



Pediatric Patient with Klippel-Trenauney-Weber Syndrome and Clubfoot - Case Report

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Abstract

A congenital deformity that causes limb overgrowth in childhood has multiple genetic and environmental etiologies. One of them is the Klippel-Trenauney-Weber syndrome (SKT), a rare condition characterized by blood vessel, soft tissue and bones abnormalities, which may affect structures like fingers toes or the whole limb, and may worsen preexisting deformities such as clubfoot. We present the case of a 9-year-old patient with SKT and congenital clubfoot.

Keywords: Klippel-Trenauney-Weber; Paediatric; Vascular malformation; Angiodysplasia; Limb overgrowth; Clubfoot

Introduction

SKT is a rare congenital disease characterized by the triad of varicose veins, capillary malformations and hypertrophy of soft tissue and bone. This can cause limb overgrowth and deformities mainly in fingers and toes and may present life-threatening vascular complications. Its etiology is unknown. The treatment is multidisciplinary, intended to improve quality of life, surgical correction of deformities, attend complications and avoid sequels. We present the case of a 9-year-old patient with SKT and congenital clubfoot.

Case Report

A 9-year-old female patient with no relevant family history. Since the age of 6 she presented asymmetry of the lower extremities and clubfoot, edema of the left pelvic limb and claudication. In 2011, surgery was performed to correct the clubfoot, however, it persisted along with the asymmetry and the claudication, getting worse with time. On physical examination, the left pelvic limb was 4 cm larger compared to the right. An increase in volume was also noted mainly in the leg and ankle, due to the muscles, lymphatic vessels and varicose veins abnormalities. Port-wine stains were observed on thorax, left leg and abdomen. In addition,

a “cafe-au-lait” skin stain was seen on the same leg (Figure 1). Angio-CT scan of pelvic limbs reported multiple varicose venous malformations and arterio-venous fistulas in the left pelvic limb, with early venous filling, and soft tissue and bone hypertrophy, suggestive of SKT (Figure 2). Genetic studies reported 46 XX genotype without numeric or structural chromosomal abnormalities. Biopsy of the “cafe-au-lait” skin stain was taken from the left leg to rule out neurofibromatosis discarding this diagnosis because none were found. Other diagnostic possibilities associated with limb overgrowth such as Beckwith-Wiedemann, Soto or Proteus syndrome were also excluded. With all the previous data, the diagnosis of SKT was confirmed.

To correct the asymmetry of the pelvic limbs, an epiphysiodesis of the left distal femur was performed. An anterior and posterior Blump’s staples were placed between the diaphysis and the metaphysis temporarily to improve symmetry by slowing bone growth (Figure 3). Six months later, to correct completely the asymmetry, proximal distal and tibial femoral epiphysiodesis and clubfoot plasty were performed. The patient evolved adequately; the clubfoot was completely corrected. With physiotherapy she improved her walking. During follow-up, the patient's growth was assessed and the asymmetry was corrected. To preserve symmetry, further epiphysiodesis of the right limb was proposed

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if needed. Currently, the patient is walking normally, without pain and performing her daily activities without difficulties. She attends medical consultation for follow-up and periodic examinations to detect other possible complications of SKT.



Figure 1: Discrepancy of 4cm in length between lower extremities, with increased muscle mass and port-wine stain in the left limb, and a “cafe-au-lait” skin stain in the same leg.

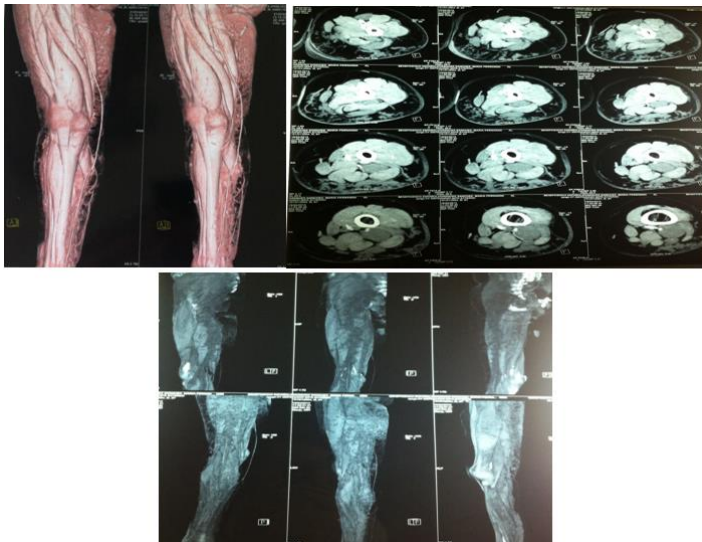


Figure 2: Angio-CT scan with soft tissue hypertrophy and multiple venous malformations.



Figure 3: Epiphysiodesis with Blump's staple placement.

Discussion

SKT is a rare congenital disease of unknown cause, characterized by a triad that consists of vascular malformations mainly of the deep venous system and capillaries, skin color changes (port-wine stain) in up to 80-98% and varicosities in 70-80% of cases [1].

These are the most frequent clinical manifestations and the causes of most of the life-threatening complications. These anomalies affect the extremities causing hypertrophy of muscle, lymphatic, fat and bone tissue. They usually occur in only one limb, although in rare cases it can affect two at the same time. The main symptoms are pain and walking abnormalities. Overgrowth of the limb, hypertrophy and muscular and tendon flaccidity can cause or worsen other associated deformities such as clubfoot like the case of the patient reported here, and should be taken into account for the complete management of this problem [2,3].

The frequency of this pathology is unknown; however, it has been reported in 1: 100,000 live births [4]. In patients with a first-degree family history it increases up to 1: 880 [5]. Although it can affect both men and women, “it seems to have certain predilection for men” goes Ceballos et al. [6] mentioned that many cases of SKT are de novo since there are no first-degree relatives with a diagnosis of this disease. However, in those in which the disease has been traced in the family tree, the presence of an autosomal dominant pattern has been demonstrated. This suggests that it may be caused by a genetic defect in homozygous patients. The association with angiogenic factors such as the AGGF1 and PIK3CA genes related with vascular and lymphatic overgrowth seems to be of relevance [7]. This disease can be associated with other genetic syndromes that affect the skin and vascular system such as neurofibromatosis [8]. In this patient who had suggestive lesions that looked like “cafe-au-lait”, neurofibromatosis was ruled out.

The etiology is still unknown. There are theories that point to an alteration during fetal growth, in the process of development of vascular structures. These alterations usually manifest themselves in childhood or adolescence. They may be limited to the skin, subcutaneous tissue or muscles, however, in some cases they affect all these areas causing progressive deformities especially in lower extremities. The most frequent and serious complications are disseminated intravascular coagulation (DIC) 88% and pulmonary thrombosis in 10%, which are linked to the vascular malformations. Bleeding from the digestive tract has also been reported [9,10]. The disorders that are associated with the limb overgrowth in pediatric patients have a multifactorial etiology. There are endocrine, nutritional and environmental factors, with different genetic causes such as those identified in other pathologies classified overgrowth syndromes in those with vascular involvement such as SKT, and those with only somatic components [11]. The overgrowth of soft and bone tissue caused by abnormal vascular proliferation causes the increase in volume, diameter and length of the limb. Among all the malformations mentioned in the literature caused by this disease, limb deformities have been reported between 50 and 94%, with the lower extremities being the most affected in up to 95% of cases unilaterally. Vascular malformations with venous and lymphatic

hypertension that cause alterations of the extremities may be present since intrauterine life.

McGrory et al. reported in a series of 108 patients the deformities in the SKT. Most of them were found in fingers and toes such as macrodactyly, syndactyly, polydactyly or clinodactyly. Other deformities reported were, five patients with idiopathic scoliosis, one with clubfoot and other with flat foot and patellar subluxation, one patient with congenital hip dislocation, another with knee hemartrosis, another with carpal tunnel syndrome and one with Ehlers-Danlos syndrome [12]. Due to the type of associated pathologies in SKT that have been found in some case reports and series such as the one mentioned above, a hypothesis that a collagenopathy could be associated with SKT can be made since most of these pathologies may have a defect of this protein, possibility that has been not studied yet as far as we know. Collagen abnormalities as proposed in one of the new theories of the pathogenesis of the clubfoot, such as "fibrous retraction," may be involved [13]. The diagnosis of this disease is possible in the presence of the mentioned clinical signs. Especially when the vascular malformations, the port-wine skin stain, the presence of varicose veins, the overgrowth of a limb, or the complete triad that characterizes this disease is present, supported by imaging studies. The most helpful studies for diagnosis are the Doppler ultrasound to evaluate vascularity abnormalities, complemented with contrasted computed angio-tomography to assess the extent of the problem and magnetic resonance with gadolinium to distinguish lymphatic malformations. The limbs length asymmetry can be evaluated with plain X-rays [14]. There is no definitive cure for SKT. The management of this problem must be multidisciplinary, aiming primarily to improve the quality of life and functionality, and to prevent or treat the complications such as coagulopathies. As a treatment for capillary lesions, laser therapy is recommended, especially if the lesions are on face and trunk. For the treatment of varicose veins and lymphedema in the extremities, compression stockings or sclerotherapy are useful. Anti-angiogenic medications are promising for the treatment of vascular malformations and the reduction of complications [1]. Surgery is indicated in patients with symptoms or complications associated with this problem that cannot be solved with conventional treatment. If complications such as exaggerated limb growth in both length and volume, coagulopathies, incoercible bleeding or deformities that cannot be corrected with medical or surgical treatment, limb amputation may be indicated. To treat the overgrowth and asymmetry of the limbs, corrective surgery is necessary. Epiphysiodesis is one of the most used procedures when the asymmetry is greater than 2 cm as in the case of this patient [15].

Conclusion

SKT is a rare disease, difficult to diagnose, which should be suspected in the pediatric patient presenting vascular abnormalities and limb deformities, to implement appropriate early prevention measures and avoid complications. In some cases, such as the one reported here, they can be associated with other malformations such as clubfoot that can be treated with opportune surgery.

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