CASE REPORT

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Two-stage procedures in an 11-year-old patient with Klippel-Trenaunay syndrome: A case report

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ABSTRACT

Introduction: Klippel-Trenaunay Syndrome (KTS) is a cutaneous vascular malformation syndrome that occurs as a result of a triad of limb hypertrophy, capillary, and venous malformation. As the etiology of KTS remains incompletely understood, no definitive consensus has been reached regarding its optimal treatment or standardized management. Thus, this study aims to report the management of KTS in an 11-year-old patient.

Case description: An 11-year-old male patient presented with right lower extremity varicose veins, a bluish red cutaneous nodule of the right thigh, and hemihypertrophy that was suggestive of KTS. Doppler ultrasonography revealed multiple dilated superficial veins along the lateral aspect of the right femur extending to the right foot. The Great Saphenous Vein (GSV) and Small Saphenous Vein (SSV) were notably enlarged, with maximum diameters of 9 mm and 11 mm, respectively. No arterial abnormalities suggestive of high-flow arteriovenous malformations or fistulas were identified in the right lower limb. Varicose veins along the lateral aspect of the right lower limb were treated with Endovenous Laser Ablation (EVLA). At 3 months post-EVLA, no prominent dilated veins were observed along the lateral, medial, or posterior aspects of the limb. Due to the patient's high-impact activities, vein ligation was planned to eliminate reflux within the lateral marginal vein. The procedure was performed at four sites along the lateral marginal vein of Servelle under ultrasound guidance. Four weeks after surgery, the patient showed marked clinical improvement, reporting no pain or discomfort. Physical examination revealed no evidence of recurrent varicose veins or other complications.

Conclusion: The combination of EVLA and vein ligation has the potential to decrease the likelihood of varicose veins and recanalization caused by blood reflux. Since there is no accepted protocol for treating KTS, the two-stage procedure may be considered as a treatment option in selected KTS cases, particularly in patients with high-impact activities.

Keywords: Endovenous Laser Ablation (EVLA), Klippel-Trenaunay Syndrome (KTS), vein ligation.
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INTRODUCTION

The Klippel-Trenaunay syndrome (KTS) was first documented in 1900 by Maurice Klippel, a French neurologist, and Paul Trenaunay, a physician from Paris. It is a congenital disorder characterized by the presence of three main features, including cutaneous haemangiomas (abnormal growth of blood vessels in the skin manifested as port-wine stain), varicosities in unusual locations, and hypertrophy of soft tissues and bones in the limbs.[1] The estimated prevalence is approximately 2 to 5 cases per 100,000 individuals and is observed in both males and females at an equal rate.[2]

KTS is known to be associated with a genetic pathway. This syndrome is linked to somatic mutations in the PIK3CA gene, causing cell overgrowth and dysregulation of the mTORC2 pathway. These mutations occur during embryonic development, affecting angiogenesis.[3] Other clinical presentations include gastrointestinal bleeding caused by gastrointestinal vascular malformations, superficial thrombophlebitis, lymphatic malformation, and recurrent deep vein thrombosis resulting in pulmonary embolism.[4–6]

The management of venous malformations in pediatric KTS remains challenging due to the heterogeneity of the affected structures, the wide spectrum of clinical manifestations ranging from gait abnormalities to psychological impairment, and the variability in patient age groups. A multidisciplinary approach is crucial for optimal patient management. As the etiology of KTS remains incompletely understood, no accepted consensus has been established regarding its optimal treatment or standardized management. Therapeutic strategies are therefore often individualized according to the extent of vascular involvement, symptom severity, associated complications, and patient characteristics.[1]

The management of KTS involves the use of conservative and surgical methods. Conservative therapy involves employing non-invasive methods such as wearing compression stockings and taking analgesics, antibiotics, and corticosteroids.[7,8] Surgical intervention is only considered for situations that do not respond to medical treatment. It involves the use of endovenous ligation to close off embryonic veins and stripping for severe

varicose veins.[9] Ligation and stripping procedures have become less popular due to the exacerbation of symptoms that occur after these surgeries.[10] Nevertheless, a recent study examining 53 surgeries for KTS utilizing ligation with or without stripping revealed that after 5 years, 59% of patients experienced relief from incapacitating pain and 74% were spared from additional treatments, resulting in a notable enhancement of the Venous Clinical Severity Score.[11] Other KTS management, such as minimally invasive intervention with endovenous laser ablation (EVLA) targeting the greater saphenous vein, has also emerged as a minimally invasive treatment option for patients with KTS, particularly for the management of symptomatic varicosities associated with venous reflux.

Evidence regarding staged EVLA combined with vein ligation in pediatric patients with persistent lateral marginal vein of Servelle remains limited. Furthermore, the optimal treatment strategy and short-term outcomes in this population have not been well established due to the rarity of the disease. The patient's involvement in high-impact physical activities was considered an important factor in treatment planning, as repetitive increases in venous pressure and mechanical stress may aggravate venous reflux and progressive dilatation of incompetent superficial veins. Previous studies have demonstrated a higher prevalence of reflux in the great saphenous and non-saphenous veins among individuals with high physical activity levels.[12] Therefore, EVLA followed by vein ligation was selected to interrupt reflux within the persistent lateral marginal vein and reduce the risk of symptom progression and venous complications. This report aims to describe the short-term outcome of staged EVLA followed by vein ligation in an 11-year-old male with KTS, presenting with a port-wine stain on the right thigh since birth and a prominent tortuous cutaneous vein along the ipsilateral lateral region.

CASE DESCRIPTION

Patient Presentation

A 11-year-old male patient presented with right lower extremity varicose veins, bluish red discoloration of the right thigh, and hemihypertrophy. Previously, the patient was brought to a dermatologist and labeled as having a vascular disorder. The patient then referred to the vascular surgery clinic for further investigation. Upon further questioning, the mother stated that she began to notice the bluish red discoloration since the patient was born, but only the size of a corn seed. Later to the age of 7, the discoloration became increasing in size and varicose veins started to appear. The mother also noticed a slight increase in the size of the right leg and a distinct gait of his son. There was no drug history or surgical intervention before. None of the patient's family had similar clinical manifestations. The patient is a boarding school student and amateur football athlete. Prior to the physical examination, informed consent for publication of this report and the accompanying images was obtained from the patient.

On physical examination, the weight and height of the patient were 38 kg and 141 cm. Right lower limb showing a bluish red cutaneous nodule of the lateral aspect, prominent dilated veins on the right lateral, medial, and posterior aspect (**Figure 1**). Lower limb length was measured using a tape measure by determining the distance from the anterior superior iliac spine (ASIS) to the medial malleolus on each side. The length of the right and the left lower limb was 65,4 cm and 63 cm, respectively. The right lower limb also showed slight hypertrophy. The respiratory and cardiac exams were within normal limits.

Diagnostic Assessment

Doppler ultrasonography showed multiple dilated superficial veins along the lateral aspect of the right femur until the right pedis. The presence of a dilated vein on the lateral side of the right thigh indicates the continued existence of the lateral marginal vein of Servelle. The vein had a maximum diameter of 17 mm. There were significant enlargements in the Great Saphenous Veins (GSV) and Small Saphenous Veins (SSV) with maximum diameter 9 mm and 11 mm, respectively. None of the arterial system of the right lower limb indicates high-flow arteriovenous malformations or arteriovenous fistulas. Advanced imaging techniques, such as Magnetic Resonance Imaging (MRI) and Computed Tomography (CT) venography, were examined to assess the severity of venous and lymphatic abnormalities. However,



Figure 1. A) Right lower limb showing varicose veins, bluish red cutaneous nodule, and slight hemihypertrophy. B) Closer look at the bluish red cutaneous nodule (port-wine stain)

these tests were not performed because duplex ultrasonography had adequately demonstrated the persistent lateral marginal vein and venous reflux required for procedural planning, and the patient had no clinical evidence of significant deep venous or lymphatic involvement.

Management

The varicose veins on the lateral region of the right lower limb were treated using EVLA. Prior to the procedure, the patient was given compression stockings and analgesics. EVLA was performed under local anesthesia, with continuous vital sign monitoring. The patient was placed in the Trendelenburg position to allow for venous distention and ultrasound-guided percutaneous access to the target vein via a micropuncture method. A 0.035-inch J-tip guidewire was inserted into the venous lumen, followed by the 4F laser sheath and dilator. The guidewire and dilator were then replaced with a laser fiber that was guided to the saphenofemoral junction using ultrasonography. Tumescent fluid containing 0.9% sodium chloride solution at 40°C was injected circumferentially around the vein with an 18-G needle under ultrasound guidance to induce perivenous compression, prevent heat-related damage, and increase laser fiber contact with the venous wall.

Laser ablation was then performed with gradual withdrawal of the laser fiber, followed by ultrasonographic evaluation confirming the absence of venous flow and reduced compressibility of the treated vein. Compression was administered at the injection site of the sheath introducer using a sterile gauze, followed by the placement of an elastic bandage. During the 3-week follow-up, a noticeable decrease in varicose veins was observed in the right lower limb. The ultrasound scan revealed a decrease in the size of the GSV (5 mm) and decreased compressibility of the treated GSV without evidence of deep venous thrombosis. Three months after EVLA, a bluish red cutaneous nodule was still present, but we did not see prominent dilated veins on the right lateral, medial, and posterior aspect (**Figure 2**). Compression stocking was advised to be used by the patient.



Figure 2. Lateral view of the right lower limb 3 months after EVLA



Figure 3. Four locations of the vein ligation procedure

The patient demonstrated clinical improvement 3 months after EVLA, but follow-up evaluation still showed persistent venous patency and residual reflux within the lateral marginal vein. Therefore, vein ligation was performed as part of the planned staged management to achieve a more definitive interruption of abnormal venous flow and reduce the risk of recurrence and future complications. Vein ligation was performed under general anesthesia as a second-stage procedure. Under ultrasound guidance, four separate segments of the lateral marginal vein were identified and ligated through small skin incisions along the course of the vein (**Figure 3**). Intraoperatively, the vein appeared dilated and tortuous without evidence of active thrombosis or significant surrounding tissue adhesion. No significant intraoperative complications or technical difficulties were encountered during the procedure. The incision sites were subsequently closed and covered with sterile gauze and elastic bandages. Compression therapy using compression stockings was continued after each procedure and maintained for 2 weeks postoperatively.

Outcome and Follow-Up

Four weeks after the surgery, the patient's condition has significantly improved. At follow-up evaluation, physical examination demonstrated resolution of the previously prominent varicose veins without evidence of recurrent venous dilatation. The surgical wounds showed good healing with no signs of infection, hematoma, abnormal swelling, or skin necrosis. The patient was able to ambulate normally and resume daily activities without functional limitation. Duplex ultrasonography demonstrated the absence of significant reflux within the treated lateral marginal vein, with no evidence of deep venous thrombosis or other procedure-related complications.

DISCUSSION

KTS is a syndrome characterized by the presence of vascular malformations in the skin, veins, and lymphatics, along with the abnormal growth of soft tissue and bones in the affected limb. This syndrome is also known as capillary-lymphatic-venous malformation (CLVM), which describes

the alterations observed in those vessels. This condition was initially documented in 1900 by two French physicians, Maurice Klippel and Paul Trenaunay.[7]

Recent studies have discovered a connection between the cause of KTS and specific genetic mutations in the PIK3CA gene. Through the dysregulation of the mTORC2 pathway, the activation of phosphatidylinositol-3-kinase (PI3K)/protein kinase occurs, resulting in cell overgrowth. Changes happen during the early stages of development that involve the growth of blood vessels, which is consistent with what is observed in this particular condition.[3,13] Now, KTS is classified within the broader category of overgrowth syndromes known as PIK3CA-related overgrowth spectrum (PROS). Numerous syndromes characterized by similar clinical features and caused by various mutations in the PIK3CA gene have been discovered. Occasionally, there have been reports of translocations involving chromosomes 5-11 and 8-14.[14]

Diagnosing KTS involves identifying at least two of the three common signs, including localized cutaneous capillary malformations, venous abnormalities, and limb hypertrophy. Typically, diagnosis is determined through clinical and radiological evaluation.[14] There is an absence of guidelines on diagnostic criteria for managing the disease, given its unclear cause. An initial assessment can be made using a color Doppler ultrasound to check for varicosities, venous malformation, or the presence of thrombus formation. If arteriovenous malformations are present, it is now recognized as Parkes-Weber syndrome, a distinct entity from KTS.[14,15]

The treatment of KTS involves a combination of conservative and surgical methods.[7,8] The management of KTS should involve a cautious approach, focusing on treating the symptoms with non-invasive methods. For most cases of KTS, patients are typically recommended to wear either elastic or non-elastic compression stockings. These stockings are combined with additional conservative measures such as regular leg elevation, physiotherapy, lifestyle adjustments, and stringent cleanliness maintenance.[7] Analgesics, antibiotics, and corticosteroids are frequently used to treat cellulitis and thrombophlebitis. Surgical intervention may be considered in cases where medical treatment is ineffective. This procedure entails the utilization of endovenous closure of embryonic veins and the removal of severe varicose veins.[9] Endovenous laser therapy can be utilized to treat varicosities in patients with KTS by targeting the larger saphenous veins.[7]

Further study is required to investigate drug treatment options for patients with KTS in order to avoid the advancement of anomalies that can lead to significant clinical complications. There have been encouraging findings regarding the effectiveness of rapamycin. In the field of medical research, rapamycin has demonstrated promising outcomes in the treatment of KTS. It functions by inhibiting mTOR, thereby impeding the advancement of vascular malformations and cellular growth.[1] Sirolimus has been used in a total of twenty-nine patients who have capillary lymphatic venous malformations, including patients with KTS and Congenital Lipomatous Overgrowth, Vascular malformations, Epidermal nevi, and Scoliosis/Skeletal/Spinal anomalies (CLOVES). Ninety-three percent of patients experienced enhanced quality of life, while 86% observed relief in at least one of their symptoms.[16] The observed side effects encompassed neutropenia, lymphopenia, infections, and aphthous ulcers/stomatitis, whereas no indications of toxicity were detected.

In our case, we discussed what therapeutic modalities could be performed on the patient before reaching a final decision. The treatment we performed also included conservative therapy such as elastic bandage application, leg elevation, and pain management. In this patient, we decided to perform a two-stage operation, which includes EVLA and vein ligation. EVLA has been reported to be able to treat varicose veins in patients with KTS and remains our first choice of treatment. In this case, EVLA was selected as the first stage because it was expected to decrease venous flow and collapse the abnormal superficial vein, thereby facilitating subsequent surgical management. The endovenous laser emits pulses of heat sufficient to create vapor bubbles, resulting in thermal damage to the inner lining of the veins. This leads to the formation of a blood clot that blocks the target vein.[17]

Despite clinical improvement after EVLA, follow-up ultrasonography demonstrated persistent residual patency and reflux within several segments of the lateral marginal vein. Therefore, vein ligation was performed as the second-stage treatment to achieve more definitive interruption of the remaining abnormal venous flow and reduce the risk of recurrence and future venous complications. Reports are stating that vein ligation can avoid the recurrence of GSV and perforator incompetence.[18] EVLA was not performed in the second procedure due to the consideration that EVLA could cause damage to the peroneal nerve if performed on the lateral marginal vein of the servelle. This vein is a significant tributary that contributes to the formation of the SSV. The SSV is closely associated with the nerves in its vicinity. Within the popliteal fossa, the SSV may come into contact with either the tibial or common peroneal nerves. In certain cases, the sural nerve may connect with the SSV at different levels when the SSV ends below the popliteal fossa.[19] At the ankle, the nerve consistently comes into contact with the SSV and may even encircle it. Performing EVLA on the distal below the knee carries a significant risk of nerve damage. This is due to the distance between the vein and the nerve appears to be decreasing distally.[20]

Although EVLA is considered a minimally invasive treatment modality, its application in pediatric patients remains relatively limited, and careful procedural planning is required to minimize complications. One important concern is the risk of thermal nerve injury, particularly in venous systems located close to adjacent sensory nerves, such as the sural nerve near the SSV and lateral marginal vein. Ultrasound guidance and circumferential tumescent fluid administration were therefore utilized to increase the distance between the vein and surrounding tissues, provide thermal protection, and reduce the risk of nerve injury during ablation. In the present case, no postoperative neurological deficit or procedure-related complication was identified.

The patient is a high-impact amateur football player who attends a boarding school remote from his parents. Recurrence is not uncommon after varicose vein surgery, and while the recurrence can be influenced by several factors, physical strain from high-impact activities is one of the potential contributors.[21] Engaging in high physical activity, especially activities that increase venous pressure in the legs, such as running or heavy lifting, may lead to the recurrence of varicose veins. The stress on the venous system from these activities can promote the reappearance of venous reflux, a key factor in varicose vein formation.[12] Therefore, we consider EVLA followed by vein ligation to interrupt reflux within the persistent lateral marginal vein and reduce the risk of symptom progression and venous complications. Although in some reports ligation can worsen complaints after surgery, we did not find any complaints from patients after the two-step procedure was performed. The combination of EVLA with high ligation of the GSV, ligation of perforator veins when complicated by primary deep venous insufficiency (PDVI), has the potential to decrease the likelihood of varicose vein recurrence and recanalization caused by blood reflux.[18]

This report is limited by its single-patient design and short follow-up duration, which preclude definitive evaluation of long-term efficacy and recurrence prevention. Advanced imaging modalities such as MRI or CT venography were not performed. Therefore, the generalizability of these findings remains limited. This report shows the presentation of a real-world pediatric KTS case managed using a staged treatment approach tailored to persistent venous reflux. Both EVLA and vein ligation were performed under ultrasound guidance to optimize procedural accuracy and safety. In addition, serial clinical photographs provided objective documentation of the postoperative clinical improvement.

CONCLUSION

Klippel–Trenaunay syndrome is a rare and complex vascular malformation disorder for which no standardized treatment strategy has yet been established. In this case, staged EVLA followed by vein ligation was well tolerated and associated with short-term clinical improvement. This approach may be considered in carefully selected pediatric KTS patients after individualized vascular assessment. However, longer follow-up and larger studies are required before broader recommendations can be established.

DISCLOSURES

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Conflict of Interest

The authors do not have a conflict of interest to declare.

Author Contribution

All authors have made the same contributions to this study. Every author is responsible for preparing the manuscript and must provide their consent for this final version to be submitted.

Ethical Consideration

Informed consent was obtained from the patient for publication of this case and related clinical information.

Generative AI Statement

The manuscript was edited using an English-language writing assistant software tool for language improvement, including grammar, spelling, and clarity. The authors created all scientific content, interpretations, and conclusions.

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