Giant Central Ossifying Fibroma of the Maxilla: Case Report and Literature Review

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Abstract

The central ossifying fibroma is part of the fibro-osseous lesions and is considered a benign bone tumor. It occurs almost exclusively in the jaws, although cases have also been reported in frontal, orbital, paranasal and temporal bones. In its presentation in the jaws, it is generally an asymptomatic pathology of slow growth; but as its size increases, it becomes disfiguring and can interfere with the basic functions of mastication, swallowing, phonation and even breathing. Because it is a lesion with defined borders, the treatment of choice is surgical excision. In this article we present the case of a 39-year-old female patient with a giant central ossifying fibroma in the anterior maxilla, accompanied by the clinical, imaging and histopathological findings and treatment used, and a review of recent literature on the characterization of fibro-osseous lesions.

Keywords: Fibro-Osseous Lesions; Central Ossifying Fibroma; Benign Neoplasm; Maxillary Sinus

Introduction

According to the World Health Organization (WHO), the ossifying fibroma is part of the group of fibro-osseous lesions, together with fibrous dysplasia, cemento-osseous dysplasia, and familial gigantiform cementoma; all characterized by replacement of normal bone architecture with fibroblasts, fibrous tissue, and varying amounts of mineralized tissue [1,2].

The central ossifying fibroma (COF) is considered a benign neoplasm affecting the bones of the craniofacial complex, with peak incidence between the third and fourth decade of life and a clear predilection for the female sex, with a female to male ratio of 5:1 [3].

The most common anatomical site of presentation is the maxilla, associated with greater frequency with the molar (52%) and premolar (25%) regions of the mandible [1,2] so its origin has been proposed as the mesenchymal cells of the periodontal ligament. Yet, cases have been reported in craniofacial bones other than the maxilla, making this theory questionable [4-8], and so other proposals have emerged such as mutations on the CDC73 or APC genes, among others [9,10].

Although the lesions tend to be clinically asymptomatic, COF has potential for continuous growth if not treated [11,12] and can reach a large volume, thus resulting in facial asymmetry. It can present as an expansion of the buccal and lingual/palatal tables, even expanding...
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the mandibular basal area or the floor of the maxillary sinus, and thinning and perforation of cortices. Epistaxis and nasal obstruction can develop when COF presents in the maxilla. Radiographically it is observed as a well-defined radiolucent zone, expansive, unilateral and with radiopaque areas that suggest calcifications. Histology describes a well-defined encapsulated lesion showing a fibroblast stroma, with hyperchromatic nuclei associated with calcium and bone structures, without cellular pleomorphism or associated mitosis. It is detailed that these structures can join and form curvilinear trabeculae that can be acellular [2,3,7].

Below we present the clinical case of a patient who is in her fourth decade of life, with a giant central ossifying fibroid in her jaw, and a review of the literature.

Case Report

A 39-year-old female patient with no significant medical history came to our service because she presented a large tumor involving the anterior and posterior area of the right maxilla, of approximately two years of evolution and non-specific symptoms, with evident facial asymmetry in the right hemiface (Figure 1). During the intraoral exploration, a mass of approximately 10 cm in diameter, with a hard-rubbery consistency was observed. The mucosa was of normal characteristics, similar to the adjacent tissue, although it presented ulcerated areas. There were root remains of the first and second upper right molars and first and second upper premolars of the same side (Figure 2).

Figure 1: Facial asymmetry due to the deforming mass in the right hemicaria, with effacement of the nasogenian fold.
Initial panoramic radiographic examination revealed a radiolucent unilocular image with radiopaque foci, spanning from the canine region to the ipsilateral maxillary tuberosity. In the computed tomography (CT) scan, alteration of bone architecture was clearly observed, with a lesion of mixed intensity delimited by a hyper dense halo involving the maxillary sinus and displacing the vestibular cortical, as well as a displacement of the lateral wall of the nasal fossae, but without compromising the floor of the orbit (Figure 3A-3C).

**Figure 2:** Juxtaosseous mass of 8 x 5 x 5 cm, protruding into the edentulous mandibular space, hard/rubbery, mobile, covered by healthy mucosa, partially obliterating the oropharynx.

**Figure 3:** Tomographic image showing an expansive mass of 8 x 6 x 5 cm with soft tissue density causing bone destruction, volume with cortical expansion and disruption in some areas. Inside it presents amorphous and dense material with the appearance of osteoid material. A. Sagittal section. B. Coronal section. C. Axial section.
An aspiration was performed in which no content was obtained. Under general anesthesia, an incisional biopsy was performed for histopathological analysis. Fibrous, non-bleeding tissue was obtained. Histological sections stained with hematoxylin-eosin showed fibrous connective tissue, with various degrees of cellularity and mineralized material (Figure 4). Portions of trabecular, osteoid, and basophilic cellular spheres that were similar to cement were observed in the hard tissue specimen (Figure 5). The lesion was separated from the thin bone cortex by fibrous connective tissue. The findings were compatible with a benign fibro-osseous lesion.

**Figure 4:** Mucosal epithelium with hyperplasia and underlying reparative changes, fusiform stromal, collagenized, little cellularity, homogeneous with areas of mature ossification without atypia, without malignancy.

**Figure 5:** Neoformed bone spicules and rounded calcifications with a cementitious appearance.
**Diagnosis and treatment**

Based on the clinical and imaging characteristics, and the initial histopathological examination, the presumptive diagnosis of central ossifying fibroma was established. Considering the extension of the lesion and its defined margins, the patient was taken to surgery and a resection was performed under general anesthesia. The solid mass, well circumscribed, soft and firm, was separated in block from the underlying bone, and flaps from neighbor palate and cheek were made to cover the defect (Figure 6 and 7). The specimen (Figure 8) was sent for histopathological study and the diagnosis of COF was confirmed. The patient was discharged 48 hours after surgery without any complication (Figure 9).

*Figure 6: Bone and soft tissue defect remaining after surgical resection of the lesion.*
Figure 7: Closing the defect with rotation of local flaps.

Figure 8: Specimen made up of two fragments of rubbery, smooth, firm, cream-colored and solid white, homogeneously cut fabric. It measures 10 x 8 x 8 cm.
Discussion and Literature Review

Fibro-osseous lesions are a group of pathologies characterized by the replacement of normal bone architecture by fibrous tissue, with variable degree of mineralization that may correspond to metaplastic bone or material similar to root cement [1,2]. Over time, the entities that make up this group have changed. In the latest WHO classification (2017), fibro-osseous lesions encompass fibrous dysplasia, cemento-osseous dysplasia, familial gigantiform cementoma and central ossifying fibroma [3].

Due to their similarities from a clinical point of view, fibro-osseous lesions are very complex, and the differential diagnosis between them and with other tumor and pseudo-tumor lesions such as osteosarcoma, ameloblastoma, giant keratocyst and Paget’s disease, among others, pose difficulties [13]. Assessing the location, delimitation, distribution by age, sex and association with syndromes, can help clarify the diagnosis.

Fibrous dysplasia, formerly known as Jaffé-Lichtenstein fibrous dysplasia, can affect any bone in the body, with the skull being one of the most common locations, and can cause fragility and deformity in affected bones. According to the WHO, its etiology is in a mutation of the GNAS gene, it has no sex predilection but has a higher prevalence in the first two decades of life [3]. Clinically, fibrous dysplasia can present in four forms: monostotic, which affects only one bone; polyostotic, which affects several bones and is more aggressive; polyostotic associated to the McCune-Albright Syndrome, which consists of osseous injuries accompanied with “café-au-lait” skin pigmentation and endocrine alterations like precocious puberty and/or hyperthyroidism; and finally, the craniofacial variant, limited to the bones that form this complex [3,13,14]. The latter is considered a poorly defined lesion both from the radiological and morphological point of view, which difference it from COF. From a histological point of view, despite fibrous dysplasia sharing similarities with other fibro-osseous lesions, it presents a pathognomonic pattern of trabeculae that assume curvilinear forms resembling “Chinese letters” [15-17]. Treatment consists of bone remodeling when the lesion reaches a significant size, generating facial deformity or compromising neighboring structures by displacement. In severe cases, such as when orbital compression is present, aggressive surgical resection in block is necessary. Research on medical management with bisphosphonates continues [18,19].
Cemento-osseous dysplasia originates exclusively in the bone that supports the dental structures, is of unknown etiology, and presents a strong predilection for black women between the fourth and fifth decade of life. It is clinically asymptomatic [20] and radiologically it can be radiopaque, radiolucent or mixed, according to its stage of maturity. It is generally well defined, with a fine radiolucent edge and without loss of space of the periodontal ligament [21]. Dental vitality is preserved, which serves as the differential diagnosis with other periapical pathologies [3]. Three clinical variants of cemento-osseous dysplasia exist, which are defined solely by their location in the dental arch, as they are histologically indistinguishable. These variants are periapical cemento-osseous dysplasia, in mandibular anterior teeth; focal cemento-osseous dysplasia, in posterior teeth; and florid cemento-osseous dysplasia, which is multi-quadrant. Histologically, these lesions are characterized by irregular bone tissue intermingled with fibroblasts and numerous blood vessels delineated by endothelium of normal appearance and full of erythrocytes, and with areas of dense lymphoplasmocyte inflammatory infiltration [22-24]. They usually do not require treatment, but radiological follow-up is suggested, more strictly for florid cemento-osseous dysplasia, since complications have been reported due to mucosa perforation with exposure of the lesion, leading to secondary infection that progresses to osteomyelitis [25-27].

Familial gigantiform cementoma is a rare form of ossifying fibroma, benign but locally aggressive, that presents as multi-quadrant expansive lesions that grow significantly, causing extreme facial deformity [28-30]. No other bones are affected. It is caused by an autosomal dominant mutation and there are few cases described in families in different parts of the world, including the United States, Italy, Korea, and the Philippines. It typically occurs in the first or second decade of life, with a higher incidence in Asian and Caucasian ethnicities and no sex predilection. Radiologically, familial gigantiform cementoma is observed as a large, mixed-density, well-defined mass that generally cross the midline of the jaws [27,31]. Histology is similar to that of COF, characterized by proliferation of non-cellular fibrous tissue with benign-looking spindle cells, and multiple irregular spicules of non-lamellar bone and cement-like material in the middle. There is no cellular pleomorphism or mitosis [3,32]. Therefore, differential diagnosis is mainly clinical. Treatment is controversial, as simple bone remodeling is considered to cause accelerated growth of the lesions, but radical treatment results in mutilation in the young patient it usually affects. However, the recommendation is resection of the altered bone with immediate or deferred reconstruction that can produce acceptable aesthetic and functional results [3,33,34].

Ossifying fibroma (OF) was first described by Menzel in 1872, and the term was first used by Montgomery in 1927 [35,36]. Until 1948, it was thought that fibrous dysplasia and ossifying fibroma were the same disease or that one was a variant of the other [37]. In the 1950s, Sherman and Sternberg presented clinical, radiological, histological, and pathological aspects of these diseases and divided them into two different entities [38]. Since the beginning of the 1990s, the name ossifying fibroma was adopted by the WHO.

OF is defined as a characteristic, but not exclusive, benign bone neoplasm of the jaws, consisting of fibrous connective tissue with variable amounts of metaplastic bone and mineralized masses [39]. Its etiology is still controversial: initially, it was believed that the lesions were exclusive to the jaws, and therefore their origin was attributed to mesenchymal cells of the periodontal ligament. Later, with literature reports showing presentation in other facial bones [4-8], this changed. Currently, theories of an origin in genetic mutation of some genes, such as CDC73 and APC, are gaining strength [9,10].

There are three histopathological variants: central ossifying fibroma (COF), and two types of juvenile ossifying fibroid: juvenile trabecular ossifying fibroma (JTOF) and juvenile psammomatoid ossifying fibroma (JPOF). All three are potentially deforming expansive lesions [3].

JTOF is a rare, fast-growing, locally aggressive bone tumor. Although asymptomatic, it causes great facial asymmetry. It occurs most often in association with the upper maxilla and the adjacent structures sinuses, frontal-ethmoid bones and orbit, while it is rare in the mandible. It is frequently diagnosed in the first two decades of life, and 70% of the cases occur in children under 15, but has no sex predilection [40,41]. Imaginologically it is a well-defined lesion, usually ovoid or circular, expansive, with a density that varies according to

the degree of maturity of the lesion, from low density - radiolucent in Rx/hyper dense in CT- in the initial stages to areas of higher density - radiopathic in Rx/hyper dense in CT- that increase in quantity, being classified within the group of mixed lesions. It can present cortical thinning and perforation [37,42,43]. The WHO describes the histopathological characteristics as a proliferation rich in polyhedral or spindle-shaped cells with few collagen fibers, immature osteoid cell tissue and multinucleated giant cells in a non-encapsulated lesion but well differentiated from the underlying bone [3]. It has a characteristic disorganized architecture. The osteoid develops directly from the fibrous stroma and forms long, thin strands that have been compared to brushstrokes; and occasional mitosis can be observed in stromal cells. It is considered to be a pathology with a high potential for recurrence (between 30% and 58%), so the radical block resection is the treatment of choice [39,44]. A differential diagnosis should be made with frequent malignancies in young patients such as osteosarcoma, chondrosarcoma, Ewing's sarcoma and Burkitt's lymphoma [45].

JPOF is also a rare slow-growing but expansive tumor that shares the characteristics of local JTOF aggression. Unlike the latter, JPOF presentation in maxillary bones is infrequent: JPOF lesions affect the periorbital, frontal and ethmoid bones, and in general the walls of the paranasal sinuses, and can cause proptosis, visual alterations and nasal obstruction, among others, depending on the structures involved [40]. It is common between the second and fourth decade of life, although cases have been reported of patients between the ages of 3 months and 72 years. It has no predilection for sex. Imaging shows well-defined borders, thinning of the cortices, invasion of adjacent structures and mixed spherical shape, which may cause displacement of dental structures without rhizolysis [46,47]. Histologically, it is characterized by a stroma that varies from being lax and fibroblastic, to intensely cellular with little amount of collagen. It presents trabeculae of osteoid material that is mineralized and organized in concentric forms similar to the bodies of psammoma, hence its name of psammomatoid. It may show giant cells and cystic changes [3,44] and although no malignancy potential has been demonstrated, block resection is necessary because of its high recurrence rate with conservative management (30% - 60%) [42].

COF is a rare lesion, corresponding to 0.1% of all odontogenic tumors [48]. Due to its clinical and pathological characteristics, COF is currently on the list of fibro-osseous lesions. A study carried out by Su., et al. [1] reported higher prevalence of COF in patients between 10 and 29 years of age and no sex predilection. Yet, most authors agree that it typically affects more women (5:1) between the third and fourth decade of life, in line with the clinical case we present here. COF has a higher incidence in the mandibular molar and premolar areas. Less commonly, it can be found in the maxilla (as in our patient's case), zygomatic bone, ethmoid, frontal, orbital region and others [49-53]. COF appears as a hard and painless, localized, slow-growing tumor that displaces teeth, and has intact mucous lining. When untreated, it reaches great size, generating facial asymmetry. It gradually causes expansion, thinning and perforation of bone cortices. In diagnostic images, like for JTOF and JPOF, a mixed image is observed in different degrees, being well-defined, unilocular and with areas suggestive of calcifications [37,41]. In histology, an encapsulated well-defined lesion is observed; and some researchers have suggested that this is the only difference with bone dysplasia. It also presents a fibroblast stroma with hyperchromatic nuclei associated with calcium and bone structures, that can join together to form curved, sometimes acellular, trabeculae. There is no cellular pleomorphism or mitosis. Thanks to its low recurrence percentage (up to 28%) and to the capsule in its macroscopic conformation, handling is conservative and allows cleavage point to perform complete surgical excision [54,55]. Block resection is only suggested if there is recurrence after conservative treatment [56]. In our patient's case, the lesion was completely encapsulated, which facilitated its removal without complications, and no recurrence was observed during follow-up.

Although JTOF, JPOF and COF are considered histological variants of the ossifying fibroma, it is clear that in terms of clinical behavior they present differences that condition their aggressiveness potential and the treatment to be followed.

When evaluating these pathologies, it is important to consider lesions with similar characteristics, such as solitary bone cyst, keratocyst, ameloblastoma, central giant cell granuloma, myxoma, cementoblastoma and odontogenic adenomatoid tumor. Differential diagnosis with malignant entities such as multiple myeloma and low-grade osteosarcoma should also be considered. The age and sex of the patient, the location and the imaging characteristics serve as an initial filter to guide the diagnosis, although histopathology remains the gold standard for definitive diagnosis.

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Conclusion

The review of the literature and the clinical case described allow the following considerations to be made:

- Fibro-osseous lesions are usually very similar to each other, hindering diagnosis. Clinical presentation, imaging and histopathology have to be considered to achieve the best diagnosis. But even so, in occasions it is difficult to reach a final diagnosis.

- The ossifying fibroma is a benign neoplasm, with three histological variants that differ in terms of local behavior and surgical requirements.

- Although central ossifying fibroma occurs mainly in the molar and premolar region of the mandible, cases in the maxilla have also been reported, even displacing important structures and causing severe facial asymmetries, as observed in our patient.

- Thanks to the macro and microstructure of the COF, recurrence is low and conservative management is sufficient to guarantee the success of the treatment.

Bibliography


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