Osteofibroma in type I neurofibromatosis. A case report

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Case Report

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Background: Neurofibromatosis type 1 is an autosomal dominant genetic disorder caused by a mutation in the NF1 gene on chromosome 17q11.2. There is insufficient evidence in the literature regarding the prevalence and incidence of neurofibromatosis type 1 in Hispanic populations, including Mexico. However, globally, the prevalence is estimated at 1 in 3,164 individuals and the incidence at 1 in 2,662 individuals. Due to its multisystemic alteration, a wide variability of the clinical spectrum is presented and bone manifestations and the presence of an increased risk of tumor development stand out, no cases have been reported where osteofibromas are a characteristic clinical manifestation of the disease, however, in this work we present the case of a female patient in her sixth decade of life with Neurofibromatosis type 1 with no other relevant history who has undergone multiple local resections of neurofibromas in different parts of the body, but with the presence of an osteofibroma in the left parietoccipital region, considered an uncommon clinical entity within those described in the characteristic clinical manifestations of Neurofibromatosis type 1. A multidisciplinary approach has been taken to manage osteofibroma, however, to date, no specific medical-surgical management has been defined.

Keywords: Osteofibroma, neurofibromatosis.

Neurofibromatosis is an autosomal dominant genetic disorder caused by a mutation in the NF1 gene located on chromosome 17q11.2. Neurofibromatosis type 1, or von Recklinghausen disease, has a prevalence of 1 in 3,000 births, according to reports in the literature [3]. Regarding its pathophysiology, the mutation in the NF1 gene causes dysfunction of neurofibromin leading to the development of multiple types of benign and malignant tumors, including neurofibromas, malignant peripheral nerve sheath tumors, and optic pathway gliomas [5]. The diagnosis of NF1 is eminently clinical. Although The musculoskeletal involvement of Neurofibromatosis Type 1 is well documented, ossification within the neurofibroma has been poorly documented in the current literature. In this paper, we address the case of a female in her sixth decade of life with a long history of Neurofibromatosis Type 1. She has undergone several surgical resections of neurofibromas in different areas of her body but has an osteoma in the left frontoparietal region, yet to undergo medical or surgical treatment. There is still no effective pharmacological agent for disease remission, and symptomatic treatment largely depends on surgical resection of the tumors. [1]

Case report

This paper presents the case of a female in her sixth decade of life. She was admitted to the hospital in August 2024 with a diagnosis of Neurofibromatosis type 1, diagnosed at 7 years of age. Her mother and maternal grandmother were also diagnosed with Neurofibromatosis type 1, and the remaining history was clinically unrelevant. She has undergone several surgical procedures, including resections under local anesthesia of several neurofibromas in different parts of her body (left hand, left hemicervical region, frontal region, and right upper eyelid), the most recent being in December 2024. She presents a neurofibroma in the left parieto-occipital region that has been present for 10 years *(Figure 1)*. She reports that it has increased in size over time, representing an increase of approximately 66%. Measuring 20 x 15 cm in diameter, it has a stony consistency, regular edges, indurated, and non-tender to palpation. Stress causes pain and a sensation of pressure on that side of the skull. A cranial CT angiography was performed in March 2025 *(Figure 2)* using multidetector equipment with axial acquisition from the skull base to the convexity in a single phase, followed by venous angiography. A benign bone tumor was present in the

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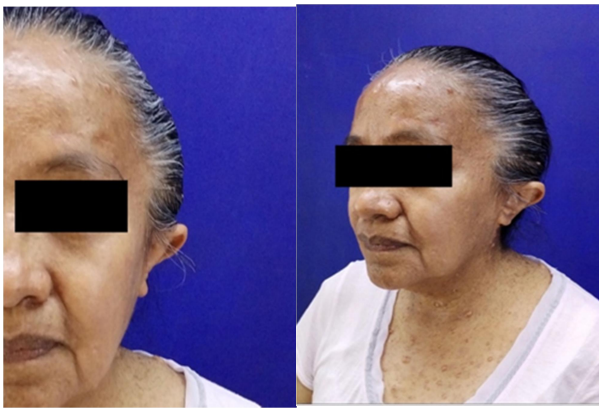

Figure 1. Front and three quarter view.

left temporal squama, suggesting an osteoma. Neurofibromas in the soft tissue of the neck.

A calcified lesion was seen outside the anterior table of the skull in the left parieto-occipital region, consistent with osteofibroma, measuring 20 x 15 cm in diameter. The patient was referred from the General Plastic Surgery Clinic for evaluation and management. Due to its location, it was decided to refer the patient to the Neurosurgery Department. No specific management at this time due to a lack of evidence in the literature regarding its presence as a clinical manifestation in this pathological entity and its therapeutic approach.

Discussion

Neurofibromatosis is a genetic disorder with an autosomal dominant inheritance pattern, caused by a mutation in the NF1 gene located on chromosome 17q11.2. Type 1 is the most common, with a prevalence of 1 in 3,000 live births, as described in the literature. [3]. Regarding its pathophysiology, the NF1 gene mutation leads to dysfunction of neurofibromin, a GTPase-activating protein (GAP), resulting in the overactivation of multiple signaling pathways, including the RAS pathway. This contributes to the development of various benign and malignant tumors, such as neurofibromas, malignant peripheral nerve sheath tumors (MPNSTs), and optic pathway gliomas [5]. Penetrance is complete since it is an autosomal dominant disorder, meaning all generations are affected without skipping [6].

Diagnosis of NF1 is primarily clinical and requires the presence of at least two or more of the following manifestations: 6 or more café-au-lait macules (prepubertal >5 mm or postpubertal >15 mm), two or more neurofibromas anywhere on the body or one plexiform neurofibroma, bone abnormalities (with sphenoid dysplasia being the most common), freckling in the axillary or inguinal regions (Crowe's sign), 2 or more Lisch nodules in the iris, a first-degree relative with a confirmed diagnosis of

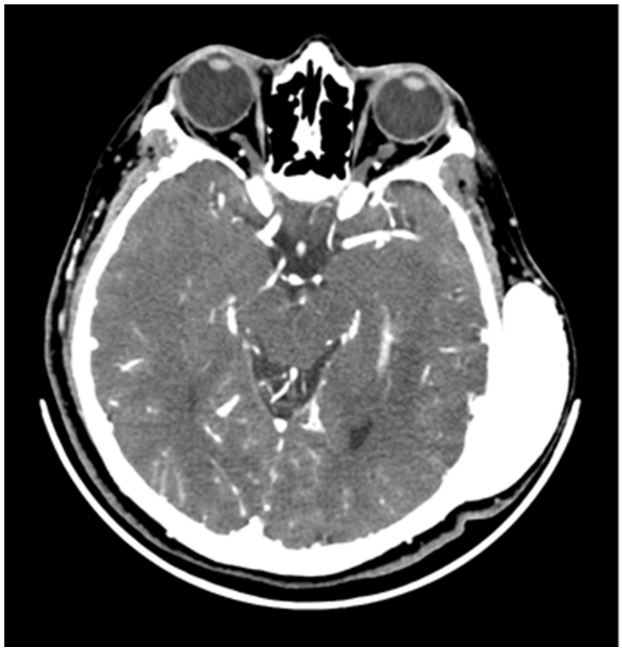

Figure 2. Cranial angiography parenchymal window.

Neurofibromatosis Type 1 (NF1) [3]. Bone lesions associated with NF1 or bone dysplasias encompass a wide range of clinical entities. The absence of the greater wing of the sphenoid bone is the most common craniofacial bone anomaly and is nearly pathognomonic in NF1 patients [4]. Osteomas are not typically among the expected manifestations of Neurofibromatosis Type 1. In our literature review, we found only one reported case (2024) describing the ossification of a frontal neurofibroma, confirmed after tumor resection and histopathological examination. No causally directed treatment of NF1 is yet available. The most important elements of management are early diagnosis and symptom-oriented treatment. Genetic counseling is especially important. Cutaneous neurofibromas can be surgically resected for either esthetic or medical reasons (pain or inflammation) [7].

Conclusion

The presence of osteofibromas as a clinical manifestation of neurofibromatosis type 1 is not very common, and there is insufficient medical-scientific evidence to address them under a single reference, which poses a significant challenge for surgeons. It is important to highlight that we could be dealing with a case of neurofibroma ossification, which is poorly documented and extremely rare. However, to confirm this diagnosis, we would need to remove the tumor and conduct a histological analysis to determine whether it is indeed an ossified neurofibroma. At this time, this is not possible, as the patient is awaiting evaluation by neurosurgery and has not expressed interest in the immediate removal of the tumor. The purpose of this article is to present this case due to its

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rare presentation and to emphasize the multiple bone manifestations that can occur in neurofibromatosis type 1. Although these manifestations are uncommon, they require proper diagnosis and management.

Conflicts of interests

It is declared that there are no conflicts of interest related to the publication of this work.

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