

Bone complication of a plexiform neurofibroma – Case report

Complicação óssea de um neurofibroma plexiforme – um relato de caso

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ABSTRACT: Neurofibromatosis type I is an autosomal dominant disease whose diagnosis is made based on clinical criteria. The three main manifestations are neurofibromas, café-au-lait spots and Lisch nodules occurring in more than 90% of patients until puberty. This article reports the case of a diagnosed neurofibromatosis type I young patient with orthopedic complications due to elephantiasis caused by a plexiform neurofibroma.

Keywords: Type I neurofibromatosis; Plexiform neurofibroma; Elephantiasis.

RESUMO: A neurofibromatose tipo I é uma doença autossômica dominante cujo diagnóstico é feito com base em critérios clínicos. As três principais manifestações: neurofibromas, manchas café com leite e nódulos de Lisch ocorrem em mais de 90% dos pacientes até a puberdade. Relatamos o caso de uma paciente jovem com diagnóstico de neurofibromatose tipo I com complicações ortopédicas devido à elefantíase causada por um neurofibroma plexiforme.

Palavras-chave: Neurofibromatose tipo I; Neurofibroma plexiforme; Elefantíase.

INTRODUCTION

Neurofibromatosis type I, or Von Recklinghausen disease, is a phakomatosis, in other words, a genetic disease originating from the neuroectoderma affecting skin and nervous system¹. It is clinically characterized by skin lesions known as café-au-lait spots, ephelids in folds areas (Figure 1), neurofibromas (Figure 2), hamartomatous lesions in bones, eyes, glands and nervous system². Another common associated manifestation is plexiform neurofibromas, which are benign lesion, usually only that compromise nerve roots. Macroscopically plexiform neurofibromas are shown as tortuous cords that extend along a neural segment. They

are highly vascularized, therefore, tend to grow over time, being able to infiltrate adjacent tissues and cause functional impairment^{3,4,5}.

Regarding epidemiology, there is no ethnic, racial or gender rate^{6,7}. The average age of clinical diagnosis in men is lower than women and life expectancy in individuals affected by this disease is lower, due to higher occurrence of neoplasm such as gastrointestinal, colon, ovarian, breast cancer, among others tumors^{8,9,10}.

For this reason, it is extremely important to know its pathophysiology in order to avoid possible complications.

This article has the objective to show the rarity of the case, lack of other similar case reports published in this advanced stage of evolution and complications.

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Figure 1: Axillary ephelides



Figure 2: Characteristic lesions of NF1: neurofibromas

METHODOLOGY

For the construction of the report, scientific articles were searched on the PubMed and Scielo platforms using

the keywords “Type I neurofibromatosis”, “plexiform neurofibroma”, “elephantiasis”. Were used articles published between 2004 and 2020 which had a more complete review on the subject or were related to this paper. The consent for the case report was made electronically, with the patient’s authorization.

CASE REPORT

Female patient, 34 years old, merchant, diagnosed with neurofibromatosis type 1 in childhood. She reports chronic pain in the right lower limb, which aggravate in the last five months, presenting at rest and worsens while mobilization of the foot. She also indicated loss of plantar and thermal sensitivity in right medial malleolus region. She has a history of plexiform neurofibroma excised at age four in the same limb with recurrence and it got worse at 12 years old until recent appointment. In addition, she has multiple cutaneous neurofibromas and complains of recurrent nail infections in toes of the affected limb.

On physical examination in 2018, blood pressure of 100 x 70 mm Hg, café-au-lait spots, ephelids and diffuse cutaneous neurofibromas were described, in addition to a massive plexiform neurofibroma in the right leg, (Figures 3, 4 and 5) with preserved superficial and deep sensitivity. In this appointment, she brought a Magnetic Resonance Imaging (MRI) of the right leg performed in 2017 (Figure 4) with the report of: (1) distortion architecture of the bone structure in leg and foot (some with liquid infiltration); (2) diaphyseal enlargement of tibia; (3) fibular diaphysis irregularity; (4) diffuse osteolytic lesions; (5) diffuse pseudoarthrosis; (6) atrophy and liquid infiltration of musculature. The conduct at the time was to refer to orthopedist to assess limb amputation.

After consultation with an orthopedist, the patient underwent a computed tomography scan (CT) of the same limb, which demonstrated: (1) leg, calcaneus (with erosive lytic lesion) and foot bone architecture distortion; (2) tibia diaphyseal enlargement; (3) talus lytic lesion. However, the orthopedist did not indicate amputation of the limb due to the risk of recurrence and, unfortunately, did not offer an alternative solution.

In the last appointment (2020), she reports bilateral oophorectomy and total hysterectomy in August 2019 due to a myoma, endometriosis and cystic disease. Physical examination was similar to that of 2018, except for right foot elephantiasis, with points of hardened and painless consistency and loss of thermal sensitivity in right medial malleolar region. The patient had difficulty walking and wearing shoes. Thus, she was instructed on the affected limb function loss and risks of having a secondary infection due to lack of awareness and proper hygiene. Under these circumstances, it was approached about the amputation possibility associated with psychological counseling for demonstrating reluctant to subject.



Figure 3: Lateral vision of right foot elephantiasis due to a plexiform neurofibroma



Figure 4 – Posterior vision of right foot elephantiasis due to a plexiform neurofibroma

DISCUSSION

Despite of the fact that the phenotype of patients with NF-1 is well described and known, bone alterations



Figura 5 – Anterior vision of right foot elephantiasis due to a plexiform neurofibroma

are underemphasized in clinical studies and in genetic discussions related to the disease¹.

Bone involvement occurs in most patients, with a variable clinical presentation, sometimes being extremely severe, appearing at birth or becoming evident in childhood and increasing with age, as described in the current case. The natural progress and pathogenesis of bone abnormalities resulting from the altered function of the NF-1 gene are little known. Consequently, therapeutic options for these conditions are often limited, which explains the divergences adopted by orthopedists in relation to the conduct regarding our patient^{13, 14, 15}.

In addition to bone dysplasia, some of the bone changes observed in these patients are secondary to tumors, which compress the bones due to their continuous growth, or due to metastases. Most often, these tumors are plexiform neurofibromas¹.

NF-1 is a syndrome that grants the patient a greater predisposition to neoplastic lesions due to the presence of mutation and loss of function of the NF1 gene, that has autosomal dominant inheritance. The transcription product of this gene originates neurofibromin, a cytoplasmic protein that is found mainly in the central nervous system and, to a lesser extent, in other tissues. This protein regulates the activity of the Ras p21 protein, which ultimately decreases the cell mitogenic signaling pathway. Therefore, the NF1

gene mutation generates a non-functional neurofibromin that results in the uncontrolled activation of this signaling pathway for cell proliferation^{11, 12}.

NF-1 skeletal phenotypes can be generalized or focal. Manifestations of generalized skeletal abnormalities, most often osteopenia or osteoporosis with short stature are common, but with few clinical implications. Focal lesions such as tibial dysplasia, short-angled scoliosis and sphenoid wing dysplasia are less common but cause significant morbidity, as described for this current case, with broad focal impairment of the left lower limb (dysplasia and lytic lesions)^{6,8}.

Children may present a unilateral anterolateral curvature of the lower leg, notably the tibia, although the child may also be born with fractures and/or pseudarthrosis or even develop these conditions shortly after birth. Deformities may appear before other manifestations of NF-1, such as cafe-au-lait spots. Tibial curvature is usually

evident within the first year of life, with fractures not uncommonly occurring around 2-2.5 years. Pathological fractures usually occur before the age of three, often with minimal trauma⁵.

Subsequent fracture healing may not occur spontaneously and sometimes requires amputation of the affected extremity. In this way, it is important to analyze the exact point at which this procedure would be performed to avoid possible recurrences, favored by the maintenance of tissues compromised by the disease after amputation.¹³

Thus, a multidisciplinary assessment of patients is necessary so that they have a correct understanding of the disease, its evolution and the proposed therapeutic. As it is a disease, until today, without cure and with physical and psychological damage to the patient, a longitudinal follow-up is essential for better adherence and quality of life for those affected by NF-1.

Consent: An informed consent was electronically presented to the patient for the realization and use of the photographs taken for academic purposes and scientific publication.

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