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Case Report

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Klippel-Trenaunay-Weber syndrome complicated with cerebral venous thrombosis

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ABSTRACT

Klippel-Trenaunay-Weber syndrome is a rare and little known congenital disease among physicians, characterized by vascular stains, soft tissue and bone asymmetric hypertrophy, varicose veins, lymphedemas, and arteriovenous fistulas. Alterations in the vascularization of the central nervous system are rare in these cases. This article presents the case of a 32-year-old puerperal black woman, with a history of recurrent lymphangitis, chronic right lower limb lymphedema since childhood, and treatment with oral contraceptives, who came to the Emergency Room presenting left-side hemiparesis and hypoesthesia. Physical examination showed motor and sensory defect, as well as flat hemangioma in the plantar face of the left foot, and right hemi-body hypertrophy. Computed axial tomography and magnetic resonance imaging evidenced the presence of cerebral venous thrombosis and arteriovenous malformation in the right parieto-occipital region.
Key words: Klippel-Trenaunay-Weber syndrome, Intracranial sinus thrombosis, Arteriovenous Fistula, Skin abnormalities

Síndrome de Klippel-Trenaunay-Weber complicado con trombosis venosa cerebral

RESUMEN

El síndrome de Klippel-Trenaunay-Weber es una enfermedad congénita rara y poco conocida entre los médicos que se caracteriza por manchas vasculares, hipertrofia asimétrica de tejidos blandos y huesos, várices, linfedemas y fístulas arteriovenosas. Las alteraciones en la vascularización del sistema nervioso central en estos casos son poco frecuentes. En este artículo se presenta el caso de una puérpera de 32 años de edad, color negro de piel, con antecedentes de linfangitis a repetición, linfedema crónico del miembro inferior derecho desde niña y tratamiento con anticonceptivos orales, que acude al Cuerpo de Guardia por presentar hemiparesia e hipoestesia del hemicuerpo izquierdo. Al examen físico se constata el defecto motor y sensitivo, así como hemangioma plano en la cara plantar del pie izquierdo e hipertrofia del hemicuerpo derecho. La tomografía axial computarizada y la resonancia magnética nuclear evidenciaron la presencia de trombosis venosa cerebral y malformación arteriovenosa en región parieto-occipital derecha.
Palabras clave: Síndrome de Klippel-Trenaunay-Weber, Trombosis de los senos

INTRODUCTION

Klippel-Trenaunay-Weber syndrome (KTWS) is defined by a clinical triad: 1) Skin alteration: vascular stain, 2) Tissue alteration: soft tissue and bone asymmetric hypertrophy, 3) Circulatory and lymphatic system alteration: varicose veins and lymphedemas[1,2].

The disease pathogenesis is unknown; however, genetic factors are presumed to be involved in the recent discovery of mutations in the RAS1 and PIK3CA genes that cause somatic mosaicisms[2,3].

French doctors Maurice Klippel and Paul Trénaunay described this disease for the first time in 1900. Years later, Parkes Weber published the case of a patient with similar manifestations accompanied by arteriovenous fistula[4,5].

This syndrome is a rare clinical condition, with a prevalence of approximately 1 per 20-40,000 live births[4,5]. In the literature consulted, there are few published cases in Cuba, and until now there is none in the province of Villa Clara.

CASE REPORT

A 32-year-old female, black skin, with a history of recurrent lymphangitis, chronic right lower limb lymphedema since childhood, and treatment with oral contraceptives for 9 years. Obstetric history of two previous uncomplicated pregnancies and a third cesarean delivery at 38 weeks' gestation, 17 days before her current hospital admission. On this occasion she went to the Emergency Room at "Arnaldo Milián Castro" Hospital for presenting a sudden onset of «numbness» and «weakness» of the left

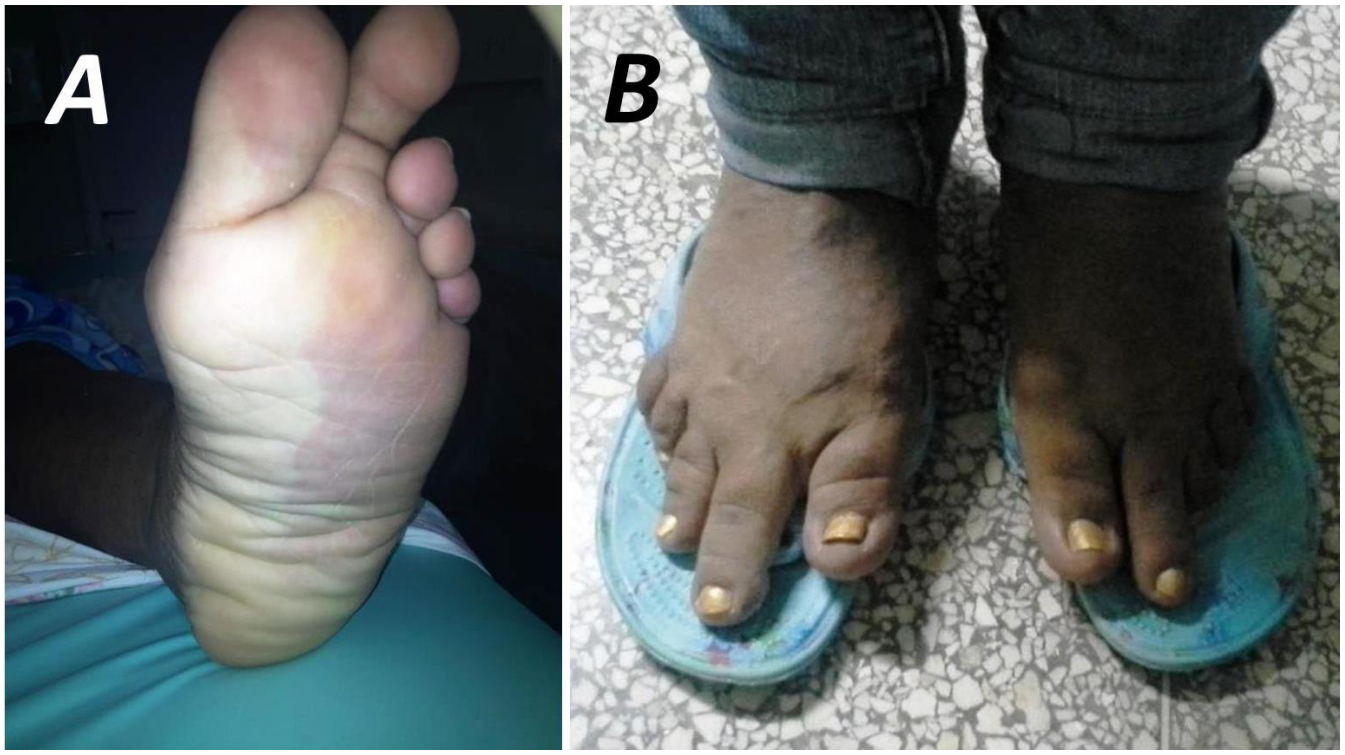

Figure 1. A. Plantar face of the left foot of the patient affected by flat hemangioma. **B.** Image showing right lower limb hypertrophy and macrodactyly of the second toe in both feet.

hemibody, so it was decided to admit her in the Neurology Department for better study and treatment.

Physical examination

Skin: A violaceous spot covering the hemithorax and the inner side of the right arm, that which respects the midline. Vascular spot on the left foot, well defined, flattened edges, occupying the plantar side of the first finger, half of the plant, the metatarsal region, and respects the calcaneus of that foot. It clinically corresponds with flat hemangioma (**Figure 1A**).

Infiltration of the subcutaneous tissue of the right lower limb and hypertrophy of the right upper and lower extremities, and macrodactili of the second toe of both feet, were detected (**Figure 1B**). An exploration of the nervous system revealed left-side hemiparesis and hypoesthesia.

Table. Most representative values of blood count and biochemistry.

Complementary	Result
Hematocrit	0.39
Leukocytes	$8x10^9$/L
- Neutrophils	0.69
- Lymphocytes	0.30
- Eosinophils	0.00
Capillary glycemia	4.46 mmol/L
Urea	77 mmol/L
Platelet count (macro-platelets)	200 x 10^9/L
Coagulation time	8 minutes
Bleeding time	1 minute
Prothrombin time	Control: 14 Patient: 15
Thromboplastin time partial activated	Control: 29 Patient: 32
Coombs test	Negative
Lupus Anticoagulant	Negative
C-reactive protein	Positive
Addis Count	
- Proteins	0.00 mg/min
- Leukocytes	2800 /min
- Red blood cells and cylinders	0.00 /min

Complementary

- Blood count and biochemistry: Are shown in the **table**.
- Peripheral blood smear: Normocytic and normochromic red blood cells, normal leukocytes, and giant platelets.
- Computed axial tomography of the skull: Slight right parieto-occipital hypodensity, with subarachnoid space effacement, as well as loss of the gray/white matter ratio and effacement of the circumvolutions at this level. Ventricular asymmetry, due to the greater size of the right lateral ventricle, no hydrocephalus, no bone lesion, and normal posterior fossa. No alterations in the rest of encephalic structures.
- Magnetic resonance imaging of the skull: Variable intensity image in the right parieto-occipital region, with signal annulment in its interior, measuring approximately 42x28mm axially, with associated vasogenic edema and little mass effect, which weakly restricts HASTE diffusion probably related with arteriovenous malformation. In the TOF sequence, the absence of a right transverse sinus signal, compatible with probable thrombosis, is striking. Transverse left and upper sagittal sinuses are shown to be permeable (**Figure 2**).

COMMENT

It is a rare disease and may lead to inadequate follow-up and delay in diagnosis, including delay or failure to detect possible associated manifestations that may lead to a potentially preventable functional limitation in the patients[6]. The patient in question reached adulthood presenting the classic symptoms and signs of this disease, but she had not been correctly diagnosed.

Cerebral alterations found in KTWS include: hemorrhages, infarcts, hemimegacephaly, cavernomas, aneurysms, hydrocephalus, choroidal plexus abnormalities, atrophy, calcifications, cortical dysplasia, seizures and arteriovenous malformations[2].

Cerebral venous thrombosis usually occurs in women between 20 and 25 years of age, especially during pregnancy (12%), puerperium (60-80%), and

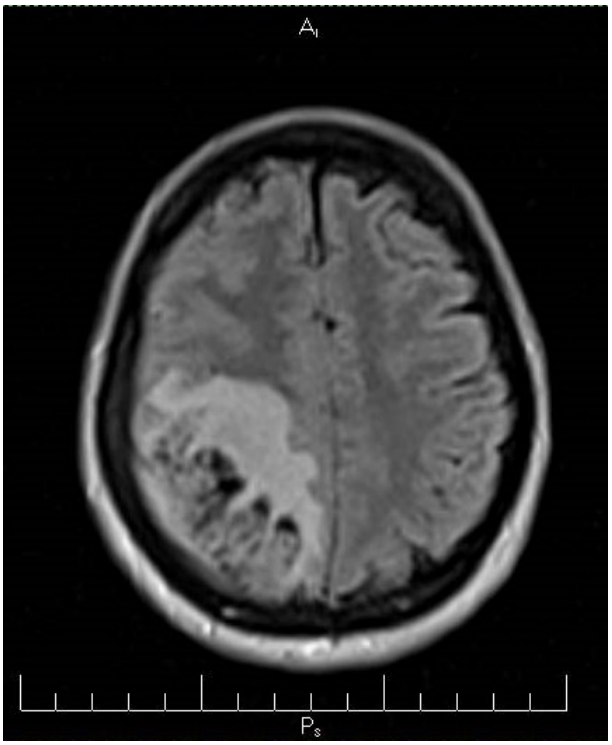

Figure 2. Magnetic resonance imaging of the skull (T2 Flair) showing a variable intensity image in the right parieto-occipital region, with signal annulment in its interior and associated vasogenic edema, in relation to arteriovenous malformation.

in oral contraceptive users, who present a risk increased by 30%[7]. In this case, besides presenting these risk factors, clinical manifestations and imaging findings (computed axial tomography) suggested the presence of cerebral venous thrombosis, and a possible cerebral arteriovenous malformation was suspected, which was confirmed by performing a magnetic resonance imaging.

KTWS cases presenting alterations in the central system vascularization are extremely rare. Angiomatosis and arteriovenous malformations have been reported in the spinal cord, oblongata and cerebellum[8,9].

It is important to mention that arteriovenous malformations usually increase in size together with the patient's growth, but they may have a rapid development precipitated by hormonal factors (puberty, pregnancy, hormonal therapy), trauma, infections or surgery[10], data of particular importance in the clinical context of the case presented.

This clinical case highlights the importance of exhaustive medical and physical examination, allowing the association of skin, tissue, and vascular lesions with a KTWS diagnosis. When patients suffering this disease present neurological symptoms, even in the presence of other vascular risk factors that justify the clinical setting, clinical consensus should guide to discard, through imaging studies, the presence of arteriovenous malformations in the central nervous system

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