

Ossifying Fibroma of maxilla: Updated Review of Literature and a Case Report

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Abstract:

Objective: In this article, an updated review of Ossifying fibroma including but not limited to its etiology, clinical presentation, radiological and histopathological appearance. In addition to reporting a case of Ossifying Fibroma affecting maxilla (uncommon site) and encroaching maxillary sinus and the treatment using intraoral approach to shell out this lesion with maxillary antrum reconstruction. **Methods:** A literature search was conducted using the keywords Ossifying Fibroma and its alternative names, Cementifying fibroma and cemento-ossifying fibroma in different databases. Full texts were retrieved for publications reviewed or reported cases of Ossifying fibroma and its variants in gnathic and extra-gnathic bone. **Results:** Fifty-one cited articles were included. A number of classifications have been proposed to group these pathological processes. In the last edition of World Health Organization considered Ossifying fibroma as part of Benign Odontogenic tumors including Juvenile ossifying fibroma. Etiology of Ossifying Fibroma is unclear, but several hypotheses were listed. It affects mainly the mandible more than maxilla in 70-90% and in second to fourth decade of life. The majority present as painless swelling, slowly growing and can be discovered during routine radiograph. Rare cases reaching giant size causing erosions and ulcerations. Complete excision of this tumor has become a necessity to avoid recurrence. **Conclusion:** Based on our review, Ossifying Fibroma is an Odontogenic tumor presenting a diagnostic dilemma for both clinician and pathologist due the overlap in clinical and histological features. The recurrent rate is about 30-38% so regular follow up is mandatory.

Key words: Ossifying Fibroma/ Benign Odontogenic Tumor/ Fibro-osseous lesion/ Maxilla.

Introduction:

There are many classifications in literature but they all agreed about the fact that that ossifying fibroma considered one of a spectrum of lesions known as benign Fibro-osseous lesion includes fibrous dysplasia (FD), florid osseous dysplasia (FOD) and focal osseous dysplasia (FocOD) [1]. Despite of behavior difference, those lesions share similar histopathological and radiological

characteristics where the normal bone architecture is replaced by fibroblasts and collagen fibers containing variable amounts of calcified material whether lamellar bone or cementum or both [2]. In 1872, ossifying fibroma was first describing and given a name by Menzel as cemento-ossifying fibroma in that group [3]. In 1971, the World Health Organization (WHO) classified the cementum producing lesions into 4 distinct types reducing the name cemento-ossifying fibroma to ossifying fibroma and 3 more lesions, Fibrous dysplasia, Cemento-ossifying fibroma and Cementifying fibroma [4]. Other name was also given to OF ;“osteofibrous dysplasia” by Campanacci in 1976 to remind that there is still similarity between OF and monostotic fibrous dysplasia with the respect of the different pathological entity. Kempson was able finally to isolate ossifying fibroma from fibrous dysplasia based on its histopathological entity and aggressive and destructive behavior [5]. In 2005, WHO reclassified them as a variant of three; Ossifying fibroma, fibrous dysplasia, and osseous fibroma [6]. In 2017, the fourth edition of WHO reclassified the bone producing fibrous neoplasms into two major well distinct types as differentiation from the non-neoplastic fibro-osseous lesions comprises fibrous dysplasia, osseous dysplasias, central giant cell lesion/granuloma, cherubism, aneurismal bone cyst and simple bone cyst [7]. Bone producing fibrous neoplasms are:

- 1- Cemento-ossifying fibroma as benign Odontogenic (ectomesenchymal) tumor
- 2- Juvenile ossifying fibroma (more aggressive form affecting children):
 - a. Trabecular juvenile ossifying fibroma (TrJOF).
 - b. Psammomatoid juvenile ossifying fibroma (PsJOF) [8].

Cemento-ossifying fibroma has both structures; cementum and bone that are differentiated from one cell of origin that is pluripotential stem cells of the periodontal ligament [9]. They originate from tooth bearing areas and so are of odontogenic origin [10]. Another reason justified the name (tumor), is the chance (although its low rate) to recur [11]. TrJOF and PsJOF are fewer common types as they are affecting wide range of age mostly younger one. PsJOF targets the ethmoidal sinus while TrJOF targets the gnathic bones [12].

Case report:

32-year-old, Ethiopian lady reported to department of oral and maxillofacial surgery with complain of painless swelling in her right cheek for 8 months. The patient is otherwise healthy, not on any medications or known for any allergies with unremarkable family history. General physical examination was non-significant. The swelling is asymptomatic but progressive started 3 months back resulted in facial asymmetry in right cheek but with normal skin appearance. There was a slight elevation of right nasal alar with no signs of nasal obstruction nor nasal discharge (fig 1). There was also no dysphagia or dyspnea and no visual field disturbance. Intraoral examination showed hard bony swelling (about 4 cm in mesiodistally), with more buccal than palatal bone involvement started from tooth 11 till 16 with grade II mobility involving those teeth. The patient has good oral hygiene with no evidence of periodontal problem (fig 2).

Radiograph revealed a well-defined spherical, mixed hypo- and hyper-dense lesion involving the roots of those teeth with cortical thinning encroaching the maxillary sinus (fig 3).

The tumor was removed under general anesthesia for purpose of reconstruction. The approach was intraorally and the lesion “shelled out “ easily which is characteristic of OF .The gross

measures of the specimen were approximately $4 \times 2.5 \times 4$ cm (fig 4). It was delivered to histopathology department in 10% formalin for evaluation. On histopathological examination report came up as ossifying fibroma.

Post- operative course was favorable, and the patient was referred to Prosthodontics to replace her missing teeth. A year later, the patient showed up for follow up with no complaint and satisfactory wound healing as it was confirmed with panoramic radiograph showed good bone regeneration (fig 5&6).

Discussion:

The etiology of OF is really unclear but it can be Odontogenic, developmental, or traumatic [13]. In literature some postulated hypothesis:

- Hamner et al in 1968 considered ossifying fibromas to be formed from pluripotent mesenchymal cells that originate from the periodontal ligament and so most of the fibro-osseous lesions [14].
- According to Kempsoh and based on electron microscopic studies, he found that ossifying fibroma is formed by fibrous tissue as repairing attempts to a bony defect [15].
- Suggestion by Marx et al, induction error in the mesenchymal cellular level can be related to the development of OF [16].
- Trauma can stimulate the progenitor cells, another suggestion by Weing [4].
- Pimenta et al.recently reported association of new tumor suppressor gene (HRPT2) mutation with OF and suggested that these lesions could arise as a result of haploinsufficiency of the particular gene [17].

Alghonaim et al, have presented a case of OF affecting the paranasal sinuses with a history of bone grafting that area (right maxilla) harvested from the mandible and the mandible was free from any pathology. He thought it might be Odontogenic, developmental or traumatic [18].

Clinical presentation

OF can affect any part in facial bones and skull with 70% affecting head and neck region mainly the jaws [19]. Ossifying fibroma affects mainly mandible (molar and premolar region) in 70-90% [20] followed by maxilla and few cases reported in sinonasal bones, skull base and orbit. Lesions in maxilla commonly affect the posterior region but few reported cases in anterior (sinus antrum) region [21]. Rarely affects the calvarium mostly frontal bone associated with paranasal sinuses [22]. Gnathic OF is reported more commonly in female patients in their second to fourth decade of life, while sinonasal tract OF occurs later in life [23]. According to reported case, geographical distribution is another differential factor. Ossifying fibroma found more common in middle aged African women and least common in Caucasian [6]. Moreover, clinical behavior is different. In the Africans, it does not tend to grow much as in Caucasians based on retrospective study done by Titinchi, et al[24]. It starts as painless swelling, slowly growing can be discovering during routine radiograph. “Giant Ossifying Fibroma” a name given for the lesion exceeding 8 cm in largest diameter and has more fibrous than osseous tissue [25]. Although large lesions are rare but massive lesions can reach up to 10 cm and more [20]. Another clinical

presentation include surface ulceration and perforation of cortical bone when reaching a considerable size [26]. OF tend to grow as round- shaped masses by equal expansion in all directions due to their centrifugal growth pattern[27].Extension to the inferior border of the mandible may cause parasthesia of inferior alveolar nerve. Lesions in maxilla can cause obliteration in oral vestibule or facial swelling. It may extend to the nasal cavity cause epistaxis or obstruction. Moreover, it may extend to orbital cavity causing epiphora or bulging of the eye [28].

Although OF usually comes as isolated lesion in patients without any significant medical conditions. Reported case of maxillary OF affecting patient with tuberous sclerosis complex (TSC). TSC is a major neurocutaneous syndrome can be associated with gingival hyperplasia or fibromas but still OF is a very rare finding [29].OF is found as monostotic in 80% but it can be found as multiple lesions although it's very rare. Only 11 cases have been reported in literature from 1968 till 2011 [30].

It is very common to see OF as solitary lesion affecting patients with no medical background. However, co-existence in patient with other medical conditions is not rare. Association of OF with many syndromes (mainly neurocutaneous disorder) have been reported in literature. Syndromes like Sturge-Weber syndrome, Gnathodiaphyseal dysplasia, Buschke–Ollen- dorff syndrome and Oculocerebrocutaneous syndrome, Encephalocraniocutaneous lipomatosis, and neurofibromatosis. Two reported cases in a patient with neurofibromatosis type-1 (an autosomal dominant multisystem disorder) in calvarial and maxillary bone. Suggestion about the incidence of OF in those type of disorders may be related to developmental background, as it arises from multipotent cells of periodontal membrane that are considered a neural crest in origin [31].Sometimes it associated with hormonal disturbance like hypercalcemia secondary to hyperparathyroidism. Hyper parathyroidism- jaw tumor syndrome develop 30–40% of single or multiple OF cases. (HPT-JT) is an autosomal dominant disorder characterized by multiple fibro-osseous lesions in maxilla and mandible. 24 reported cases was found in literature.Diagnosis of HPT-JT is always paramount in the treatment and prognosis by testing the level of calcium, phosphate, and parathyroid hormone [32].Inactivation of HRPT2 gene is considered the main etiology for HPT-JT. The treatment of those lesions is surgical removal with possible recurrence[33].

Radiographic features

According to the age of the lesion, OF shows different radiographical pictures. It starts to appear as well defined, unilocular radiolucency with sclerotic rim [34]. When the lesion starts to be calcified a mixed picture of radiolucency with radiopaque foci which is more common. When it gets fully mineralized, it appears as radiopaque with a rim of radiolucency [35]. It may displace the roots rarely causing their resorption. Root divergence has been reported in 17% of the cases [36].

Fibro-osseous lesions look similar and can be as first differential diagnosis. Fibrous dysplasia is the main lesion in the differential diagnosis of OF [37].Despite of the differences between OF and FD both radiologically and histopathologically, distinguishing them is still challenging [12].

The differences can be summarized in the table:

Table 1: Difference between Ossifying Fibroma (OF) and Fibrous Dysplasia (FD)[13,32].

OF in its early radiolucent stage mimic cemento-osseous dysplasia (34). Among the osseous dysplasia is focal osseous dysplasia (FOD), in early, intermediate, and late stage, is an important differential diagnosis for OF [7]. In contrast to OF, FOD occurs more frequently in older patients and usually presents ill-defined radiographic borders. Moreover, FOD are smaller than in OF and affect more frequently the periapical region [38].

Other than fibro-osseous lesions, other diseases can be included in the differential diagnosis of OF according to its radiographic appearance. In early radiolucent stage, Odontogenic cysts, ameloblastoma, periapical granuloma, radicular cyst and central giant cell lesion [33]. In mixed radiolucent and radio-opaque radiographic appearance, calcifying cystic Odontogenic tumour, adenomatoid odontogenic tumor, osteoblastoma and calcifying epithelial odontogenic tumor may also include [35]. For matured lesion, completely radio-opaque resembling retained root, complex odontoma, idiopathic osteosclerosis, condensing osteitis, or osteoblastoma (if its associated with the roots) [34].

Histopathological features

Ossifying fibroma has variable histological appearance, but mainly composed of fibrous stroma and bony elements with various degree of maturation [39]. The connective tissue stroma consists of matured, proliferating fibroblasts and collagen [40]. The hard tissue found in OF consists of four configurations: lamellar bone, woven bone (most common), ovoid deposits and anastomosing curvilinear trabeculae[41]. It has a more uniform pattern of hard tissue differentiation distinguish it from fibrous dysplasia [42]. Cementifying fibroma characterized by compact basophilic nodules, whereas ossifying fibroma has trabeculae of osteoblasts and osteocyte cavities [43]. Ossifying fibroma stains positive for cytokeratin [44].

Treatment and prognosis

The treatment will vary according to the clinical behavior and radiological finding into the following treatment options:

- 1- Enucleation with or without grafting, when the lesion is not very large in size and well demarcated from the surrounding osseous structure. Usually they shell out easily in surgical procedure and it's easier to be done in the mandible than maxilla [45].
- 2- Curettage, when there are no well-defined line of separation between the lesion and surrounding bone or due to its size and poor access.
- 3- Radical Treatment, in cases with massive and aggressive lesion, reaching inaccessible areas like nasal cavity to avoid recurrences [46]. OF has the ability to infiltrate about 1-2 mm, 5 mm resection is more than enough [24]. This usually requires bone grafting or reconstructive surgery [47]. Result of more functional and esthetical impairments in addition to the high cost for the treatment [24]. Sarcomatous transformation has not been documented [48].

The recurrence rate is 0-28% thus some authors advocate surgical resection, However, others

still prefer the conservative treatment and rather a long follow up since the recurrence is infrequent [2]. In literature, the follow up period ranged from 6 months to 7 years. The longest follow up period in study done by MacDonald-Jankowski and Li, revealed only one case has recurrence [24]. Marvel et al, have presented 3 cases of locally aggressive OF. They believed that OF behave more aggressively and tend to recur when they affect the midface and paranasal compared to that in mandible [49]. The cause of recurrent is unclear, may be due to dental infection or trauma in the area stimulate periodontal membrane proliferation [24]. Another cause for maxillary lesions recurrence is access difficulty and the size of the lesion at the time of presentation [50]. Radiographic evaluation of any recurrence is still with great challenge as with Eversole and co-authors who reported a 28% recurrence rate without detecting any radiological features that could predict a recurrence [51].

Conclusion:

Based on our review, Ossifying Fibroma is an Odontogenic tumor presenting a diagnostic dilemma for both clinician and pathologist due the overlap in clinical and histological features. The recurrent rate is about 30-38% so regular follow up is mandatory.

Disclosures:

- **Ethical Approval and Consent to Participate:**
The patient consented to participate by her data.
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Table 1: Difference between Ossifying Fibroma (OF) and Fibrous Dysplasia (FD).

	OF	FD
Age group	Fourth decayed	2 nd decayed of life
Radiological appearance	Well-demarcated border spherical or ovoid in shape mixed radiolucent and radiopaque image according to the maturation of the lesion	Appears as a diffuse, homogeneous ground-glass, radiodense region
Histological feature	Contain thick mature lamellar bone with osteoblastic rimming.	Only irregular shaped trabeculae of woven bone.
	Ratio between the mineralized and fibrous tissue is variable	Uniformed
Biological behavior and treatment modality	Neoplasm and has the feature of growing and exhibit considerable bone destruction if left untreated	Considered a developmental anomaly and its growth stop when bone matures.
	Well demarcated and easily	Intermingles with the

	separated from the surrounding normal bone	surrounding osseous structure
Molecular level	Strong immunoreactivity for osteocalcin than OF	Mutation in GNAS gene is commonly seen with FD

Figures:



Figure 1: Worm's eye view of a 32 aged female with a right maxillary enlargement. Note right alar elevation.



Figure 2: Clinical view (hard bony round swelling involving buccal cortical plate, extending from the maxilla).

right side anterior to posterior maxillary vestibule, teeth number 3 to 8).

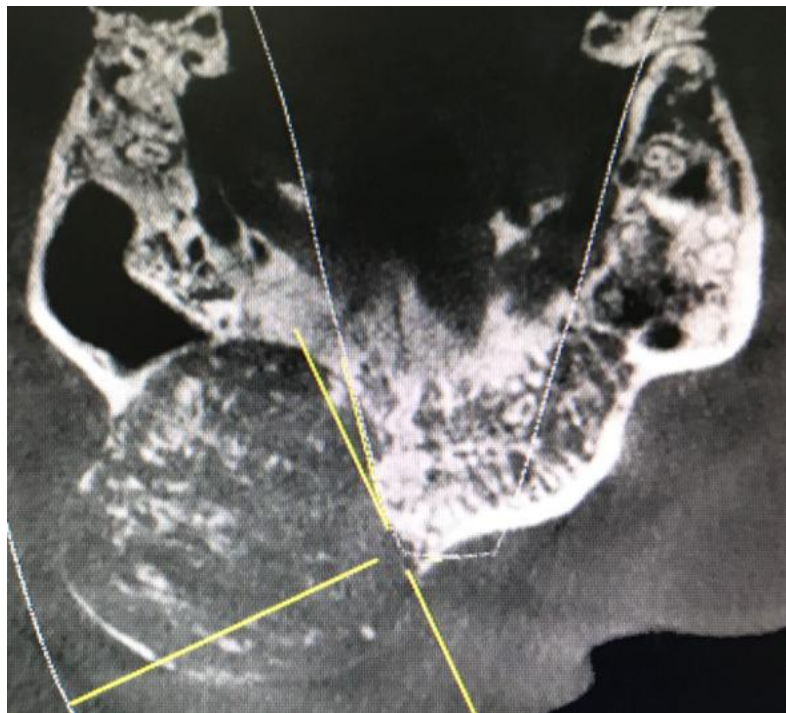


Figure 3:Computed tomography axial section shows a well-defined mixed hyperdense and hypodense mass and partially obliterates the right maxillary sinus).



Figure 4: The surgical specimen (gross appearance).



Figure 5&6: A year post op clinical photos showing patient satisfaction with prosthetic replacement of her missing teeth.