Management of Klippel-Trenaunay Syndrome from a Single Center in India: Experience Shared

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Abstract

India with a population of about 1.3 billion and diverse cultures holds within its large land mass an encyclopedia of medical cases, several un/underdiagnosed. Klippel-Trenaunay syndrome (KTS) is one such condition. Over the years, as the understanding of our team increased about the condition, we were able to share the same with our colleagues across the institution and publish the brief article. This resulted in an increased referral pattern from within the institution and across the country. At our institution, we managed 127 cases of KTS between October 2009 and December 2017. In this article, we share our experience about managing the cases, lessons learnt, and the challenges we face.

Keywords: Congenital vascular malformations, Klippel-Trenaunay syndrome, lateral marginal vein, sclerotherapy, segmental excision, venous malformations

Introduction

Vascular malformations (VMs) are essentially the result of the developmental arrest of vascular tissues and hence are inborn errors that occur at various stages of embryogenesis affecting both venous and lymphatic channels.\[1-4]\n
One of the most common combined forms of congenital vascular malformation (CVM) is a lymphovenous malformation which consists of a venous (VM) and lymphatic malformation (LM) component.\[5\]

Klippel-Trenaunay syndrome (KTS) is a popular name based eponym that describes a rare clinical condition, which represents a combination of CVM’s.\[6,7\] KTS has been named after two French physicians, Maurice Klippel and Paul Trenaunay who in 1900 described hemangiomatous lesions of the skin associated with asymmetric soft tissue and bone hypertrophy, and described as nevus variqueux osteo-hypertrophique, in two patients.\[8\] The triad that defines KTS consists of port-wine stain which is caused by capillary malformations (CM), bone and soft tissue hypertrophy, and lower extremity varicosities, which are typically, mostly lateral, varicose veins.\[9\]

The syndromes usually have two components to them– one a clinical description of the primary vascular lesion and the secondary one that includes the nonvascular lesions and clinical findings.\[9\] That is to say that in KTS, the CVM is the primary lesion and the secondary effects such as bone and soft tissue hypertrophy and varicosities [Figure 1].\[9,10\]

At our institution, we followed the Modified Hamburg Classification system and based on this KTS is a hemo-LM, which consists of VM, LM, and CM.\[5\] If, on examination or imaging an arterio-venous malformation component is found then the condition is called as Parkes-Weber syndrome (PWS).\[12,13\]

Our institution is a tertiary care center that caters to patients from all over India. A significant number are from the South and East of our country.

As our understanding of CVM’s and in particular KTS increased, we started to maintain data electronically and can clinically differentiate between KTS– PWS, Proteus syndrome, Cloves syndrome, and Servelle-Martorell syndrome.

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How to cite this article: Premkumar P, Stephen E, John JM, Kota AA, Samuel V, Selvaraj D, et al. Management of klippel-trenaunay syndrome from a single center in India: Experience shared. Indian J Vasc Endovasc Surg 2018;5:149-53.

Received: March, 2018. Accepted: June, 2018.
METHODS
Following approval by the Institutional Review Board we retrospectively analyzed our database using our electronic medical record system.

We have 127 patients from October 2009 to December 2017.

RESULTS
The patient demographics are shown in Figures 2-4.
- Age: Male – 6–72 years; Female: 7–39 years
- Gender - 19% Female; 81% male
- Side - Unilateral 87%; 13% Bilateral
- Deep vein patency – 72% patent; 28% hypo/aplastic.

Diagnosis
All the patients had a venous duplex as a baseline investigation and in those cases where the duplex did not help assess the deep venous anatomy adequately, and obese patients an magnetic resonance imaging (MRI) was performed with T1/T2 images or a computed tomography venogram, as well. Direct puncture venography was performed in two patients [Figure 5]. Analysis of the LM component was performed with a combination of the duplex and MRI imaging.

Over the past year, we have added D-dimer and platelet count for those patients who presented with a bleed, secondary to localized intravascular coagulation (LIC).[5]

A whole body blood pool scintigraphy (WBBPS), RI lymphoscintigraphy, transarterial lung perfusion scintigraphy (TPLS) were not performed on any of the cases.

DISCUSSION
Once a diagnosis of KTS was confirmed, each component (VM, LM, CM) was sub-classified as truncular or extra-truncular. Parents of children in the pediatric age group were advised symptomatic treatment, until they were at least 18-year-old. The importance of good skin care, height correction footwear, compression (either short stretch bandage or 25–33 mm of Hg stockings), manual decongestive therapy (MLD), and need for regular follow-up was impressed on them. One of our patients used the sole of a “slipper/flip-flop” to work as a height correction filler, as he was unable to come for follow up for 2 years. This we feel was an innovative idea and could be put to use in situations where patients do not have access to a orthotics or cobbler [Figure 6].

To reduce the edema (in adult patients) a short course therapy of – tablet daflon 1 g once a day – 3 months, tablet chlorthalidone 12.5 mg alternate days for a month were added to the above-mentioned plan. This we found improved compliance with the use of compression hosiery and MLD, as they saw a reduction in limb girth.

In patients with a lymphatic component that was “weeping” and in those with smaller veins in the leg/foot we offered foam sclerotherapy (FS). The foam was made with 3%
sodium tetradecyl sulfate in a ratio of room air to agent mix of −1:4. FS was offered based on symptoms at follow-up.

Segmental excision of the lateral marginal vein (LMV) was performed in 8 patients over the past 2 years with an effective reduction in edema [Figure 7]. The reduction in edema is because there is venous stasis that occurs secondary to the presence of “avalvulosis” and resultant lack of venous valves leading to venous hypertension and progressive chronic venous insufficiency. There is also evidence that this is a VM and not a varicose vein and because of the lack of media/smooth muscle cell layer can potentially cause a catastrophic pulmonary embolism. We operated on two children (7-year-old female, 12-year-old boy) with normal deep venous systems to reduce the effect of the vascular bone syndrome. In children with hypoplastic veins, staged excision of the LMV is recommended to prevent worsening edema. Venous thromboembolism (VTE) prophylaxis was used in patients with abnormal D-dimer values pre- and post-operatively. Patients who presented with bleeding had a D-dimer and platelet count done, and if D-dimer was elevated they were started on low molecular weight heparin (LMWH), and compression bandaging and the D-dimer repeated on day 3 with a platelet count. Once the bleeding stopped, LMWH was discontinued 2 weeks later, with the intention of healing of the wound (C5) while on multilayer bandages [Figure 8].

Complications
We had two complications in our series, following the intervention. One major and the other minor. One of our patients who had been receiving FS on follow up’s for a year with the good cosmetic result regarding reduction of leg varices, underwent FS of foot veins. He presented 72 h later with significant forefoot pain and pregangrenous changes in the foot. He was started on an infusion of unfractionated

Endovenous ablation (EVA) and coil embolization were not offered as these are associated with higher risk of VTE, coil embolization due the avalvulosis and lack of media/smooth muscle in the LMV. As a result of the later, the vein expands around the thrombus/coil and hence embolizes. Skin necrosis is also high with EVA. Patients who presented with bleeding had a D-dimer and platelet count done, and if D-dimer was elevated they were started on low molecular weight heparin (LMWH), and compression bandaging and the D-dimer repeated on day 3 with a platelet count. Once the bleeding stopped, LMWH was discontinued 2 weeks later, with the intention of healing of the wound (C5) while on multilayer bandages [Figure 8].

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heparin, aiming for full heparinization [Figure 9]. The forefoot progressed to forefoot dry gangrene and the trans metatarsal stump healed with secondary intention. The complication occurred probably from an inadvertent injection into the foot arch vessels.

The other complication was a lymphatic leak following segmental excision of the LMV. The LM lesion in the KTS limb, especially if extratruncular can be life-threatening if there is a lymphatic leak and if there is added infection. A patient could progress to systemic sepsis. This, in turn, could lead to LIC and disseminated intravascular coagulopathy [Figure 10].

The patient was managed with oral antibiotics, dry dressings, and good skin care. The leak stopped 4 weeks post-operatively.

A third patient developed sepsis secondary to his ulcer in the leg getting infected and flexion deformity at the knee. He required management with epidural analgesia, regular dressings, and intravenous antibiotics. Once the ulcer was clean, we applied 4-layer bandaging, to the ulcer healed [Figure 11].

Lessons learnt

Over the years, we have understood the importance of classifying each component (VM, LM, CM) for optimal treatment and also noting the primary and secondary components.

The number of female patients is low in our cohort, and this could be secondary to cultural practices in India. As awareness increases and doctors learn how to manage KTS, we could see these numbers increase.

Attention to good skin care and nutrition is vital. The former reduces the incidence of infection and therefore decreases fibrosis and ulceration. Malnourished patients could have excess edema secondary to reduced plasma osmotic pressure from hypoalbuminemia. Obesity too adds to edema due to venous obstruction above and below the inguinal ligament, especially when patients sit. We have found MLD to be very useful in reducing edema and softening areas of lipodermatomal skin. As we know the venous and lymphatic systems are mutually complementary and inseparable in nature, therefore, if one or the other system is defunct the other plays an auxiliary role and reduces the edema. Adding a low dose diuretic for a short period along with Daflon improved compliance with the use of MLD, as patients noticed a reduction in edema almost immediately.

Height correction footwear using locally available in sole’s was an eye-opener and should be mentioned to patients who do not have access to orthotics or cobblers.

The use of LMWH preoperatively and postoperatively in patients undergoing intervention, if their D-dimer was elevated has prevented any VTE event, thus far.

The use of Sirolimus in two patients with a large VM component helped reduce girth and low dose steroid use in a patient with bleeding complication, stopped the bleeding when used in conjunction with LMWH and sirolimus. These patients were all managed with the help of our pediatric hem oncologist.

We take additional care to avoid incisions over the region of skin that has LM when excising the LMV, and have not had any more lymphatic leaks after the initial case.

Managing patients with KTS requires a multi-disciplinary team or an interest group consisting a vascular and endovascular
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surgeon, orthopedic surgeon (adult and pediatric), plastic surgeon, physiotherapist, and an orthotics, which we have at our institute.

Challenges

- Late presentation of the patient’s, for example, with anemia following bleeding, spinal deformity secondary to vertebral body stapling (VBS). Long distances that patients need to travel to get to the center with experience in managing KTS, is the reason
- Encouraging patients to come for regular follow-up and buy compression garments, which often are customized
- As most patients are not insured, cost of treatment is a great limiting factor
- Convincing surgical and interventional colleagues against the use of EVA and coil embolization, for reasons, mentioned earlier in this article.

Future

We would like to conduct a randomized controlled trial to see the outcome after use of Sirolimus and steroids in this subset of patients, especially those that present with bleeding, lymph leak, early cases of VBS and disabling pain. A discussion with our pediatric orthopedic team is nearing implementation, regarding the use of an epiphyseal plate in the effected limb to curtail the VBS, while the normal limb grows. Thereby reducing the spinal deformity and pelvic tilt. We will add WBBPS, TLPS, lymphoscintigraphy, genetic testing to our armamentarium of assessment.

To form a nationwide interest group so that patients all across India can have access to the standard of care and we could learn from each other’s experiences.

Conclusion

KTS is a CVM that vascular surgeons, dermatologists, orthopedic surgeons, interventional radiologists and family doctors will see more of in the coming years. A good understanding of the embryology, presentation, management, and limitations of when and how far to intervene, will improve patient outcomes.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

Financial support and sponsorship
Nil.

Conflicts of interest
There are no conflicts of interest.

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