Management of fibrous dysplasia
A report on 36 cases

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A consensus on the clinical course of fibrous dysplasia has not yet emerged in the literature. We retrospectively evaluated 36 patients who were diagnosed with fibrous dysplasia in our institution and were followed for a mean duration of 56.5 months (range 7-210 months). Their mean age was 25.8 years (range 5-67 years) ; 46.7% were male. The most frequent presenting complaints were pain (66% of patients) and pathological fracture (20%). Osteosarcoma developed in one patient 20 years after he had undergone radiation therapy for fibrous dysplasia in the tibia. Mazabraud syndrome was encountered in two patients, and aneurysmal bone cyst associated with fibrous dysplasia was seen in one patient. Fibrous dysplasia is generally considered a static disease, but with long-term follow-up it is found to have a more dynamic nature. For this reason, patients with fibrous dysplasia should be followed carefully over the long term.

Keywords : fibrous dysplasia ; orthopaedic procedures ; follow-up studies.

INTRODUCTION

Fibrous dysplasia is a rare condition in which bone tissue is replaced by fibro-osseous lesions (*6*). These benign skeletal lesions may involve one bone (monostotic) or multiple bones (polyostotic). The lesions can occur throughout the skeleton but tend to occur in long bones, ribs and craniofacial bones ; they represent 5-7% of all benign bone tumours (*4*). The first symptoms usually appear between 5 and 20 years of age, and the more extended the dysplasia, the earlier the onset of symptoms (*1*). The exact pathogenic mechanism of fibrous dysplasia is unknown but recent studies indicate that genetic factors may be responsible, and the disease has been linked to a mutation in the $G_s\alpha$ gene located on chromosome 20q13.2-13.3 (*21*).

Polyostotic fibrous dysplasia tends to occur in a unilateral distribution. Monostotic lesions are generally identified incidentally, and in some cases clinical observation is the choice of treatment. In monostotic dysplasia, lesions generally cease to be

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active with the onset of puberty. However, polyostotic fibrous dysplasia tends to continue after skeletal maturity, and severe skeletal deformity may develop (*10*). The maxillary bones, proximal femur and tibia are the most frequent sites of disease. These are followed by humerus, ribs, radius and iliac bone (1). In the extremities, fibrous dysplasia is generally seen in the metaphysis of long bones. Fibrous dysplasia appears to affect males and females equally (*10*).

Treatment for fibrous dysplasia generally consists of prophylactic surgery (curettage and grafting) and clinical observation. Recent studies have reported that bisphosphonate therapy may be effective in some patients with fibrous dysplasia (*2, 4, 12*). Diseases to be considered in the differential diagnosis of fibrous dysplasia include chondroma, simple bone cyst**,** non-ossifying fibromas, osteofibrous dysplasia, Paget's disease of bone, osteoblastoma, chondroblastoma, fibromyxoma of bone, adamantinoma and low-grade intramedullary osteosarcoma (*1, 4, 7, 9*). The purpose of the current study is to report our experience of fibrous dysplasia in a series of 45 patients, 36 of whom with continued follow-up.

MATERIALS AND METHODS

We retrospectively evaluated 36 patients who were diagnosed with fibrous dysplasia in our institution and were followed for a mean duration of 56.5 months (range 7-210 months).

Diagnosis was made via Jam-Shidi needle biopsy (8 patients), open biopsy (15 patients, 9 of these during surgery for pathological fracture), or with imaging techniques (22 patients). Standard radiographs and computed tomography (CT) were performed for all patients, and magnetic resonance imaging (MRI) was performed in 15 patients. We used technetium bone scintigraphy in 8 patients to assess the extent of lesions. If polyostotic disease was discovered, patients were examined for endocrine abnormalities.

Of the 45 patients in the study, 32 were treated with surgery. Nine patients were lost to follow-up, and of the 36 patients with continued follow-up, 29 underwent surgical treatment.

In one patient, polyostotic fibrous dysplasia was treated with radiation therapy at another centre in 1980, before the period covered by this study. Eight patients who continued in follow-up had pathological fractures ; two of these were treated with a cast brace only, and the other six were treated surgically. In one patient who received surgery, a cast brace had been initially applied. For the surgical procedure, curettage and bone graft or bone cement were generally used. If bone stability was not good during the surgical procedure, the use of an implant was preferred.

In three patients who had shepherd's crook deformity of the proximal femur, corrective osteotomy was made. For patients who had moderate tibia vara, curettage and bone cementing was performed. In one patient who underwent surgery for pathological hip fracture, a custom-made hip prosthesis was implanted because of severe hip deformity. One patient who had extensive fibrous dysplasia in the scapula underwent total scapulectomy.

RESULTS

A total of 45 patients (24 female, 21 male ; mean age 26.2 years, range 5-67 years) were diagnosed as having fibrous dysplasia in our department of orthopaedic oncology from March 1986 to January 2006. Of these patients, 30 had monostotic disease and 15 had polyostotic disease. For the 36 patients who continued in follow-up, the mean period of follow-up was 56.5 months (range 7-210 months). Pain was the most common presenting symptom (66% of patients). Pathological fractures were the presenting complaint in nine patients (20%). Table I gives the frequency distribution of anatomic sites affected by fibrous dysplasia.

In the one patient who had received radiation therapy for fibrous dysplasia, osteosarcoma developed 20 years later in his left tibia, which had been irradiated. The patient died due to pulmonary metastases from the tumour, one year after the osteosarcoma was diagnosed.

In two patients we diagnosed polyostotic fibrous dysplasia with soft tissue myxoma, a condition known as Mazabraud syndrome (*17, 20*). Both patients complained of a soft tissue mass. One was treated surgically ; the other, who also had vertebral tuberculosis, did not accept surgical treatment. She was successfully treated for tuberculosis and at 58 months follow-up her Mazabraud symptoms were unchanged.

Table I. — Locations of fibrous dysplasia

Location	% of all tumours
Femur	35.05
Tibia	17.52
Humerus	11.34
Ilium	11.34
Maxillofacial bones	8.24
Thorax	4.12
Radius	3.09
Fibula	3.09
Vertebrae	2.06
Scapula	2.06
Ulna	2.06
Total	100%

In three patients who had shepherd's crook deformity, corrective osteotomy was made. Two of these patients had no problem at 13 and 66 months follow-up, respectively. In the third patient, the affected leg was 4 cm shorter than her other leg. One patient who had polyostotic fibrous dysplasia developed a distal radius deformity 14 months after surgery.

In a 13-year-old female patient, graft resorption and recurrence of fibrous dysplasia occurred at 8 months after curettage and bone grafting. However, the patient had no complaints 60 months after surgery. In two patients who had fibrous dysplasia in the upper femur and femoral neck respectively, pain was lessened but not eradicated by surgery.

In one patient, an aneurysmal bone cyst developed secondary to fibrous dysplasia in the scapula 108 months after the patient had been diagnosed with polyostotic fibrous dysplasia. The aneurysmal bone cyst was treated with curettage and bone grafting.

In 4 patients refracture or stress fracture occurred within 9 months after the initial operation. These patients were treated surgically. No complications related to infection were encountered in any patients.

DISCUSSION

In our series of 45 patients with fibrous dysplasia, there were slightly more females than males (24 females, 21 males), and in 15 patients the symptoms of fibrous dysplasia began after 30 years of age. The gender distribution in our series is consistent with previous studies (*1, 10*), but the onset of symptoms after age 30 in one-third of our patients is in contrast to the general observation that symptoms usually begin between the ages of five and 20 (*1*). Fibrous dysplasia accounts for 3.6% of all benign bone tumours diagnosed in our department of orthopaedic oncology, which is slightly less than the 5-7% reported in the literature (*4*). In our series, monostotic was more frequent than polyostotic fibrous dysplasia, which is consistent with other studies (*4, 10*). The ratio of monostotic to polyostotic fibrous dysplasia in our series was 2/1.

Plain radiographs of fibrous dysplasia lesions generally show cortical thinning, expansion of the medulla, loss of the normal trabecular pattern and a "ground-glass" appearance. For evaluating the extent and shape of lesions, CT is the best technique. In our series, all patients underwent CT and 15 also underwent MRI. Radionuclide bone scintigraphy is also useful in determining the extent of lesions, particularly in polyostotic disease. We used scintigraphy in 8 patients with polyostotic fibrous dysplasia to determine the location of the lesions. In the other patients with polyostotic fibrous dysplasia, lesions were localized with radiographs covering all regions of the body. In diagnosing fibrous dysplasia, we used imaging methods alone in 22 patients.

Polyostotic fibrous dysplasia may be associated with skin pigmentation, endocrine abnormalities, and precocious pubertal development, and this combination is known as Albright's syndrome (*14, 15, 18*). Fibrous dysplasia may also be seen with hypophosphataemic osteomalacia (*14*). In our patients with polyostotic fibrous dysplasia we found no endocrine abnormalities. Skin pigmentation was noted in one of them.

Pain was the most common presenting symptom (66% of patients) in this series. We suspect that pain can arise from microfractures occurring in the dysplastic bone. In one patient who had pain, no definite fracture was visible on radiographs, CT or MRI, but during surgery an incompletely healed fracture was found (fig 1-4). Pathological fracture

Fig. 1. — On this plain radiograph of a patient who presented with a 2-month history of pain in the left hip, the signs of fibrous dysplasia are visible : ground-glass appearance, medullary expansion and cortical thinning.
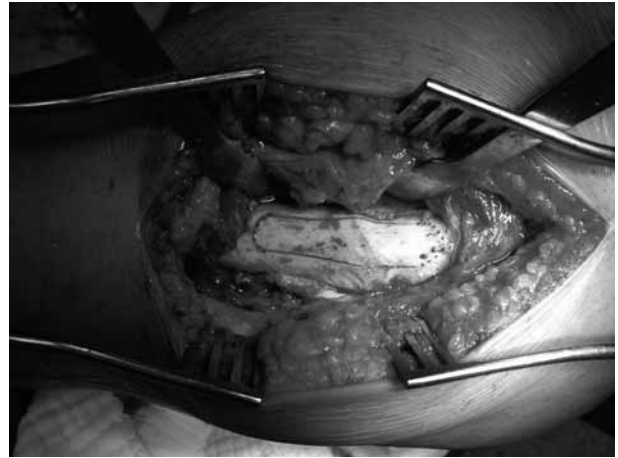

Fig. 2. — This photograph of the affected region of the femur shows a healing fracture line.

Fig. 3. — A cortical window encompassing the fracture line was removed from the bone, and the fracture was more apparent on the interior surface, as shown here.

was the second most common cause of presentation, presence of a mass was third, and limping was fourth. In two patients fibrous dysplasia was discovered fortuitously.

Fibrous dysplasia can cause skeletal deformity. For example, shepherd's crook deformity is seen in the proximal femur. A possible mechanism for this deformity is repeated microfracture and malunion, with the femur becoming laterally bowed and enlarged due to mechanical insufficiency. Bowing of the tibia may also be seen, and may due to the same reasons. Corrective osteotomy was performed in three patients who had shepherd's crook deformity (aged 6, 12 and 36 years respectively). The 12-year-old developed lower leg discrepancy during skeletal growth. The other two patients had

no problem at 13 and 66 months follow-up, respectively, but we are planning close follow-up through skeletal maturation for the 6-year-old patient.

An area of fibrous dysplasia in bone may undergo rapid enlargement, and this can be due to cystic degeneration, aneurysmal bone cyst or malignant transformation (5, 19). In determining the nature of this enlargement, MRI can be helpful. One patient in our series complained of intractable pain and rapid enlargement occurring within one week at his

Fig. 4. — Coronal MRI shows cystic degeneration in the proximal femur.

tibial bone lesion. MRI revealed cortical destruction and soft tissue enlargement suggesting malignancy. Open biopsy revealed osteosarcoma. In four patients we diagnosed fibrous dysplasia with cystic degeneration at the time of diagnosis (fig 4). In these patients MRI did not suggest malignant changes. A patient with polyostotic fibrous dysplasia suffered from severe pain and enlargement of the lesion in her scapula. MRI revealed a fluid level, which suggested a diagnosis of aneurysmal bone cyst secondary to fibrous dysplasia. In this patient, histological examination of biopsy specimens confirmed the radiological diagnosis.

Malignant changes in fibrous dysplasia are rare, occurring in less than 1% of all cases (*1, 11, 22*). The most common malignant tumour in this setting is osteosarcoma followed by fibrosarcoma and then chondrosarcoma (*18*). Although sarcomas in fibrous dysplasia can develop without prior irradiation (*11, 22*) the role of radiation therapy in the occurrence of sarcoma in fibrous dysplasia is well known. For this reason radiation therapy should be avoided in the treatment of fibrous dysplasia (*1, 18, 20, 22*). In our series, one patient developed osteosarcoma 20 years after receiving radiation therapy.

Scoliosis may be seen with polyostotic fibrous dysplasia (*13*). However, the two patients in our series who had vertebral involvement had no spinal deformities.

The relationship between fibrous dysplasia and myxoma (Mazabraud syndrome) remains unclear. The syndrome is quite uniform, and mostly occurs in women. Malignant transformation from fibrous dysplasia to osteosarcoma or fibrosarcoma in Mazabraud syndrome has been reported in the literature (*15, 20*). Our two patients with Mazabraud syndrome were female, one of whom did not accept surgical intervention. In this latter patient, after 58 months of follow-up there was no progression of the lesions.

In patients with fibrous dysplasia, if there are no symptoms or if there is no impending fracture, surgical treatment may not be necessary (*1*). The patients at greatest risk for pathological fractures are those who have large painful lesions in weight-bearing bones, and these patients should be evaluated for prophylactic treatment (*4*). Curettage and bone grafting has been the standard treatment for symptomatic and asymptomatic lesions in fibrous dysplasia (*8*). For patients with symptomatic dysplasia in the femur, surgical treatment alternatives include curettage and bone grafting, valgus osteotomy, plating (*8*), intramedullary nailing (*6*), and oblique wedge osteotomy (*23*). The modified Pauwels' intertrochanteric osteotomy can be used in the treatment of pathologic femoral neck fractures secondary to extensive lesions of fibrous dysplasia (*16*). In our series, surgical treatment was generally preferred due to symptoms, skeletal deformity or the risk of pathological fracture. For femoral deformity, dome-shaped osteotomy was preferred in our series. A total of 23 patients underwent surgery (curettage, graft or corrective osteotomy) for lower extremity lesions. Refracture or stress fracture developed in four patients during follow-up.

In summary, although fibrous dysplasia is generally considered a static disease after skeletal maturity, with long-term follow-up the disease is found to have a more dynamic nature which can include cystic degeneration, aneurysmal bone cyst, and malignant transformation. Pain in fibrous dysplasia

is usually explained in general terms of mechanical insufficiency, and as a specific source of pain we propose microfractures that are not readily apparent on imaging studies. A final point is that pathological fractures may occur with no warning symptoms, and this was the case in 20% of the patients in this series. Given these characteristics of fibrous dysplasia, we suggest that patients with this disease should be followed carefully over the long term.

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