

# Clinicopathological analysis of 55 cases of ossifying fibroma of the jaw

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## Research

**Keywords:** ossifying fibroma, clinical, pathological, jaw

**Posted Date:** February 28th, 2020

**DOI:** <https://doi.org/10.21203/rs.3.rs-15458/v1>

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# Abstract

**Objective :** The purpose of this study was to investigate 55 cases of ossifying fibroma to analyze their clinical and pathological data.

**Methods :** The clinical data, age, imaging performance, serology and their prognosis of 55 cases were analyzed and also Chi-square Test for statistical analysis were made.

**Results :** The COF took up 70.9%, JPOF took up 20.0%, and JTOF took up 5.5%. 62.5% COF were the females, 75% JPOF concentrated in females, 66.7% JTOF concentrated in males. 66.7% COF located in the mandible. 54.5% JPOF were in the maxilla, in which 4 cases (4/11,36.4%) involved the para-nasal sinus. JTOF mainly concentrated in the mandible (66.7%). 2 cases (3.6%) exhibited multi-lesions. 7 cases (12.7%) were found the level of serum ALP up-regulated, and the up-regulation concentrated in younger patients (0~29 years) (  $P < 0.05$ ). In radiographic presenting, only 7.3% displayed unclear borderline, and 87.3% exhibited mixed lesions, 7.3% was X-ray transparent, 5.5% was X-ray opaque. 29.1% had thinning bone cortex and 1 cases was found the bone cortex destructed (1/55,1.8%).18.2% OF appeared tooth displacement, and 9.1% displayed the amputated-like absorption of tooth root. 32 cases were followed up, 31.3% underwent conservative treatment suffered relapse, there was significant differences between the conservative and radical treatment (  $P < 0.05$ ).

**Conclusions:** The main subtype of OF was COF, JPOF and JTOF were relatively less. The majority of sporadic OF was single lesion, multi-lesions were rare. COF occurred with the female predilection in mandible, while JPOF occurred with the female predilection in maxilla; JTOF was the youngest, most occurred in adolescent males in mandible. Tooth displacement was often seen, and the root appeared as an amputated-like resorption. Younger patients were more likely to have elevated ALP. The patients underwent conservative curettage had relatively higher rate of relapse, the lesion should be resected radically to prevent relapse. **Keywords:** ossifying fibroma, clinical, pathological, jaw

## Background

The ossifying fibroma (OF) is a common fibrous-osseous lesion in the maxillofacial region, composed of fibrous tissues as well as multiple mineralized tissues[1]. In 2005, the WHO classified the OF as three subtypes: the Conventional OF (COF), the Juvenile Trabecular OF (JTOF) and the Juvenile Psammomatoid OF (JPOF)[2]. There are many overlap in the clinical and pathological characteristics between the three subtypes. Benign fibro-osseous lesions (BFOL) are a clinically diverse group of bone disorders that share similar histologic features including Ossifying fibroma (OF), fibrous dysplasia (FD), and osseous dysplasia (OD) are three forms of BFOL[3]. It has been reported that there is certain relationship between alkaline phosphatase (ALP) elevation and recurrence of FD[4]. The surgical methods of OF is always controversial on enucleation or complete surgery. In this study, we collected 55 cases of OF, and investigated the imageological, clinical and pathological characteristics, as well as analyzed the prognosis, for the purpose of further understanding on this tumor.

## Methods

The paraffin-embedded samples of OF were collected in the period of 1994 ~ 2019, from the Department of Stomatology, The First Affiliated Hospital of Bengbu Medical College. All the samples were treated with HE staining and estimated by three pathologists, and the corresponding data of clinical record, imageology and surgery were analyzed again. The cases without complete data were discarded.

The clinicopathologic data were analyzed according to the classification standard of OF suggested by WHO in 2005[2]. The OF cases were classified into three subtypes according to their histopathological characteristics, as well as the corresponding data about the patients' gender, age and clinical exhibition. The imageology and therapy of every patients were recorded, the prognosis was analyzed with the follow-up information. And also Chi-square Tests were made for statistical analysis.

## Results

### The Clinical characteristics of OF

The cases of OF generally displayed painless bulge in the face and jaw, the majority of them appeared deformation and malaise in the jaw; only two cases exhibited pain and one of them occurred ulcer for one year. The lesion in the maxilla always accompanied with nasal obstruction, exophthalmos, visual impairment, headache and sometime the infection; while the lesion involved the mandible sometime exhibited numbness of lower lip (4/55,7.3%). The time before surgery varied from 1 month to 8 years.

### Age and gender in the cases of OF

The age of OF patients was 6~61, the mean age was  $25.5 \pm 12.4$  (Fig.1 A-D, Table1); the COF was diagnosed at the age of 6~47, the mean age was  $24.9 \pm 11.5$ ; the age of JPOF patients was 10~61 with the mean age of  $27.5 \pm 14.5$ ; the age of JTOF was between 11 and 17 with the mean age of  $14.7 \pm 2.6$ . The COF took up 70.9% (39/55), JPOF took up 20.0% (11/55) and JTOF took up 5.5% (3/55). The majority of COF were the females with the age between 30 and 40 (25/40,62.5%); JPOF concentrated in females with the age between 20 and 30 (9/12,75%); in contrast with the other subtypes, the JTOF concentrated in males (2/3,66.7%) of the age between 10 and 20.

### The regions of the OF

The regions of OF lesions were listed in table 2. In the 39 cases of COF, 13 cases (13/39,33.3%) occurred in maxilla, most of the lesions appeared in the posterior of maxilla (the region of molars). 26 cases (26/39,66.7%) of COF appeared in the mandible, most of which occurred in the region of pre-molars and molars. In the 11 cases of JPOF, 6 cases (6/11,54.5%) was in the maxilla and 5 cases (5/11,45.5%) in the mandible, 4 cases (4/11,36.4%) of the maxillary lesions involved the para-nasal sinus. JTOF mainly concentrated in the posterior-ramus of mandible (2/3,66.7%). 2 cases (2/55,3.6%) exhibited multi-

lesions(Fig2-3). Case 1 involved the two sides of mandible, and Case 2 involved both the maxilla and mandible.

#### The laboratory assay

7 cases (7/55,12.7%) were found the level of serum ALP up-regulated, the up-regulation concentrated in younger patients (0~29 years) (table3-4). And the ALP level restored to normal after the surgery. Chi-square Test for ALP level showed that there was significance between the age groups ( $P<0.05$ ).

#### Imageology

The majority of lesions that 51 cases (51/55,92.7%) exhibited circular or oval shape with clearly borderline, only 4 cases (4/55,7.3%) displayed unclear borderline, 35 cases (35/55,63.6%) exhibited lesions with sclerotic borderline. 48 cases (48/55,87.3%) exhibited mixed lesions containing both high and low density regions. Only 4 cases (4/55,7.3%) were X-ray transparent, 3 cases (3/55,5.5%) were X-ray opaque(Table 5). In the cases involved the mandible, 16 cases (16/55,29.1%) had thinning bone cortex of which 1 cases was destructed (1/55,1.8%). 10 cases (10/55,18.2%) appeared tooth displacement, 5 cases (5/55,9.1%) displayed the absorption in amputated type of the tooth root (Fig.4).

#### Histopathology

The COF exhibited the fibrous tissue containing abundant storiform fibroblasts, the mature woven or lamellar bone were surrounded by osteoblasts, sometimes the scattered spherical psammomatoid and capsule could be investigated (Fig.5A). JPOF was composed of bony body and stroma cells, it was characterized by basophilia and concentric body without osteoblasts, accompanied with woven or lamellar bone trabecular, sometimes the stroma contained mucoid degeneration, cystic degeneration or the infiltration of multi-nuclear giant cells (figure 5B); however, the JPOF in older cases exhibited increased calcified masses, the concentric psammomatoids fused each other (Fig.5C). JTOF was mainly composed of immature bone trabecular and fibrous stroma, the trabecular was thin and woven as lattice, the dense arrayed osteoblasts surrounded those bone trabecular (Fig.5D).

#### The therapy and follow-up

The therapy included conservative and radical treatment. 21 cases (21/55,38.2%) were treated with conservative curettage, 34 cases (34/55,61.8%) underwent extended excision of bone. Some of them were treated by bone transplanting for restore aesthetics and function

32 cases were followed up for 6 months to 10 years. 10 cases (10/32,31.25%) underwent conservative treatment suffered relapse, in which 5 involved maxilla and 5 in mandible (Table 7). A patient at the age of 10 suffered two times of relapse within two years. The patients underwent extended excision of bone displayed no relapse. Statistical analysis were made that there was significant difference between the conserved and radical treatment ( $P<0.05$ ).(Table 6).

## Discussion

The ossifying fibroma (OF) was firstly named by Montgomery in 1927[1]. In 1972, WHO classified the ossifying fibroma as a bone derived tumor, while the cementifying fibroma as a subtype of cementoma, however, both of them were then reclassified by WHO in 1992 as one type of bone derived tumor, the cemento-ossifying fibroma[5]. But in 2005, WHO had renamed the cemento-ossifying fibroma as ossifying fibroma (OF) again, and which was reclassified as three subtypes: the COF, the JTOF and the JPOF[2]. In this study, the 55 cases of OF included: OF 70.9%, JPOF 20.0%, JTOF 5.5%. JTOF was relatively rare.

There are different mean age between the three subtypes. The mean age of the occurrence of COF is 35, while the age is younger in JPOF. The age of onset of JTOF is younger, the mean age of JTOF is 8.5–12[6]. The range of age of JTOF is relatively wide, 62.8% patients of JTOF is diagnosed between 5–15, but there still reports about JTOF patient at the age of 80[6]. The latest research showed that the mean age of the patients with JPOF ( $18.9 \pm 12.0$  years) was significantly higher than that of the patients with JTOF ( $11.5 \pm 6.0$  years)[7]. In this study, of the COF patients, the female between 30 and 40 also took up a relatively high proportion, it was almost consistent with previous reports. However, in JPOF patients, the female patients were a little more than the males. It was a little different from the previous reports that some researches showed that male patients was a little more than the females[8, 9]. The real adolescent OF is the JTOF, varied between 11 ~ 17, the male (2/3,66.7%) inclination made it different with the two other subtypes.

The three subtypes of OF also have characteristics of the sites. COF always occurred in the posterior of mandible supporting teeth and frequently in females[10]. According to previous studies, JPOF occurred more frequently in the fronto-naso-orbitoethmoidal region than OF, which predominantly affected the jaws, with a slight predilection for the maxilla[7]. Some cases that mainly affected the maxillary sinuses also affected the ipsilateral nasal cavity or the orbit. It was reported in the literature that the paranasal sinuses (70% in the paranasal sinuses, followed by 20% in the maxilla and 10% in the mandible) were the most common sites[11]. In this study of JPOF, 55.5% patients in the maxillaries, and 36.4% patients involved the para-nasal sinus. JTOF almost occurred in the jaw bone only, 50% in the maxilla, 44% in the mandible and 6% involved the para-nasal sinus[8, 9, 12]. However, in this study, 66.7% JTOF occurred in the mandible. In addition, we found 2 cases of multi-lesion (2/55,3.6%), one involved both the maxilla and mandible, and the other one involved the two sides of mandible.

The imaging features of OF present different imaging findings according to its stage of development. The OF display X-ray transparent shadow with low density, the mixed shadow containing both the transparent and opaque region or the X-ray opaque high density changes[13]. Consistently, most cases in this study exhibited the sclerotic fringe surrounding mixed shadow with definitely borderline, but the lesion in the maxilla displayed confused borderline because of the neighbouring bones. 1(1/55,1.8%) cases exhibited the cortical destruction in the mandible, it can be identified from the FD which rarely display the cortical destruction. The growth of OF always results in the impede of tooth eruption, displacement and loss, but

the root absorption is relatively rare[14, 15]. It was consistent with previous studies in which 17%-33% of OF occurred displacement and 10%-44% occurred root absorption[1, 15, 16]. In this study, 10 cases (10/55,18.2%) of OF displayed tooth displacement, 5 cases (5/55,9.1%) exhibited absorption in amputated type. However, in our experience, there was no report showed that root absorption in amputated type in FD. Whether root absorption in amputated type can be differentiated from the diagnosis of OF and FD requires further investigation. The mechanism of the root absorption of OF perhaps is similar to the ameloblastoma, as a real tumor, cause the tooth displacement, absorption and the destruction of canales mandibulae[17].

The clinical treatment of OF always has been controversial, the surgery of OF is determined by its size and region, mainly includes conservative curettage and extended resection. The completed resection is necessary to prevent relapse, while the bone transplant help to restore aesthetics and function[18]. Slootweg et al. investigated no difference between conserved and radical treatment[19, 20]. When the patient was young, the majority of scholars suggested conservative treatment instead of radical resection until the complete development of the maxillofacial region[1, 3, 21, 22]. In this study, 10 cases (10/32,31.3%) of OF suffered relapse after curettage, for relatively younger age and large size of tumor. There was significant difference between the two surgical methods ( $P < 0.05$ ). The first surgery of extended resection seemed important to prevent the relapse of OF.

With the onset of OF, there are also some changes in the serum level of ALP. The bone metastasis of tumor would result in the imbalance of bone absorption and formation. Correspondingly, the serum level of ALP, Ca and IP change. The bone alkaline phosphatase (BALP) is a glycoprotein secreted by mature osteoblasts, BALP could be hydrolyzed and connected with Phosphatidylinositol and polysaccharide then embed into cell membrane before being released into blood as ALP[23]. As the osteoblast developing into osteocytes, the ALP decomposes organophosphorus compound into phosphate, which combines the  $Ca^{2+}$  form hydroxylapatite and then result in the bone mineralization with the help of osteocalcin(OCN). The up-regulation of serum ALP always suggests the attenuation of bone mineralization as a result of the stasis of osteoblasts[23]. We investigated 7 cases (7/55,12.7%) of OF exhibited increased ALP, which concentrated in childhood and adolescent. Chi-square Test for ALP level showed that there was significance between the age groups( $P < 0.05$ ). The younger the patients were, the higher increased rate of ALP. It suggested the osteoblasts differentiation actively in the adolescent OF patients.

OF needs to be differentiated from FD, OD and HPT-JT. As the Benign Fibro-Osseous Lesions (BFOL), the OF, FD and OD exhibit similar pathological, imageological and clinical characteristics, but different treatment[24]. Comparing with FD, first of all, the OF displays clear or sclerotic fringe, while the FD exhibits inconspicuous lesion which fuses with normal bone; secondly, the OF containing bone trabecula is surrounded by osteoblasts, but the FD containing immature trabecula surrounded by fibrous tissue without osteoblasts[2]; finally, the OF always causes the tooth displacement, distortion of dental arch as well as the bulge of the jaw bone[25]; however, the FD patient could maintain the shape of dental arch despite of thin cortical bone, and there is little tooth absorption[26]. In addition, the mutation of GNAS gene in FD is frequent, as a cause of FD, the GNAS mutation could be used as an identification for FD and

other fibrous-osseous diseases[4].OF also requires differential diagnosis with OD. OD is one type of non-tumorous fibrous-osseous disease, it always appeared in mandibles and associated with the root of tooth. Summerlin et al. described it as X-ray transparent-opaque mixed image with amorphous and wide range; the surgery sample was difficult to be separated from the bone and easily to be bleeding[27]. The classical imageological exhibition of OD is that the high density fringe surrounds the mass of relatively low density, which is associated with the root of tooth; the connective tissue contains irregular bone like or cementum like masses, sparse collagen fiber scatters within the cementum mass and trabecula[27].The Hyperparathyroidism-jaw tumor syndrome (HPT-JT) is a autosomal dominant inherited disease, the patient displays hypercalcemia and high parathyroid hormone, the parathyroid adenoma, the lesion in the jaw and the cyst of kidney are common clinical symptoms. 25–50% HPT-JT patients have the ossifying fibroma[28–30], but the high level blood calcium and parathyroid hormone are the main identification of the syndrome and sporadic OF. Once the patient has been diagnosed as HPT-JT, it would better to excise the parathyroid to avoid parathyroid adenoma[31, 32].

The majority of sporadic OF are single lesions, multi-lesions are rare. The ratio of multiple lesions of OF cases is unclear, but we have found only 2 cases (3.6%) in 55 cases (Fig. 2–3). Also we have reported another two multiple cases in previous research[33]. Sporadic multiple OF need to be differentiated from HPT-JT. In this study, the level blood calcium (2.51 mmol/L,2.29 mmol/L,2.15–2.55 mmol/L) and parathyroid hormone (21.53 pg/ml,49.70 pg/ml,15–65 pg/ml) of the two multiple cases were normal. Recently, the candidate tumor suppressor gene HRPT2 then as CDC73 have been identified in chromosome 1q24-q32, encoding a novel protein of 531 amino acids named parafibromin[28]. Some studies show that Germline mutations and somatic inactivation of CDC73 are associated with HPT-JT and sporadic carcinoma and adenomas of parathyroid[4, 34]. Alterations in the tumor suppressor gene CDC73 in ossifying fibroma have recently been reported. In one series, which included four cases with OFs, mutations in CDC73 were found in two of the cases, suggested that CDC73 might be a key factor in the etiology of OFs[35]. However,Yan Chen et al. found that two somatic mutations were identified in 40 cases of OF (5%)[36]. The mutations of CDC73 of sporadic OF previously reported in the literatures were reviewed, and only 4 cases were identified the mutations of CDC73 (Table 7).These findings indicate that the CDC73 mutation is not common in the development of sporadic ossifying fibroma, and therefore may not be used as a marker for diagnosis[37]. The effect of mutated CDC73 on sporadic OF needs to be studied further.

## Conclusions

The main subtype of OF was the COF, JPOF and JTOF were relatively less. The majority of sporadic OF were single lesions, multiple lesions were rare. COF occurred with the female predilection, while JPOF also occurred with the female predilection; JTOF was the youngest, occurred in adolescent males. COF tend to occur in the region of pre-molar and molar in the mandibles; while the JPOF displayed maxillary predilection, the JPOF in the maxilla always involved paranasal sinus; the JPOF tend to occurred in the mandibles. Tooth displacement was often seen, as the root resorption appeared as amputated-like.

Younger patients were more likely to have elevated ALP. The patients underwent conservative curettage had relatively higher rate of relapse, the lesion should be resected radically to prevent relapse.

## Abbreviations

OF

Ossifying fibroma; COF:Conventional ossifying fibroma; JPOF:Juvenile psammomatoid ossifying fibroma; JTOF:Juvenile trabecular ossifying fibroma;

BFOL

Benign fibro-osseous lesion; FD:Fibrous dysplasia; OD:osseous dysplasia;

HPT-JT

Hyperparathyroidism-jaw tumor syndrome;

## Declarations

### Acknowledgements

The Stomatological staff also gratefully acknowledge the Pathology staff of The First Affiliated Hospital of Bengbu Medical College for their cooperation.

### Funding

This work was supported by Research Grants from the Natural Science Foundation of The First Affiliated Hospital of Bengbu Medical College (BYKY18105).

### Authors' contributions

TTW and YSH participated in the histopathological evaluation, performed the literature review, acquired photomicrographs and drafted the manuscript. JLX , YRO and KZ established the diagnosis of the case described in figures and performed the radiological examination.KZ conceived and designed the study, and revised the manuscript for important intellectual content. All authors read and approved the final manuscript.

### Competing interests

The authors declare that they have no competing interests

### Consent for publication

Not applicable

### Ethics approval and consent to participate

The study protocol was approved by the Ethical Committee for Human Experiments at The First Affiliated Hospital of Bengbu Medical College.

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## References

1. Perez Garcia S, Berini Aytes L, Gay Escoda C. Ossifying fibroma of the upper jaw: report of a case and review of the literature. *Med Oral*. 2004; 9(4): 333-339.
2. Barnes L, Eveson JW, Reichart P, Sidransky D. World Health Organization classification of tumours: pathology and genetics of head and neck tumours. Lyon: ARC Press, 2005.
3. Eversole R, Su L, El-Mofty S. Benign fibro-osseous lesions of the craniofacial complex. A review. *Head and neck pathol*. 2008; 2(3): 177-202.
4. Shi RR, Li XF, Zhang R, Chen Y, Li TJ. GNAS mutational analysis in differentiating fibrous dysplasia and ossifying fibroma of the jaw. *Mod pathol*. 2013; 26(8): 1023-1031.
5. Kramer IRH, Pindborg JJ, Shear M. Neoplasm and other lesions related to bone. Berlin, 1992; 28-31.
6. MacDonald, D. S. Fibro-osseous lesions of the face and jaws. *Clin Radiol*. 2004; 59(1): 11-25
7. Chrcanovic BR, Gomez RS. Juvenile ossifying fibroma of the jaws and paranasal sinuses: a systematic review of the cases reported in the literature. *Intl J Oral maxillofac surg*. 2020; 49(1): 28-37.
8. Nelson BL, Phillips BJ. Benign Fibro-Osseous Lesions of the Head and Neck. *Head and neck pathol*. 2019; 13(3): 466-475.
9. El-Mofty S. Psammomatoid and trabecular juvenile ossifying fibroma of the craniofacial skeleton: two distinct clinicopathologic entities. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod*. 2002; 93(3): 296-304.
10. Akcam T, Altug HA, Karakoc O, et al. Synchronous ossifying fibromas of the jaws: a review. *Oral Surg Oral Med Oral Pathol Oral Radiol*. 2012; 114(5 Suppl): 120-125.
11. Barrena Lopez C, Bollar Zabala A, Urculo Bareno E. Cranial juvenile psammomatoid ossifying fibroma: case report. *J Neurosurg Pediatr*. 2016; 17(3): 318-323.
12. MacDonald DS. Maxillofacial fibro-osseous lesions. *Clin Radiol*. 2015; 70(1): 25-36.

13. Kolomvos N, Theologie-Lygidakis N, Christopoulos P, Iatrou I. Benign fibro-osseous lesions of the jaws in children. A 12-year retrospective study. *J Craniomaxillofac Surg.* 2013; 41(7): 574-580.
14. Bernaerts A, Vanhoenacker FM, Hintjens J, et al. Tumors and tumor-like lesions of the jaw mixed and radiopaque lesions. *JBR-BTR.* 2006; 89(2): 91-99.
15. Posnick JC. Fibrous dysplasia of the craniomaxillofacial region: current clinical perspectives. *Br J Oral Maxillofac Surg.* 1998; 36(4): 264-273.
16. Alsharif MJ, Sun ZJ, Chen XM, Wang SP, Zhao YF. Benign fibro-osseous lesions of the jaws: a study of 127 Chinese patients and review of the literature. *Int J Surg Pathol.* 2009; 17(2): 122-134.
17. More C, Taylor M, Patel HJ, Asrani M, Thakkar K, Adalja C. Radiographic analysis of ameloblastoma: a retrospective study. *Indian J Dent Res.* 2012; 23(5): 698-670.
18. Su L, Weathers DR, Waldron CA. Distinguishing features of focal cemento-osseous dysplasias and cemento-ossifying fibromas: I. A pathologic spectrum of 316 cases. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod.* 1997; 84(3): 301-309.
19. Slootweg PJ, Panders AK, Koopmans R, Nikkels PG. Juvenile ossifying fibroma. An analysis of 33 cases with emphasis on histopathological aspects. *J Oral Pathol Med.* 1994; 23(9): 385-388.
20. Slootweg PJ. Lesions of the jaws. *Histopathology.* 2009; 54(4): 401-418.
21. Sciubba JJ, Younai F. Ossifying fibroma of the mandible and maxilla: review of 18 cases. *J Oral Pathol Med.* 1989; 18(6): 315-321.
22. Abuzinada S, Alyamani A. Management of juvenile ossifying fibroma in the maxilla and mandible. *Journal of maxillofacial and oral surgery.* 2010; 9(1): 91-95.
23. Boumaza I, Srinivasan S, Witt WT, et al. Autologous bone marrow-derived rat mesenchymal stem cells promote PDX-1 and insulin expression in the islets, alter T cell cytokine pattern and preserve regulatory T cells in the periphery and induce sustained normoglycemia. *J Autoimmun.* 2009; 32(1): 33-42.
24. Brannon RB, Fowler CB. Benign fibro-osseous lesions: a review of current concepts. *Adv Anat Pathol.* 2001; 8(3): 126-143.
25. Alawi F. Benign fibro-osseous diseases of the maxillofacial bones. A review and differential diagnosis. *Am J Clin Pathol.* 2002; 118 Suppl: 50-70.
26. McCarthy EF. Fibro-osseous lesions of the maxillofacial bones. *Head and neck pathol.* 2013; 7(1): 5-10.
27. Summerlin DJ, Tomich CE. Focal cemento-osseous dysplasia: a clinicopathologic study of 221 cases. *Oral Surg Oral Med Oral Pathol.* 1994; 78(5): 611-620.
28. Carpten JD, Robbins CM, Villablanca A, et al. HRPT2, encoding parafibromin, is mutated in hyperparathyroidism-jaw tumor syndrome. *Nat Genet.* 2002; 32(4): 676-680.
29. Haven CJ, Wong FK, van Dam EW, et al. A genotypic and histopathological study of a large Dutch kindred with hyperparathyroidism-jaw tumor syndrome. *J Clin Endocrinol Metab.* 2000; 85(4): 1449-1454.

30. Hobbs MR, Pole AR, Pidwirny GN, et al. Hyperparathyroidism-jaw tumor syndrome: the HRPT2 locus is within a 0.7-cM region on chromosome 1q. *Am J Hum Genet.* 1999; 64(2): 518-525.
31. Sarquis MS, Silveira LG, Pimenta FJ, et al. Familial hyperparathyroidism: surgical outcome after 30 years of follow-up in three families with germline HRPT2 mutations. *Surgery.* 2008; 143(5): 630-640.
32. Guarnieri V, Bisceglia M, Bonfitto N, et al. Re: Familial hyperparathyroidism: surgical outcome after 30 years of follow-up in three families with germline HRPT2 mutations. *Surgery.* 2008; 144(5): 839-840.
33. Wang TT, Zhang R, Wang L, Chen Y, Dong Q, Li TJ. Two cases of multiple ossifying fibromas in the jaws. *Diagn Pathol.* 2014; 9: 75.
34. Shattuck TM, Valimaki S, Obara T, et al. Somatic and germ-line mutations of the HRPT2 gene in sporadic parathyroid carcinoma. *N Engl J Med.* 2003; 349(18): 1722-1729.
35. Pimenta FJ, Gontijo Silveira LF, Tavares GC, et al. HRPT2 gene alterations in ossifying fibroma of the jaws. *Oral Oncol.* 2006; 42(7): 735-739.
36. Chen Y, Hu DY, Wang TT, et al. CDC73 gene mutations in sporadic ossifying fibroma of the jaws. *Diagn Pathol.* 2016; 11(1): 91.
37. Toyosawa S, Yuki M, Kishino M, et al. Ossifying fibroma vs fibrous dysplasia of the jaw: molecular and immunological characterization. *Mod Pathol.* 2007; 20(3): 389-396.

## Tables

Due to technical limitations, the tables are only available as a download in the supplemental files section

## Figures

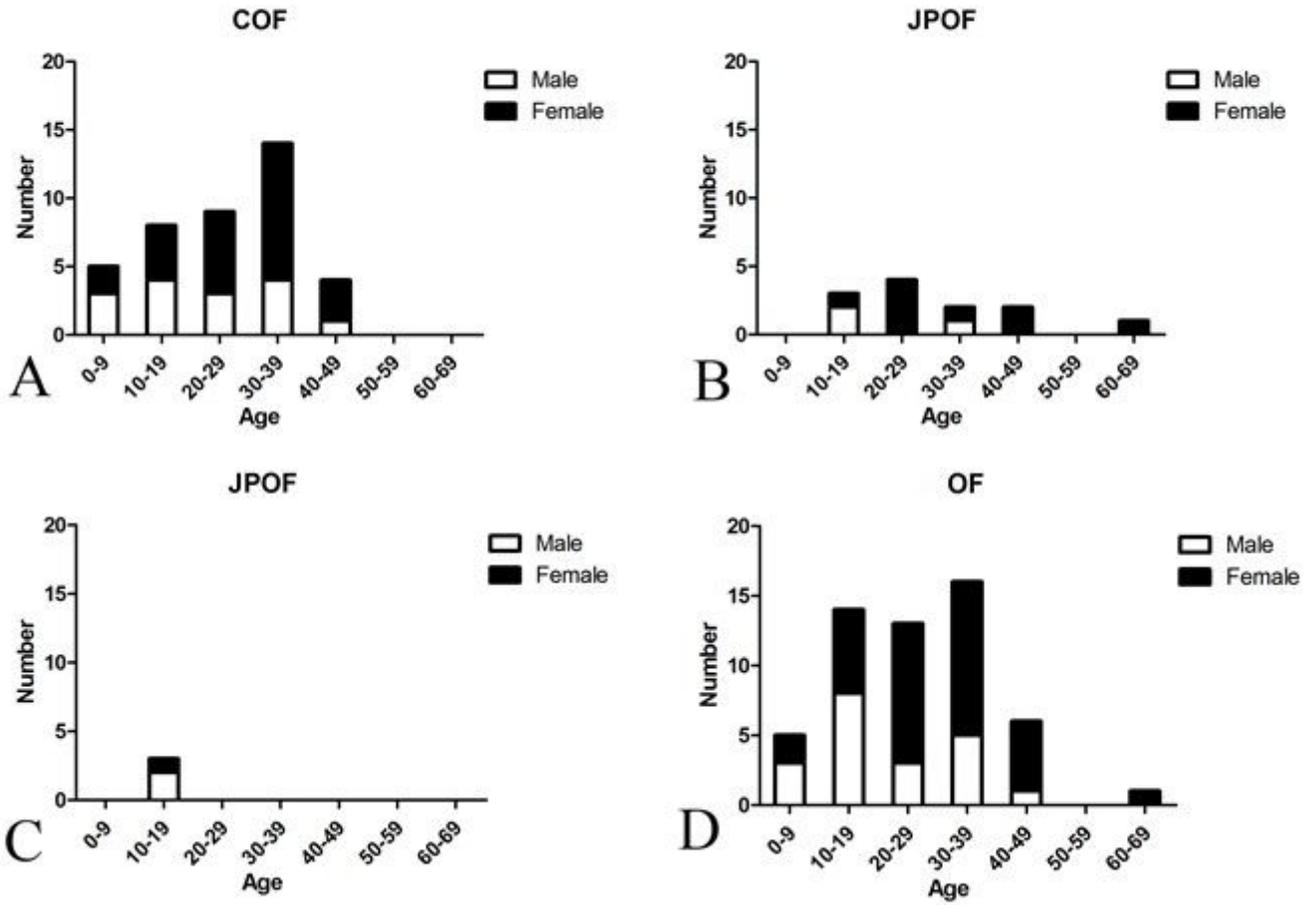
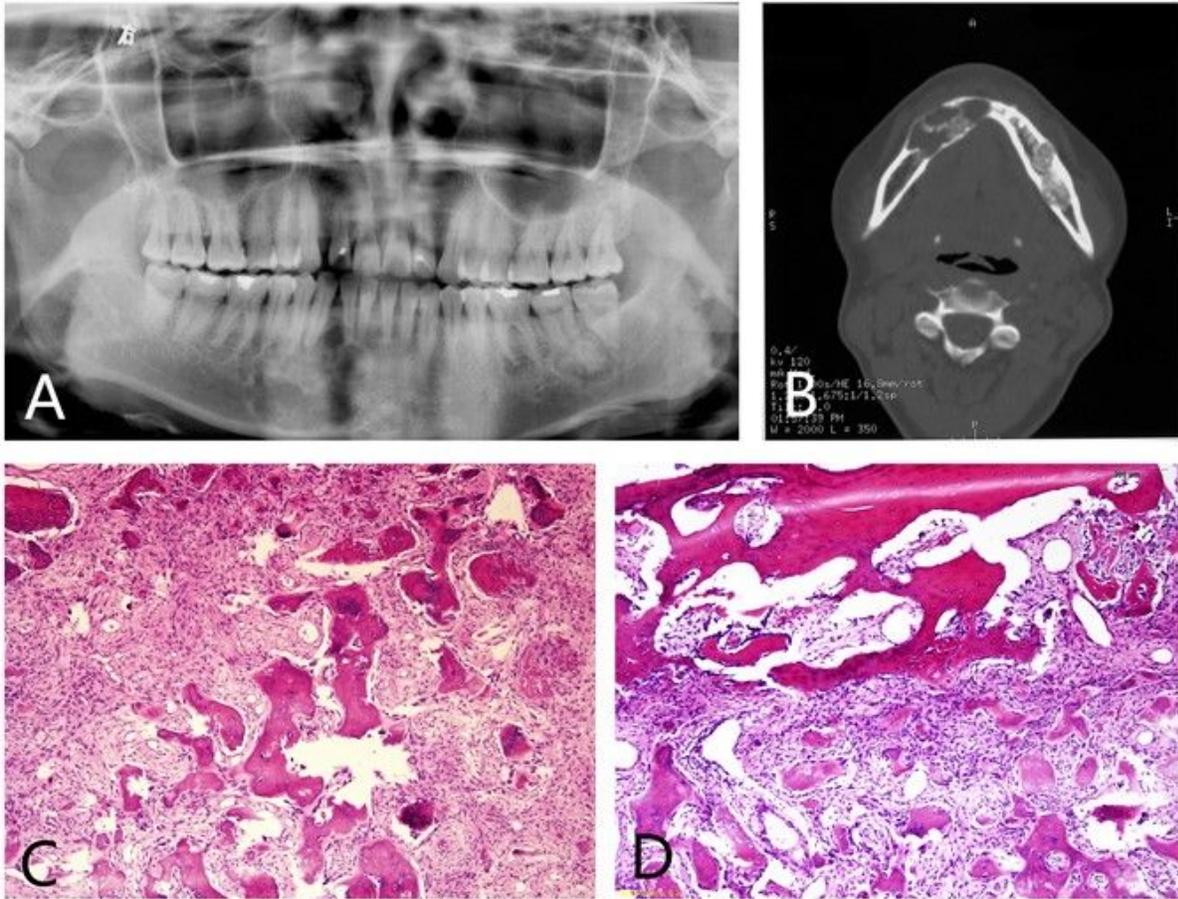


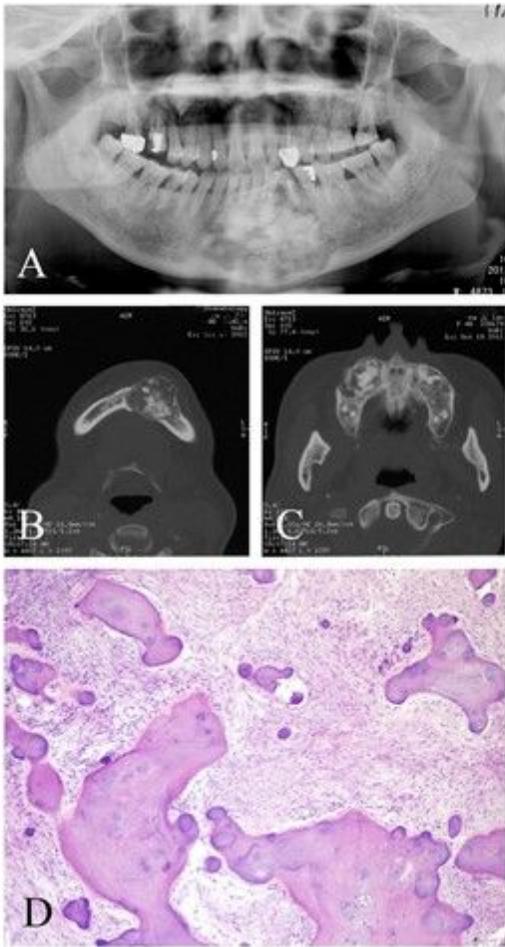
Figure 1

The age and gender of three subtypes of ossifying fibroma



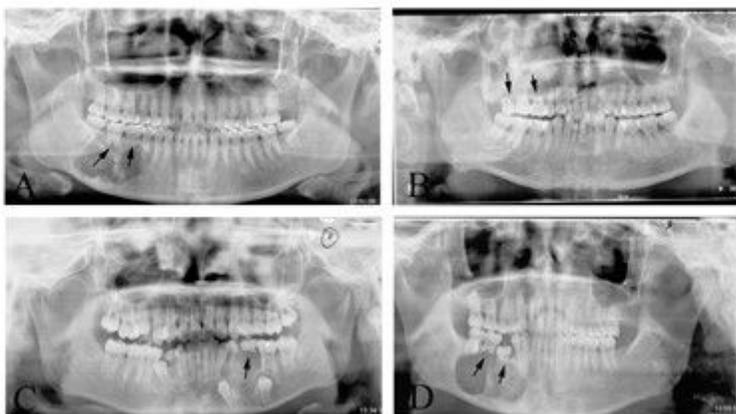
**Figure 2**

Mutiple ossifying fibroma of case 1 A-B Panoramic radiograph and CT showing two well-demarcated mixed-density lesion bilaterally in the mandible. C Haematoxylin and eosin stain of the right lesion(100×) D Haematoxylin and eosin stain of the left lesion(Magnification: 100×)



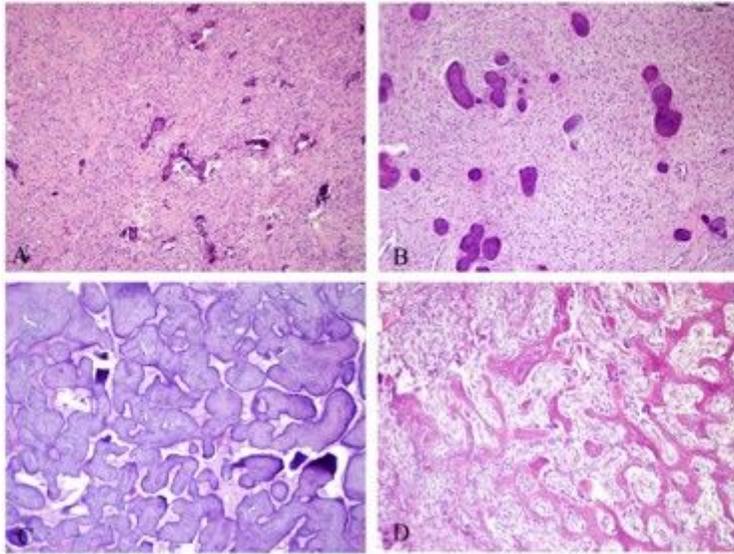
**Figure 3**

Mutiple ossifying fibroma of case 2 A-C Panoramic radiograph and CT showing well-demarcated mixed-density lesions both in maxilla and mandible. D Haematoxylin and eosin stain of the lesion showing JPOF(Magnification: 100×)



**Figure 4**

## Root resorption in amputated type of ossifying fibroma



**Figure 5**

The histopathological manifestations of ossifying fibroma. A The Conventional OF (COF); B The Juvenile Trabecular OF (JPOF); C The Juvenile Psammomatoid OF (JPOF) of older patients, concentric circle shaped psammomatoid; D The Juvenile Trabecular OF (JTOF). (Magnification: 100×)

## Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- [Tables.pdf](#)