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Image in Medicine

Proteus syndrome: case report

Síndrome de Proteus: relato de caso

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Proteus syndrome is a rare hamartomatous syndrome, a congenital disorder of genetic origin. It was first described in 1979 by Cohen and Hayden¹ as a hamartoma syndrome, and was subsequently named "Proteus syndrome" in 1983 by Wiedeman.² The syndrome has characteristic malformations caused by an excess and multifocal growth of tissue derived from all three germ layers, which determine partial gigantism of the limbs, pigmented nevi, subcutaneous tumors, macrocephaly, and visceromegalies, but normal mental development.²⁻⁴ Lindhurst et al. confirmed that the syndrome was genetically inherited in 2011, after performing the genetic sequencing of 29 patients with the syndrome and finding a somatic mutation in the AKT1 oncogene, thus demonstrating the presence of somatic mosaicism for a mutation that is lethal in the non-mosaic state. It was also demonstrated that a dysfunction in the PI3K-AKT pathway is related to the overgrowth.⁵

This article reports a case of Proteus syndrome in a 24-year-old female patient. This is a unique case in the family, whose onset started at birth with epidermal nevi located in the right upper limb and trunk. During childhood, the patient experienced disproportionate growth of the limbs, which currently show hemihypertrophy of the left leg due to lipomatous overgrowth and of the right arm due to a vascular malformation, shown in Figures 1 and 2, respectively. This asymmetric hemihypertrophy resulted in scoliosis, with consequent upper and lower back pain.

The arm shows a few lymph vesicles and hardened nodules – likely foci of thrombosis in this limb, which are characterized by foci of vascular channels in Figure 2. The patient presents splenomegaly as a visceral abnormality, shown in Figure 3. Neuropsychomotor development is normal. The syndrome diagnosis was established by the abovementioned clinical findings associated with lesion presentation pattern, which are: mosaic distribution, progressive course, and sporadic occurrence. The patient came to the clinic complaining of heaviness in the right arm, and is being followed by a multidisciplinary team that includes genetic services, plastic surgery, orthopedics, vascular surgery, and diagnostic imaging. The proposed surgical treatment consists of partial correction of the deformities, including amputation of the right arm and splenectomy. The patient and family are considering the possibility of having them performed, as they have been informed of the surgical risks of bleeding and vascular complications.

The remarkably high variety of clinical manifestations of Proteus syndrome predisposes to difficulties in attaining a diagnosis. The diagnostic criteria for Proteus syndrome were reviewed by Biesecker et al. in 1999. The mosaic distribution pattern of the lesions, progressive course, and sporadic occurrence are mandatory characteristics. Among the specific criteria, connective tissue nevi, when present, are almost pathognomonic. The other findings, when combined, can help to establish the diagnosis, such as the presence of two of

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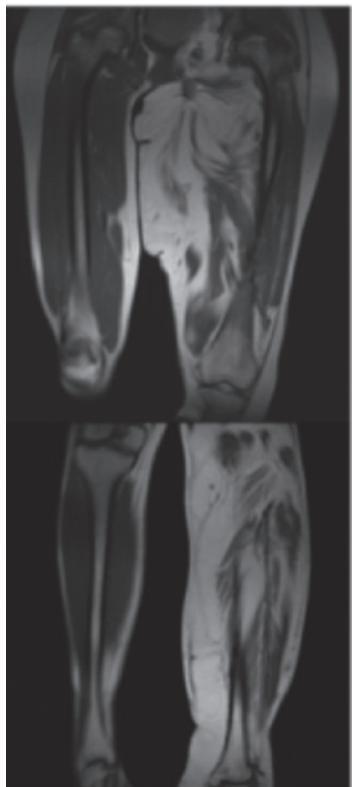


Fig. 1 – Magnetic resonance imaging of lower limbs with coronal T1-weighted sequences showing diffuse left leg enlargement due to extensive proliferation of adipose tissue associated with atrophy of adjacent muscle groups.

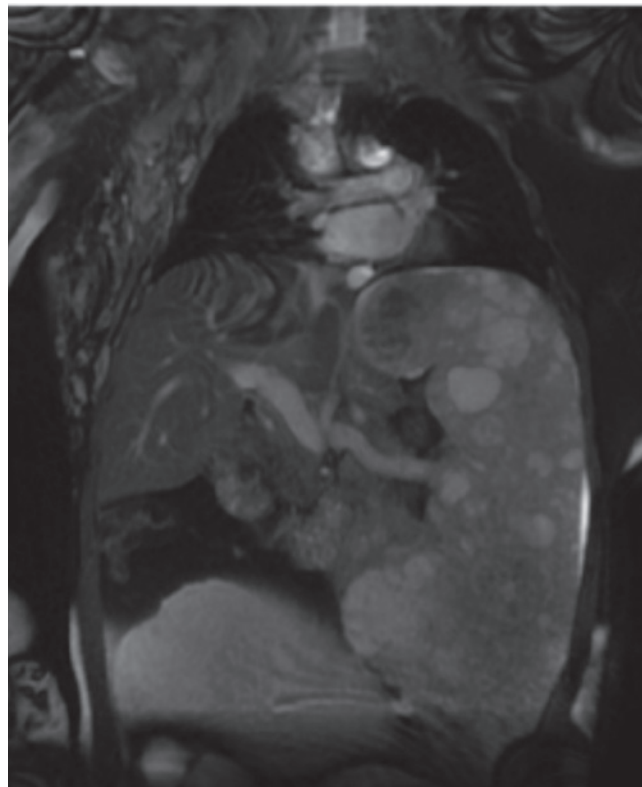


Fig. 3 – Magnetic resonance imaging of the upper abdominal region with coronal T2-weighted sequence, showing splenomegaly with multiple nodular images and hyperintense signal on T2, characteristics of angiomatosis.

the following: epidermal nevi; disproportionate overgrowth of limbs, vertebrae, or viscera; macrocephaly or hyperostosis; bilateral ovarian cystadenoma or monomorphic adenoma of the parotid gland; or three of the following adipose tissue dysregulations, vascular malformations, or facial phenotypes.³

The visceral abnormalities are less common than the musculoskeletal; the following have been reported:

splenomegaly, macrocephaly, white matter abnormalities, nephromegaly, and cystic and emphysematous lung alterations.⁴ Most patients have normal psychomotor development. Life expectancy is 9 months to 29 years, according to the severity of the abnormalities.⁴ The fourth leading cause of premature death is pulmonary thromboembolism and respiratory failure, which are predisposed by vascular

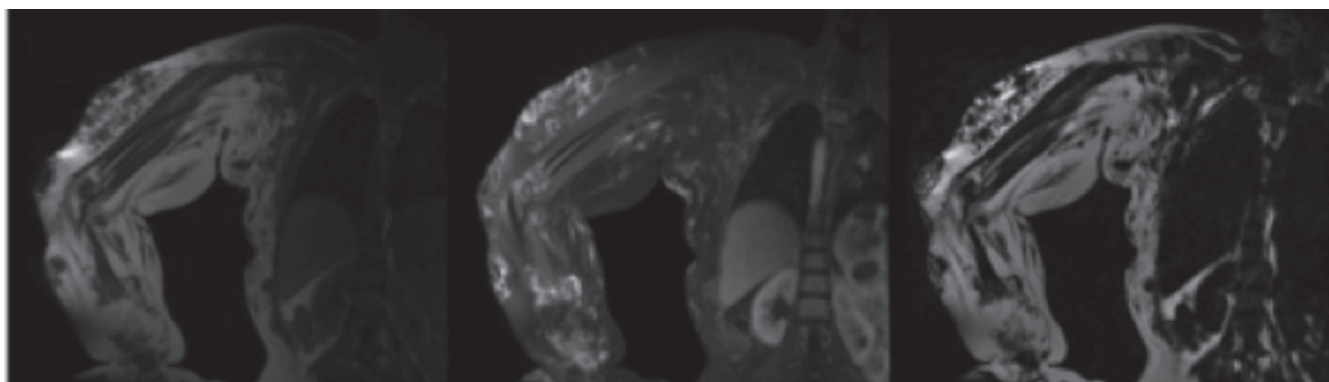


Fig. 2 – Magnetic resonance imaging of the right arm with coronal T1-weighted sequences before and after administration of paramagnetic contrast, showing diffuse limb enlargement due to the presence of multiple images with low signal on T1 and intense enhancement after contrast, characteristics of hemangioma associated with adjacent muscle atrophy.

malformations, surgical convalescence, and (in extreme cases of deformity) by restricted mobility.⁶ Benign neoplasms associated with the syndrome include lipomas, ovarian cystadenomas, and monomorphic adenoma of the parotid gland; malignant neoplasms include papillary adenocarcinoma of testicles, mesothelioma of the *tunica vaginalis*, and peritoneal mesothelioma.^{3,4} Differential diagnoses include vascular and pigmented syndromes and lipomatoses, mainly Klippel-Trenaunay syndrome and hemihyperplasia/lipomatosis syndrome.^{3,4,6}

Treatment is multidisciplinary, including clinical and psychological support. Proteus syndrome results in significant social stigma, due to its rarity and disfiguring features; thus, these patients must undergo psychological counseling.⁷ Genetic counseling provides information on the nature, inheritance, and implications of genetic disorders to help individuals and families to make medical and personal decisions. Skeletal overgrowth can result in biomechanical dysfunction and functional limitation; the correction of these conditions involves epiphysiodesis, limb shortening, reduction of asymmetries, stretching, arthrodesis, arterial ligation, and even amputation; however, deformity recurrence is common.⁸ The most urgent and life-threatening complications include deep vein thrombosis and pulmonary embolism, which may have a late diagnosis due to their very low incidence in pediatric patients. Patients should be treated with anticoagulants.⁹

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