Fibrous dysplasia

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Chapter 9

Clinical course and management of fibrous dysplasia of the humerus

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ABSTRACT

Background: Fibrous dysplasia (FD) is a rare bone disorder that can cause pain, deformity and fractures at the site of lesions. Although the humerus is often affected, evidence on the clinical course and treatment of FD lesions located at the humerus is scarce.

Purposes: In this retrospective study we evaluated (1) the clinical characteristics of FD of the humerus; (2) risk factors for pathological fractures; and (3) outcomes of conservative treatment, surgery and sclerosing injections of cystic lesions at this site, with a good outcome being defined as revision-free follow-up with no recurrent fracture, delayed union or complications.

Methods: Out of the 255-strong cohort of patients with FD, treated at the Leiden University Medical Center between 1990–2015, 50 had FD of the humerus (57 humeri) and were included in the study. Data were collected from medical records on age at diagnosis, sex, type of FD, clinical features including pain and fractures, endocrinopathies, and history of surgical interventions. Potential risk factors for a fracture were analysed on conventional radiographs and MR-imaging of FD lesions and included anatomical localization of the lesions, involvement of the cortex and the presence of cysts. Primary outcomes of surgery and of injections of the cysts with sclerosing agents were the absence of newly sustained fractures and/or need for revision surgery.

Results: Thirty-one of the 50 patients (62%) had monostotic FD, 11 (22%) had polyostotic FD and 8 (16%) had McCune-Albright syndrome. Mean follow-up after diagnosis was 9.4 years (± 12.5 SD) and 27 patients (54%) had sustained at least one pathological fracture at a mean age of 19.1 years (± 15 years SD). A fracture was the presenting symptom in 22 patients (44%). The presence of cystic degeneration in an FD lesion was identified as a risk factor for fracture in logistic regression analysis (OR 4.1, p = 0.033, 95% CI 1.1–14.9). Conservative treatment of fractures resulted in a good outcome in 70% of patients. Three of five patients who were treated with cancellous allogeneic bone grafting had a good outcome, with the other two needing revision surgery. Two of three patients who had cortical bone grafting had a good outcome and one sustained a fracture, which successfully healed on conservative treatment. Three of five patients who received sclerosing injections of cystic lesions had good outcomes, one sustained a subsequent fracture and one required additional surgery.

Conclusion: FD of the humerus is associated with a relatively mild course. Although pathological fractures occur in half of patients, two third of these heal successfully on conservative treatment. Cystic degeneration of an FD lesion represents a risk factor for fractures. Surgical treatment with a view to decrease pain or stabilize impending fractures appears to be more beneficial with the use of cortical rather than cancellous bone grafting, although definite recommendations on this type of treatment should await results of studies performed in larger cohorts.

INTRODUCTION

Fibrous dysplasia (FD) is a rare bone disorder in which healthy bone is locally replaced by fibrous tissue of poor quality. The lesions can be present in a single bone (monostotic FD) or several bones (polyostotic FD), and in combination with a number of endocrinopathies in the context of the McCune-Albright Syndrome (MAS), which include precocious puberty, growth-hormone and prolactin excess and hyperthyroidism and with café-au-lait skin lesions. FD is caused by a missense mutation of the GNAS-gene that occurs post-zygotically and results in a net increase of intracellular cAMP in affected cells.[1] The mosaic distribution of the mutation causes a wide variation in clinical expression of FD, varying from completely asymptomatic patients, to patients with severe pain, deformities, and fractures. Although FD is predominantly localized in the proximal femur and craniofacial bones, the bones of the upper extremity, especially the humerus, may also be affected.[2] Literature on the natural history and treatment of FD of the humerus is scarce, with reports on the management of FD generally focusing on the lower extremities, which are more prone to complications because of their weight-bearing properties.[3,4] In our experience, FD lesions of the humerus may also be symptomatic, although behaving differently from FD lesions of the lower extremities. This led us to retrospectively evaluate (1) the clinical characteristics of FD of the humerus; (2) risk factors for pathological fractures; and (3) the surgical and non-surgical treatment of FD lesions at this site.

PATIENTS AND METHODS

Study design

Our FD database consists of 255 patients with different types of FD, evaluated and followed-up at our tertiary referral centre for rare bone diseases between 1990–2015. From this cohort, we identified from medical records 50 patients (male/female ratio 25:25) with an FD lesion at 57 humeral sites. The diagnosis of FD was established on the basis of clinical and radiological features, with conventional radiographs being available in all patients, and MR imaging performed as required. In case of doubt about the diagnosis, this was confirmed on the basis of histological evaluation of a biopsy of the lesion and/or the case was referred for evaluation to the National Netherlands Committee for Bone Tumours. All patients had to have a minimum follow-up of 1 year to be included in the study. The study was approved by the Medical Ethical Committee of the Leiden University Medical Center.

Data collection

Data retrieved from patients' medical records included age at diagnosis, sex, type of FD (e.g., monostotic, polyostotic or McCune-Albright syndrome), clinical features including pain, endocrinopathies in the context of MAS such as precocious puberty, GH-excess, presence of café-au-lait patches, prevalence of pathological fractures of the affected humerus, and history of surgical interventions. The radiological studies were evaluated by an experienced skeletal radiologist (HMK).

Potential risk factors for pathological fractures (Fig. 9.1) were assessed according to the findings of a previous study on the risk of pathological fractures in patients with femoral metastasis and included: 1) Localization of the lesions (metaphysis, epiphysis, diaphysis or a combination); 2) Cystic degeneration of the FD lesions on MR imaging (yes/no); 3) Maximal length of the (biggest) lesion in mm. 4); Circumferential cortical involvement (> 50%); 5) Transverse cortical involvement (> 50%); 6) Axial cortical involvement (> 30 mm).[5] Evaluation of the presence of cystic components in a

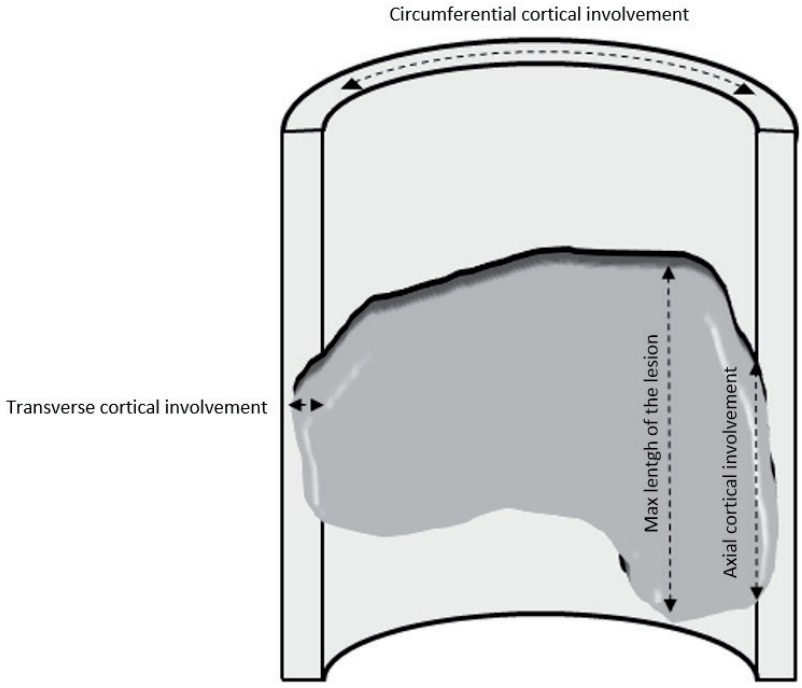


Fig. 9.1 Potential risk factors for fractures in fibrous dysplasia of the humerus. Schematic drawing of potential risk factors for fractures in fibrous dysplasia of the humerus, including maximal length of the lesion, circumferential extent of cortical involvement (> 50%), transverse cortical involvement (> 50%), axial cortical involvement (> 30 mm), anatomical localization of the lesion (metaphysis, epiphysis, diaphysis) and presence of cystic degeneration.

fibrous dysplasia lesion could only be reliably performed by MR imaging, including T2-weighted and T1-weighted post-contrast fat suppressed sequences, and was, therefore, solely conducted in patients with available MR scans (n = 19).

Different surgical and non-surgical interventions were evaluated and categorized as follows: 1) Fracture treatment; 2) Surgical treatment of FD of the humerus for various indications; 3) Minimally invasive injections of cystic FD lesions with sclerosing agents to prevent pathological fractures. A good outcome was defined as no need for reoperation, no (re)fracture and no delayed union or non-union. All interventions were further evaluated for complications.

Statistical analysis

Statistical analysis was performed using SPSS for Windows, version 23.0 (SPSS, Inc., Chicago, IL, USA). Unless stated otherwise, results are presented as mean ± SD, or as a percentage in case of categorical data. Clinical predictors for pathological fractures were assessed in a univariate logistic regression analysis and subsequently in a multivariate logistic regression analysis to correct for age and sex.

RESULTS

Patients characteristics (Table 9.1)

Out of the 255 patients from our FD cohort, 50 (19.6%) patients (25 male and 25 female) had FD lesions of the humerus, with 7 having bilateral lesions, totalling 57 humeral lesions for study. Thirty-one patients (62%) had monostotic FD, 11 (22%) had polyostotic FD and 8 (16%) had MAS. Mean age was 35.7 ± 18.8 years, and mean age at diagnosis was 22.7 ± 16.7 years in MFD patients, 26.4 ± 16.6 years in PFD patients and was significantly lower in MAS patients at 4.1 ± 4.6 years (p = 0.002). Mean follow-up after diagnosis was 9.4 years (± 12.5 SD).

Humeral fibrous dysplasia lesions

Humeral FD lesions were generally large with a mean length of 143 mm (± 82.5 SD) and the cortex was often involved (95%). In 37% of lesions, only the diaphysis was affected, in 20% the diaphysis and metaphysis, in 11% only the metaphysis and the whole of the humerus was affected in 33% of humeral lesions. Over half of the cortical circumference of bone was affected in 87% of cases, and more than half of the transverse width of the cortex was affected in 84%. Mean axial cortical involvement was 99.1 mm (± 60.0

Table 9.1 Patient characteristics

Patient ID	Gender	Side	Age at diagnosis (years)	Type of fibrous dysplasia*	Fracture of the humerus	Age at time of first fracture (years)	Cystic deformation**	Follow-up in years
1	Female	Left	13	MFD	Yes	13	Yes	4
2	Male	Right	9	PFD	No	-	NA	26
3	Female	Left	8	MFD	Yes	8	NA	1
4	Female	Both	3	MAS	No	-	NA	19
5	Female	Left	4	MAS	No	-	NA	39
6	Male	Right	13	MFD	Yes	10	NA	3
7	Female	Right	24	MFD	Yes	24	Yes	1
8	Female	Right	31	MFD	Yes	31	Yes	4
9	Male	Left	16	MFD	Yes	13	NA	11
10	Male	Right	7	MFD	Yes	8	NA	36
11	Female	Left	29	MFD	Yes	29	NA	7
12	Male	Left	29	MFD	No	-	NA	15
13	Female	Left	19	PFD	No	-	No	3
14	Female	Left	38	MFD	No	-	No	1
15	Female	Both	0	MAS	Yes	28	NA	50
16	Male	Right	9	MFD	Yes	10	No	3
17	Male	Left	59	MFD	No	-	NA	1
18	Female	Left	10	MFD	Yes	11	NA	2
19	Female	Both	0	MAS	No	-	NA	41
20	Male	Right	11	MFD	Yes	11	No	8
21	Female	Left	5	MFD	Yes	5	NA	8
22	Male	Right	31	PFD	Yes	27	NA	18
23	Male	Left	7	MFD	Yes	7	NA	7
24	Male	Right	14	MFD	Yes	15	Yes	1
25	Female	Left	30	MFD	Yes	31	Yes	1
26	Female	Right	57	MFD	Yes	57	Yes	2
27	Male	Left	10	MFD	Yes	10	Yes	5
28	Female	Right	4	PFD	No	-	NA	32
29	Female	Left	5	PFD	No	-	No	13
30	Female	Right	21	PFD	No	-	NA	32
31	Female	Both	6	MAS	No	-	NA	2
32	Female	Both	1	MAS	Yes	62	NA	61
33	Male	Left	12	MFD	Yes	13	NA	13
34	Male	Left	11	PFD	No	-	NA	1
35	Male	Left	10	MFD	Yes	11	Yes	1
36	Female	Left	49	PFD	No	-	NA	1
37	Male	Left	60	MFD	No	-	NA	1
38	Male	Right	12	MFD	Yes	12	NA	10
39	Male	Right	20	MFD	No	-	Yes	1
40	Male	Left	10	MFD	Yes	11	Yes	2

Table 9.1 continues on next page

Table 9.1 *Continued*

Patient ID	Gender	Side	Age at diagnosis (years)	Type of fibrous dysplasia*	Fracture of the humerus	Age at time of first fracture (years)	Cystic deformation**	Follow-up in years
41	Male	Right	50	PFD	No	-	NA	3
42	Female	Right	63	MFD	No	-	No	1
43	Male	Right	16	MFD	Yes	16	NA	6
44	Female	Right	29	MFD	Yes	29	Yes	1
45	Female	Left	35	PFD	No	-	No	5
46	Female	Left	32	MFD	No	-	NA	11
47	Male	Right	24	PFD	No	-	NA	5
48	Male	Right	32	MFD	No	-	Yes	11
49	Male	Both	5	MAS	Yes	16	NA	12
50	Male	Both	14	MAS	No	-	NA	11

* MFD = monostotic fibrous dysplasia; PFD = polyostotic fibrous dysplasia; MAS = McCune-Albright syndrome.
** NA = Not analysed (no MRI).

SD) and in 81% axial cortical length was over 30 mm. Cystic degeneration of humeral FD lesions was observed in 74% of cases in which an MRI had been performed and the cystic component comprised more than half of the lesion in 64% of these. In 77% of patients with cystic degeneration of the FD lesion and a fracture, this ran through the cystic part of the lesion (Fig. 9.2).

Clinical predictors for pathological fractures

Twenty-seven patients (54%) had sustained at least one pathological fracture at a mean age of 19.1 years (± 15 years SD) and a fracture was the presenting symptom in 22 patients (44%). None of these patients were using crutches at the time of the fracture. In univariate logistic regression analysis (Table 9.2) only the presence of cysts was predictive for a pathologic fracture (OR 3.5, p = 0.027, 95% CI = 1.6–10.8). This was still significant after correction for age and sex (OR 4.1, p = 0.033, 95% CI 1.1–14.9). No other factors were found to be significantly associated with a fracture at the site of a humeral FD lesion, although there was a trend for circumferential cortical involvement to do so (OR 8.3, p = 0.064, 95% CI 0.9–78.3).

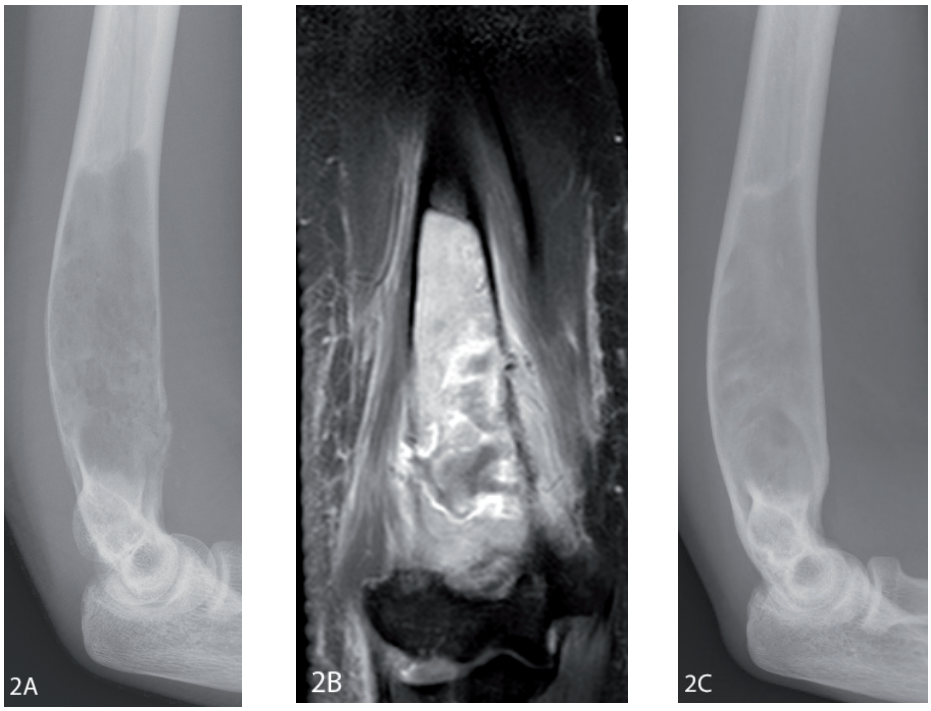


Fig. 9.2 Cystic degeneration of a fibrous dysplasia lesion of the humerus. Patient nr. 8 with an osteolytic lesion in the distal part of the humerus with evident cortical thinning and a fracture on the anterior side of the humerus (2A). Formation of cysts visible in the fracture area on T1-weighted fat supressed post-contrast MR-images, (2B). The fracture was treated with a cast resulting in good healing and no recurrent fractures. Conventional radiographs 6 years after the fracture showing increased cortical thickening and slightly increased sclerosis of the lesion compared to radiographs at diagnosis (2C).

Table 9.2 Logistic regression

	Factor	Odds ratio	Sig.	95% CI
Univariate	Age	1.03	0.100	0.99–1.07
	Gender	2.47	0.189	0.77–7.92
	Length of the lesion (mm)	1.00	0.764	0.99–1.01
	Transverse cortical involvement (> 50%)	2.10	0.377	0.41–10.80
	Circumferential cortical involvement (> 50%)	8.33	0.064	0.89–78.31
	Axial cortical involvement (> 30 mm)	3.43	0.116	0.74–15.91
	Cyst in the lesion	*3.54*	*0.027*	*1.16–10.81*
After correction for age and gender	Length of the lesion (mm)	1.00	0.731	0.99–1.01
	Transverse cortical involvement (> 50%)	2.56	0.292	0.45–14.66
	Circumferential cortical involvement (> 50%)	7.28	0.089	0.74–71.87
	Axial cortical involvement (> 30 mm)	2.84	0.195	0.59–13.81
	Cyst in the lesion	*4.08*	*0.033*	*1.12–14.89*

Conservative treatment

All 27 humeral fractures were primarily treated conservatively using a cast, a sling, or a brace, which resulted in a good outcome (no recurrent fracture, no non-union or delayed union and no indication for further surgery) in 16 patients (59%). Three patients sustained at least one recurrent fracture (two patients had 1 recurrent fracture and one patient had 2 recurrent fractures), prior to a good outcome using repetitive conservative treatment of the fracture. Eight patients eventually required at least one further intervention after a median of 13 months (range 1–100 months) following the primary fracture, including allogeneic graft surgery in 4 patients and sclerosing injections in cystic FD lesions of 5 patients.

Surgical treatment

Eight patients underwent 10 surgical interventions (Table 9.3). Primary indication for surgery was pain (n = 4), or an impending fracture after conservative treatment of an initial fracture (n = 4). Five patients were treated with allogeneic cancellous bone grafting (CBG). Three of these had a good outcome, but two patients required additional surgery due to continuous pain (n = 1) or continuous risk of an impending fracture (n = 1). The second intervention consisted of cryosurgery in the patient with persistent

Table 9.3 Surgical treatment

Patient ID	Gender/age at first surgery (years)	History of a fracture	Indication	Type of surgery**	Failure mechanism	Second intervention
9	M/17	Yes	Impending fracture*	CBG		
20	M/11	Yes	Impending fracture*	Cortical allograft	Fracture	Cast
22	M/35	Yes	Impending fracture*	Cortical allograft		
29	F/4	No	Pain	CBG	Pain	Cryosurgery
38	M/11	Yes	Impending fracture*	CBG	Impending fracture	Cortical autograft
45	F/37	No	Pain	Cortical allograft + nail		
46	M/32	No	Pain	CBG		
48	M/13	No	Pain	CBG		

* Impending fracture after a previous fracture with insufficient healing.
** CBG = cancellous bone grafting with allografts.

pain, which failed to decrease pain levels, and a cortical allograft in the patient with a continuous risk of a pathological fracture that resulted in a good outcome. Three patients were primarily treated with cortical allografts (Fig. 9.3), supplemented with a titanium nail in one patient. Two patients had good outcomes with no further complaints of pain and no need for additional surgery, and one patient sustained a fracture at the site of the reconstruction after a traumatic injury. The fracture was treated conservatively and showed good healing with no further intervention necessary.

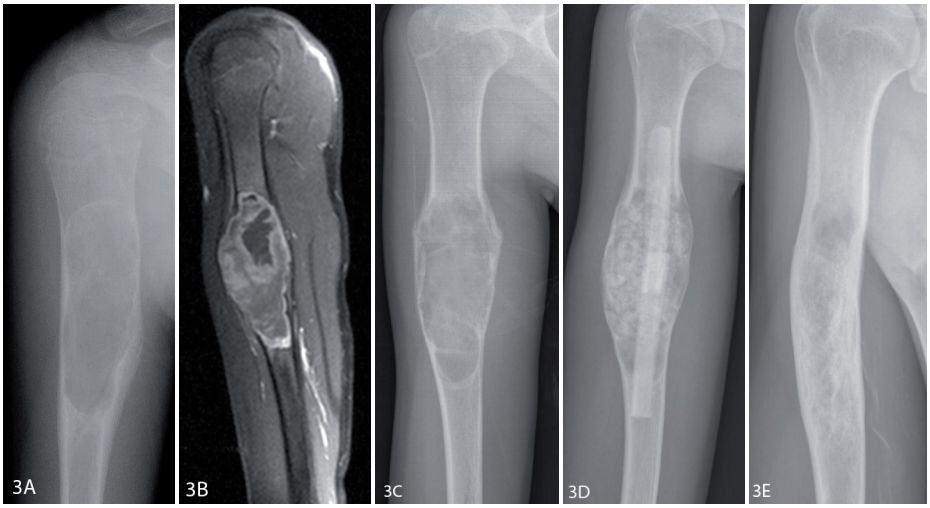
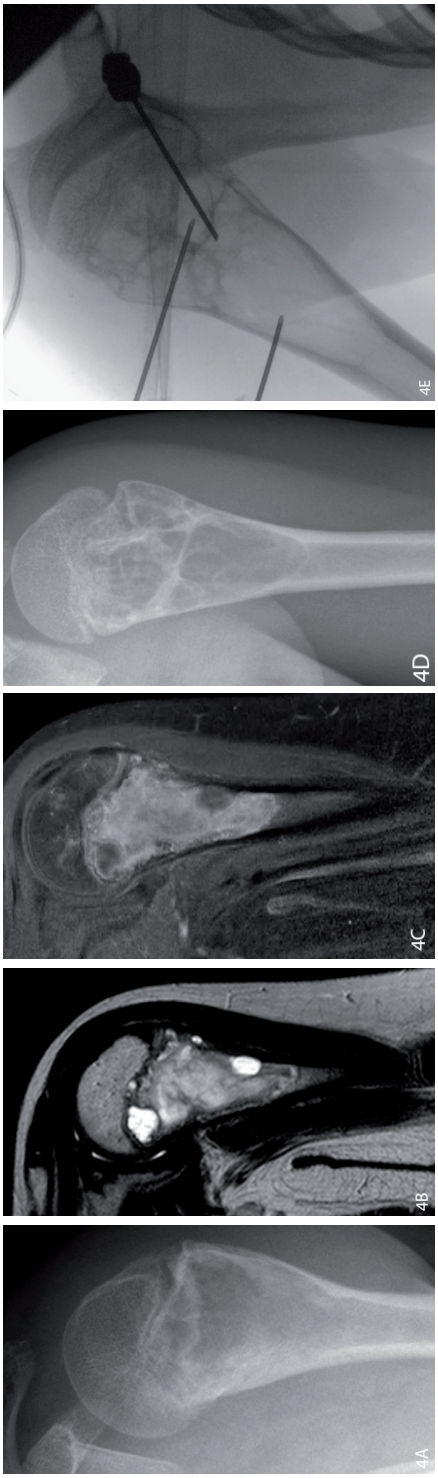


Fig. 9.3 Allogeneic strut grafting in fibrous dysplasia of the humerus. Patient nr. 20 presented with a fracture of the humerus. The fracture healed after conservative treatment with a cast (3A). Two years later, the patient sustained a recurrent fracture. After initial immobilization using a cast, he was treated with injection of a sclerosing agent. However, pain persisted and three years later a coronal T1-weighted fat suppressed post contrast MR images showed a fibrous dysplasia lesion with cystic degeneration (3B). Histologic evaluation confirmed the diagnosis. A repeat MRI scan performed a year after diagnosis showed increased cortical thinning (3C). Two cortical allografts were placed in the lesion, which was additionally filled with autogenous iliac crest bone (3D), which resulted in complete relief of his pain and full restoration of function of the right arm. Control radiographs 9 years later show largely resorbed strut grafts, but also evident cortical thickening, well-mineralized bone and no suggestion of an impending fracture (3E).

Injections

Five patients received injections in the cystic part of the FD lesion using different sclerosing agents, including aethoxysclerol 3% (8–15 ml), depomedrol (120 mg) or ethibloc (7.5 ml) to prevent impending fractures and decrease pain (Table 9.4). Four patients received multiple injections. Three patients had a good outcome, with disappearance of pain complaints, no fractures and progressive filling and cortical thickening of the lesion on conventional X-rays (Fig. 9.4). One patient sustained



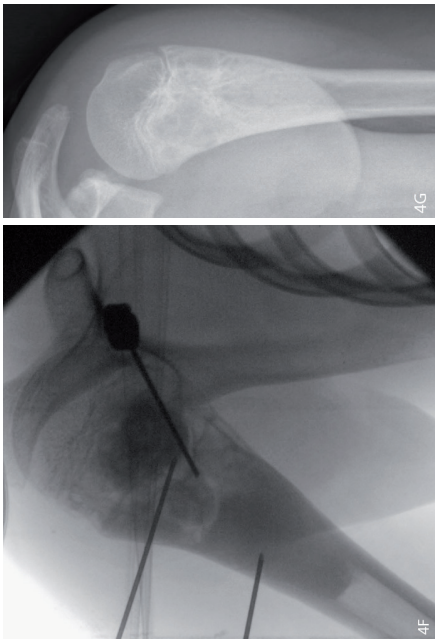


Fig. 9.4 Cystic embolization in fibrous dysplasia of the humerus. Patient nr. 40 presented with a pathologic fracture of the humerus after a minor trauma. Radiographs showed an osteolytic lesion of the diaphysis and metaphysis with cortical thinning (4A). Sagittal MR imaging showed a lesion with intermediate signal intensity on T1-weighted images (4B) in combination with focal islands with high intensity, a high signal on coronal T2-weighted images and inhomogeneous signalling after administration of contrast (4C). A diagnosis of fibrous dysplasia with cystic degeneration was made. Two years later further cortical thinning indicative of an impending fracture was seen on conventional radiographs, (4D). This was treated with an injection of aethoxysclerol in order to prevent recurrent fractures (4E and F) resulting in complete relief from pain, free range of motion of the upper arm and good mineralisation of bone on a control radiograph 1 year after treatment (4H).

Table 9.4 Embolic injection of the cysts

Patient ID	Gender/age at first injection (years)	Indication	Number of injections	Agent(s)	Failure
1	F/13	Impending fracture Growth plate at risk	2	Depomedrol	No
20	M/11	Impending fracture	3	Depomedrol (2) & Ethibloc (1)	Reoperation with cortical allograft due to an impending fracture
23	M/7	Impending fracture	2	Depomedrol	Fracture
33	M/14	Impending fracture	3	Depomedrol	No
40	M/12	Impending fracture	1	Polidocanol (3)	No

Five patients received injections in the cystic part of the FD lesion with different embolic agents, including depomedrol (120 mg), aethoxysclerol 3% (8–15 ml) or ethibloc (7.5 ml).

several fractures after treatment with sclerosing injections and one patient required additional surgery.

DISCUSSION

In this study we evaluated clinical features, management and prognosis of FD lesions of the humerus in a relatively large cohort of 50 patients with predominant monostotic FD. In our 255-strong FD cohort, the prevalence of FD of the humerus was 20%, and as previous reported, we also observed a higher prevalence of humeral lesions in polyostotic and MAS patients.[2,6] More than half of the patients with humeral FD (53%) developed a fracture at the affected humeral site, and the majority had a good outcome after initial conservative treatment (59%) or conservative treatment in recurrent fractures (n = 3, 11%). Surgical treatment failed in two out of five patients with allogeneic cancellous bone grafting and in one out of three patients with cortical bone grafting. Sclerosing injections of cysts adequately prevented pathological fractures in three out of five patients, which is an important finding as cysts were identified as risk factors for pathological fractures of the humerus.

Fibrous dysplasia is a heterogeneous disorder and its clinical course appears to be significantly different in lesions of the humerus compared to the more commonly situated lesions of the lower extremity, in which weight-bearing forces give cause

to a high incidence of deformities and fractures, often associated with pain and ultimately with more impaired Quality of Life (QoL).[2,3,7-9] Although FD of the humerus is believed to run a milder course than that of the lower limbs, our findings from this study suggest that the majority of the patients with humeral lesions had sustained at least one fracture at the site of the lesion. Importantly, none of these patients were using crutches at the time of their fracture, which is especially relevant in polyostotic patients with lesions of the lower extremity, as the use of crutches would put weight-bearing forces on the humerus. In a study on fractures in 35 patients with polyostotic FD, Leet et al. reported that fractures of the humerus accounted for 19% of a total of 172 fractures.[10] In our Leiden FD cohort, we observed that phosphaturia and a high skeletal burden score were associated with high fracture rates at a younger age. As all three of these factors are related to disease severity in FD, it is likely that patients with extensive disease are more prone to sustain pathologic fractures. Our current study is the first to address fracture risk in FD based on radiologic characteristics of the lesion. Our findings are in keeping with those of a study of fracture risk in femoral bone metastases, in which both axial cortical involvement > 30 mm and circumferential cortical involvement > 50% were identified as risk factors for pathological fractures.[5] Despite the common assumption that larger lesions are more prone to fractures, the length of a humeral FD lesion was not associated with an increased risk of developing a fracture. However, in contrast to the study on femoral metastases, in which circumferential cortical involvement of more than 50% was significantly associated with pathological fractures, in our study, we only found a non-significant trend for this ($p = 0.064$), possibly because of the relatively small number of patients studied. The only factor that was significantly associated with fractures in the current study was cystic degeneration of the FD lesions. The development of cysts in FD has been specifically reported in the humerus, although these cysts have never been associated with an increased risk of fractures.[6,11-13] It appears that the presence of cysts may further weaken bone and decrease its stability, thereby increasing the risk of fracture, whereas the size of a lesion or involvement of the cortex may not. These findings suggest that routine MRI should be advocated in FD of the humerus to assess the risk of developing a fracture, as cystic degeneration cannot be reliably evaluated on conventional plain radiographs. Our findings of promising outcomes of specifically targeting humeral cysts with injections of sclerosing agents suggest that this intervention may represent a minimally invasive method to reduce the risk of fractures in cystic FD lesions of the humerus.[14,15] However, it is of note that two of the five patients in our series who underwent sclerosing therapy of FD lesions still fractured their humerus or needed surgery after multiple injections with sclerosing agents.

Despite the relatively high fracture rate in the current study, patients with humeral FD are reported to have fewer deformities, less pain and better QoL compared to those with FD lesions of the lower extremities.[7,16,17] Due to the lack of weight-bearing forces acting on the humerus, conservative treatment of these fractures appears to be on the whole adequate in the majority of the patients. Our results are in keeping with those of a number of studies reporting good outcomes conservative treatment of pathological fractures of humeral FD lesions, with success rates of 93% and 94%.[10,18] No cases of delayed union or non-union were reported in any of the published studies, suggesting that bone healing is not impaired in FD of the humerus.

In FD there is a difference in outcome between cancellous and cortical allogeneic bone grafting, with the latter believed to being superior due to better mechanical loading and lower resorption rates.[4,19,20] In keeping with our results, Stephenson et al. reported failure of two out of four CBG procedures in FD of the humerus.[18] However, failure rates of this procedure in the lower extremity have been reported to be up to 100%, suggesting that outcomes of graft surgery are better in FD lesions of the humerus compared to those of the femur.[21] Although low numbers preclude any firm conclusions on this, cortical bone grafting does appear to be associated with a slightly better outcome, as four studies that reported on outcomes of this procedure in a total of 14 patients with humeral FD reported no reoperations, no graft resorption, and good functional outcomes.[22-25] In contrast to the case in femoral localisations, reconstruction with osteosynthesis is sporadically used in humeral FD, with additional benefit in specific cases with the use of devices such as Prevot pins.[26]

Our study has some limitations. Although we were able to study FD of the humerus in a relatively large cohort, we also appreciate the small number of patients included in the study, may have precluded the identification of factors other than cystic degeneration for increased fracture risk in this FD localization. A further limitation of our study may be the potential of a selection bias in our inclusion of symptomatic patients, whereas FD of the non-weight bearing bones is often asymptomatic, possibly explaining the relatively high fracture-rate observed in our study, with true fracture-rate being possibly lower. As the majority of patients included in the study presented with a fracture, there were no available MR images prior to the fracture. Hypothetically cystic degeneration might develop after a fracture, instead of being a risk factor for it. However, there are to our knowledge no data supporting this premise in FD lesions of the humerus. Lastly, due to the low number of interventions of different types performed over time, we were only able to use descriptive statistics in the evaluation of treatment of FD of the humerus.

In conclusion, FD of the humerus is associated with a relatively mild course despite the development of pathological fractures in 50% of patients, although two third of these can be successfully treated with conservative measures. Whereas the size of an FD lesion of the humerus does not appear to influence the risk of developing a fracture, we identified cystic degeneration within a humeral FD lesion as a significant risk factor for developing pathological fractures, suggesting that routine MR-scanning should be advocated in FD at this localization to allow the timely management of these lesions, which holds a generally good outcome. Surgical interventions aiming at decreasing pain or stabilizing impending fractures should include the use of cortical rather than cancellous bone grafts, although definite recommendations relating to the choice of surgical interventions should await results from larger studies.

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