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Klippel-Trénaunay Syndrome and Angiokeratoma: Case Report of a Rare Condition

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Abstract **Case Report**

***Introduction*:** Klippel-Trénaunay syndrome is a rare congenital vascular disorder characterized by a triad of cutaneous capillary malformations, varicosities and hypertrophy of soft tissues and overgrowth bones. Among the cutaneous malformations are angiokeratomas, which appear as a papule from 2 to 10 mm in diameter, usually dark red in color, although they may be blue or black, and their surface is keratotic on palpation. Angiokeratomas pose a therapeutic challenge, especially in cases of multiple or extensive lesions. Laser modalities have demonstrated efficacy and may be successful treatment options. ***Clinical Case*:** A 13-year-old male patient with a clinical history of Klippel-Trénaunay syndrome diagnosed at birth. He came to the outpatient services because he presented dermal nodular lesions at the inguinal region, painful on palpation, with a duration of one week. In addition, he had an increase in diameter of the left lower limb with multiple varicose veins, ochre dermatitis on the inner side of his left leg. On the right lower limb there are violaceous patches with the presence of euchromic papules grouped together, of hard consistency at the left knee region. He also presents multiple violaceous keratotic papules on the scrotum, thigh and left knee bleeding on manipulation and trauma. Skin excision was performed in the right inguinal region for biopsy, which reported macroscopically fibrous, multinodular element measuring 0.7x0.5x0.3cm, whitish surface of firm consistency and whitish heterogeneous surface upon sectioning. Microscopic inspection was carried out with hematoxylin and eosin technique, which reported skin with epidermis showing acanthosis, hyperkeratosis, papillary dermis with congestive dilated vessels, negative for malignancy and compatible with angiokeratoma. Among the treatment options, it was decided to initiate CO2 laser therapy with satisfactory results. ***Conclusions*:** Klippel-Trénaunay syndrome is an extremely rare vascular pathology of genetic origin, associated with mutation in the PIK3CA gene. Its association with the presence of angiokeratomas is infrequent, making its treatment even more difficult and it generally has a poor evolution. Different types of treatment have been proposed, among which surgical excision, cauterization and cryotherapy of angiokeratomas stand out. However, the results are not encouraging due to the high risk of complications. Currently, laser therapy of different types has become an option with good results. In our case, carbon dioxide laser was used, with which a good response was obtained.

Keywords: Klippel-Trénaunay syndrome; vascular malformations; angiokeratoma.

INTRODUCTION

Klippel-Trénaunay syndrome is a rare and sporadic congenital disorder characterized by the classic triad of Port Wine Stains, varicose disease plus bone and soft tissue hypertrophy. Some vascular malformations may be associated with other anomalies, such as tissue overgrowth. The PIK3CA-related overgrowth spectrum (PROS) is a group of rare genetic disorders with asymmetric overgrowth caused by somatic mosaic

mutations in the PI3K-AKT-mTOR pathway that encompasses a heterogeneous group of rare disorders that are associated with the occurrence of overgrowth. Cloves syndrome and Klippel-Trénaunay syndrome are PROS diseases [1]. Symptoms of Klippel-Trénaunay syndrome include pain, swelling, lymphedema and bleeding, venous involvement can produce symptoms of superficial thrombophlebitis and deep vein thrombosis. In most cases, a complete history and clinical examination are sufficient for the diagnosis of Klippel-Trénaunay syndrome. However, when certain complications occur, non-invasive imaging techniques are used for the diagnosis and evaluation of the disease in patients [2].

CLINICAL CASE

A 13-year-old male patient with a clinical history of Klippel-Trénaunay syndrome diagnosed at birth. He came to the outpatient services because he presented dermal nodular lesions at the inguinal region, painful on palpation, with a duration of one week. In addition, he had an increase in diameter of the left lower limb with multiple varicose veins, ochre dermatitis on the inner side of his left leg.

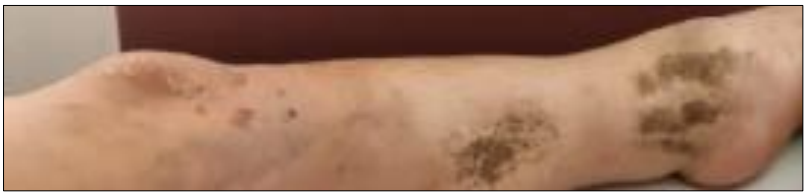

Figure 1: Lymphedema is observed at the calf region in addition to ocher dermatitis.

On the right lower limb there are violaceous patches with the presence of euchromic papules grouped together, of hard consistency at the left knee region. He also presents multiple violaceous keratotic papules on the scrotum, thigh and left knee bleeding on manipulation and trauma.

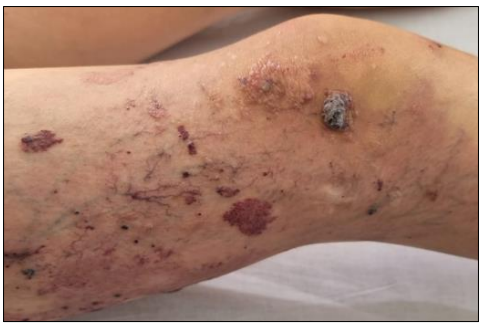

Figure 2: Presence of violaceous patches on the right lower limb and papules.

Figure 3: Presence of multiple violaceous keratotic papules on the scrotum, presence of isolated papules, some of them pedunculated on the right inner thigh.

Skin excision was performed in the right inguinal region for biopsy, which reported macroscopically fibrous, multinodular element measuring 0.7x0.5x0.3cm, whitish surface of firm consistency and whitish heterogeneous surface upon sectioning. Microscopic inspection was carried out with hematoxylin and eosin technique, which reported skin with epidermis showing acanthosis, hyperkeratosis, papillary dermis with congestive dilated vessels, negative for malignancy and compatible with angiokeratoma.

Among the treatment options, it was decided to initiate CO2 laser therapy with satisfactory results.

DISCUSSION

Klippel-Trénaunay syndrome is uncommon and there is still no consensus on the correct approach to its investigation and treatment. It was first described as a single pathological entity by Klippel and Trénaunay in 1900. Unlike Parkes Weber syndrome, the involved tissues do not contain hemodynamically significant arteriovenous communications, but other soft tissue, lymphatic, and bony abnormalities are often present [3].

It belongs to a spectrum of limb overgrowth syndromes (PROS), with whose members it shares many similarities. Genetic research has confirmed that a mutation in the PIK3CA gene has been implicated in Klippel-Trénaunay syndrome associated and members of the related limb overgrowth spectrum (PROS). The existence of other genes such as the RASA-1 gene in Parkes Weber syndrome and AKT1 gene in Proteus syndrome has been noted, allowing researchers a better and more detailed understanding of the role of molecular genetics in this type of pathology [4].

It can be diagnosed, clinically by an experienced physician, as it is a disease of recognition, based on distinct clinical findings and specific features on multimodality imaging. The observation of a triad of cutaneous capillary malformations, varicosities and hypertrophy of soft tissues and overgrowth bones are characteristics of this pathology. Furthermore, although this classic presentation is usually seen in a single extremity, multiple and even full body cases have been described [5].

As we can see in our patient, the physical examination reveals varicosities in the extremities and multiple cutaneous manifestations, which he has developed since childhood. Capillary malformations correspond in most cases with the so-called Port Wine Stains predominantly in the lower extremity, being more infrequent the involvement of upper limbs and the trunk. Lymphedema may be observed. It is necessary to know the possible complications associated with this syndrome, such as bleeding from abnormal vessels in the digestive or genitourinary tract, as well as local and systemic thrombotic phenomena [6].

Angiokeratoma is a relatively rare vascular malformation. The current classification of angiokeratomas distinguishes between localized and systemic forms [8]. It presents clinically as a papule from 2 to 10 mm in diameter, usually dark red, sometimes blue or black, whose surface is keratotic on palpation. Histologically, these are dilated subepidermal vessels associated with epidermal hyperplasia such as acanthosis or hyperkeratosis. These lesions are usually asymptomatic, but are at risk of hemorrhage, thrombosis and repetitive trauma [7]. Our patient presents angiokeratomas in the inguinal region, thigh and knees, which produce bleeding upon frictional trauma.

Depending on the type of vessel involved and its flow characteristics, Klippel-Trénaunay syndrome is classified as a slow flow complex combined capillary venous or capillary venous lymphatic malformation.

Traditional treatment options for angiokeratomas include surgical excision, cauterization and cryotherapy. However, these methods may result in hemorrhage, atrophy and abnormal scarring, especially in cases of large or multiple lesions [5]. The use of several laser modalities has been described as treatment alternatives as promising options for angiokeratomas, including argon laser, pulsed dye laser, copper vapor laser, potassium titanyl phosphate laser, carbon dioxide (CO2) laser [9].

Angiokeratomas can pose a therapeutic challenge, especially in cases of multiple or extensive lesions. The included laser modalities have demonstrated efficacy and may be suitable treatment options. However, understanding of the relative efficacy of these lasers is currently limited [9]. Our patient, after undergoing carbon dioxide laser treatment sessions, showed improvement of the discomfort, being in this case an effective treatment.

CONCLUSIONS

Klippel-Trénaunay syndrome is an extremely rare vascular pathology of genetic origin, associated with mutation in the PIK3CA gene. Its diagnosis is usually clinical with the observation of classic signs. Its association with the presence of angiokeratomas is infrequent, making its treatment even more difficult and it generally has a poor evolution. Different types of treatment have been proposed, among which surgical excision, cauterization and cryotherapy of angiokeratomas stand out. However, the results are not encouraging due to the high risk of complications. Currently, laser therapy of different types has become an option with good results. In our case, carbon dioxide laser was used, with which a good response was obtained. However, further studies are required to evaluate long-term evolution as well as the risk of recurrence.

Conflict of Interest: We, the authors, declare that we have no personal, financial, intellectual, economic, and corporate conflicts of interest.

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