CASE REPORT

Monostostic fibrous dysplasia with nonspecific cystic degeneration: A case report and review of literature

Afreen Nadaf, MB Radhika[1], K Paremala[1], N Srinath[2]

Departments of Oral Pathology, Government Dental College, Jammu and Kashmir; [1]Oral and Maxillofacial Pathology, Krishnadevaraya College of Dental Sciences, Bangalore, Karnataka; [2]Oral and Maxillofacial Surgery, Krishnadevaraya College of Dental Sciences, Bangalore, Karnataka, India

Address for correspondence:
Dr. Afreen Nadaf,
Department of Oral & Maxillofacial Pathology
Govt. Dental College & Hospital, Srinagar,
Jammu and Kashmir - 190 015, India.
E-mail: aanadaf@gmail.com

ABSTRACT

Fibrous dysplasia (FD) has been regarded as a developmental skeletal disorder characterized by replacement of normal bone with benign cellular fibrous connective tissue. It has now become evident that FD is a genetic disease caused by somatic activating mutation of the Gsα subunit of G protein-coupled receptor. Here we report a case of bilateral monostotic FD in a middle-aged female showing a classic histological picture, but radiologically presenting as a mixed radiolucent radiopaque lesion showing nonspecific cystic degeneration.

Key words: Fibrous dysplasia, monostotic, nonspecific cystic degeneration

INTRODUCTION

Benign fibro-osseous lesions of the craniofacial complex represent a variety of disease processes that are characterized by pathologic ossifications and calcifications in association with a hypercellular fibroblastic marrow element.[1] The designation fibro-osseous lesion is not a specific diagnosis and describes only a process. Fibro-osseous lesions of the jaws include developmental (hamartomatous) lesions, reactive or dysplastic processes, and neoplasms.[2]

Fibrous dysplasia (FD) a developmental tumor-like condition still remains as a clinicopathologic challenge for many reasons. Although usually easily diagnosed, FD may present with clinical and radiographic features that may border with other benign fibro-osseous lesions of the skeleton and (although rarely) may be confused with certain elusive types of malignancies.[2,3] Mention of FD first appeared in the literature in 1937 when Albright and coworkers reported a disease showing cutaneous pigmentation and endocrine disorder in addition to FD.[4]

The term FD of bone was first used by Lichtenstein in 1938 to describe a condition to which attention had been drawn by Hunter and Turnbull (1931). They stated: "Of much more common occurrence than the generalized disease is a focal osteitis fibrosa. This condition affecting one or more bones; usually not disabling; of slow progress; and showing a tendency to become arrested. It occurs chiefly in adolescence and is often symptomless until spontaneous fracture occurs. The figures for serum calcium and phosphorous are invariably normal". This a description of FD which has since hardly been improved.[5,6]

FD represents 5-7% of benign bone lesions.[5,7] Although the FD of the extracranial skeleton is a relatively common bone lesion, the involvement of the facial bones is much rarer.[8] Being a sporadic benign skeletal disorder, it can affect one bone (monostotic form), or multiple bones (polyostotic form). Polyostotic form may form part of the McCune-Albright syndrome (MAS) or of the Jaffe-Lichtenstein syndrome (JLS). JLS is characterized by polyostotic FD and cafe-au-lait pigmented skin lesions, while MAS has the additional features of hyperfunctional endocrinopathies manifesting as precocious puberty, hyperthyroidism, or acromegaly.[9]

Gender prevalence of FD is equal. The monostotic form is more common, affects the 20-30 years age group and commonly affects the jaw bones.[2] Polyostotic FD has its onset mainly in children younger than 10 years of age, the lesions grow with the child and stabilize after puberty and commonly involve craniofacial bones, ribs, and metaphysis or diaphysis of the proximal femur or tibia. The ratio of occurrence of polyostotic to monostotic FD is 3:7.[9]

The craniofacial bones are affected in about 10% of cases of monostotic FD and in 50-100% of cases of polyostotic

Access this article online

Quick Response Code:

Website: www.jomfp.in

DOI: 10.4103/0973-029X.119765

FD. When only the cranial and facial bones are affected by FD, the term craniofacial FD is used. The prevalence of the polyostotic craniofacial FD ranges from 71 to 91% and monostotic form from 10 to 29%. FD of the jaws affects the maxilla more frequently than the mandible and affects females more frequently than males.[9]

Any cranial or facial bone can be affected by FD and associated clinical features will depend upon the bone or bones affected. Signs and symptoms can include facial pain, headache, cranial asymmetry, facial deformity, tooth displacement, and visual or auditory impairment.[9]

Here, we present a case of monostotic FD occurring bilaterally in the mandible of a middle-aged woman. A literature search revealed very few cases of bilateral monostotic FD and our case could add to this frugal list.

CASE REPORT

A 40-year-old female patient reported to our college, with a chief complaint of swelling in the lower right and left posterior teeth region since 6 years. The swelling was asymptomatic. Her medical history was noncontributory. Extraoral examination revealed a swelling on the right posterior region of the mandible. The swelling extended anteroposteriorly 1.0 cm from the commissure to 4.0 cm in front of the angle of the mandible and superoinferiorly 1.0 cm above the lower border of the mandible to 0.5 cm from the commissural line and measured 4.0 × 3.0 cm in dimension. It was ill-defined, hard, and nontender; with overlying normal skin [Figure 1]. Intraorally, the swelling extended from the mesial aspect of 44 to the distal aspect of 47 with slight obliteration of the buccal vestibule. The lingual cortex showed slight expansion. The overlying mucosa was stretched but intact.

Extraoral examination revealed a diffuse swelling on the left lower border of the mandible extending 2.0 cm behind the angle of the mouth to 5.0 cm from the angle of the mandible and measured 3.0 × 2.0 cm in dimension, was hard and nontender with overlying normal skin [Figure 2]. Intraorally, the swelling extended from mesial aspect of 34 to distal aspect of 37 with no obliteration of the buccal vestibule. The overlying mucosa was normal. Submandibular lymph nodes were palpable on both sides, solitary, mobile, and nontender.

The orthopantomograph showed a well-defined multilocular radiolucency with specks of radiopacity in the right and left posterior mandible. Radiolucency extended from 43 region to the ramus of the mandible on right side and from 34 to 37 region on the left side of the mandible, 36 was missing. The lower border of the mandible was intact [Figure 3].

Occlusal radiograph showed expansion of the buccal and lingual cortices on both right and left side of the mandible. Ground glass appearance of the mandible was visible [Figure 4]. Computed tomography (CT) scan revealed well-defined lytic lesion with radiopacities involving right and left posterior mandible region with buccal and lingual cortical expansion [Figure 5].

Routine blood and urine investigations along with serum examination for alkaline phosphatase activity and calcium profile were performed and the values were within normal limits.

Surgical note

Under general anesthesia, a degloving incision was placed on the right side and the lesion was surgically recontoured. The lesional tissue did not separate out from the bone easily. The same procedure was followed on the left side and cystic cavities were seen which were empty [Figure 6] and the lesion did not separate out easily. Hemostasis was achieved, betadine wash given, and primary closure was achieved. Specimens were submitted for histopathological examination with a clinical diagnosis of fibro-osseous lesion. Patient was kept under postoperative observation

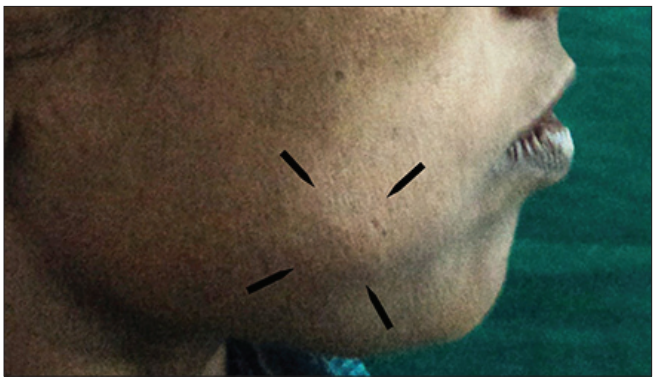

Figure 1: Clinical photograph showing swelling on the right side of the mandible

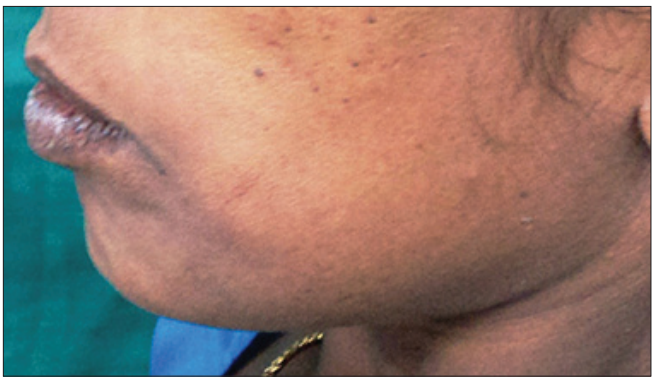

Figure 2: Clinical photograph showing diffuse swelling on the left lower border of the mandible

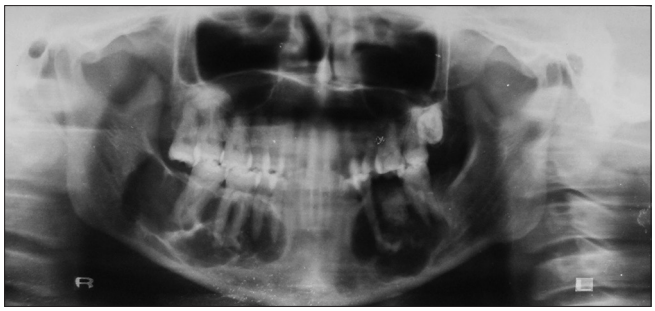

Figure 3: Orthopantomogram showing well-defined multilocular radiolucency with specks of radiopacity in the right and left posterior mandible

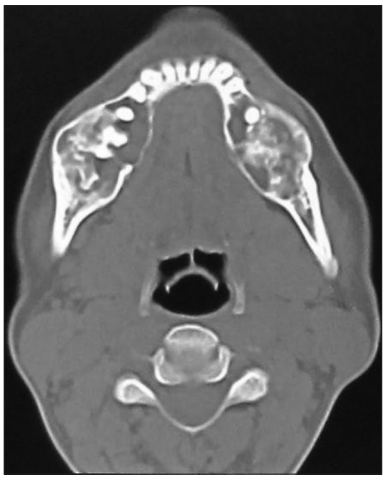

Figure 5: Computed tomography scan showing well-defined lytic lesions involving right and left posterior mandibular region with thinning and expansion of buccal and lingual cortical plates

and recovered without any postsurgical complications. The healing was uneventful.

PATHOLOGY

Macroscopic findings

Multiple hard tissue specimens were received from both the right and left lesional area. The specimens from the left side were creamish white in color, smooth surface was seen on the buccal aspect, and were bony hard in consistency. Cystic cavities with hemorrhagic areas were seen on the inner aspect of the tissue specimen [Figure 7]. The largest specimen measured 3.0 × 2.0 × 1.0 cm.

The right side specimens were creamish white in color, with smooth surface and bony hard in consistency, largest specimen measured 2.8 × 2.0 × 0.7 cm. The specimens were subjected to decalcification in 5% nitric acid and processed routinely.

Microscopy

The 4 μm thick hematoxylin and eosin (H and E) stained sections of the lesion on the right side showed numerous delicate

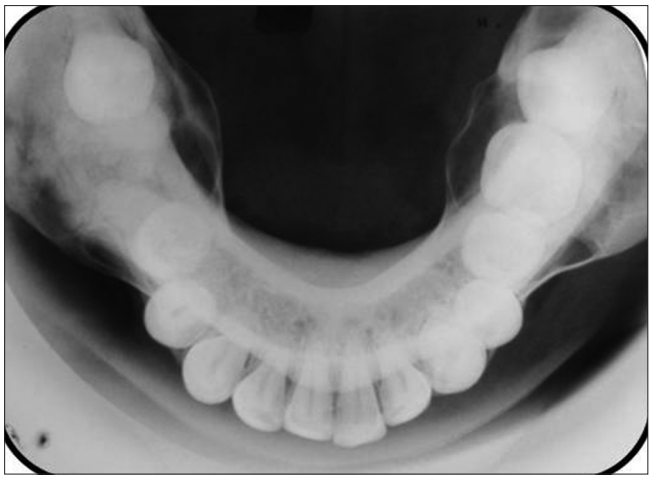

Figure 4: Occlusal radiograph showing expansion and thinning of the buccal and lingual cortex on both sides of the mandible with ground glass appearance

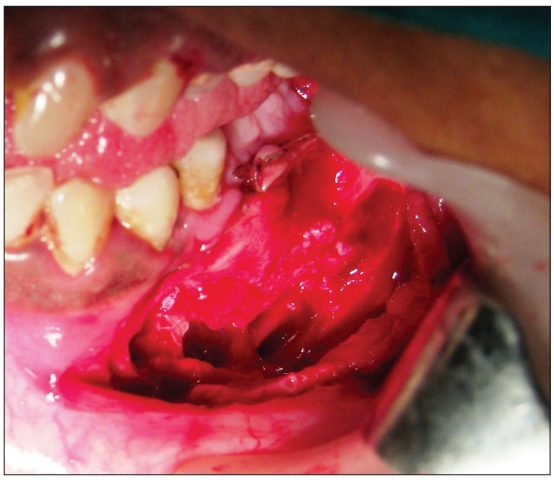

Figure 6: Cystic cavities in relation to the swelling on the left side of the mandible which were empty on surgical exploration

trabeculae arranged in different forms lacking osteoblastic rimming. Intervening spaces showed fibrous proliferation. Typical Chinese letter pattern of the trabeculae was evident. Few marrow spaces with blood vessels were present. The fibrous connective tissue was mature and well-formed. The bony trabeculae were merging with the surrounding normal bone [Figure 8a-c].

The H and E stained sections of the left side showed cellular connective tissue. Fibrocellular tissue was seen, along with trabeculae of woven bone. Trabeculae were intermixing with each other and were fused with the surrounding normal bone. Osteoblastic activity was seen. Numerous osteoclasts were also seen resorbing the normal bone. Few areas showed calcified spherules resembling psammoma bodies in fibrous stromal background [Figure 9a-c].

The patient is under a postsurgical follow-up since 6 months which has been uneventful so far.

DISCUSSION

FD first appeared in 1937 in the literature, reported by Albright and coworkers. In 1938, Lichtenstein defined polyostotic myelofibrous lesions without cutaneous pigmentation and endocrine disorder as polyostotic FD. Lichtenstein and Jaffe in 1942 included the monostotic and polyostotic forms in FD of bone and Schlumberger (1946) termed the monostotic form; monostotic FD.[4]

The term facial FD, as advocated by Thoma, may be appropriate for lesions involving the facial bones other than mandible. As mandible is a single bone unlike the bones of the facial skeleton, we classified the present case as a monostotic FD.[4]

Many theories were proposed to explain the etiology signifying trauma with a nonspecific disturbance in local bone reaction or a congenital anomaly or "perverted" activity of mesenchymal bone-forming cells and a complex endocrine disturbance with local bone susceptibility as etiological factors.[7] Of these, Lichtenstein's theory of abnormal growth of undifferentiated osteogenic mesenchymal tissue is well accepted.[4]

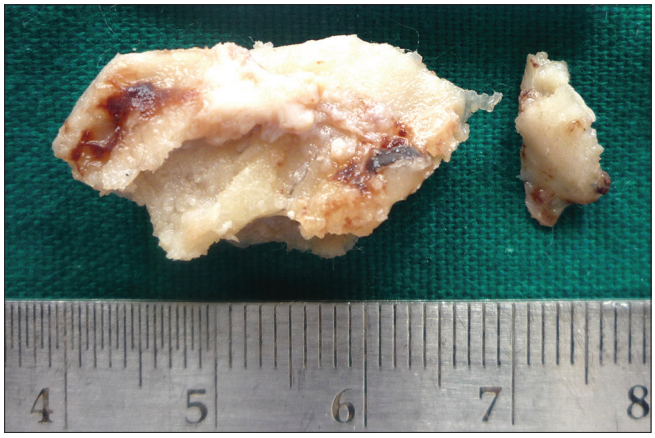

Figure 7: Macroscopic picture of the resected lesional hard tissue of the left side, creamish white in color, with irregular surface. Cystic cavities with hemorrhagic areas are seen on the inner aspect

The etiology of FD is now believed to be a developmental error in which primitive fibrous tissue proliferation within the bony medulla that encroaches upon the cortex often producing expansion.[6,10] However, the fact that the three different systems involved in the polyostotic FD arise from different embryological tissues gives some countenance to the theory of a central or nervous system lesion.[10]

Recent studies have shown that the disease is a genetic non-inherited condition caused by missense mutation in the GNAS1 gene. The molecular underpinning of this related group of diseases is a mutation in the gene on chromosome 20 that encodes the G protein α-subunit (Gsα), of the stimulatory G protein-coupled receptor that couples cyclic adenosine monophosphate (cAMP) to hormone receptors. These mutations result in guanosine triphosphatase (GTPase) perturbations that lead to prolonged Gsα activation and stimulation of endocrine receptors.[1,9,11] The activating mutations occur postzygotically, replacing the arginine amino acid residue with either a cysteine or a histidine amino acid. The mutation selectively inhibits GTPase activity, resulting in constitutive stimulation of AMP-protein kinase A intracellular signal transduction pathway;[9] and this induces an alteration in the transcription and expression of several downstream target genes, including c-*fos*, a proto-oncogene.[11]

The systemic manifestations of the mutated Gsα protein-coupled receptor complex include autonomous function in

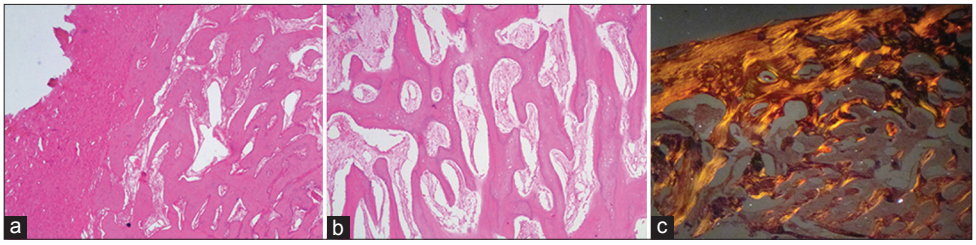

Figure 8: Photomicrograph of the lesion on the right side showing numerous delicate trabeculae arranged in different forms lacking osteoblastic rimming. Intervening spaces showed fibrous proliferation (H&E stain,; (a) ×40, (b) ×100). (c) Polarizing microscopic photomicrograph showing normal bone on the periphery, cascading into immature bone (H&E stain, x40)

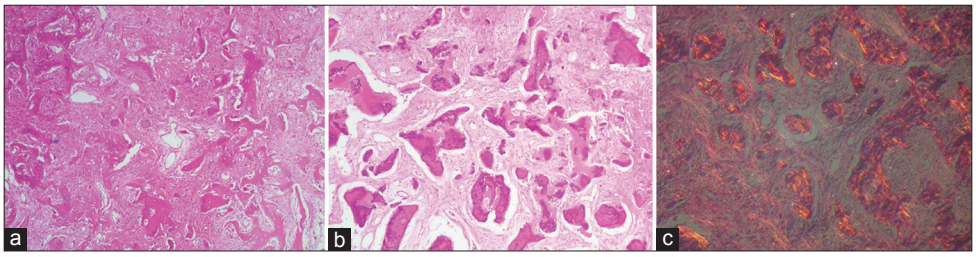

Figure 9: Photomicrograph of the lesion on the left side showing calcified spherules composed of immature bone. Intervening spaces showing fibrocellular proliferation (H&E stain (a) ×40, (b) ×100). (c) Polarizing microscopic photomicrograph showing calcified spherules composed of immature bone (H&E stain, x40)

bone through parathyroid hormone receptor leading to FD; in skin through melanocyte-stimulating hormone receptor manifesting as cafe-au-lait spots; in ovaries through the follicle-stimulating hormone receptor; and in the thyroid and the pituitary gland, through the thyroid and growth hormone receptors, respectively.[9]

FD is a somatic mosaic disorder with a broad spectrum of phenotypic heterogeneity. The extent of the disease is related to the stage at which the post-zygotic mutation in Gsα had occurred, whether during embryonic development or postnatally.[9]

If the mutation occurs in undifferentiated stem cells during histodifferentiation phase, that is, pregastrulation mutation; the mutated pluripotent cell develops into a mutated clone of cells affecting bones in the case of FD, and affecting multiple organs together with bones in the case of MAS.[9] If the mutation occurs after histodifferentiation and cell migration is complete, that is, postgastrulation mutation, progeny of that mutated cell are essentially confined to just one site resulting in FD affecting a single bone.[2,9]

The postnatal manifestation of FD is not a reflection of the stage of development when the mutation occurred, but indicates the time that the dynamic equilibrium between mutated and normal osteogenic cells in the mosaic fibrous dysplastic bone favored the mutated cells. Possible factors influencing the dominance of mutated over normal cells include growth factors and hormones, and it is probable that there is a 'critical mass' of mutated cells necessary for the development of FD. The burden of mutated cells in FD frequently declines with age, owing to imponderable suppressive influences shifting the balance of transformed to normal cells towards predominance of normal cells, resulting in arrest of FD.[9]

Monostotic FD can occur in the jaw, frontal, ethmoidal, temporal, and calvarial bones. Clinically, the maxilla is affected more often than the mandible and lesions are first detected in the late 1st and early 2nd decades without any gender or racial predilection. The disease is characterized by painless osseous expansion with facial asymmetry.[1]

Polyostotic FD may present in two forms: JLS and MAS.[12] Involvement of two or more bones is seen and is a relatively uncommon condition. The number of involved bones varies from a few to 75% of the entire skeleton. When seen with cafe-au-lait it is termed JLS. Polyostotic FD also may be combined with cafe-au-lait pigmentation and multiple endocrinopathies with manifestations such as sexual precocity, pituitary adenoma, or hyperthyroidism. This pattern is known as the MAS. In the jaws, the lesion presents as a facial asymmetry; but symptoms are usually dominated due to the involvement of long bones. Pathologic fracture with resulting pain and deformity is frequently noted.[2,12]

The cafe-au-lait pigmentations occur due to activating Gs-alpha mutation in skin which involves tyrosinase gene activation in affected melanocytes. They present as well-defined, generally unilateral tan macules on the trunk and thighs, oral mucosal macules may also be present. These pigmented lesions may be congenital. The margins of the cafe-au-lait spots are typically very irregular, resembling a map of the coast line of Maine. This is in contrast to the cafe-au-lait spots of neurofibromatosis, which have smooth borders (like the coast of California).[2,5]

In MAS, sexual precocity is the most common endocrine manifestation of the syndrome, particularly in females. Menstrual bleeding may occur during the first few months of life. Breast development and pubic hair may be apparent within the first few years of life in affected girls.[2] Other less common manifestations of MAS include hyperthyroidism, adenomas of various endocrine glands including the pituitary gland, Cushing syndrome, acromegaly, benign ovarian cysts, linear epidermal nevi, and neonatal cholestasis.[11]

In our case the patient did not present with any other symptoms or pigmentations except for single bone involvement, hence apt to be called as a monostotic variety of FD.

Radiographic features vary depending upon the stage of the disease. Early onset lesions are radiolucent and later progressively calcify, culminating in a ''ground glass'' or mottled mixed radiolucent/radiopaque pattern. Critical to the diagnosis is the fact that FD fails to manifest any discrete margins; rather, the lesional bone subtly blends into the surrounding normal appearing bone.[1]

Involvement of the mandible often results not only in expansion of the lingual and buccal plates but also bulging of the lower border. Superior displacement of the inferior alveolar canal is common. Periapical radiographs of the involved dentition often demonstrate narrowing of the periodontal ligament space with an ill-defined lamina dura that blends with the abnormal bone pattern. When the maxilla is involved, the lesional tissue displaces the sinus floor superiorly and commonly obliterates the maxillary sinus. Imaging studies in cases with maxillary involvement may show increased density of the base of the skull involving the occiput, sphenoid, roof of the orbit, and frontal bones.[2]

But our case showed well-defined margins with multilocularity, which was distinctly different from the regular radiographic appearance of FD.

Results of laboratory studies, that is, serum examination for alkaline phosphatase activity and calcium profile in FD are characteristically within the normal limits and our case too showed no abnormal levels of serum alkaline phosphatase and calcium.[2]

There are no distinguishing histological features between the three types of FD.[13] In the early formative phase, pronounced

osteogenesis is seen with thin osteoid anastomosing trabeculae that are rimmed with osteoblasts. The stromal fibroblastic element is proliferative and hypercellular. As the disease progresses, trabeculae thickens and assumes the classic "Chinese letter" characteristics, yet the osseous collagen pattern remains woven. The fibrous element continues to be hypercellular. In later stages of the disease, woven bone is replaced by lamellar bone trabeculae; extensive remodeling may result in a mosaic pattern of resting and reversal lines.[1]

A characteristic feature of FD is that the lesional bone merges imperceptibly with adjacent cancellous bone or with the overlying cortex. Also the fibrous tissue has a monotonous cellularity and the fine pattern of bony trabeculae is repeated throughout the entire lesion. Spherical, cementicle or psammomatoid calcifications may be seen in a minority of lesions, but they are never prominent. In older or mature lesions there may be lamellar bone with mature trabeculae arranged in elongated parallel arrays.[13] Our case too showed similar histological presentation.

Early craniofacial FD is characterized by minimally mineralized deposits of woven bone with a continuum progressive lamellation of the woven bone trabeculae as FD becomes mature. This is in contrast to FD lesions in long bones where mature lamellar bone is not found.[9]

Nonepithelial lined cysts occasionally occur in association with various benign and malignant bone lesions; including FD, giant cell tumor, chondroblastoma, ossifying fibroma, benign osteoblastoma, cemento-osseous dysplasia, fibrous histiocytoma, fibrosarcoma, and osteosarcoma. These cysts vary in nature; some are aneurysmal bone cysts, some are simple bone cysts, and others are nonspecific cystic degenerations.[14]

The first reports of FD complicated by nonspecific cystic degeneration have been attributed to Jaffe and Schlesinger, Keats and Ruoff.[14]

Nonspecific cystic degeneration occurring in FD of the jaws has rarely been reported in the literature. Obwegeser, Freihofer, and Horejs reported two cases of FD that demonstrated radiographic and clinical evidence of cyst formation. Fisher reported two cases of bone cavities in fibro-osseous lesions in the maxillofacial skeleton. A single case of FD of the mandible complicated by a large simple bone cyst was published by Hara *et al*. The occurrence of aneurysmal bone cyst in FD of the jaws is more frequently reported. A review of 53 cases of fibro-osseous lesions of the jaws found associated aneurysmal bone cysts in 21%.[14] So our case was one of the interesting cases showing nonspecific cystic degeneration.

Mazabraud's syndrome is a rare disease with association of single or multiple intramuscular myxomas with monostotic or polyostotic forms of FD.[11,15]

Although rare, malignant transformation of FD has been reported in patients with craniognathic disease, most malignant neoplasms develop in patients who previously have undergone radiation therapy of the affected area. However, de novo sarcomatous transformation has been identified in a few rare cases. Overall, 0.4-0.5% incidence of secondary malignant neoplasms in FD was found frequently in males with polyostotic disease. Osteosarcoma accounts for more than half of all the malignant neoplasms in FD, the next commoner being fibrosarcoma and chondrosarcoma. Secondary angiosarcomas and a malignant fibrous histiocytoma have also been reported.[11]

The growth of FD often tends to stabilize and occasionally stops when skeletal maturity is attained, surgical intervention in children and adolescents with more extensive lesions should be delayed as long as possible. However, in some cases, FD may persist into late adult life. Treatment in young patients with significant cosmetic or functional deformity is limited to a contouring procedure, without complete resection to minimize morbidity. Complete surgical resection is recommended for patients with rapidly expanding FD, lesions that encroach on the orbit. Radiation therapy is contraindicated owing to the increased risk of malignant transformation. Long-term clinical and radiographic follow-up is recommended for any patient with FD.[11,16]

In summary, we report a case of bilateral monostotic FD in a middle-aged female showing a classic histological picture, but radiologically presenting as a mixed radiolucent radiopaque lesion showing nonspecific cystic degeneration.

REFERENCES

1. Eversole R, Su Lan, ElMofty S. Benign fibro-osseous lesions of the craniofacial complex. A review. Head Neck Pathol 2008;2:177-202.
2. Neville BW, Damm DD, Allen CM, Oral maxillofacial pathology, 2nd ed. Philadelphia: Saunders; 2002. p. 553-7.
3. Ippolito E, Bray EW, Corsi A, De Maio F, Exner UG, Robey PG, *et al*. European Pediatric Orthopaedic Society. Natural history and treatment of fibrous dysplasia of bone: A multicenter clinicopathologic study promoted by the European Pediatric Orthopaedic Society. J Pediatr Orthop B 2003;12:155-77.
4. Bessho K, Tagawa T, Murata M, Komaki M. Monostotic fibrous dysplasia with involvement of the mandibular canal. Oral Surg Oral Med Oral Pathol 1989;68:396-400.
5. Di Caprio MR, Enneking WF. Fibrous dysplasia. Pathophysiology, Evaluation, and Treatment. J Bone Joint Surg Am 2005;87:1848-64.
6. Henry A. Monostotic fibrous dysplasia. J Bone Joint Surg Br 1969;51:300-6.
7. Kalsotra P, Manhas M. Cranio-facial fibrous dysplasia. JK Sci 1999;1:124-6.
8. Pound E, Pickrell K, Huger W, Barnes W. Fibrous dysplasia (Ossifying Fibroma) of the maxilla: Analysis of 14 Cases. Ann Surg 1965;161:406-10.
9. Feller L, Wood NH, Khammissa RA, Lemmer J,

Raubenheimer EJ. The nature of fibrous dysplasia. Head Face Med 2009;5:22-7.
10. Strassburger P, Garber CZ, Hallock H. Fibrous dysplasia of bone. J Bone Joint Surg Am 1951;33:407-20.
11. Alawi F. Benign fibro-osseous diseases of the maxillofacial bones. A review and differential diagnosis. Am J Clin Pathol 2002;118 Suppl 1:S50-70.
12. Riminucci M, Fisher LW, Shenker A, Spiegel AM, Bianco P, Gehron Robey P. Fibrous dysplasia of bone in the McCune-Albright syndrome: Abnormalities in bone formation. Am J Pathol 1997;151:1587-600.
13. Speight PM, Carlos R. Maxillofacial fibro-osseous lesions. Curr Diagnc Pathol 2006;12:1-10.
14. Feretti 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.
15. Kabukcuoglu F, Kabukcuoglu Y. Mazabraud's syndrome: Intramuscular myxoma associated with fibrous dysplasia. Orphanet Encyclopedia 2005:1-4. Available from: https://www.orpha.net/data/patho/GB/uk-Mazabraud.pdf. [Last accessed on 2010 Dec 21]
16. Waldron CA. Fibro-osseous lesions of the jaws. J Oral Maxillofac Surg 1993;51:828-35.

How to cite this article: Nadaf A, Radhika MB, Paremala K, Srinath N. Monostostic fibrous dysplasia with nonspecific cystic degeneration: A case report and review of literature. J Oral Maxillofac Pathol 2013;17:274-80.
Source of Support: Nil. **Conflict of Interest:** None declared.