Monostotic Fibrous Dysplasia of the Maxilla: A Case Report and Review of Literature

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Fibrous dysplasia (FD) is caused by the abnormal proliferation of fibrous tissue interspersed with normal or immature bone because of poorly differentiated, mutated osteoblasts. It is found in 3% of all bony tumors and in over 7% of all non-malignant tumors of bone. It can also be associated with hyperpigmentation and endocrinological disorders. Mutations in Gs-α of osteoblastic cells are implicated in the development of the disease. In this article, we report a case of monostotic FD in a 24-year-old male patient with a brief overview on FD and its pathogenesis. Clinical, radiographical, and histopathological features were the diagnostic evidence in this case.

**Keywords:** Bone neoplasm, Developmental, Fibrous dysplasia, Maxilla

INTRODUCTION

In 1938, American pathologist Louis Lichtenstein was the first to use the term “fibrous dysplasia (FD).” In 1942, Lichtenstein and Henry Lewis Jaffe described FD as a congenital anomaly caused by a disturbance of the bone-forming mesenchyme.¹ FD is found in 3% of all bony tumors and in over 7% of all non-malignant tumors of bone.² It can occur in one or several bones, either as monostotic or polyostotic FD.³ 80-85% of patients who have FD have the monostotic form.¹ Polyostotic FD accounts for 20-25% of FDs and may affect up to 75% of the skeleton, and the craniofacial region is affected in 40-60% of the cases. The term Jaffe’s type is used for the polyostotic FD with skin pigmentation, whereas Albright’s disease must exhibit a triad of characteristics: Polyostotic FD, hyperpigmentation of the skin, and endocrinopathies among which peripheral precocious puberty is the most common. Hyperthyroidism, acromegaly, and hypercorticism are present in some patients. Renal phosphate wasting and soft-tissue myxomas (Mazabraud syndrome) may also be encountered.³⁻⁴ In the craniofacial region, the maxilla is affected twice as frequently as the mandible, and the posterior aspects of the jaw are affected more frequently than the anterior aspects.¹ Lesions in other craniofacial bones, such as the zygoma, frontal bone, sphenoid bone, orbital plates, and occipital bone, have been reported. The age range of 96% of the patients is within the first four decades.³

The aim of this article is to present clinical, radiological, and microscopic findings of a case diagnosed as FD of the maxilla.

CASE REPORT

A 24-year-old male patient reported to the oral medicine and radiology clinic with a chief complaint of swelling on the right side of the face present for the last 12 years. There was a gradual slow enlargement of the swelling since his childhood resulting in facial asymmetry, and it remained constant for the last 4 years. He did not have any history of associated pain, visual disturbance, headache, or nasal obstruction. He denied any relevant past or family medical history.

Extraoral examination revealed a single diffuse swelling over the right side of the face, involving the infraorbital region, and extending over the zygoma region. Obliteration of the nasolabial fold and a raised nasal ala was noted due to the swelling. The surface texture of overlying skin appeared normal. On palpation, the swelling was afebrile, non-tender, bony hard in consistency, immobile, and the overlying skin was not fixed to the swelling. On the affected side, an intraoral bony hard swelling was palpable in the...
maxillary buccal vestibule extending from 1-4 to 1-6 region. The expansion was smooth and covered with normal appearing mucosa. No displacement or mobility of the teeth were noted. On general examination, no abnormal skin pigmentation could be found, and no bony deformities were seen in any other parts of the body. Right deviated nasal septum was present. On vitality testing, 1-1 to 1-8 were vital. Transillumination test was also performed which showed no illumination of light from the right maxillary sinus suggesting obliteration of the sinus.

Panoramic radiograph disclosed diffuse opacification of the right antrum encroaching the lateral nasal wall and causing thinning of the inferior orbital wall. Complete opacification of the right maxillary sinus was seen in Waters view. The lateral wall of the sinus was expanded. Periapical and occlusal radiographs revealed the classic “ground glass” appearance involving the alveolar bone extending from the incisor region to the tuberosity and extending to involve the right half of the palate. Margins of the abnormal bone merge imperceptibly with the adjacent bone. The bone trabeculae display an altered morphology and are more numerous than normal trabeculae causing an increased density of the bone. Expansion of the lateral aspect of the maxilla was evident with thinning of the cortical border. No displacement or resorption of the teeth was observed.

Computed tomography (CT) revealed the monostotic involvement of the entire maxilla with ground-glass opacification. Mediolaterally, extended from the midsagittal region of the maxilla to involve laterally the zygomatic process of the right maxilla. The periphery of the lesion extends to involve all borders of the right maxilla, with thinning of the cortical walls. It has resulted in the expansion of all the walls of the maxilla including right half of the palate causing significant narrowing of the right maxillary sinus with displacement of the right lateral wall of the nose medially. Mild narrowing of the right infundibulum and thinning of the right inferior orbital margin were noted. Deviation of the nasal septum and left inferior turbinate hypertrophy was seen. Right infraorbital nerve canal and the nasolacrimal duct appeared normal. Bilateral frontal, ethmoid, and sphenoid sinuses are clear. Orbits appeared normal.

Biochemical parameters including serum calcium, phosphorus, and alkaline phosphatase levels were normal. (serum alkaline phosphatase: 130 IU/L, serum calcium: 10.6 mg/dl, serum phosphate: 3.8 mg/dl). Microscopic analysis revealed irregular trabeculae of woven bone without osteoblastic rimming within a fibrous stroma. Some of the trabeculae showed c-shaped or Chinese pattern arrangement. Stroma contained few collagen fibers, large number of plump fibroblast proliferating into stroma arranged in a swirled pattern. These findings were consistent with FD. Surgical recontouring of the maxillary bone was carried out for the patient and is under regular follow-up.

**DISCUSSION**

FD is caused by the abnormal proliferation of fibrous tissue interspersed with normal or immature bone because of poorly differentiated, mutated osteoblasts. Activating mutations in Gs-α (GNAS1) of osteoblastic cells are implicated in the development of the disease. In 1991, mutations of the GNAS1 gene were documented in the lesions of patients with McCune-Albright syndrome. In 1995, the same mutations were identified in monostotic FD. GNAS1 encodes α subunit of G proteins (guanine nucleotide proteins) that act as signal transducers. G proteins consist of three different subunits, α, β, and γ, which are linked with transmembrane receptors (G protein-coupled receptors) of hormones and growth factors. One of two specific point mutations of GNAS1 is the cause of McCune-Albright syndrome, polyostotic FD, monostotic FD, and pituitary adenoma. These mutations are either C→T, which results in Arg201Cys, or G→A, which results in Arg201His. They occur in somatic cells after conception (post-zygotic mutations) either during embryonic development or after birth. The extent and form of the disease depend on the stage of development and the location at which the mutation occurs. The earlier during embryogenesis the mutation occurs, the more generalized the FD. This missense mutation results in the loss of guanosine triphosphatase activity of GNAS1 with consequent activation of adenylate cyclase, overproduction of cyclic adenosine monophosphate (cAMP), increased cell proliferation, and inappropriate cell differentiation. Hence, mutational analysis has been used as an additional and useful tool for the diagnosis of FD in selected cases. Somatic mutation in the GNAS1 gene may also stimulate osteoblastic cell proliferation by inducing chronic stimulation of early genes such as c-fos and c-Jun result in overproduction of fibrotic bone matrix. All of the structural and biochemical abnormalities that are observed in mature bone-forming cells in FD can in fact be related to the effects of excess cAMP. Long-term effects of cAMP on mature osteoblasts dysregulate the expression of several bone matrix proteins. Malfunction of mature osteoblasts might disrupt a homeostatic balance between immature (preosteoblastic) and mature (osteoblastic) compartments of the osteogenic lineage. Continued recruitment and accumulation of fibroblast-like pre-osteogenic cells results the fibrosis of marrow spaces adjacent to bone surfaces. Defective osteoblast differentiation is also evidenced by the abnormal collagen organization in the immature bone. The collagen fibers are not parallely oriented, a characteristic of immature woven bone. The collagen fibers sometimes
appear perpendicular to the bone surface, showing a comb-like structure. In addition to this, non-collagenous protein synthesis is affected. Osteonectin level is increased, whereas osteopontin and bone sialoprotein are decreased in dysplastic bone, reflecting the immature composition of the matrix.

Conventionally, FD has been considered to be a bone disorder. Cohen suggested that FD is a benign neoplasm based on four pieces of evidence: (1) the same activating mutation that causes FD also causes pituitary adenoma, which is a neoplasm, (2) high levels of c-fos proto-oncogene expression were found in cells of FD lesions in eight patients, (3) GNAS1 mutations have been identified in a few neoplasms, (4) McCune-Albright syndrome is associated with ovarian cysts and neoplasms, such as thyroid tumors, parathyroid adenoma, and intramuscular myxoma.

Clinically, FD leads to expansion, thickening and, then, sclerosis in the involved bone. Headache is the most common symptom, but the other symptoms due to mass effect and compression emerge as the lesion grows. Orbital and periorbital bone involvement leads to hypertelorism, visual impairment, and blindness; sphenoid and temporal bone involvement leads to vestibular dysfunction, facial paralysis, trigeminal neuralgia, tinnitus, and hearing loss; paranasal bone involvement to nasal obstruction, sinusitis symptoms, nasal bleeding, and anosmia; and finally, the mandibular and maxillary bone may involve may cause teeth disorder and loss of teeth. Radiologic findings are characteristic and not pathognomonic. Biopsy and histopathologic examination are necessary for a definitive diagnosis. Radiological characteristics differ regarding to the bone and fibrous matrix ratio; they include and usually seen as three patterns: Pagetoid pattern: Rate of the bone-fibrous matrix is equal. It has a ground glass or orange peel appearance. Sclerotic pattern: Bone structure is in the foreground but the normal trabecular appearance disappears in the latter. Radiolucent pattern: Fibrous matrix is in the foreground. Cystic degeneration, simple bone cyst, and aneurysmal bone cyst can also account for the radiolucency in FD. The lesion leads to expansion of the bone as it grows and surrounds with a reactive bone tissue. Cortical structure of the bone gets thinner although it always maintains its integrity. Loss of lamina dura due to replacement of normal bone may be one of the diagnostic signs of FD. The literature suggests that FD in women can be reactivated during pregnancy. This association is more commonly seen with the polyostotic form. Cystic lesions resembling aneurysmal bone cysts have been noted in association with the monostotic form. Differential diagnosis includes Paget disease, osteo FD, ossifying fibroma, and sarcoma. CT can be shown clearly to the expansion, cortical borders, and lesion’s internal structure. CT criteria of use for the differential diagnosis include involvement of the inner table (usually spared by FD), periosteal new bone formation (outer table expansion in FD), and surface irregularities (smooth surface in FD). In MR imaging, there is considerable variability in signal intensity depending on the amount of bony trabeculae, cellularity, and collagen. Usually, areas of involvement have low signal intensity on T1-weighted images and low, intermediate, or high signal intensity on T2-weighted images. Post-gadolinium enhancement is low, intermediate, or high with a uniform, central patchy, or rim configuration. This variability, together with the poor visibility of tissue mineralization, limits the diagnostic usefulness of magnetic resonance imaging (MRI), which should be viewed as a second-line imaging study. MRI is crucial for identifying cystic degeneration or a secondary aneurysmal bone cyst and, when a malignancy is suspected, for detecting soft-tissue involvement. 3D reconstruction can assist the surgeons in planning by computer-aided manufacture model-making. Bone scintigraphy is the best imaging technique for mapping the FD lesions, which usually exhibit increased uptake. In scintigraphy, a significant involvement is observed, especially if the lesion is active, like in the adolescence period. This involvement decreases as the lesion matures. Serum alkaline phosphates are rarely observed as high in the laboratory examination. Calcium, parathormone, 25 hydroxyvitamin D, and 1,25 dihydroxyvitamin D are normal. Hypophosphatemia, hyperphosphaturia, and osteomalacia may be seen in polyostotic FD. Malignant change is rare, roughly 0.5% for the monostotic form and 4% for McCune-Albright syndrome. The cause of the malignant change of FD still remains unknown, but irradiation is believed to be the main cause. Development of soft-tissue mass or increase in serum alkaline phosphatase would be the sign of malignant change, so clinicians should be aware of these findings. Early radiologic features of sarcomatous transformation are moth-eaten or cystic areas of osteolysis, cortical destruction, and gradual formation of a soft-tissue mass. Recently, the benefit of F-18 fluorodeoxyglucose positron emission tomography was discussed for the early detection of malignant transformation of FD. Treatment necessary for this condition depends on its location in the craniofacial skeleton, its effect on function, and, ultimately, cosmetics. Skeletal deformities can require surgical approach which includes two different approaches: Conservative or radical. Conservative shaving or osseous contouring has been recommended by some authors who maintained that periodic contouring could be performed until a static phase was reached. Radical surgical therapy permits the complete removal of the lesion followed by immediate reconstruction.
REFERENCES


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