Nonspecific Cystic Degeneration in Craniofacial Fibrous Dysplasia: A Rare Finding

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Abstract

Fibrous dysplasia (FD) is a developmental pathology of the bones in which normal bone is replaced by fibrous tissue and immature bone. It can affect single bone (monostotic) or multiple bones (polyostotic), sporadically or in association with McCune-Albright syndrome, Jaffe-Lichtenstein syndrome, or Mazabraud syndrome. When multiple bones in the craniofacial region are affected, the term "craniofacial FD" is used. Nonspecific cystic degeneration occurring in FD of the jaws has rarely been reported in the literature. Here, we present a 52-year-old male patient who reported with a longstanding gradual expansion of the mandible unilaterally. Investigations revealed the presence of mixed radiolucent radioopaque appearance in the mandible and dense sclerotic multiple craniofacial bones. In addition, a lytic lesion in the mandible was appreciated. Histopathological examination of the mandible confirmed the diagnosis of FD with nonspecific cystic degeneration.

Keywords: *Bone diseases, craniofacial fibrous dysplasia, fibrous dysplasia of bone, mandible*

Introduction

Fibrous dysplasia (FD) is a nonheritable genetic disorder characterized by the replacement of normal bone by haphazardly distributed immature bony and fibrous tissue.[1] It is an unusual developmental condition caused by postzygotic mutation of the GNAS1 gene, resulting in the persistent activation of the G protein-stimulatory subunit. Activation of the G-protein complex leads to inappropriate maturation of osteoblasts and deposition of fibro-osseous tissue in place of bone. Clinically, FD may manifest as monostotic, polyostotic or syndromic depending on the timing of the mutation. The term craniofacial FD (CFD) is used when the maxilla and its contiguous bones such as sphenoid, frontal, zygomaxillary, and base of the skull are involved.[2] Diagnosis requires close correlation primarily between clinical and radiological features with histologic confirmation desirable in some cases.

Case Report

A 52-year-old male patient reported to our institution with a complaint of swelling in the lower jaw. He gave a history of having swelling since childhood. He also reported that removal of the swelling had been done around 20 years back in a private dental clinic. However, he had lost the records of the same. Subsequently, he noticed the reappearance and gradual increase of the swelling over the years. On extraoral examination, swelling of size 2 cm × 3 cm was seen on the left side extending from below the corner of the lip till the angle of the mandible [Figure 1a]. It was bony hard and nontender with no rise in local temperature. Intraoral examination showed a slight obliteration of the lower left vestibule and missing 35, 36, and 37 [Figure 1b]. The patient reported that these teeth were removed during the previous surgery. Orthopantomogram (OPG) was taken and showed a mixed radiolucent radiopaque lesion extending from the premolar region till the angle of the mandible with expansion and bowing of the lower border on the left side [Figure 2]. With a provisional diagnosis of the fibroosseous lesion, an incisional biopsy was done. Microscopic examination of this tissue showed only peripheral bone with irregular surface indicative of resorption [Figure 3]. Since the incisional biopsy was not definitive, the surgeons went ahead with further investigations.

Laboratory investigations such as routine blood examination and serum

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alkaline phosphatase levels were done and found to be within normal limits. Multidetector computed tomography neuronavigation (head) showed a well-defined lytic lesion with intact cortex and sclerosed margin measuring 3.9 cm × 3.3 cm × 4.4 cm (anteroposterior × transverse × craniocaudal) in the body of the mandible on the left side [Figure 4a]. Furthermore, diffuse dense and sclerosed appearance of the left maxilla, zygoma, sphenoid body, left squamous and petrous part of the temporal bone, left mastoid and anterior ethmoid bone was noted [Figure 4b]. Whole-body computerized tomography (CT) scan ruled out the involvement of other bones including long bones and vertebrae. A provisional diagnosis of CFD with the possibility of concomitant aneurysmal bone cyst was then considered. Considering the presence of lytic lesion in the mandible with continuing expansion, a wide local excision extending from the angle of the mandible on the left side to contralateral canine with reconstruction using free fibula flap was done. The excised bone was sent for histopathological examination. The resected specimen showed open cavitary defects extending from the premolar region to the posterior end [Figure 5]. On sectioning the mandible, smaller cystic areas were seen. The scanty soft tissue within the cystic areas was scooped out and given for microscopic examination along with the decalcified bone. The hard tissue specimens showed a fibro cellular connective tissue stroma with mineralization. The mineralized component was in the form of immature bone of different shapes and sizes which were not interconnected and the absence of osteoblastic rimming in most of the areas [Figure 6a]. At the periphery, more mature bone blending with the adjacent normal cortical bone was noted [Figure 6b]. The connective tissue stroma showed proliferation of spindle cells with numerous endothelial lined vascular spaces of varying sizes with small foci of immature bone. The soft-tissue specimen showed cellular connective tissue with the proliferation of spindle cells in a loose stroma [Figure 7a]. Numerous endothelial lined vascular spaces of varying sizes filled with red blood cells were seen throughout [Figure 7b]. The cystic areas showed only compressed connective tissue without any epithelial lining [Figure 8a and b]. These findings were consistent with nonspecific cystic degeneration in a case of FD. Correlating with the radiological features, a final diagnosis of CFD with nonspecific cystic degeneration in the mandible was given. Since the skull lesions were asymptomatic, the patient was asked to come for regular follow-up. At the past follow-up, 6 months after the surgery, the patient had adjusted well to the mandibular prosthesis. As the patient was otherwise asymptomatic, imaging studies are planned for the next follow-up visit.

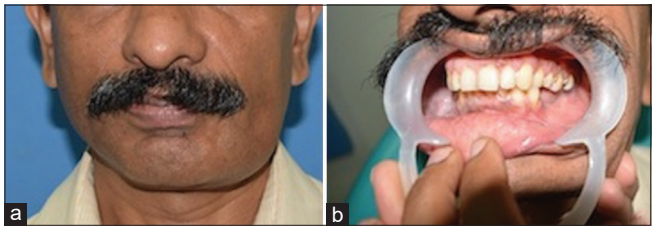

Figure 1: Clinical photograph of the patient. (a) Extra-oral photograph showing the swelling in the left side of the mandible. (b) Intraoral photograph showing mild obliteration of buccal vestibule

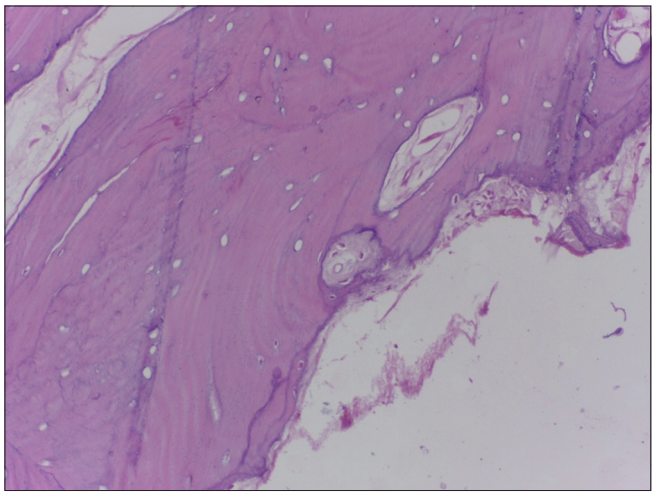

Figure 3: Histopathology of incisional biopsy specimen showing resorptive bone with irregular borders (hematoxylin and eosin, ×20)

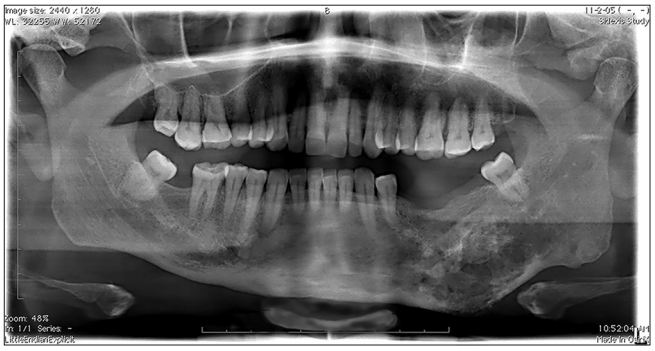

Figure 2: Orthopantomogram showing mixed radiolucent radiopaque lesion extending from premolar region till angle of the mandible on the left side with bowing of lower border

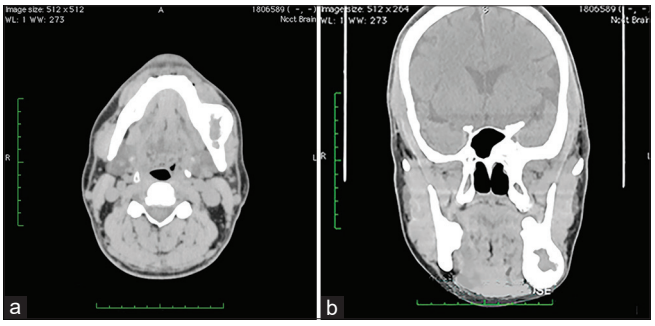

Figure 4: Multidetector computed tomography (head). (a) Well-defined lytic lesion with intact cortex and sclerosed margin in the body of the mandible on the left side. (b) Diffuse homogeneous dense sclerosed appearance of the left maxilla, zygoma, sphenoid body, left squamous and petrous part of the temporal bone, left mastoid, and anterior ethmoid bone

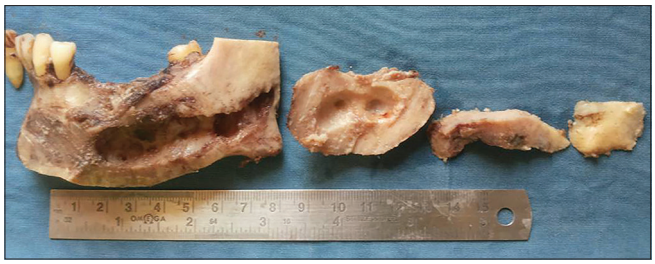

Figure 5: Resected specimen showed open cavitary defects extending from the premolar region to the angle of the mandible

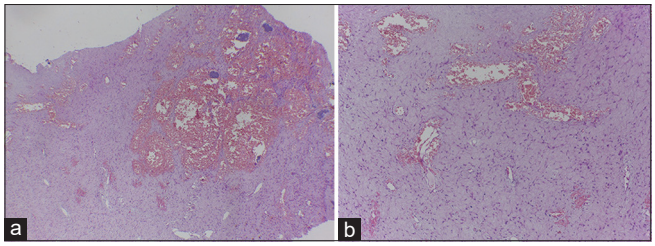

Figure 7: Histopathology of soft-tissue within the bone showing (a) Cellular connective tissue with proliferation of spindle cells in a loose stroma (hematoxylin and eosin, ×4). (b) Numerous endothelial lined vascular spaces of varying sizes filled with red blood cells (hematoxylin and eosin, ×20)

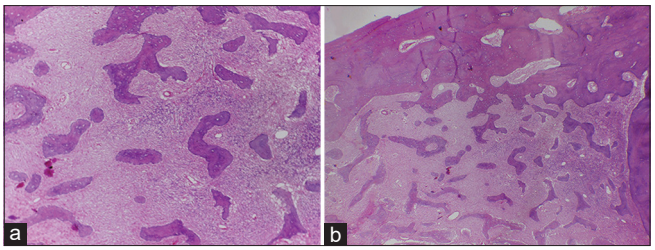

Figure 6: Histopathology of decalcified mandible showing (a) Immature bone showing characteristic "Chinese character" pattern in a fibro cellular matrix (hematoxylin and eosin, ×10). (b) At the periphery, immature bone is seen merging with the cortical bone (hematoxylin and eosin, ×10)

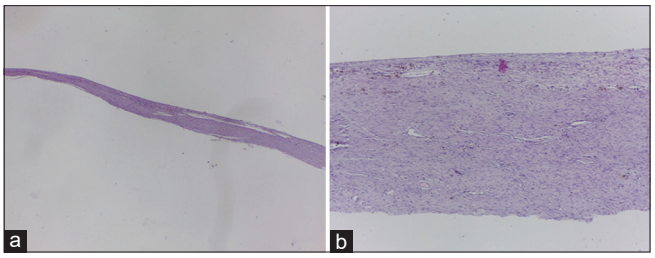

Figure 8: Specimen from the cystic cavity showed (a) Only compressed connective tissue (hematoxylin and eosin, ×4). (b) Magnified image showing absence of epithelial lining (hematoxylin and eosin, ×20)

Discussion

CFD is typically a slow-growing lesion that maybe identified incidentally on routine radiography or when gradual swelling and facial asymmetry becomes noticeable.[1] The most affected bones in the craniofacial region are maxilla, mandible, sphenoid, ethmoidal, and frontal bones, whereas occipital and temporal bones are the least affected.[3] Moreover, FD is relatively rare in the craniofacial region accounting for only 20% of all locations.[4] CFD may cause gradual expansion and thickening of skull bones leading to asymmetry and deformity. Their behavior may change if associated with other rapidly growing lesions such as aneurysmal bone cysts or other endocrinopathies.[1] The main symptoms other than facial asymmetry are mainly due to the compression such as headache, visual disturbances, sinusitis, nasal obstruction, and neuralgias depending on the bone involved. Unusually, our patient presented with only facial asymmetry and craniofacial involvement was diagnosed upon subsequent investigations. FD usually presents in the younger age group and stabilizes over time. As our patient was 55-year-old, the disease progression must have been long-standing but with a slow progression. Since the previous surgical reports were missing, we only had the patient's verbal summary of the disease progression.

Radiographic findings in FD, though not pathognomonic, are very characteristic with the lesional bone showing merging with adjacent normal bone. The radiographic presentation may vary depending on the ratio of bone and fibrous matrix and is usually seen as three patterns: (i) Pagetoid - where the bone and fibrous matrix are equal and is seen as ground-glass appearance, (ii) sclerotic - more amount of bone is seen, and (iii) radiolucent - fibrous matrix is more.[3] CFD typically demonstrates dense and sclerotic lesions.[5] The presence of secondary changes such as cystic degeneration, aneurysmal bone cyst, or simple bone cyst can also contribute to radiolucent picture. CT without contrast can show the radiographic extent of the lesion. Bone scintigraphy is useful as a skeletal survey for the extent of the disease process. Magnetic resonance imaging (MRI) is most helpful for cases that are suspected to have a malignant change.[1,5] The radiographic features noted in our case was mixed radiolucent radiopaque appearance in the OPG while the lytic changes were detected only in the CT images. The extent of craniofacial involvement was also seen in the CT scan.

The classic microscopic appearance of FD is described as immature, delicate, and curvilinear bony trabeculae with variable degree of mineralization and displaying classic "Chinese character" pattern with minimal or no osteoblastic rimming within a vascularized fibrous stroma of variable cellularity.[2] The histopathologic picture is dependent on the stage of the disease. Early stages may show thin woven bone with hypercellular stroma. As the disease progresses, the immature woven bone becomes thicker in the hypercellular stroma. The woven bone, in the later stages, maybe replaced by lamellar bone with prominent resting and reversal lines. Evidence of lesional bone blending with the unaffected bone at the periphery is most useful in diagnosis.[2] Secondary changes in FD includes the formation of cyst, peritrabecular clefting, osteoblastic rimming, lamellar bone pattern, resting and reversal lines, and cementoid bodies.[2] The classic picture

of woven bone showing Chinese character pattern was seen in our case along with merging or blending with the unaffected bone. In some areas, hypercellular stroma with minimal bone formation and prominent blood vessels were noted. Incision biopsy sample did not show the features of FD and this could be attributed to superficial sampling.

Nonepithelial lined cysts can occur occasionally in association with various benign and malignant bone lesions including FD. These cysts vary in nature; they maybe aneurysmal bone cysts, simple bone cysts, and nonspecific cystic degenerations.[6] Nonspecific cystic degeneration is a term used to describe a lesion that fails to meet the histologic criteria for either an aneurysmal or simple bone cyst.[7] Although the exact pathogenesis is unknown, these changes seem to occur in longstanding cases. Since aneurysmal bone cyst and simple bone cysts are thought to originate due to local alteration in hemodynamics, nonspecific cystic degeneration may also have a similar etiology. The first reports of FD complicated by nonspecific cystic degeneration have been attributed to Jaffe and Schlesinger, Keats, and Ruoff.[7] In their case series, Diah *et al*.[8] observed that changes of cystic degeneration were noted between 1 and 7 years after initial diagnosis. They also noted that sudden enlargement and pain are the common symptoms of these patients. There are seven cases of nonspecific cystic degeneration in CFD previously published in the English literature [Table 1]. The cystic cavity seen in our case was lined by compressed connective alone without the presence of any lining epithelium and hence, can be considered as nonspecific cystic degeneration.

As the behavior and progression of CFD may vary considerably in each case, the management also becomes difficult and complex and requires a case-based approach. It was earlier believed that it may become quiescent in late adolescence, but now not believed to be the case with some patients experiencing growth late into adulthood.[9] The treatment options include observation, medical therapy, surgical remodeling, radical excision, and reconstruction.[5,9] Asymptomatic cases may be followed regularly while surgery is indicated for rapid enlargement and compression.[8] However, given the difficulty in accessing areas such as the skull base, observation is recommended. CT imaging maybe repeated as needed for symptomatic lesions in adulthood.[5] The use of anti-resorption drugs like bisphosphonates may be considered for pain reduction and to reduce rate of growth.[10] Resection and reconstruction were done in our patient as the surgeons felt that recontouring or shaving may result in pathologic fracture due to the presence of lytic changes in the mandible.

Table 1: Summary of previously reported cases of nonspecific cystic degeneration in craniofacial fibrous dysplasia

Authors	Age (years)	Gender	Presenting complaint
Diah *et al*.[8]	10	Female	Sudden enlargement*
Diah *et al*.[8]	11	Female	Pain*
Diah *et al*.[8]	22	Female	Sudden enlargement, pain, visual disturbances
Diah *et al*.[8]	21	Female	Sudden enlargement, pain
Diah *et al*.[8]	40	Male	Pain*
Bowers *et al*.[13]	24	Female	Visual disturbances*
Singh *et al*.[14]	16	Male	Sudden enlargement, pain
Present case	52	Male	Enlargement

*Case where histopathologic report was unavailable

All cases of CFD require long-term follow-up. Cystic degeneration or malignant transformation can occur spontaneously, and patients may develop symptoms such as sudden enlargement and pain.[8] Malignant transformation has been reported to occur in 0.4%–4% of cases of FD.[11] Cystic degeneration can be detected by CT scans and biopsy to exclude malignancy in questionable cases is recommended.[8] To differentiate between the two, imaging modalities such as CT and MRI are essential. Resection and reconstruction may result in less regrowth and fewer operations than more conservative debulking and recontouring techniques.[12] Careful follow-up is advised as recurrences after removal of cyst has been reported.[8]

To conclude, we are reporting a rare occurrence of nonspecific cystic degeneration in a case of CFD in a 52-year-old male patient who reported with a long-standing jaw swelling. This is only the eighth such case reported in the English literature. Nonspecific cystic degeneration can occur in longstanding cases of FD and this should be borne in mind when clinicians suspect FD in older patients.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Nil.

Conflicts of interest

There are no conflicts of interest.

References

1. Ricalde P, Magliocca KR, Lee JS. Craniofacial fibrous dysplasia. Oral Maxillofac Surg Clin North Am 2012;24:427-41.
2. Davidova LA, Bhattacharyya I, Islam MN, Cohen DM, Fitzpatrick SG. An analysis of clinical and histopathologic features of fibrous dysplasia of the jaws: A series of 40 cases and review of literature. Head Neck Pathol 2020;14:353-61.
3. Hanifi B, Samil KS, Yasar C, Cengiz C, Ercan A, Ramazan D. Craniofacial fibrous dysplasia. Clin Imaging 2013;37:1109-15.

4. Chandavarkar V, Patil PM, Bhargava D, Mishra MN. A rare case report of craniofacial fibrous dysplasia. J Oral Maxillofac Pathol 2018;22:406-9.
5. Kushchayeva YS, Kushchayev SV, Glushko TY, Tella SH, Teytelboym OM, Collins MT, *et al.* Fibrous dysplasia for radiologists: Beyond ground glass bone matrix. Insights Imaging 2018;9:1035-56.
6. Eversole R, Su L, ElMofty S. Benign fibro-osseous lesions of the craniofacial complex. A review. Head Neck Pathol 2008;2:177-202.
7. Ferretti C, Coleman H, Dent M, Altini M. Cystic degeneration in fibrous dysplasia of the jaws: A case report. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 1999;88:337-42.
8. Diah E, Morris DE, Lo LJ, Chen YR. Cyst degeneration in craniofacial fibrous dysplasia: Clinical presentation and management. J Neurosurg 2007;107:504-8.
9. Kim DD, Ghali GE, Wright JM, Edwards SP. Surgical treatment of giant fibrous dysplasia of the mandible with concomitant craniofacial involvement. J Oral Maxillofac Surg 2012;70:102-18.
10. Lee JS, FitzGibbon EJ, Chen YR, Kim HJ, Lustig LR, Akintoye SO, *et al.* Clinical guidelines for the management of craniofacial fibrous dysplasia. Orphanet J Rare Dis 2012;7 Suppl 1:S2.
11. Couturier A, Aumaître O, Gilain L, Jean B, Mom T, André M. Craniofacial fibrous dysplasia: A 10-case series. Eur Ann Otorhinolaryngol Head Neck Dis 2017;134:229-35.
12. Boyce AM, Burke A, Cutler Peck C, DuFresne CR, Lee JS, Collins MT. Surgical management of polyostotic craniofacial fibrous dysplasia: Long-term outcomes and predictors for postoperative regrowth. Plast Reconstr Surg 2016;137:1833-9.
13. Bowers CA, Altay T, Shah L, Couldwell WT. Pregnancy-induced cystic degeneration of fibrous dysplasia. Can J Neurol Sci 2012;39:828-9.
14. Singh V, Gupta K, Salunke P. Monostotic craniofacial fibrous dysplasia: Report of two cases with interesting histology. Autops Case Rep 2019;9:e2018092.