergluteal region, associated with a venolymphatic malformation and complicated by recurrent cellulitis.

CASE REPORT

A 12-year-old patient with KTS and extensive venolymphatic lesions in the intergluteal region presented with pain and serous drainage. Her KTS was initially suspected on prenatal ultrasound, which revealed bilateral cystic muscular abnormalities involving the buttocks and right thigh. Subsequent imaging confirmed abnormal bone development of the lower extremities at age 11 months, dilation of the saphenous and marginal veins at age three years, and progressive inflammatory and vascular malformations involving gluteal and perineal tissues by age 8. Surgical resection was performed, followed by percutaneous bleomycin sclerotherapy at age 11. Over the course of 12 years, the patient had experienced three episodes of cellulitis without systemic symptoms.

At presentation, the patient exhibited vomiting, fever (39°C [102°F]), and a painful, warm, erythematous intergluteal lesion with serous discharge, leading to limited mobility. Multiple varicose veins and scars from previous procedures were evident on the posterior right leg, particularly at the lateral gluteal level. Additionally, several hyperpigmented and lichenified plaques were present. Initial laboratory tests revealed leukocytosis (31,190/mm^3) with neutrophilia (28,200/µL) and lymphocytopenia (1,360/µL), along with an elevated C-reactive protein level (315.71 mg/dL). Arterial blood gas analysis demonstrated partially compensated respiratory alkalosis (pH 7.515, pCO_2 22.7 mmHg, pO_2 73.3 mmHg, HCO_3 17.9 mmol/L, tCO_2 41.7 vol%, EBvt –2.9 mmol/L, and SpO_2 97%).

The Department of Infectious Diseases was consulted and ordered blood cultures which grew *Streptococcus dysgalactiae* ssp. *equisimilis* in one of two sets. To evaluate the extension of the infectious process, a soft tissue ultrasound of the gluteal region was performed, demonstrating skin thickening, increased echogenicity of the subcutaneous tissue, and contour alteration without circumscribed

Figure 1. Multiple pink to violaceous vascular papules and plaques in the intergluteal and upper posterior thigh region.

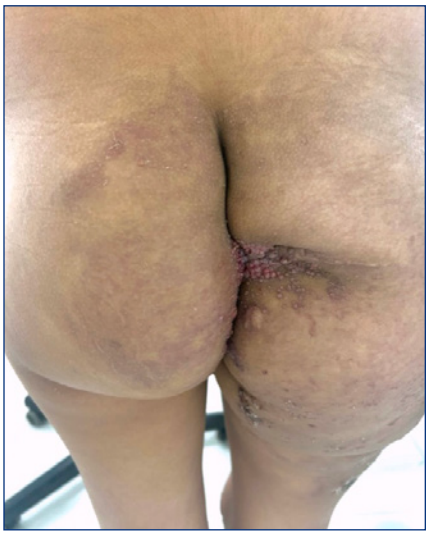


Figure 2. Multiple erosions with crusting and asymmetry in the length and thickness of the left gluteus and lower limb compared to the right.

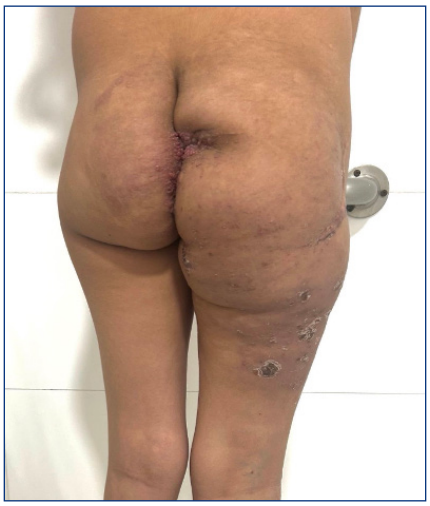
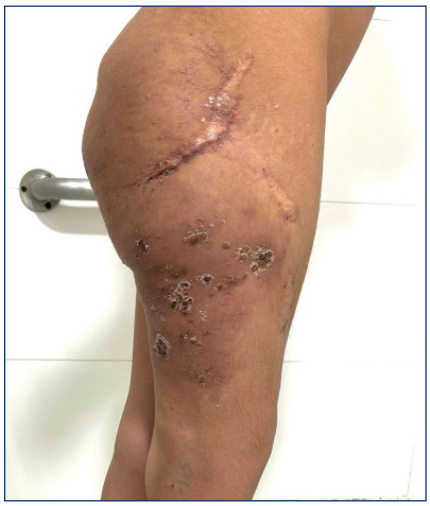


Figure 3. Varicose vein formation and scars from past procedures on the posterior side of the right leg. Surrounding the affected areas, hyperpigmented and lichenified plaques.



collections, findings consistent with gluteal cellulitis. Empiric intravenous antibiotic therapy was initiated with vancomycin (40 mg/kg/day) and cefepime (150 mg/kg/day). Subsequent rectal swab cultures grew *Klebsiella pneumoniae* subsp *pneumoniae*, identified by antibiogram as carbapenemase-producing. However, this isolate was deemed to represent colonization rather than active infection, and the initial antibiotic regimen was continued.

After one week of empiric antibiotic therapy, the lesion demonstrated significant improvement, with a marked reduction in serous discharge. On re-examination, multiple pink-to-violaceous vascular papules and plaques were observed, predominantly in the intergluteal region and upper posterior thigh [**Figure 1**]. The right posterior thigh displayed multiple erosions with overlying crusting, along with noticeable asymmetry in the length and thickness of the left gluteus and lower limb compared to the right [**Figures 2,3**].

Given the lesion's location and the severity of her presentation, the patient received a 21-day course of intravenous antibiotics, resulting in complete resolution of the infection. The patient and her mother were counseled on local hygiene practices and the importance of minimizing excessive moisture in the affected area to prevent recurrence.

DISCUSSION

KTS was first described in 1900 by French physicians Maurice Klippel and Paul Trenaunay. It is now understood to be part of the PIK3CA-related overgrowth spectrum (PROS), a group of syndromes caused by somatic mutations in the *PIK3CA* gene, which plays a central role in regulating cell growth, angiogenesis, and lymphangiogenesis.[5] It is characterized by a triad of capillary malformations, venous varicosities, and hypertrophy of one or more extremities. The condition exhibits a broad phenotypic spectrum, and its progressive nature often leads to complex complications that often require a collaborative and multidisciplinary approach.

KTS is associated with a range of complications, including cellulitis, deep vein thrombosis, pulmonary embolism, chronic venous insufficiency, and hemorrhage, all of which may contribute to limb length discrepancies. Additional complications include lymphedema, neurologic involvement, orthopedic abnormalities, and internal organ complications, such as hematuria or gastrointestinal bleeding, both of which can be life-threatening.[6] Cellulitis is a common consequence of the underlying vascular and lymphatic malformations and may recur, particularly in the lower extremities. Venous hypertension and stasis in the affected limb further increase the risk of cellulitis due to altered hemodynamics.[7]

In the present case, the anatomical location of the venolymphatic malformation presents a significant clinical challenge. The intergluteal area is particularly susceptible to excessive moisture, friction, and hygiene-related issues that may promote bacterial overgrowth and contribute to recurrent cellulitis and delayed wound healing. These factors further exacerbate the risk of chronic inflammation, fibrosis, and long-term scarring. A recent retrospective study evaluating cutaneous complications in KTS reported cellulitis in 74 of 410 patients, including 12 cases involving lesions in the buttocks, perineum, or genitalia.[7] Notably, KTS lesions in this region were identified as a predictor of cutaneous complications (odds ratio 1.92; $P = 0.009$).[7] This finding underscores both the heightened risk in patients with gluteal involvement and the relative rarity of cutaneous manifestations in this anatomical area.

The management of cellulitis in patients with KTS should account for the increased risk of complications, including deep infections and sepsis. Radiologic assessment is strongly recommended to evaluate the extent of infection, and a multidisciplinary approach should be the standard of care. For patients with recurrent lower-extremity cellulitis, prophylactic low-dose daily oral antibiotics may reduce recurrence.[8,9]

The impact of cellulitis on quality of life in patients with KTS should not be underestimated. This patient reported significant pain, consistent with previous research identifying pain as one of the top ten symptoms in individuals with KTS.[10] Moreover, pain in KTS may be associated with an increased risk of future psychiatric diagnoses.[11] Thus, early diagnosis and appropriate treatment of cellulitis are essential not only to minimize physical morbidity but also to mitigate psychological consequences.

Given these multifactorial challenges, a comprehensive and individualized approach is essential to optimize outcomes in patients with KTS and venolymphatic malformations. Exploring adjunctive management strategies, including targeted pharmacologic therapies, advanced wound care modalities, and minimally invasive interventions, may offer additional therapeutic benefits. However, the scarcity of research on optimal treatment approaches for venolymphatic malformations in this anatomical region underscores the need for further investigation. Advancing our clinical understanding of these complex cases will be critical in developing more effective, evidence-based strategies to improve long-term patient outcomes.

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