

KLIPPEL-TRENAUNAY-WEBER SYNDROME — A CASE REPORT

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Klippel-Trenaunay-Weber syndrome is a rare congenital syndrome involving enlarged veins and arteries, limb hypertrophy and capillary malformations. In 1900, French physicians, Klippel and Trenaunay, first described what became known as Klippel-Trenaunay syndrome after two patients presented with a triad of symptoms — port-wine stain, varicose veins, and bony and soft tissue hypertrophy involving an extremity (Klippel and Trenaunay, 1900).

Later in 1907, Parkes Weber, who was unaware of Klippel and Trenaunay's earlier work, described a patient who also presented with these three symptoms as well as an arteriovenous malformation of an affected extremity, hence the condition became known as Klippel-Trenaunay-Weber syndrome.

Pathophysiology

Klippel-Trenaunay-Weber syndrome affects females and males equally and presents at birth or during early infancy/childhood. Patients tend to develop degenerative joint disease at an early age.

The exact aetiology of Klippel-Trenaunay-Weber syndrome is unknown, but suggested causes include:

- ▶ Arteriovenous anastomoses
- ▶ Underlying mixed mesodermal and ectodermal dysplasia
- ▶ Deep vein abnormalities, with resultant obstruction of venous flow, leading to venous

hypertension and the development of varicosities

- ▶ Lymphoedema
- ▶ Limb hypertrophy.

Although there are some genetic studies underway, no specific genes that may cause Klippel-Trenaunay-Weber syndrome have been identified to date.

Varicosities may affect the superficial, deep, and perforating venous systems and may remain stable in size or gradually expand.

Symptoms

The Klippel-Trenaunay vein, as it has become known, is a large superficial vein extending from the lower leg all the way up to the buttocks. It is a symptom of Klippel-Trenaunay-Weber syndrome often seen at birth, although it may not be obvious until later in childhood.

Varicosities, one of the main symptoms of Klippel-Trenaunay-Weber syndrome, are congenital and may be extensive, although they may not affect the saphenous vein and its function. They are seen below the knee, laterally above the knee, and occasionally in the pelvic region. Varicosities may affect the superficial, deep and perforating venous systems, and may remain stable in size or gradually expand.

Pain and lymphoedema are also commonly reported in Klippel-Trenaunay-Weber syndrome and may worsen during pregnancy.

Haemangiomas (enlarged or abnormal vessels/collection of vessels, i.e. port wine stains) may also be present and vary in depth. They may be limited to the skin or extend deeper into subcutaneous tissue, including muscle and bone. Visceral organs, such as the pleura, the spleen, the liver, the bladder and the colon may also be affected.

Klippel-Trenaunay-Weber syndrome generally affects a single extremity, although cases of multiple affected limbs have been reported. The leg is the most common site, followed by the arms, the trunk, and rarely the head and the neck.

Limb hypertrophy causes increased length (bony involvement) and/or increased girth (soft tissue involvement). Hypertrophy may be apparent at birth and usually progresses during the first years of life. Although lymphoedema is also seen in patients, true hypertrophy of the affected soft tissues is always present. Occasionally, the affected limb may be atrophied rather than hypertrophied.

Other common features of Klippel-Trenaunay-Weber syndrome include lymphatic obstruction, chronic venous insufficiency, stasis dermatitis, poor wound healing, ulceration and thrombosis.

In a study of 20 patients by Noel et al (2000), pain was the most common complaint in patients with Klippel-Trenaunay-Weber syndrome (16 patients; 80%), followed by swelling (15 patients; 75%), bleeding (eight patients;

40%), and superficial thrombophlebitis and cellulitis (three patients; 15%).

Diagnosis

In many instances, a thorough history and physical examination are all that is required to diagnose Klippel-Trenaunay-Weber syndrome. However, when complications are present, imaging studies can be useful. If a patient was to undergo surgery, e.g. for leg shortening or genital swelling, pre-operative X-rays or ultrasound might be necessary. Also, duplex Doppler scans may be required to fully assess vascular insufficiency.

Management

At present, many of the symptoms of Klippel-Trenaunay-Weber syndrome may be treated, but there is no cure. The following interventions are considered best practice by the author.

Compression garments

Compression garments are indicated for chronic venous insufficiency, lymphoedema, recurrent cellulitis and recurrent bleeding from capillaries or venous malformations of the extremity. Compression garments may protect the limb from trauma and intermittent pneumatic compression (IPC) pumps may also help.

However, in some patients with absent or hypoplastic deep venous systems, elastic compression may increase venous stasis and cause discomfort (Clayton and Irvine, 2008).

Pain management

Pain management is an important aspect of caring for patients with Klippel-Trenaunay-Weber syndrome. Referral to a pain clinic and/or a multidisciplinary team, including a pain management specialist, may be necessary.

Cellulitis and thrombophlebitis

Cellulitis and thrombophlebitis can be managed with analgesics, elevation, antibiotics and corticosteroids. In patients with a history of recurrent cellulitis, intermittent or prophylactic antibiotics may be considered, as

indicated in the consensus document for the management of cellulitis in lymphoedema (visit: www.thebls.com).

Anticoagulant therapy is indicated in acute thrombosis and can be given as a prophylactic before surgical procedures associated with Klippel-Trenaunay-Weber syndrome.

Given the risk of thrombotic events, women with Klippel-Trenaunay-Weber Syndrome should avoid using oral contraceptive pills.

Laser treatment is most effective when performed on very early flat superficial lesions, especially if they appear in cosmetically significant areas.

Limb hypertrophy

In the case of limb hypertrophy, heel inserts are generally sufficient for discrepancies of 1.5cm or less. For greater discrepancies, orthopaedic surgery may be considered. In rare cases, amputation is required due to recurrent infections, non-healing ulcers or recurrent bleeding.

Pregnancy

Women with Klippel-Trenaunay-Weber syndrome have been reported to have normal pregnancies (Andreasen et al, 1999). These patients should be monitored carefully with serial ultrasound as previously asymptomatic arteriovenous malformations within the uterine wall may become pronounced with the additional blood flow to the uterus which takes place during pregnancy.

Laser treatment

Laser treatment of any haemangioma can be effective in lightening the colour of the port-wine stain. Laser treatment is also indicated in the case of ulceration — ulceration of haemangiomas can be painful and impair functional abilities, i.e. when dressings are worn the ability to take baths or showers may be limited. Also, ulceration can affect an individual's

ability to wear particular items of footwear, i.e. trainers for exercise.

When treated with lasers, ulcers often heal more quickly than with standard treatment with dressings and compression bandaging and can lead to a more permanent improvement. Laser treatment is most effective when performed on early flat superficial lesions, especially if they appear in cosmetically significant areas, as it can improve the long-term appearance of the port-wine stain and improve the function of the superficial capillaries. Unfortunately, raised lesions or lesions under the skin do not respond to laser treatment.

Typically, many treatments are required to achieve the desired effect and laser treatment only helps with the superficial section of the haemangioma.

Surgical intervention

Surgery in the treatment of varicosities and venous malformations is controversial as it can be complicated by infection, lymphorrhoea and skin necrosis (Gloviczki et al, 1991). Some surgeons feel that surgery only gives a temporary improvement and may damage venous and lymphatic structures, leading to increased oedema in the affected limb.

However, surgery can be considered in either significant cosmetic deformity or where there are symptoms of pain, heaviness of the leg, bleeding, or infectious complications.

Venous stripping, ligation, excision, or sclerotherapy are contraindicated unless the surgery involves the superficial system and the underlying deep system is normal or demonstrates only mild-to-moderate reflux.

The management of patients with Klippel-Trenaunay-Weber syndrome continues to be primarily non-surgical, but those patients with patent deep veins can be considered for excision of symptomatic varicose veins and venous malformations. Although the recurrence rate is high, clinical improvement is

significant and further operations can be performed if needed. Occasionally, deep vein reconstruction, excision of peripheral superficial veins (PSVs), or subfascial endoscopic perforator surgery (facilitates healing of a leg ulcer through dissection of the perforator veins) is indicated.

Inadequate evaluation before excision can increase surgical complications. Evaluation of the deep venous system using computed tomography (CT) arteriography, duplex scanning contrast venography, ultrasonography, contrast venography or magnetic resonance imaging (MRI) can show the extent of vascular impairment and highlight any arteriovenous fistulae. These can affect the success of any surgery to the leg, including healing time and infection risk. Patients also need pre-operative screening for any concurrent medical problems.

When adequate preoperative examination is performed, symptomatic superficial varicosities can be removed without harm.

Although Baskerville et al (1985) demonstrated that some 90% of treated varicosities redevelop, conservative treatment can provide improvement that may last for years.

Successful treatment of incompetent valves in the femoral vein of the affected limb with contralateral saphenous vein transplant has been reported (Cardon et al, 1999).

Debulking procedures have limited use and may damage venous and lymphatic structures, leading to increased oedema in the affected limb.

Radiotherapy

Radiotherapy has been reported to be of help in some cases of Klippel-Trenaunay-Weber syndrome as the radiation may help to induce regression of haemangiomas, however the results can be slow to develop (Yildiz et al, 2005).

Endovenous laser therapy

Managing varicosities by using endovenous laser therapy on the greater

saphenous vein is gaining support in patients with Klippel-Trenaunay-Weber syndrome. Using a very narrow optical fibre introduced under local anaesthetic, endovenous laser therapy treats the vein directly and without the need for removal. The procedure lasts between 1–2 hours and is popular as patients can walk immediately and return to normal daily activities, such as work, the following day (Huang et al, 2005). This therapy has been used alone and in combination with other surgical interventions and is a novel and minimally invasive approach for the management of some varicosities.

Case report

At the end of 2003, patient X, a 17-year-old student who also worked part-time in a fast-food restaurant, was referred to the lymphoedema clinic by a consultant general and vascular surgeon for assessment and treatment of lymphoedema caused by Klippel-Trenaunay-Weber syndrome.

Patient X attended his initial outpatient's appointment in early 2004 with his mother and they reported that when he was six weeks old, both patient X's right lower and left upper limb had been larger in girth than the unaffected arms and legs. At the same age he had also developed a birthmark all over his trunk, left arm and right leg.

Between the ages of 10 and 12, patient X was treated with laser therapy, which considerably reduced the cutaneous angiomas over his left arm, improving the cosmetic appearance by reducing the high colour. At age 12, patient X had an epiphyseal plate fusion to reduce the length of his right lower leg (epiphyseal plates, which are formed of hyaline cartilage, are present in growing long bones and are located at one or both ends of the bone between the epiphysis [end] and the diaphysis [shaft]).

On examination by the author at the lymphoedema clinic, patient X's right lower leg was longer and larger in girth than the left (excess limb volume 1,259mls, which was 22.8% larger than the other limb). Cutaneous angiomas

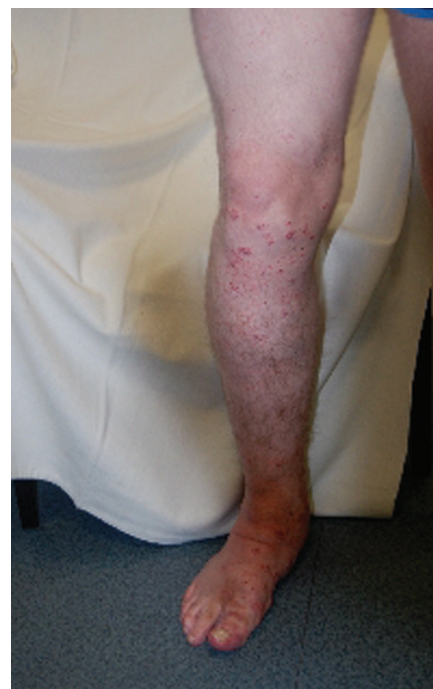


Figure 1. Anterior aspect of the affected right lower limb.

were also present, along with evidence of underlying venous disease (Figure 1) (discolouration to the foot, skin that was cool to touch and a small ulcer to the inner aspect of the patient's right big toe).

Oedema was present below the knee, especially in the foot and ankle where the subcutaneous tissues were soft and non-pitting. The leg was also clammy, but other than the small ulcer the skin was intact.

Patient X's left leg was normal, however there was considerable scrotal oedema together with multiple angiomas over the scrotal skin, the right inguinal, suprapubic region and the trunk. There was also a hydrocele to the right side of the scrotum.

Patient X's left arm also showed features of Klippel-Trenaunay-Weber syndrome (Figures 2 and 3), with angiomas, increased girth and length, and fingers that were larger and longer than those on his right hand.

Patient X felt that his biggest problem was the aesthetic appearance of his scrotum, as well as the appearance of his arm and leg (Figure



Figure 2. Posterior view of the affected left upper limb.



Figure 3. Medial aspect of the affected left upper limb, note the large haemangioma to the wrist.



Figure 4. Cutaneous angiomas to the right posterior thigh.

4). He was not yet sexually active, but did have a girlfriend and was embarrassed about the possibility of her seeing him naked.

Patient X was prescribed a treatment plan of:

- ▶ Skin care: to maintain the integrity

and hydration of his skin and to reduce the risk of infection. This included dressings to be applied to the ulcerated area, daily washing, thorough drying, and treating any trauma appropriately

- ▶ Exercise: to enhance venous and lymphatic return. Patient X was a keen football player and was actively involved in a number of other team sports at least three times a week
- ▶ Strong compression hosiery: patient X was fitted with a below-the-knee stocking to wear daily — this was to be removed at night.
- ▶ Scrotal bandaging was to be carried out as tolerated.

In 2005, patient X was referred to a specialist centre for further assessment and diagnostic investigation, especially with regards to the scrotal swelling. It is standard treatment in the author's clinic to refer any children or adolescents to the specialist centre for thorough assessment and diagnostic tests to ensure nothing is being missed. This also represents an opportunity for genetic testing in some cases. In patient X's case, there was a query regarding the scrotal swelling and the author felt that he may be a suitable candidate for genital surgery.

Clinicians at the specialist centre confirmed a diagnosis of a variant of Klippel-Trenaunay-Weber syndrome with limb hypertrophy. It was suggested that addressing the scrotal swelling was a priority due to the obvious concerns of the patient and the fact that it would deteriorate with time. Patient X was therefore referred to a consultant urologist who works in association with the specialist lymphoedema centre.

It was also suggested that the level of venous reflux in the limbs be assessed, as well as to what extent the superficial veins could be treated (if deep veins are normal, further surgical treatment to the superficial veins can go ahead and may offer cosmetic improvement and a reduction in ulceration). For classification purposes, he was also to be seen by the consultant clinical geneticist.

During the time period of his treatment, patient X had finished his final school examinations and gone on to attend university. Treatment was ongoing and his scrotal swelling was being maintained by a scrotal support and the leg swelling had reduced with the use of strong compression hosiery (excess limb volume 963ml, a 15% difference between the two legs).

In September 2005, patient X was seen by the consultant urological surgeon, who noted remarkable hemiscrotal enlargement with haemangiomas and thickening associated with the right hydrocele. The left hemiscrotum was entirely normal but the left testicle was smaller. Patient X was considered entirely suitable for hemiscrotectomy and lasering of the haemangiomas, which would take place in the Easter holidays of the following year to reduce any interruptions to his university timetable.

In 2006, patient X underwent scrotal surgery, which was a complete success. He was delighted with the results and no longer needed the scrotal support. His confidence increased and he stated that he no longer felt embarrassed. He also said that he was considerably less affected by the appearance of his leg and arm.

Over the next 12 months the mild swelling to patient X's leg continued, although he still played football twice a week. He wore compression hosiery for activities of daily living and sport and continued the skin care regimen. The ulceration to his right big toe was a problem occasionally, but he was able to care for the area by applying dressings to any ulceration, washing the area daily, and treating any trauma appropriately and therefore no infection developed.

In 2007 as suggested by the specialist centre, patient X was re-referred to the consultant vascular surgeon to ascertain the level of venous reflux in his limbs. An increase in the haemangiomas in his left upper arm was noted and he was referred for

further laser treatment. Patient X is still waiting for an out-patient appointment from a hospital in another area that offers this specific treatment.

Patient X was last seen by the author's lymphoedema clinic in September 2008. He has now finished university and is looking for a full-time job. His right lower limb swelling is under control with skin care, exercise and below-the-knee compression hosiery for activities of daily living.

Patient X still experiences occasional breakdown to the skin of his big toe and it was noted that he had been using the same pair of insoles for the last 10 years, therefore he was re-referred to the orthotics department.

Patient X had also read about a new treatment on the internet (foam sclerotherapy) and was keen to learn more. Foam sclerotherapy involves injecting a foam (which may either be a prepared product, or produced by mixing a chemical with air or other gas) into the affected vein. This inflames the vein and causes it to close, although patients may sometimes need more than one injection to block the vein.

In a study by Bergan et al (2006), nine patients with Klippel-Trenaunay-Weber syndrome were treated with ultrasound guided foam sclerotherapy. All nine patients had angiomas, four had painful non-healing ulcers, six had swelling, and all had aesthetic complaints.

Venous access was obtained percutaneously through specific targeted veins. Bergan et al (2006) state that the treatment goals (mainly cosmetic but with some wound healing and pain reduction targets), but not cure were achieved in the patients' affected limbs. There was also an acceptably low level of adverse incidents.

The technique was discussed between the author and the consultant vascular surgeon, who felt that there

was not enough information to support the use of foam sclerosant in patients with Klippel-Trenaunay-Weber syndrome, and that as patient X was young, fit and healthy there were real concerns about the possibility of negative side-effects, including blindness and cerebral vascular accident.

It is planned that patient X will be seen annually at the lymphoedema clinic, and it is hoped that he will undergo further laser treatment.

Conclusion

Klippel-Trenaunay-Weber syndrome is not a static disease process. Patients should be reviewed annually and if there is any disease progression, appropriate management strategies should be implemented or appropriate referrals made.

Noel et al (2000) suggest that as Klippel-Trenaunay-Weber syndrome is rare, patients should receive multidisciplinary care in qualified vascular centres. With their knowledge and expertise in chronic disease management, the selection/fitting of compression hosiery and sequential pneumatic compression, lymphoedema therapists are essential members of any multidisciplinary team managing patients with Klippel-Trenaunay-Weber syndrome. **JL**

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Key points

- ▶▶ Klippel-Trenaunay-Weber syndrome is a rare congenital syndrome involving enlarged veins and arteries, limb hypertrophy and capillary malformations.
- ▶▶ Pain and lymphoedema are also commonly reported in Klippel-Trenaunay-Weber syndrome.
- ▶▶ At present many of the symptoms may be treated, but there is no cure.
- ▶▶ Klippel-Trenaunay-Weber syndrome is not a static process. Patients should be reviewed annually and if there is any disease progression, appropriate management strategies should be implemented or appropriate referrals made.