Klippel Trenaunay syndrome
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Identity
Alias: Angio-osteohypertrophy syndrome
Note: Various disorders with varying combination of limb hypertrophy, vascular lymphatic malformation and other features like naevi include Klippel Trenaunay syndrome (KTS), Sturge Weber syndrome, Proteus syndrome and isolated hemihypertrophy are clinically distinct entities and need to be appropriately diagnosed.
Inheritance: Most cases of KTW syndrome are sporadic, through familial aggregations are reported. However, a strong doubt has been raised about familial cases as in most of these cases the family members may have isolated vascular naevi or varicose veins which are not uncommon in general population. Presence of cases with variable severity and locations of manifestations in family members can be explained by paradominant inheritance. It means a mutation is passed from one generation to another and heterozygous individuals are normal unless the other copy of the gene gets mutated. The mutation in other copy of the gene in early stages of embryogenesis might be giving rise to a clonal population of cells with homozygous for KTS mutation. This also explains mosaic pattern of lesions.

Fig 1a
Clinical photograph of a patient.
Thanks to Dr Shridevi Hegde [Clinical Geneticist, Bangalore, India] for Figure 1a and 1b.
**Clinics**

**Phenotype and clinics**

KTS syndrome consists of:
1. Combined vascular malformation of the capillary, venous and lymphatic types;
2. Varicosities of unusual distribution, in particular the later an various anomaly observed during infancy or childhood and;
3. Limb enlargement.

The lower limb is involved in about 95% of patients while upper limb involvement is seen in 5% of cases. Rarely only the trunk is involved. Capillary malformations are seen as pink to bluish macular lesions of varying sizes (Fig 1).

There is hypertrophy of soft tissue and bones of the involved limb. Venous varicosities develop in about 80% of patients. Lymphatic involvement is seen as lymphatic vesicles on the surface of cutaneous capillary malformation and there may be ooze of lymph. Varicosity of veins in KTS is different from the commonly occurring varicose veins. It appears in infancy or early childhood and lateral venous anomaly is seen in 80% of cases. A prominent vein seen on the surface of capillary malformations is known venous flares. The deep veins may be involved and the defects of deep veins include agenesis, atresia, hypoplasia, vascular incompetence, aneurismal dilatation (Fig 2).

Arteriovenous malformation are not seen and in presence of such high flow lesion a label of Park Weber syndrome is given as suggested by Cohen, Jr (2000). Presence of involvement of face and leptomeninges is characteristic of Sturge Weber syndrome. But cases with features overlapping with KTS and Sturge Weber syndrome are seen.

**Neoplastic risk**

Not known to be increased. Eleven tumours have been reported in KTS till 2005. This low number indicates very low risk of tumourogenesis. Lapunzia (2005) has recommended annual physical examination and minimal follow-up.

**Treatment**

No definitive treatment is possible. Treatment primarily remains to be non surgical. Imaging studies like contrast enhanced MRI, ultra-sonography and Doppler study may be needed for documentation of vascular lesions for diagnostic purposes. These studies also help to delineate the extent of lesion and plan interventions if indicated. The active intervention needs to be attempted only for localized lesions or in case of serious complications like bleeding or cardiac failure. Vascular interventions do not affect the limb hypertrophy. Discrepancy in limb length may need to be taken care by special shoes. Many cases may have significant problems due to limb hypertrophy, which may be difficult to be corrected by surgical procedure. The same may be cause of cosmetic issues in many cases.

**Evolution**

There is increase in the size of vascular malformation proportionate to the increase in the size of involved limb. Ulcerations, thromboembolic phenomenon, Kasabach-Meritt syndrome (thrombo-cytopenia due to conceptive coaguloapthy) are described. Bleeding from rectum, uterus etc may occur depending on the location of vascular lesions. Cardiac failure may occur if there is associated high flow lesion in cases which are labeled as Park Weber syndrome.

**Cytogenetics**

**Note**

Reciprocal translocations t(5;11) and t(8;14) and ring chromosome of 18 are reported in association with KTW syndrome.

**Genes involved and proteins**

**Note**

No genetic defect has been identified yet. By studying the break points of translocation between chromosomes 8 and 14, Tian et al (2004) identified VG5Q gene.
which was considered to be a susceptibility gene for KTS syndrome. But the change E133K in VG5Q observed in 5 of 130 cases of KTS syndrome was found to be a polymorphism by other studies.

References


This article should be referenced as such: