Klippel-Trénaunay Syndrome

Nomenclature

Synonyms: Klippel-Trénaunay-Weber syndrome, angio-osteohypertrophy syndrome, naevus vasculosus osteohypertrophicus

Note: the term Klippel-Trénaunay-Weber syndrome has been variably used with different meanings:

- Synonymously with Klippel-Trénaunay syndrome.
- As a separate condition, also known as Parkes Weber's syndrome (limb enlargement with a high-flow capillary malformation and arteriovenous fistula).

Current consensus separates the names into Klippel-Trénaunay syndrome and Parkes Weber's syndrome, so as to distinguish between the two conditions. This is clinically relevant because their management and prognosis differ.

Definition

Klippel-Trénaunay (KT) syndrome is a rare condition, characterised by the triad of:

- Cutaneous capillary malformations - usually port-wine stains.
- Soft tissue and bone hypertrophy (occasionally hypotrophy) - usually of one lower limb.
- Varicose veins or venous malformations.

Varicosities and limb hypertrophy are not always present at birth and may take several years to manifest. Not all cases have the full triad of features. There is wide variation in the clinical manifestations of the condition. Some patients have complex features, including internal abnormalities.

The affected limb may also have abnormalities of lymphatic channels and drainage, along with arterial malformations. Blood flow through the capillary abnormalities in KT syndrome is low-velocity, in contrast to Parkes Weber's syndrome where there is a true arteriovenous malformation with high-velocity blood flow.

The condition may affect more than one limb, an internal organ or the head and neck. Visceral involvement is thought to be more common than previously supposed, occurring in perhaps 20% of patients.

Aetiology and epidemiology

The cause is is unknown. KT syndrome is extremely rare.

The condition appears to be sporadic, although there are reports of two families in whom the condition may have been inherited.

Presentation

Cutaneous capillary malformations

- The characteristic capillary haemangioma will be visible from birth in the vast majority of cases (98% in one series).
- The skin lesion has a characteristic 'port-wine stain' appearance, usually red-purple or bluish in colour (in contrast to that of Parkes Weber's syndrome which appears bright red).
Venous malformations and varicosities
- These are mostly superficial, but may involve muscle, bone or visceral organs, including the spleen, liver, pleura, bladder or colon.
- They may be extensive in the affected limb.
- They usually manifest when the child starts walking.
- There may be lymphatic hypoplasia or aplasia with resulting lymphoedema. This can complicate the condition and contribute to the limb enlargement.

Limb abnormalities
- Limb lengthening may present initially as gait disturbance.
- Limb hypertrophy is often greater distally. The digits may be affected, with macrodactyly, syndactyly, polydactyly or oligodactyly.
- An increase in limb girth may be the main feature if soft tissues rather than bones are predominantly affected.
- Rarely, the affected limb may show atrophy rather than hypertrophy.

Complications
- Psychological problems due to cosmetic appearance.
- Chronic venous stasis and its complications:
  - Venous dermatitis, venous ulcers.
  - Chronic paraesthesiae.
  - Venous thromboembolism (VTE).
  - Thrombophlebitis.
- Kasabach-Merritt syndrome (consumptive coagulopathy) can occur with large haemangiomas. [6, 7]
Visceral bleeding: \cite{3, 8}
- This ranges from occult to massive and life-threatening.
- It usually presents in childhood.
- The most common sites of gastrointestinal bleeding are the distal colon and rectum. Other sites, such as jejunal vascular malformations and oesophageal varices, are reported.
- Splenic haemangiomas may occur.

Genitourinary:
- Bladder lesions may cause frank haematuria (usually in childhood; recurrent and painless). \cite{3}
- Erectile dysfunction due to disturbance of venous function. \cite{9}

Orthopaedic complications:
- Gait disturbance.
- Scoliosis.
- Chronic pain in the affected limb.

- Haemangiomas of the liver, kidney, heart or lungs have also been reported. \cite{3}
- One reported case involved a cerebral haemangiopericytoma (a malignant vascular tumour). \cite{10}

Differential diagnosis \cite{11}
- Parkes Weber's syndrome (where there is a high-flow arteriovenous malformation rather than capillary haemangioma, as above).
- Other syndromes involving port-wine stains and high-flow shunts - eg, capillary malformation-arteriovenous malformations syndrome, Cobb's syndrome and CLOVES syndromes (Congenital Lipomatous Overgrowth, Vascular malformations, Epidermal naevi and Spinal/scoliosis/seizures/skeletal abnormalities).
- Sturge-Weber syndrome.
- Proteus' syndrome (rare hamartomatous disorder causing asymmetrical hypertrophy of a range of tissues, possibly afflicting Joseph Merrick, the so-called 'Elephant Man').
- Congenital lymphatic atresia or obstruction.
- Maffucci's syndrome (rare dysembryoplasia causing cartilage and vessel tumours).
- Kaposiform haemangioendothelioma.

Investigations \cite{3, 12, 13}
- Investigation of the vascular or lymphatic malformations - various methods may be used; for example:
  - Doppler ultrasound.
  - Angiography or MRI/CT angiography.
  - MRI or CT.
  - CT of the abdomen and pelvis may help to identify visceral haemangiomas. \cite{3}
  - Whole-body blood pool scintigraphy.
  - Lymphoscintigraphy may be used to assess the lymphatic system and the cause of limb-length discrepancy.

- Imaging of the bone and soft tissues of the affected limb, using plain X-rays, MRI or CT scan.
- If there is gastrointestinal bleeding, it may be difficult to locate the source by endoscopy, since the venous malformations can be widely spread. Angiography can be helpful for both diagnosis and treatment of these lesions and has been used to locate and treat severe bleeding in one reported case. \cite{8}

Management \cite{1}
There is no curative therapy. Management requires a multidisciplinary and individualised approach, aiming to ameliorate the patient's symptoms and correct the consequences of limb-length discrepancy. \cite{14}
Conservative measures

- Graduated compression garments help to reduce the effect of chronic venous insufficiency in the affected limb. Intermittent pneumatic compression pumps may also be used to the same effect. These help to reduce the effects of venous insufficiency but do not affect the ultimate size of the limb.
- Prophylaxis for VTE may be appropriate.
- Standard treatments for cellulitis or thrombophlebitis.
- Pain management.
- Contraception: oestrogen-containing contraceptives are contra-indicated where there is a history of VTE and should probably be avoided in KT syndrome because of the increased VTE risk (although there is no specific UK contraception guideline for this condition).
- Pregnant women with KT syndrome need careful monitoring due to a range of haematological, obstetric and anaesthetic complications.[15]

Active/surgical measures

- Laser treatment (pulsed dye laser) for cosmetic improvement of head and neck cutaneous lesions.
- Pre-operative assessment:
  - Detailed pre-operative assessment of the venous system is important because there may be associated hypoplasia of the deep veins.[13]
  - Careful anaesthetic assessment is required, including for possible consumptive coagulopathy.[7, 16]
  - Surgery for long bone fractures in the affected limbs is associated with high risk due to increased haemorrhage. This requires careful pre-operative planning, surgical technique and intra-operative/postoperative support.[17]
- Vascular interventions:
  - Treatment of the more severe venous malformations may include:
    - Sclerotherapy with foam or with alcohol.[18]
    - Vascular surgery such as:
      - Surgical stripping.
      - Phlebectomy.
      - Subfascial endoscopic ligation of perforating veins.[13]
      - Endovenous thermal ablation.[14]
      - Rarely, deep venous reconstruction.[13]
  - Gastrointestinal bleeds may require angiographic treatment - eg, selective arterial embolisation has been used in one case; or intra-arterial infusion of vasopressin has been suggested.[8] Surgical resection of the bowel may be required.[3]
  - For splenic haemangiomas, small ones (<4 cm) have been managed conservatively; splenectomy may be considered for larger lesions.[3]
  - Erectile dysfunction has been successfully treated by ligation of the affected veins.[9]
- Orthopaedic interventions:
  - Limb length discrepancy may be treated with orthoses or orthopaedic surgery, depending on its severity.
  - De-bulking surgery for grossly enlarged limbs is occasionally used but carries a significant risk of lymphatic and venous damage.
  - Amputation may be used in cases where a limb or digit is of little functional use and causes severe symptoms or complications.

Prognosis

- Life expectancy is largely normal, depending on the severity of the malformation and thus the likelihood of complications.[1]
- Possibly about 10% of patients develop a pulmonary embolism.

Further reading & references

- Klippel-Trenaunay-Weber syndrome; Geneva Foundation for Medical Education and Research
2. Klippel-Trenaunay Support Group
5. Klippel-Trenaunay-Weber Syndrome; Online Mendelian Inheritance in Man (OMIM)

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