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Abstract

Fibrous dysplasia is a rare bone disease caused by an abnormal proliferation of fibrous tissue in bone. We retrospectively evaluated eight patients (female to male ratio 3:1, mean age 22.5 years, range 10-32) with a monostotic form who were treated between 1996 and 2006. Two each were affected in the lower jaw, the upper jaw, the midface, and the frontoparietal region. Most patients were referred because of a painless swelling. Biopsy specimens from two patients were examined, six patients had modelling osteotomies, two of whom had further operations because of progressive enlargement. There was no visual impairment or malignant transformation. Fibrous dysplasia should be treated as conservatively as possible, but in cases of functional disturbance that results from malignant transformation, or from the involvement of the optic foramen or the foramen magnum, an immediate operation is needed. Disfigurement can be another reason for operation. When there is a risk of malignant transformation, follow-up of patients is recommended.

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Abstract

Fibrous dysplasia is a rare bone disease caused by an abnormal proliferation of fibrous tissue in bone.

We retrospectively evaluated eight patients (female-male ratio: 3:1, mean age 22.5 years, range 10-32) with a monostotic form who were treated between 1996 – 2006. Two each were affected in the lower jaw, the upper jaw, the midface, and the frontoparietal region.

Most patients were referred because of a painless swelling. Biopsy specimens from two patients were examined. Six patients had modeling osteotomies, two of whom had further operations because of progressive enlargement. There was no visual impairment or malignant transformation.

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When there is a risk of malignant transformation, follow-up of patients is recommended.
Introduction

The term fibrous dysplasia was first mentioned by Lichtenstein in 1938.\textsuperscript{1} It is a rare localized disease often associated with bony deformities caused by the abnormal proliferation of fibrous tissue interspersed with normal or immature bone because of poorly differentiated, mutated osteoblasts. Some authors suggest that greater resorption of bone in affected areas\textsuperscript{2,3} is because of the activation of \( \text{G}_\text{s}\alpha \) and increased synthesis of \( \text{IL}_6 \), a cytokine involved in the differentiation of osteoclasts.\textsuperscript{2,4}

Fibrous dysplasia is found in 3\% of all bony tumours and in over 7\% of all non-malignant tumours of bone.\textsuperscript{5,6}

Malignant change is rare, roughly 0,5\% for the monostotic form and 4\% for McCune-Albright syndrome.\textsuperscript{7,8} Yabut et al\textsuperscript{6} and identified reports of 83 cases (27 in facial bones) of malignant degeneration in fibrous dysplasia; osteosarcoma was the most common, followed by fibrosarcoma, and chondrosarcoma. Malignant transformations were found mostly in the third or fourth decade of life. It is important to note that 28\% of these transformations were in patients who had had fibrous dysplasia lesions radiated.

This disease can be divided into subtypes: roughly 70\% are monostotic, roughly 30\% are polyostotic. It is also found in McCune-Albright syndrome (an association of fibrous dysplasia), precocious puberty, endocrine abnormalities, and pigmented cutaneous lesions in female patients. There seems to be no transition from one form to the other. Fries found that the skull was involved in 28 patients (72\%) with a polyostotic form and in 11 (28\%) with a monostotic form.\textsuperscript{9} The fronto-orbital region was affected in 20\% of patients.\textsuperscript{10}

Differential diagnosis includes Paget disease, osteofibrous dysplasia, ossifying fibroma, and sarcoma. The most useful diagnostic sign to fibrous dysplasia from Paget disease is a ground glass bony matrix seen on a bone window on a computed tomogram (CT) (Fig. 1) and caused by the admixture of fibrous and osseous elements. Thin cortical tables, involvement of the orbit, nasal cavity, and maxilla are also signs of fibrous dysplasia.\textsuperscript{11}

Maki et al\textsuperscript{12} retrospectively studied 90 cases of fibrous dysplasia and 17 of osteofibrous dysplasia. Osteofibrous dysplasia occurred only in the tibia or fibula. The
mean age of those with fibrous dysplasia was 24 years, compared with that of patients with osteofibrous dysplasia, which was 12.9 years.

We retrospectively evaluated eight patients (female to male ratio 3:1, mean age 22.5 years, range 10-32) with a monostotic form who were treated between 1996 and 2006.

Fig1: Typical “ground glass” matrix and enlargement of the frontal bone in the CT

Patients

Eight patients were referred to the Department of Cranio-Maxillofacial Surgery at the University Hospital, Zurich between 1996 and 2006. The female to male ratio was 3:1, mean age 22.5 years (range 10-32).

Details about the patients’ age, sex, clinical presentation, radiological extent of tumour, histopathology, microcomputed tomography (micro-CT), and treatment are shown in Table 1.

Fig 2: bony enlargement on the left side of the lower jaw Fig 3: bony enlargement on the left side of the upper jaw

Table 1: distribution of localisation
### Treatment

*Fig 5: intraoperative view*

<table>
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<tr>
<th>Sex</th>
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Table 2: summary of the patients

Seven of eight patients were referred because of a painless swelling or asymmetry (Fig. 2 and 3), and one of a suspected bony cyst. Biopsy specimens were taken in two cases (Fig 4). Six patients had modeling osteotomies, two of whom had further operations: bimaxillary osteotomy and calvarial remodeling.

The histological findings of all patients were similar with features of osseous and fibrous lesions. The osseous component consisted of trabeculae of woven bone with emanating collagen fibers. The trabeculae lacked an osteoblastic rimming. Bland spindle cells with no mitotic figures were interspersed. There were no definable borders (Fig 5).

*Figure 6: Fibrous-osseous lesion with trabeculae of woven bone and interosseous spindle cells, H&E, x50.*
The bony samples (0.5 cm) with fibrous dysplasia were examined with a SkyScan 1172 microcomputer tomograph (Skyscan, Kontich, Belgium) using a fan beam. Images were obtained with an aluminium filter and reconstructed with a three-dimensional DICAM medical viewer (Osirix®). The trabecular structure is partly not recognisable because the bone has been remodelled (Fig. 6a and b).

Discussion

Opinions about treatment range from various surgical methods to medical treatment such as pamidronate given intravenously,\(^{13,14}\) but it is clear that a conservative approach may not be suitable in all cases of craniofacial fibrous dysplasia.

Pamidronate 60mg/day given intravenously on 3 successive days to reduce osteoclastic activity has been given every 6 months for 18 months. It resulted in a decreasing intensity of bony pain, reduced bony resorption, and improved radiological features such as filling of lytic lesions in about half of the patients.\(^{14}\)

The use of calcitonin is not supported universally; some authors report good results,\(^{15}\) while others report poor.\(^{16,17}\)

We recommend that vitamin $D$ and calcium supplements are given because concentrations of serum calcium are low.\(^{3}\)

Many factors have to be considered when deciding about further treatment. One is the aesthetic implication for the patient, but functional impairment should take precedence.

In thinner bone, such as the orbital plate of the maxillary, ethmoid and frontal bones, the cortex expands more rapidly and to a greater degree than in thicker cortical bone.\(^{19}\) When the orbit is involved compression and subsequent distortion of the globe can cause errors in refraction, focusing, and accommodation,\(^{20}\) so immediate
removal of the dysplastic process and decompression of the optic nerve canal is necessary. Visual loss in fibrous dysplasia is caused by the progressive compression of venous drainage of the optic nerve, which leads to reduced retinal perfusion.\textsuperscript{21} Operation is also essential when the foramen magnum is affected to prevent life-threatening conditions.

Chen and Noordhoff based surgical treatment on four areas of involvement: excision of dysplastic bone and reconstruction with autogenous bone graft in the fronto-orbit, nasal ethmoid and upper maxilla, or the conservative shaving of the parietal and part of the occipital bone.

Orthognathic operations can be done to restore occlusion and correct disproportion of the jaw when tooth-bearing bone is involved. Yeow and Chen\textsuperscript{23} achieved long-term stability of the occlusion in one of our patients.

The risk of developing sarcoma is 400times higher in patients who have been treated previously with radiation than in non-radiated patients. Radiotherapy should not be used to treat fibrous dysplasia.\textsuperscript{5} When there is a risk of malignant degeneration follow-up of these patients is recommended. Schwarz and Alpert\textsuperscript{24} found that there was a mean interval of 13.5 years between diagnosis of fibrous dysplasia and the development of malignancy.

References


Fig 1: typical "groundglass" matrix and enlargement of the frontal bone in the CT

Fig 2: bony enlargement on the left side of the lower jaw

Fig 3: bony enlargement on the left side of the upper jaw
Table 2: summary of the patients

<table>
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Figure 6: Fibrous-osseous lesion with trabeculae of woven bone and interosseous spindle cells, H&E, x50.

Figure 7: Woven bone with emanating collagen fibers (arrow), EvG, x100.