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Maxillofacial fibrous dysplasia:A clinical analysis of 72 cases.

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Abstract

Objective: To analyse the clinical characteristics and imaging findings of maxillofacial fibrous dysplasia and the relationship between serum alkaline phosphatase and its clinical relative factors.

Method: The clinical materials of 72 fibrous dysplasia patients were reviewed and the alkaline phosphatase among monostotic fibrous dysplasia, polyostotic fibrous dysplasia and non-fibrous dysplasia group (control group) were statistically analysed by variance (ANOVA) using the SPSS 22.0 software.

Result and discussion: There were 53 monostotic fibrous dysplasia (73.6%) and 19 polyostotic fibrous dysplasia (26.4%) among the 72 cases. Most fibrous dysplasia cases were not obvious boundary but ground glass type. The X-image classification of fibrous dysplasia showed that there were 44 cases of ground glass (61.1%), 10 cases of nodular sclerosis type (13.9%), 3 cases of cystic type (4.2%) and 15 cases of mixed type (20.8%). Before operation, serum alkaline phosphatase in polyostotic fibrous dysplasia group was (216.1 ± 248.7) U/L, significantly higher than (66.2 ± 14.9) U/L in control group and (118.8 ± 92.2) U/L in monostotic fibrous dysplasia group. After treatment, the serum alkaline phosphatase was (66.2 ± 14.9) U/L in control group, significantly higher than (118.8 ± 92.2) U/L in the 53 monostotic cases and (216.1 ± 248.7) U/L in the 19 polyostotic cases, P<0.01. There was no significantly statistical difference between control group and monostotic group. There were 17 relapses. 14 cases were relapses when they were admitted to hospital. According to the observation of recurrence cases, all the monostotic fibrous dysplasia's primary site was mandible. Authors suggested that it may relate to the operative way, anatomy and morphology of the upper and lower jaw. All the follow-up recurrence cases occurred in the mandible and first symptom was like inflammation, which might be associated with the anatomical characteristics of the mandible, surgical resection extent, proper treatment, and the short follow-up time.

Conclusion: Fibrous dysplasia is a fibrous bone lesion while the maxillofacial region is one of the predilection sites. No significant gender differences in the disease. The increase of serum alkaline phosphatase may be associated with the range of fibrous dysplasia lesions. The operation type can be chosen according to the patients' condition, and the appropriate time for surgery is post-adolescence.

Keywords: Maxillofacial region, Fibrous dysplasia, Alkaline phosphatase, Treatment.

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Introduction

Fibrous Dysplasia (FD) of bone, also called fibrous dysplasia, is the sporadic bone risk with genetics base and belongs to one of the fibrous hyperplasia bone lesions, accounting for about 5%-7% in benign lesions [1-4]. It is also the most common disease among the Fibro-Osseous Lesions (FOL) [5]. Generally, the FD has 3 types: polyostotic (PFD), monostotic (MFD) and McCune-Albright [6,7]. To some extent, the Serum Alkaline Phosphatase (ALP) shows the osteogenetic activity [8,9]. This paper tries to determine serum ALP in different maxillofacial FD patients, analyses the relationship between serum ALP and relative clinical factors, and summarizes and reviews the clinical and following-up material of those patients.

Material and Method

Patients

The study is approved by the ethics committee of Ninth People's Hospital; Shanghai Jiao Tong University School of Medicine. All patients signed the informed consent form.

Subjects were 72 inpatients in our hospital during 2009-2012. There are 27 males and 45 females among the 72 patients, age ranged from 9-66 and the median age was 22. The inclusive criteria were: complete medical history, marked X-ray and CT image and clear pathological diagnosis of maxillofacial FD. The gender, age, clinical manifestation, imaging finding, operation method and following-up material of all patients were collected and analysed. The preoperative serum ALP in all patients was analysed, and serum ALP in patients with same maxillofacial tissue cyst, the same period to hospital and same age, was used as control.

Treatment

Among the 72 patients, 15 patients experienced surgery caused by FD. The relapse criteria were that the previous surgical and pathological diagnosis was clear maxillofacial FD and the lesion increased significantly compared to the previous postoperative lesions. One case received the maxillary expansion excision and titanium mesh repair; orbital zygomatic maxillary resection, orbital plasty, orbital floor reconstruction, optic nerve decompression and eyeball reduction operation were given to another case; one case of zygomatic maxillary lesions experienced zygomatic maxillary resection and fibula flap repair; two cases experienced resection of mandibular lesions and repair of the vascularized fibula muscle; one case was treated with mandibular lesions resection and free fibula flap repair; one case of mandibular lesions was treated with curettage and autogenous bone implanting; one case with polyostotic lesions was treated by surgical decompression; other cases experienced the diseased bone trimming. The recovery of patients was fine.

Follow-up

The following-up time for the 72 patients was 2 months to 3.4 years. The recurrence rate, symptoms and recovery degree of the patients were collected. X-ray was performed when needed.

Statistical analysis

Using the analysis of variance (SNK Method) to analyse the data. The difference was considered to be significant when $P<0.01$. All calculation was performed using SPSS 22.0.

Result

Clinical data

There are 27 males and 45 females among the 72 patients, age ranged from 9-66 and the median age were 22. The course was 0.1-36 year, average 10.1 years. The mean age of onset was 14, but ranged from 1-54, and 80.4% patients' onset age was before 20 years old (Table 1). Clinical manifestation was slow-development, non-symptom maxillofacial deformity. Manifestation of teeth was sparse distribution, occlusal disorder, but no loosening. The severe degree of the maxillofacial deformity was relative to the course. 13 patients (18.1%) had pain, 4 of them were the first episode with infection, showing swell and pain of the lesion site, while the anti-inflammatory therapy was effective; among the 4, 1 case also had the limitation of mouth opening. While on other 5 relapse cases, 1 case showed paroxysmal headache caused by great compression to temporal lobe, the pain was relevant to postoperative infection and symptoms also were pain in lesion area complicated with radiation; the other 4 cases had diseased region pain caused by non-inflammation. 6 cases had nasal symptoms-nasal congestion with poor ventilation; two of them had had epistaxis. 4 had eye symptom: 2 of them had optic material discomfort; one was eye elevation with diplopia and one was blind. There were 5 male and 12 female among 17 relapses (Table 2).

Table 1. *Distributions of age and age of onset in 46 patients with FD of maxillofacial bone.*

Age	Distribution of treatment age		Distribution of onset age	
(year old)	Number (n)	Percentage (%)	number (n)	Percentage (%)
0~9	1	1.4	21	29.2
10~19	20	27.8	31	43.1
20~29	28	38.9	11	15.3
30~39	14	19.5	5	7
40~49	3	4.2	2	2.7
50~59	4	5.5	2	2.7
>59	2	2.7	0	0
Total	72	100	72	100

Fibrous dysplasia classification

The maxillary disease often involved the malar bone, frontal bone, ethmoid and other parts [10]. Their clinical symptoms were similar to maxillary single bone lesion, so this group classified such lesions as monostotic lesion of single maxillae. According to this classification, there were 53 cases of monostotic FD (73.6%) and 19 cases of polyostotic FD (26.4%) in this group. No McCune-Albright type in this group. Among the monostotic FD cases, single maxillae cases were 33 (62.3%, 9 involving cheekbones, 7 sphenoid, 3 temporal bone, 1 frontal bone, 1 ethmoid, 1 palatine bone), single mandible cases were 21 (39.7%). Among 19 polyostotic FD cases, 3 involved bilateral maxillofacial bone, 16 cases involved the upper jaw, 15 cases of mandible, 16 cases of sphenoid bone, 14 cases zygomatic bone and zygomatic arch, 10 cases of temporal bone, 6 cases of frontal bone, 5 cases of turbinate, 3 cases of ethmoid, 2 cases of palatine bone, 2 cases of parietal bone, 3 cases of occipital, 1 rib case, 2 cases of femur, 1 ilium case.

Imaging findings

According to the widespread X-image classification of FD, various types of the distribution and performance are as follows: Among the 44 cases of ground glass (61.1%), there were 24 cases of maxilla, 9 cases of mandibular bone and 11

cases of polyostostic bone, showing the similar gray matter of the lesion and like ground glass. Among the 10 cases of nodular sclerosis type (13.9%), there were 3 cases of maxilla, 4 cases of maxillary, 3 cases of polyostostic bone, showing higher calcification degree, homogeneous or in-homogeneous dense image without structure. 3 cases of cystic type (4.2%) were mono-cyst and occurred in the mandible, showing irregular image change. However, the edge was not smooth, and the boundary was not clear. Among the 15 cases of mixed type (20.8%), there were 4 cases of maxilla, 6 cases of maxillary mandible and 5 cases of polystotic bone. There also were transmission and resistance, namely dense film group shadow intermingled with irregular transmission shadow.

Preoperative serum ALP

In control group, the serum ALP was (66.2 ± 14.9) U/L. ALP was (118.8 ± 92.2) U/L in the 53 monostotic cases while it was (216.1 ± 248.7) U/L in the 19 polyostotic cases. The serum ALP in the polyostotic group was significantly higher than that in control group and monostotic group, and it had difference by statistical analysis ($P<0.01$). There was no significantly statistical difference between control group and monostotic group. Statistical analysis also showed that the ALP increase had no correlation with age and gender.

Follow-up

The following-up time for the 72 patients was 2 months-3.4 years. 3 of them relapsed and the 3 cases were single mandible. The initial symptoms were swelling and pain, the anti-inflammatory therapy was effective. One of them experienced the mandibular tumor scraping in our hospital, after 7 months, the follow-up X-ray found on the side of the mandible in shadow; 1 case experienced tumor exploration, after 1 month, the swelling and pain without relief, X-ray demonstrated periosteal reaction; another experienced mandibular resection, after 0.5 years, he had the swelling and pain again. 3 relapses underwent mandible repair and postoperative recovery was good. There was no recurrence in the follow-up period.

Table 2. *Age, age of primary operation, description of recurrence and primary region of 11 patients with recurrent FD of maxillofacial bone.*

Number	Gender	Age	Initial operation age	Lesion site	Recurrence description
1	F	35	22	maxillae	After the initial surgery, the maxillae enlarged slowly; in 2003, she had another trimming surgery; but 2 years later, the swell was recovered.
2	F	13	8	mandible	She experienced 5 times surgery when she was 8; when she was 12, her chin was cut; 1 year later, she got the contralateral swelling and pain, and the anti-inflammation was effective.
3	M	24	19	Poly-bone	The swell grew slowly in postoperative.
4	M	37	17	Poly-bone	The swell grew slowly in postoperative. But 3 years ago, the swell grew faster; and 1 year ago, she had left elevation and diplopia.
5	F	35	18	Poly-bone	The swell grew slowly in postoperative; 2 years ago, she had another operation.
6	F	21	16	mandible	The swell grew slowly in postoperative.
7	M	51	45	maxillae	After 2 years, she had swelled again.
8	F	29	23	Poly-bone	After a half year, she had swelled again.
9	F	26	19	maxillae	After the first operation, the slow increase, 5 years ago, second surgery was proceeded; 0.2 years ago, anterior palate swelled again.
10	F	31	15	Poly-bone	After surgery, jaw swelled slowly; 0.1 years ago, the paroxysmal pain of pain occurred.
11	F	53	16	Poly-bone	After surgery, there was a slow swelling of the jaw, and the growth rate was not significantly accelerated.
12	M	23	18	Poly-bone	After surgery, there was a slow swelling of the jaw, and the growth rate was not significantly accelerated.
13	F	41	29	mandible	After the first surgery, the swell grew slowly; 6 years ago, another surgery was done, and then numbness of lower lip happened; 2 years ago, the swell occurred again.
14	F	22	18	Poly-bone	After surgery, the dysesthesia of the orbital area occurred.

Discussion

FD, first reported by Lichenstein in 1938, is a kind of benign fibrous bone lesion in the marrow [11,12]. There are no precise data of its incidence and prevalence [1,13]. Among the 3 types, the McCune-Albright type is accompanied by care-au-lait spots and endocrine disease [14-16]. FD has different degrees' change during the process of bone formation and growth and the discomfort can occur in any age (but most patients have onset before 30). The onset of FD is without gender predisposition and FD usually occurs in long bone, rib, maxillofacial bone and pelvis [17].

FD is considered to be a disease of development that has bone remodeling disorders from the primitive bone to lamellar bone

[18]. Immature and isolated bone trabeculae caused by skeletal development disorders is left in the dysplastic fibrous tissue. These bone trabeculaes metabolize slowly, but they can't remould the bone shape, namely pathological bone can't realign according to the mechanical forces. In addition, the immature bone matrix can cause abnormal mineralization process. Both of the lack adjustment of external force and mineralization insufficiency lead to the loss of bone mechanical strength, resulting in pain, deformity or pathological fracture process. In our group, all 72 cases had malformation and some had pain, but without pathological fracture process, which may because of the maxillofacial bone loading less than the long bone.

The cause of FD is not fully clear. It is said that the cause may be relative to the mutation of gene *Gsα* localized in 20q 13.2-13.3 chromosome [19,20]. All mutant cells display dysplasia but the clinical presentation is only determined by the location of those cells and the size of the mutant cell mass [14,21]. In pathology, the FD is characterized by non-osteogenesis: the immature bone trabeculaes scatter evenly in the fiber matrix and there are no malignant cytological characteristics under the microscope [13]. Due to the extremely similar pathological characteristics between FD and other maxillofacial FD, especially the Ossifying Fibroma (OF), the scholars consider the diagnosis need the close collaboration between clinician and pathological physician [22].

FD is the lesion of expanding asymptotic growth. Imaging features of the bone tissue show wholly swelling [23,24]. If the swell occurs in the mandibular canal of the mandible, there may be displacement. The lesions, no obvious boundary, can transit between the mandibular canal and the normal bone tissue and will not affect the continuity of the cortical bone. When the lesion becomes too large, it can involve the cortical bone. Then the imaging of mandible shows thin cortical bone or the obvious periosteal proliferation. Later, cortical line of bone cavity in maxilla can be vague or disappears. So, tooth root absorbs nothing and light tooth displacement occurs, but the boundary among proper alveolar bone, compacted bone and cancellous bone disappears, and the periodontal space exists. Despite different records of FD's imaging classification, the author recommends the clear classification of ground glass type, nodular sclerosis type, cystic type and mixed type which helps memorizing and clinical application.

Reports about preoperative serum ALP of FD patients are few [25]. By using the preoperative serum ALP, this paper suggests that the ALP in polyostotic group was higher than control group and monostotic group, and it was not significantly correlated with age. The results suggest that the raise of serum ALP may be related to the extent of the lesion. In previous report, the most notable characteristic to identify the FD and Paget's disease of bone is that ALP in patients with Paget's disease is significantly increased [21]. But in our group, the serum ALP of polyostotic FD group also increased significantly. More attention is necessary while diagnosed.

Maxillofacial bone directly relates to facial structure, morphology and beauty, so the patients with maxillofacial FD tend to require appearance improvement. For FD patients with mild lesions and no obvious deformity, clinical observation can be preceded and X-ray films were taken every 6 months [13]. Moreover, active treatments should be taken, for correcting or preventing the development of functional abnormalities and improving facial features. Generally, the slashing, enucleation or partial ostectomy of jaw were used to cure FD. All trimming in this paper was treated with method of "overkill", that is, the relatively wide resection or scraping lesions. Pressure bandage was used to prevent hematoma after operation. No relapse in postoperative and effect was satisfactory.

Osteocytes of FD lesions lose normal physiological function and the lesion area is susceptible to infection [26]. If the lesion involved the alveolar process, the bacteria can enter the lesion area easily through the alveolar bone. Compared to the maxillae, mandible's blood supply is limited [27]. That's to say, if infection occurs in mandible FD, the disease becomes more protracted. Authors of this paper believe that FD cases, with relapses and infection, or affected appearance and function, can be used as indications for repair and reconstruction.

These 14 cases were relapses when they were admitted to hospital, with gender differences. Intervals between initial operation and admission range from 4 to 37 years, but most patients clearly felt the swelling of mass after 5 years of the surgery. From the age of the first operation, among the 15 cases, 11 cases were less than 22 years old. It tends to the younger, the faster of relapse and the more severe symptoms. So the authors support the program of post-adolescent surgery. Interestingly, according to the observation of recurrence cases, all the monostotic FD's primary site was mandible. Authors suggested that it may relate to the operative way, anatomy and morphology of the upper and lower jaw. The specific reasons are awaited.

After surgery, 72 cases were followed up for 2 months-3.4 years, during which 3 cases were reoccurred. However, it is reported that the recurrence rate of the disease is more than 10% [28] and is related to the extent of surgical resection as well as the age of operation [29,30]. All the follow-up recurrence cases occurred in the mandible and first symptom was like inflammation, which might be associated with the anatomical characteristics of the mandible, surgical resection extent, proper treatment, and the short follow-up time. Authors will deeply analyse the characteristics and prognosis of the disease by many methods, such as collecting more maxillofacial FD cases and increasing the follow-up time.

Conclusion

In summary, this study analysed the clinical materials of 72 fibrous dysplasia patients and investigated effects of the alkaline phosphatase among monostotic fibrous dysplasia, polyostotic fibrous dysplasia and non-fibrous dysplasia group. Results showed that fibrous dysplasia is a fibrous bone lesion while the maxillofacial region is one of the predilection sites. The increase of serum alkaline phosphatase may be associated

with the range of fibrous dysplasia lesions. The operation type can be chosen according to the patients' condition, and the appropriate time for surgery is post-adolescence.

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