

CASE REPORT

Varicose Veins, Port-Wine Stains, and Bony and Soft Tissue Hypertrophy: Klippel-Trénaunay-Weber Syndrome

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CASE PRESENTATIONS

Case 1

Mr. X is a 26-year-old male being followed by his family physician for a recurrent left leg ulcer. The ulcer recurred five days prior to the clinic visit and was self-managed with soap, water and Polysporin® antibiotic ointment. The ulcer is not painful, with initial bloody discharge followed by white discharge. This is his second ulcer in the last year, and he has had several others throughout his lifetime, all occurring in the same location. Mr. X does not smoke or consume alcohol, has no drug allergies and is not taking any medications. The patient's medical history includes a surgical excision of left-sided phlebitis. All other past medical and family history is unremarkable.



Figure 1a. Anterior lower extremity photograph of Mr. X. The left lower extremity is longer by 1.5 cm and notably wider than the right. Varicose veins and port-wine stains are noted from the left anterior thigh to the foot on the affected limb.



Figure 1b. Left lateral lower extremity photograph of Mr. X. Port-wine stains and varicose veins are noted on the anterior thigh and extending to the dorsal and plantar surfaces of the foot.

On examination, the left lower extremity is longer by 1.5 cm (anterior superior iliac spine to the medial malleolus) and notably wider than the right. Varicose veins from the posterior thigh to the foot and anterior port-wine stains with irregular borders characterize the left leg (Figures 1a and 1b). There is a weeping, 2 cm by 1 cm ulcer over the left medial malleolus, with a significant scar tissue base (Figure 1c). All other clinical examinations are unremarkable.



Figure 1c. Anterior medial view of bilateral feet for Mr. X. Note the medial malleolus ulcer and the port-wine stains on the left foot and ankle. Mild soft tissue hypertrophy is noted on the left foot compared to the right foot.

Case 2

Baby girl Q was born by vaginal vertex delivery at 40 weeks gestation to a healthy G1 mother. Ultrasound at 18 weeks and a maternal serum screen were within normal limits. At birth, baby girl Q weighed 3.2 kg, and had Apgar scores of 7 at 1 minute and 9 at 5 minutes. On examination, her right lower limb was longer and wider than her left, and both legs had multiple hemangiomas and several bleeding ulcers. Baby girl Q was transferred to the neonatal intensive care unit for management of ongoing blood loss. Baby girl Q had stabilized by six days of age, and was discharged home with specialized dressings and compression stockings,

with subsequent plastic surgery, dermatology, medical genetics and pediatrics follow-up.

Since birth, baby girl Q has shown normal cognitive, language and fine motor development; however, gross motor development was delayed. Furthermore, the patient has significant leg-length discrepancy, extensive varicose veins, port-wine stains with irregular borders and numerous peripheral and visceral arteriovenous malformations. Baby girl Q had several surgical procedures, including debridement, right toes amputation and vascular interventions.

On examination, the patient is a happy girl who is unimpeded but aware of her physical limitations. The patient has a large bleeding ulcer on her right hip (Figure 2a) and left posterior thigh (Figure 2b). There is noticeable leg-length and size discrepancy (Figure 2c). Baby girl Q is neurovascularly intact and neurologically competent, interacting at an above-average 4-year-old level. Right toes amputation appears to be healing well (Figure 2d).



Figure 2a. Right lower extremity photograph of Baby girl Q. Note the significant varicose veins, tissue hypertrophy and port-wine stains. There is also a large weeping ulcer over the right lateral hip region.



Figure 2b. Left lower extremity photograph of Baby girl Q. Compared to Figure 1a, there is less bony and soft tissue hypertrophy on the left leg compared to the right leg. Port-wine stains and varicose veins are noted as well.



Figure 2c. Right posterior thigh photograph of Baby girl Q. Note the significant soft tissue hypertrophy of the right buttock compared to the left. There are significantly larger port-wine stains and varicose veins on the right side compared to the left side, and the right lateral hip ulcer is also noted.



Figure 2d. Right foot and ankle photograph of Baby girl Q. All distal digits were amputated and note is made of the port-wine stains on the foot. Significant bony and soft tissue hypertrophy is present in the remaining foot and ankle.

KLIPPEL-TRÉNAUNAY-WEBER SYNDROME (KTWS)

Klippel-Trénaunay syndrome was first described by two French physicians in 1900 and later in 1907 by Weber, who was unaware of the previous report. The syndrome was defined by the presence of a triad of varicose veins, port-wine stains, and bony and soft tissue hypertrophy of the extremities. In addition to the triad, Parkes Weber has also described an arteriovenous malformation in the affected limb. The latter characterization has been challenged because presence of arteriovenous malformation in some patients with this condition is associated with increased morbidity, making this group of patients different from those with the original triad.¹

The pathophysiology of this condition remains obscure. Different hypothetical mechanisms have been proposed to explain the syndrome. One group of investigators claims that

intrauterine damage to venous flow produces venous hypertension that results in varices and limb hypertrophy.² Another group of researchers implicates abnormal mesodermal development of the fetus as the leading role for persistent microscopic arteriovenous communications.³ Furthermore, some evidence suggests that mesodermal and endodermal dysplasia cause abnormalities seen in the condition.

The majority of reported cases are sporadic. However, a few families with autosomal dominant inheritance with variable expressivity have been described.⁴ The genetic basis has yet to be established. However, analysis of several reciprocal translocations that were found in association with KTWS has suggested a linkage to chromosomes 11p, 8q or 14q.⁵ Also, inadequate methylation of 11p, which is required for correct imprinting of the regulatory genes, was shown to be present in familial cases.⁶

DIAGNOSIS

The syndrome usually presents at birth or in early years and has no racial or gender predisposition. Two-thirds of the patients present with a complete triad, another third of patients presents with port-wine stains and with varicosities or single limb malformation. The affected limb is predominately a lower extremity followed by upper extremities, trunk and head (Table 1).¹

Key Points for Clinical Diagnosis of Klippel-Trénaunay-Weber Syndrome

- Predominately lower extremity
- Varicose veins
- Port-wine stains (cutaneous vascular malformations)
- Hypertrophy of bones and soft tissue (length, width, girth)
- Arteriovenous malformations

Clinical examination usually reveals a hemangioma or a port-wine stain with clearly demarcated linear border that tends not to cross the midline. The colour of the hemangiomas progress with time from a pink to deep purple; however, unlike strawberry nevi, they do not proliferate or regress. Depth of the malformation can vary from superficial to deep, including bones and internal organs. Visceral organ involvement has an inherited risk of bleeding and may manifest as hematuria or hematochezia, substantially increasing morbidity in these individuals. Consumptive coagulopathy can also occur in skin hemangiomas that sequester platelets from circulation.

Venous malformations of large, lateral, superficial veins often present later with ambulation of a child, although they may present at birth. While varicose veins can be extensive and involve superficial and deep veins, they rarely affect visceral organs. They usually produce pain and lymphedema, and may remain stable or progress slowly.

Hypertrophy of bones and soft tissue can be measured in length and girth of the extremity, and can be more severe with presence of arteriovenous malformation. Although the

difference can be greater than 10 cm, the affected limb can sometimes be atrophied.

Arteriovenous fistula, an additional feature that was identified by Weber, can present as a pulsatile mass, thrill or bruit that, if present, is usually in the spared extremities. On examination, hyperthermia and Branham's sign (induced bradycardia on occlusion of the artery proximal to the fistula) can be positive.

Multiple other bony and venous defects have been described such as spina bifida, polydactyly, and chronic venous insufficiency.

MANAGEMENT

Although the syndrome often causes cosmetic and health problems, therapy is limited. Conservative and symptomatic treatment of venous insufficiency and lymphedema can be achieved with compression stockings. In case of an inflammatory or infectious process of the effected extremity, antibiotics, analgesics, and steroids can be offered. Significant limb difference can be managed with epiphysiodesis. Laser treatment for hemangiomas can improve the discoloration of the skin. However, sclerotherapy, ligation or excision of affected veins is contraindicated. Stasis and inappropriate circulation in the affected extremities increase the risk of complications such as thromboembolic events, ulceration, hemorrhage and cellulites. In addition, discrepancy in lower limb lengths can cause compensatory scoliosis and functional limitations.

CASES REVISITED

Case 1

The ulcer was cleansed and debrided with appropriate topical antibiotics and dressings. The patient was advised to keep the dressing clean, change it on a regular basis, and continue wearing a compression stocking to alleviate the pain and swelling associated with varicose veins.

Case 2

Baby girl Q requires daily dressing changes and special compression stockings used by burn patients. The family is distressed about the costs they must tolerate to provide appropriate dressings for their child, which are not covered by provincial health insurance. The ulcers are cleansed and debrided with appropriate topical antibiotics and dressings at the clinic. The family is advised to keep the dressings clean, change them on a regular basis and continue wearing the compression stockings.

COMMENTS

KTWS is an extremely rare condition (less than 1 in 200,000 persons³), and yet these two cases of mild and severe forms presented to the same family physician. Rare conditions provide an extra burden to the patient and their health care providers. As the name implies, they are "rare", and hence not part of mainstream health care management.

This may cause major financial barriers, as the patients' required treatment may not be covered by standard health care funding.

Several private and public organizations have produced online resources with user-friendly interfaces for searching and learning about rare disorders (Box 2). These websites not only provide information about the rare disorders, but also provide much-needed contact information for patient support groups. †

Rare Conditions Websites

- National Organization for Rare Disorders (NORD): www.rarediseases.org
- Canadian Organization for Rare Disorders (CORD): www.cord.ca
- National Institutes of Health: Office of Rare Diseases (ORD): rarediseases.info.nih.gov
- University of Kansas Medical Center, Medical Genetics: www.kumc.edu/gec/support
- Genetic Alliance: www.geneticalliance.org

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Author Biographies

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