CASE REPORT

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Craniofacial Fibrous Dysplasia

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ABSTRACT Fibrous dysplasia is the replacement of cancellous bone components with fibrous tissue containing abnormal bone. Craniofacial fibrous dysplasia (CFD) invades two or more craniofacial bones. Treatment options are controversial, and follow-ups are crucial for young patients. Cone-beam computed tomography is useful for evaluation of craniofacial bones. Remaining maxillary sinus volumes can be used as a quantitative value. In this case report, we present two CFD patients with radiologic features. This case report may be a valuable addition to the literature due to the usage of quantitative values to evaluate progression of FD lesions.

Keywords: Fibrous dysplasia, craniofacial; cone-beam CT

Fibrous dysplasia (FD) results from a localised change in normal bone metabolism; which leads to the replacement of all the components of spongy bone with fibrous tissue containing varying amounts of abnormal bone and causes deformity, pain, pathological fractures, mechanical loss of strength and nerve compression.[1] Schlumberger firstly reported a disease process which was including only a single bone and defined it as "monostotic fibrous dysplasia".[2] Monostotic and poliostotic terms are still being used for stating the numbers of the affected bones. If the lesion invades one single bone, it is defined as Monostotic type FD, if it holds multiple bones, it is defined as Polyostotic type FD. Monostotic type is not a precursor sign for the poliostotic type.

Craniofacial fibrous dysplasia (CFD), another type which was described by Daves and Yardly, invades two or more craniofacial bones.[3] If the lesion involves only mandible, a diagnosis of monostotic FD can be made easily, contrary to maxillar lesions where FD can affect adjacent bones like zygoma easily. Therefore 'craniofacial FD' term was described. Frequencies of monostatic type, polyostotic type and craniofacial type are reported as 74%, 13% and 13%, respectively. Maxillary cases are two times more common than mandibular cases, often with involvement in the posterior region and are usually unilateral.[4] Although the aetiology of the disease remains unknown, genetic factors are held primarily responsible.

This article aims to present two craniofacial FD cases with a review of the literature. Informed consents of the patients were obtained.

CASE REPORTS

CASE 1

An 18-year-old male patient was referred to Department of Oral and Maxillofacial Radiology with complaint of painless swelling in his right maxillary alveolar process. His medical record was insignificant. Extraoral examination revealed that there was no significant asymmetry although the patient's right zygomatic arch seemed protruding. No history of fever, trauma and similar swelling elsewhere in the body were

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reported. In intraoral examination, there was a single, well-defined swelling which was covered with normal mucosa and hard on palpation, involving right maxillary alveolar process from #13 to #16 with the expansion of cortical plate (Figure 1).

The panoramic radiograph revealed an ill-defined ground glass appearing lesion extending from right maxillary canine to apices of right maxillary second premolar and molar tooth; besides, right maxillary sinus and orbital floor appeared to be affected by the lesion (Figure 2A). Patient's dental records have been examined, and it has been found that he referred to our clinic 3 years ago, his previous panoramic radiography also revealed a lesion in the region of interest, with a smaller size and affecting the eruption path of the right maxillary canine (Figure 2 B). However, the lesion did not preclude the eruption of the right maxillary canine only cause displacement of right maxillary canine, first and second premolar teeth.

The patient has stated that the lesion was asymptomatic back then so it can be said that the clinician failed to diagnose the lesion incidentally 3 years ago. A Cone Beam Computed Tomography (CBCT) (Newtom 5G QR, Verona, Italy) was taken for further investigation. An ill-defined heterogeneous radioopaque lesion with ground-glass appearing foci was present in the maxilla, zygoma, frontal and sphenoid bones. In the maxilla, the lesion was extending from apices of the right canine to the right tuber maxilla, causing the expansion of right maxillary alveolar bone. The right maxillary sinus was almost obstructed with lesion which was extending to the orbital floor and surrounding the infraorbital nerve. The lesion was proceeded to the zygomatic bone through the zygomaticomaxillary suture and caused significant expansion.

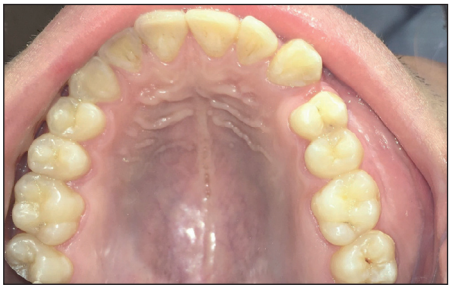

FIGURE 1: Intraoral view of Patient 1, revealing unilateral buccal swelling located at right maxillary premolar-molar region which was covered with normal mucosa.

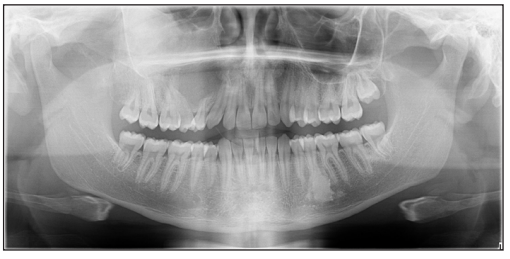

FIGURE 2A: Panoramic radiography of Patient 1, revealing a well-defined ground glass appearing lesion extending from right maxillary canine to tuber maxilla region, also right maxillary sinus appeared to be affected by the lesion.

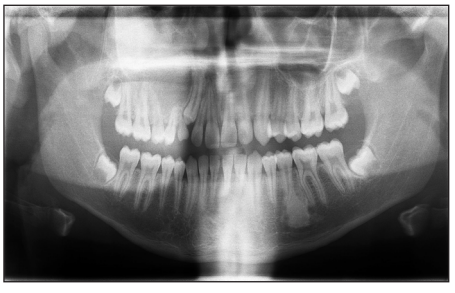

FIGURE 2B: Panoramic radiography of Patient 1 which was obtained three years ago, revealing a well-defined ground glass appearing lesion extending from right maxillary canine to the right first molar tooth, affecting the eruption path of right maxillary canine.

The borders of the lesion end with zygomaticofrontal suture (Figure 3A). In sphenoid bone; medial pterygoid plate and lateral pterygoid plate were affected and expanded significantly. Foramen rotundum and vidian canal were surrounded by the lesion and found indistinct compared to the healthy symmetric side. The lesion also surrounded the optic canal. Sphenoid sinuses were almost obstructed with the lesion (Figure 3B).

Based on the asymptomatic nature of the lesion, clinical features and imaging features showing typical ground-glass appearance with the involvement of adjacent bones, a provisional diagnosis of craniofacial FD was made, and the patient has been referred to Oral and Maxillofacial Surgery Department. An incisional biopsy was performed under local anaesthesia. Histopathologic examination revealed a fibro-osseous lesion which was compatible with advanced stage of CFD (Figure 4). Treatment options have been discussed, and it has been decided that the patient does not need surgical approach at this moment but has to be followed periodically due to the risk of expansion of the lesion and causing important symptoms such as visual impairment. CBCT scans were obtained during the sixth and twelfth month of his

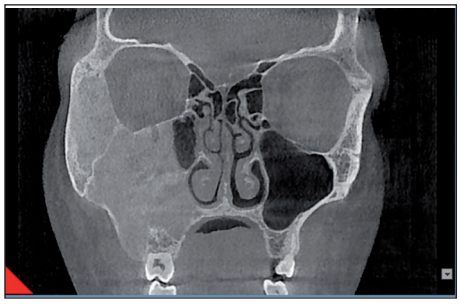

FIGURE 3A: Coronal section CBCT image indicating invasion of right maxillary sinus, zygomatic and frontal bone. Please note that infraorbital canal is surrounded by lesion.

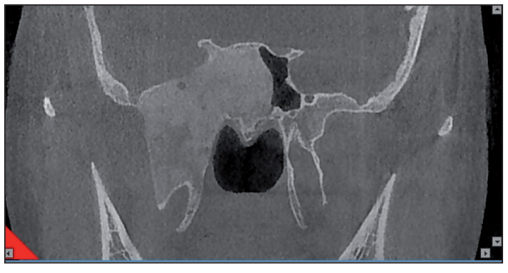

FIGURE 3B: Coronal CBCT image, revealing the affected sphenoid bone, expansion of medial pterygoid plate and lateral pterygoid plate and obstructed sphenoid sinuses. Please note that foramen rotundum and vidian canal are surrounded by the lesion and seem indefinite compared to healthy symmetric side.

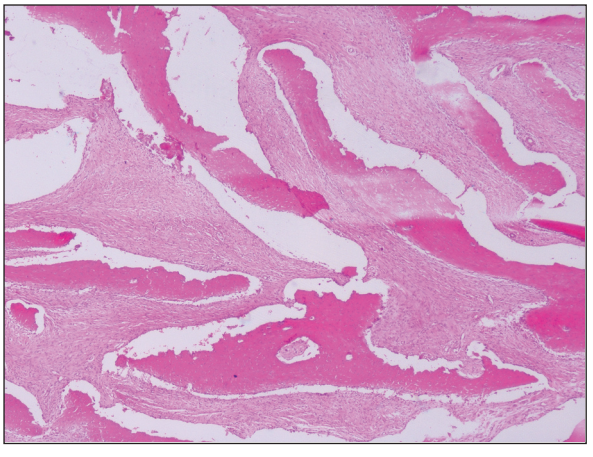

FIGURE 4: Histopathologic examination of Patient 1 reveals abnormal irregular shaped lamellated trabeculation which indicates the late stage of fibrous dysplasia. (H&Ex40).

follow up. The volume of unaffected right maxillary sinus was measured during the follow-ups with Simplant software (ver.14.0 Materialise Medical, Leuven, Belgium). The volumes were 4386.81 mm^3, 3303.37 mm^3, and 2945.27 mm^3 during the initial visit, first follow-up and second follow-up respectively (Figure 5A, Figure 5B and Figure 5C). Therefore it can easily be said that the lesion is continuing to grow in the maxilla. The lesion was accepted to be growing in zygomatic and sphenoid bones, too according to CBCT examinations. Even the lesion was accepted to be growing, a surgical approach was not seen necessary. A conservative approach is planned until the end of the adolescent period unless there is a functional or aesthetic symptom.

CASE 2

A 21-year-old male patient was admitted to Department of Oral and Maxillofacial Radiology with complaint of painless swelling in the right side of his face. Patient's medical record was insignificant. In extraoral examination right zygomatic arch was seen protruding, but there was no significant facial asymmetry. Patient's anamnesis revealed that swelling was present for 6 months and kept growing with time. In intraoral

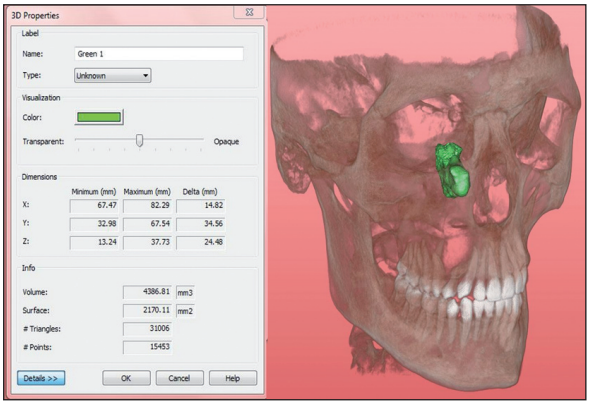

FIGURE 5A: Unaffected sinus volume measurement of Patient 1 during the initial visit.

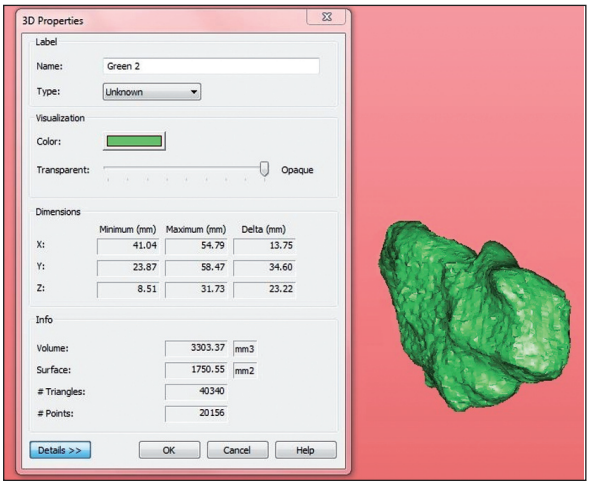

FIGURE 5B: Unaffected sinus volume measurement of Patient 1 during the first follow-up.

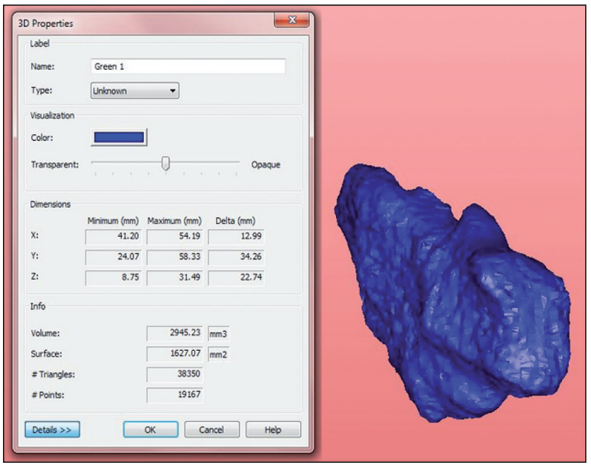

FIGURE 5C: Unaffected sinus volume measurement of Patient 1 during the second follow-up.

examination, there was no significant asymmetry in the maxillary dental arch (Figure 6). In panoramic radiography, a heterogenous radioopaque lesion, with ground-glass appearing involving the apices of right second premolar and first molar teeth, affecting maxillary sinus and reaching the orbital floor was detected (Figure 7). A CBCT scan (Newtom 5G QR, Verona, Italy) was taken for a detailed examination of craniofacial bones. CBCT evaluation showed a heterogeneous radioopaque lesion with ground glass appearance affecting maxilla, sphenoid and temporal bone. In the maxilla, the lesion was involving apices of the posterior teeth, causing the expansion of alveolar bone, filling the maxillary sinus, reaching the orbital floor and surrounding the infraorbital nerve. The lesion was limited with zygomaticomaxillary suture and it was not affecting the zygomatic bone (Figure 8A). In sphenoid bone; medial pterygoid plate and lateral pterygoid plate were affected and expanded significantly. Foramen rotundum and vidian canal were surrounded by the lesion and seemed indefinite compared to healthy symmetric side. Sphenoid sinuses were filled with the lesion (Figure 8B). In temporal bone, squamous, mastoid and petrous parts were affected by the lesion (Figure 8C).

Patient referred to Oral and Maxillofacial Surgery Department with a provisional diagnosis of CFD. An incisional biopsy was performed under local anaesthesia for diagnostic purposes. Histopathologic examination revealed early stage fibrous dysplasia. (Figure 9). Periodic follow-ups were suggested for the patient.

DISCUSSION

FD is a congenital skeletal disease, characterised with the replacement of the bone marrow with fibrous tissue.[1] Monostatic FD can be easily diagnosed if a mandibular lesion is present, but if the lesion is located in the maxilla, it can be difficult to diagnose it with absolute accuracy because maxilla is adjacent to the zygomatic and sphenoid bones and the lesion can easily affect adjacent bones.

There are many theories about the aetiology of FD. The most accepted one is the effect of a postzygomatic mutation in the GNAS1 gene. FD lesions are mostly composed by undifferentiated mesenchymal cells which produce the abnormal matrix, bone trabeculae and collagen. The time of the mutation in developmental process determinates the type and severity of the FD, if the mutation occurs in early times of the process, mutant cells can spread more

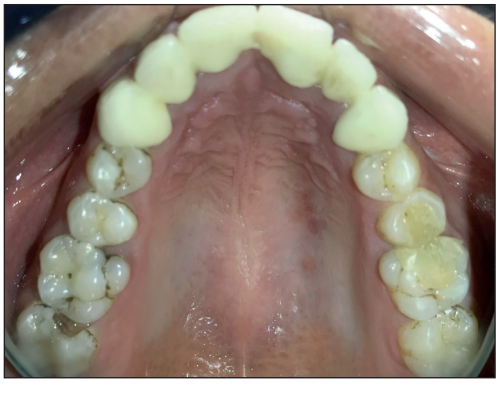

FIGURE 6: Intraoral view of the Patient 2, revealing a symmetric dental arch and no significant asymmetry.

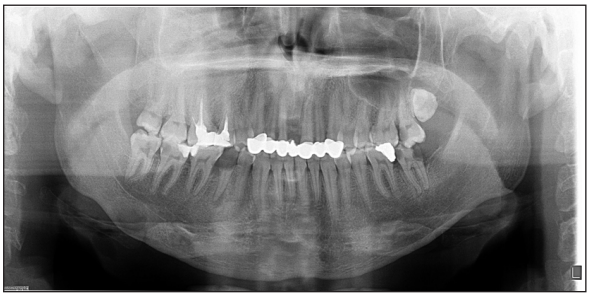

FIGURE 7: Panoramic radiography of Patient 2 revealing a heterogenous radioopaque lesion, with ground-glass appearing involving the apices of right second premolar and first molar teeth, affecting maxillary sinus and reaching the orbital floor.

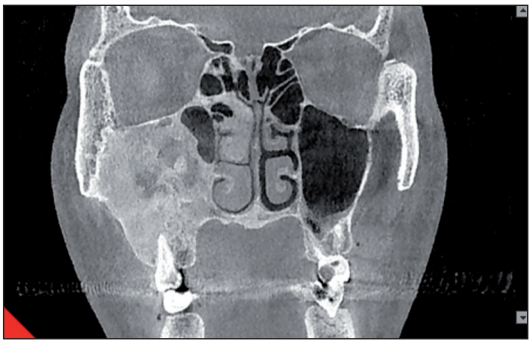

FIGURE 8A: Coronal CBCT image of Patient 2, revealing the affected right maxillary sinus. Please note that infraorbital canal is surrounded by lesion and lesion borders end with zygomaticomaxillary suture thus zygomatic bone is not affected.

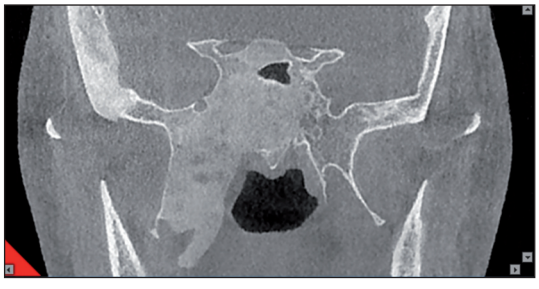

FIGURE 8B: Coronal CBCT image of Patient 2, showing the affected and expanded medial pterygoid plate and lateral pterygoid plate in sphenoid bone. Please note that foramen rotundum and vidian canal are surrounded by the lesion and seem indefinite compared to healthy symmetric side.

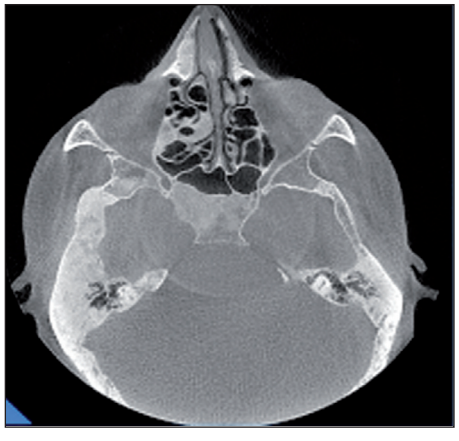

FIGURE 8C: Axial CBCT image of Patient 2 showing the expansion of squamous, mastoid and petrous parts of the temporal bone.

widely, and this results in a more severe clinical manifestation.[5]

FD can be seen in all age groups. According to MacDonald-Jankowski's systemic review, it is mostly seen in the second and third decades with a ratio of 35% and 31% respectively.[6] Most of the MFD cases are asymptomatic, and if the lesion is in craniofacial bones, it can be detected incidentally with the help of the panoramic radiographs.[1] Almost all monostotic FD cases occur unilaterally; bilateral involvement can be detected only in sporadic extensive cases; therefore, bilateral examination is useful for correct diagnosis of the disease and evaluation of pre-op or post-op symmetry.

Clinical signs can differ between disfigurement, proptosis, atypical facial pain, numbness, diplopia, nerve compression, loss of hearing and blindness. Even though there are several types of symptoms, many cases remain asymptomatic for years. FD causes expansion, thickening and sclerosis in the involving bones so if the lesion is in craniofacial bones, cranial asymmetry and facial deformities can occur. A systemic review by Macdonald-Jankowski reported the most frequent symptoms as swelling (94%) and pain (15%).[6] If the lesion invades orbital and periorbital bones, symptoms like hypertelorism, visual impairment and blindness; if the lesion invades sphenoid and temporal bones, symptoms like vestibular dysfunction, facial paralysis, trigeminal neuralgia, tinnitus and loss of hearing; if the lesion invades paranasal bones, symptoms like nasal obstruction, sinusitis symptoms, nasal bleeding and anosmia; and lastly if the lesion invades maxilla or mandible, symptoms like displacement of teeth, loss of teeth, loss of lamina dura, narrowing of periodontal space and rarely root resorption can occur.[1,7] Both of our patients did not have any visual complaints even though the le-

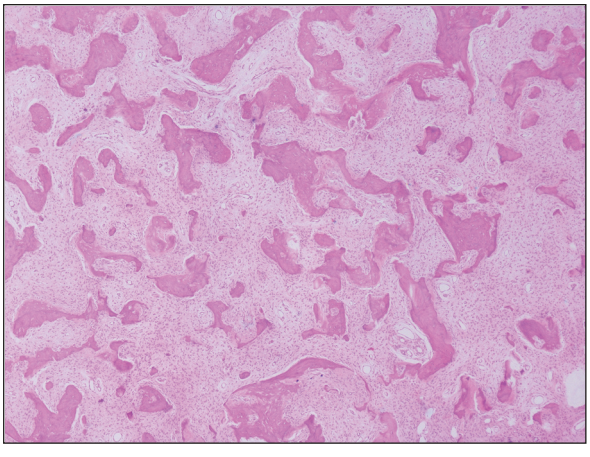

FIGURE 9: Histopathologic examination of Patient 2 revealed curvilinear metaplastic bone trabeculation without osteoblastic rimming in fibroblastic stroma which indicates the early stage of fibrous dysplasia. (H&Ex40).

sions were involving the infraorbital canal. In Patient 2, the temporal bone was affected, but the patient did not have any symptoms related to temporal bone. FD lesions usually occur after the eruption of permanent teeth therefore unerupted teeth within the FD lesions is rare. The superior displacement of the mandibular canal indicates FD and considered as a pathognomonic sign by Petrowski.[8]

The appearance of FD lesions on panoramic radiographs is well defined by their sclerotic border. There is a characteristic radiographic appearance of FD called "ground-glass"; it helps to distinguish FD from other pathologies and composed of homogeneous grey blurry density areas. Radiographic density degree directly depends on the mineralisation level. Lucent areas contain mostly fibrous component while the more radioopaque areas consist woven bone in high quantity.[1]

Computed tomography (CT) reveals an expansive lesion in ground-glass density based on the medullary cavity of the bone. A study with 46 CFD patients reported the prevalence of the radiologic patterns; mixed pattern with sclerotic and lytic areas, homogenous sclerotic, cystic or lytic as 55%, 34% and 11% respectively.[9] In maxillary cases, it is almost impossible to define the borders of the lesion with conventional radiographs. CT or CBCT is quite useful for evaluating the extension of the lesions into the antrum, orbit or nasal cavity.[1] Since CBCT is more accessible for dentists, has a lower dose of radiation compared to CT and sufficient enough to show hard tissues with high quality, it can be the method of choice for radiologic examination of CFD patients.

Most differential diagnosis options can be eliminated easily due to age, symptom severity, fever, inflammation. Even though conventional radiography and magnetic resonance imaging (MRI) images may give confusing ideas, ground-glass appearance in CT or CBCT usually verifies the diagnosis. It can be accepted that all CFD cases, even the ones with no ground-glass image in panoramic radiographs, display ground-glass image at least in some areas in CTs.[9] Differential diagnosis of CFD depends on the location and the internal structure of the lesion. FD lesions which are widely spread along craniofacial bones are more likely to be sclerotic. This type of lesions should differ from Paget's disease or osteopetrosis. Paget's disease and FD lesions may have similar features. However, the thickening of the skull with the curvature and extension of long bones helps the differentiation of Paget's disease. Besides, serum alkaline phosphatase levels are high in these patients, and the age groups they are most commonly seen are different.[1] It is also hard to differ a sclerotic FD lesion in paranasal sinuses from allergic fungal sinusitis or ossifying fibroma. Allergic fungal sinusitis may also show a ground-glass-like appearance, and it can be distinguished from FD with a careful examination. Ossifying fibroma is usually defined as a well-defined lesion, causes expansion like tumours and has a significant radiographic resemblance to FD. In differential diagnosis, it should be considered that ossifying fibroma usually has an intracortical location whereas FD lesions have central distribution.[10] If there is a reasonable amount of doubt about the radiological diagnosis; a bone biopsy is essential. A review about the reliability of the radiological diagnoses of FD states that it is almost impossible to make the diagnosis of fibrous dysplasia exclusively by imaging.[11]

The treatment plan for CFD is quite complicated, and there is no just one accepted treatment plan for all patients. Typically there are three treatment plans for CFD patients; the follow-up, conservative surgery or radical surgery. In asymptomatic patients follow-ups are sufficient. Surgical approach depends on a lot of different factors like the location of the lesion, growth rate, aesthetic complaint, loss of function, patient's request and performance status. Some authors suggested that treatment should be conservative due to the lesion's benign nature, and highlighted the importance of preserving the existing function.[7]

FD generally begins at childhood, continues during puberty and halts with adulthood. Time of surgical intervention has always been controversial, especially for children who are in the growth phase. Exponential growth may occur when surgical intervention is performed during the active growth phase.[12] In young patients, follow-ups can be suggested because of exponential growth risk and the self-limiting nature of the lesion. However early surgical intervention may be inevitable if the patient has significant functional or aesthetic problems.

Instead of any surgical approach, follow-ups with CBCT scans were suggested to both of the our patients due to the asymptomatic nature of the lesions, their young age and risk of exponential growth after surgery. Follow-up CBCTs of Patient 1 were obtained, the lesion is extending to orbit in all CBCT scans, but since he still does not have a visual symptom, surgical intervention was not considered necessary. Follow-up periods were determined as 6 months for both patients.

Malignant or sarcomatous transformation of FD is rare, only seen in 0.4-4% of the cases and the craniofacial zone is the most affected area.[1] Follow-ups are crucial for FD patients because lesions can progress to adjacent structures and have malignant changes. Symptoms like increasing pain and size, a sudden occurrence of a soft tissue mass and increasing alkaline phosphatase values should be evaluated carefully, and they can be indicating malignant transformation.[13]

Medical treatment also can be suggested along with surgical treatment. Bisphosphonate usage has been associated with good results, it helps to increase function, decrease pain and risk of pathologic fracture but this method is still under clinical investigations and controversial.[14]

Posnick&Costello suggested life-long follow-up for FD and indicated that post-op CT is needed periodically for checking the progress of residual FD lesions.[15]

CBCT is a valuable imaging method for evaluating the radiodensity of the lesion with high accuracy and identifying the long-term changes relating to progress or reactivation of the lesions. For all types of FD, it is essential to follow the patient with radiological imaging methods to detect any changes, any surgery needs and evaluating the disease progress; then make treatment decisions.

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Conflict of Interest

No conflicts of interest between the authors and / or family members of the scientific and medical committee members or members of the potential conflicts of interest, counseling, expertise, working conditions, share holding and similar situations in any firm.

Authorship Contributions

Idea/Concept: *Aykağan Coşgunarslan, Mehmet Amuk;* ***Design:*** *Mehmet Amuk;* ***Control/Supervision:*** *Aykağan Coşgunarslan;* ***Data Collection and/or Processing:*** *Hatice Cansu Kış, Neşe İspekter;* ***Analysis and/or Interpretation:*** *Aykağan Coşgunarslan;* ***Literature Review:*** *Neşe İspekter, Hatice Cansu Kış;* ***Writing the Article:*** *Aykağan Coşgunarslan;* ***Critical Review:*** *Mehmet Amuk.*

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