Denouement and Discussion

Klippel-Trénaunay Syndrome

Klippel-Trénaunay syndrome (KTS) is a rare disorder characterized by the triad of port-wine stain, hypertrophy of bone and soft tissue, and varicose veins or venous malformations. The syndrome was described in 1900 by French physicians Klippel and Trénaunay.[1] In 1907, Weber[2] noted similar findings in association with arteriovenous malformations.

The diagnosis of KTS can be made when any 2 of the 3 features are present. Jacob et al,[3] in a study of 253 patients with KTS, observed that 63% of the patients had all 3 features and that 37% had 2 of the 3 features. Port-wine stain has been observed in 98% of patients, varicosities or venous malformation in 72%, and limb hypertrophy in 67%.

The exact cause of KTS is unknown, although several theories exist. Most cases are sporadic, and a few cases could be of autosomal dominant inheritance. A new theory of paradominant inheritance was suggested in a study of monozygotic twins.[4] A novel mutation in the *RASA1* gene (OMIM139150) was found in KTS.[5]

No racial or sex predilection for KTS has been documented. The syndrome is present at birth or develops during early childhood and generally affects a single extremity. The lower extremity is the most commonly affected site (95% of patients), followed by the arms and the trunk.

The most common manifestation is capillary hemangioma or port-wine stain. Usually the hemangioma has a distinct border that follows the midline and is generally noted on the lateral aspect of the limb. Typically, the capillary vascular malformation does not progress or it regresses with time. The hemangioma can have cutaneous or deep involvement (osseous and muscular). Visceral organs such as spleen, bladder, liver, pleura, and gastrointestinal tract may also be affected.[6] Involvement of the gastrointestinal tract has been described in 20% of patients; bleeding of the distal colon and rectum is the most common symptom. Genitourinary involvement (hematuria) also may be noted in KTS.

Varicosities or venous malformations often spare the saphenous distribution, sometimes in the pelvic region. Varicose veins can be superficial, deep, or perforating. Venous stasis results from valvular insufficiency, obstructed venous outflow, or abnormal lymphatic drainage.

Bony and soft-tissue hypertrophy is another feature of KTS; increased length and circumference of the affected extremity are typical. Hypertrophy may be present at birth and progresses with time. Complications of KTS include stasis, bleeding, ulcerations, dermatitis, cellulitis, thrombophlebitis, pulmonary emboli, and abnormalities of the vertebral column.

The diagnosis of KTS is made on the basis of clinical history and findings at physical examination. Typical hemangioma associated with bony and soft-tissue hypertrophy or abnormal venous structure is sufficient for the diagnosis. A skin biopsy specimen of the hemangioma is unnecessary for the diagnosis.

If complications are present or suspected (eg, deep venous thrombosis), imaging studies such as color Doppler ultrasonography and magnetic resonance imaging can be useful. Radiographic examination can be used to define bony hypertrophy and to measure the difference in the length of the affected extremity. Imaging studies of the abdomen are required to rule out a vascular malformation in the perineum or abdomen.[7] The most common differential diagnoses are Parkes Weber syndrome and proteus syndrome.

Medical treatment of KTS is conservative and symptomatic. Some patients with KTS have severe pain in the affected limb.[8] A multidisciplinary approach is necessary when complications are present. Compression garments are required to treat chronic venous insufficiency and lymphedema. Cellulitis and thrombophlebitis are treated with elevation, compression, and analgesic and antibiotic therapy. Skin hygiene is useful in preventing cellulitis. In women with KTS, it is recommended that, to prevent deep venous thrombosis, estrogen-containing contraceptives not be used.

In addition to medical treatment, if limb discrepancies are present, surgical orthopedic procedures may be considered to prevent functional and psychologic disabilities; laser treatment of the skin lesions could be useful in treating the superficial component of the hemangioma to improve its color. Surgical treatment of varicosities is controversial. Yearly clinical follow-up of patients with KTS is recommended, with more frequent follow-up if clinically indicated.

Insofar as long-term outcome, hypertrophy of the limb is the most common problem, often impairing function and affecting mobility. All children with KTS must be monitored for growth abnormalities. An important issue is pain, which can worsen and seriously affect quality of life[8] and requires psychologic support. When the limb is grossly enlarged, amputation may rarely be required.[9]

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