

Chondromyxoid fibroma; experience of 36 cases of an intriguing entity

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Abstract

Objectives: To evaluate the clinico-pathological features and treatment options of chondromyxoid fibroma patients.

Methods: The retrospective study was conducted at the Aga Khan University Hospital (AKUH), Karachi, and comprised data of all cases of chondromyxoid fibroma of bone diagnosed between 1996 and 2013. The diagnosis had been made mostly histopathologically, but also included patients in whom preoperative incisional biopsies had been used. Histopathological and radiological findings along with various treatment options and follow-up was recorded on a proforma.

Results: Of the total 36 patients, 14(39%) were females and 22(61%) were males, with an overall mean age \pm of standard deviation 20.9 years \pm 9.8 (range: 6-51 years). Diagnosis was made histopathologically in 27(75%) patients and biopsy was used in 9(25%) cases. The most common site of involvement was tibia in 16(44.4%). The main presenting symptom was pain in 30(83.3%) and/or swelling in 6(16.6%). Radiological examination revealed no foci of soft tissue involvement. Bizarre large atypical cells were seen in 14(39%) cases and osteoid formation in 2(5.5%), leading to extreme difficulty in diagnosis. Treatment options included wide resection and marginal excision in 22(61%) cases, intra-lesional curettage in 14(39%). The mean \pm standard deviation follow-up was 48.8 \pm 40.2 months (range: 8-152 months). Follow-up details were available only for 19(53%) patients. Among them, recurrence occurred in 7(36.8%) patients. No functional loss developed after surgical treatment, but 3(16%) patients developed wound-site infection.

Conclusions: Chondromyxoid fibroma is clinically and histopathologically rare and difficult to diagnose because of the absence of typical diagnostic features in every case.

Keywords: Chondromyxoid fibroma, Bone, Benign, Bone neoplasm. (JPMA 64: S-175 (Suppl. 2); 2014)

Introduction

Chondromyxoid fibroma is a distinctly exceptional tumour, and it has comprised less than 1 per cent of the documented bone in most of the large studies done. For the first time, the true nature of the lesion was described in 1948 and despite histological variation, it has generally been believed to be benign.¹⁻³ Although clinical behaviour may be aggressive with high recurrence rate, but malignant transformation has been observed in very rare cases.

In the initial era, it had been described as originating from physis cartilage, but now more detailed analysis of its origin and aetiological factors have been proposed that include chromosomal anomalies and immunological factors.⁴ It is mostly a lesion identified in younger age group, but a wide age distribution has been seen. It generally involves

metaphysis of long bones.

Specifically, when an unusual location of development or odd age is seen, an erroneous diagnosis of malignant lesion may be sought for. In most of the surgically treatable cases, en bloc excision of the tumour and grafting is the preferred method of treatment.^{5,6} When an en bloc excision cannot be done due to peculiar location of the tumour, efficacious results can be attained by curettage and bone grafting.⁷

The current study was planned to evaluate clinico-pathological features of chondromyxoid fibroma patients. To our knowledge, it is the first such study from the region.

Material and methods

The retrospective study was conducted at the Aga Khan University Hospital (AKUH), Karachi, and comprised data of all cases of chondromyxoid fibroma of bone diagnosed between 1996 and 2013. The diagnosis had been made mostly histopathologically, but also included patients in whom preoperative incisional biopsies had been used. Demographic, histopathological and, wherever available, radiological

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findings along with various treatment options and follow-up was recorded on a proforma. All pathology material, like biopsies and curettage done at the hospital, and slides and/or paraffin blocks of material received as consultation cases from elsewhere, were also retrieved. The tissue was formalin-fixed, embedded in paraffin, and stained with routine Hematoxylin and Eosin (H&E) stain.

Cases where histological findings of chondromyxoid fibroma were not diagnostic, i.e. absence of typical lobulation along with chondromyxoid stroma, were excluded. Follow-up information of patients, when available, was taken via telephonic conversation or patient files if treated in the same hospital. At least verbal informed consent was taken in those cases where written consent could not be taken. Cases where consent could not be taken were also excluded.

Because of its retrospective nature, the study did not need approval from the institutional ethical committee, but no patient-identifiable material was used and all procedures were in accordance with the ethical standards outlined by the Helsinki Declaration.

As it was a descriptive case series, frequencies and percentages were used for the presentation of categorical data. Range, mean and median were used to define numerical data.

Results

Of the total 36 patients, 14(39%) were females and 22(61%) were males, with an overall mean age \pm standard deviation of 20.9 ± 9.8 years (range: 6-51 years). Diagnosis was made histopathologically in 27(75%) patients and biopsy was used in 9(25%) cases.

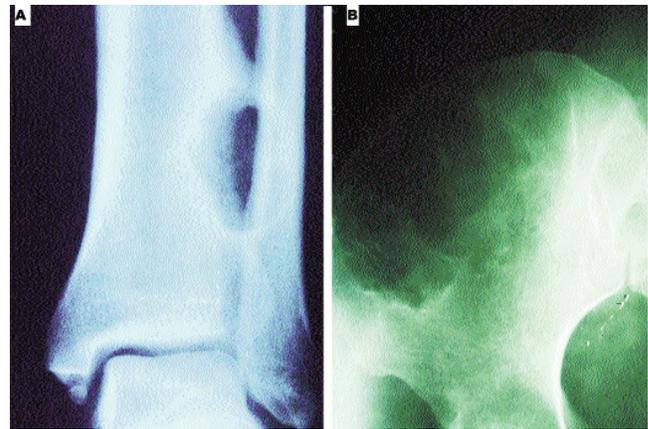


Figure-1: The typical appearance of radiology with radiolucent lesion having sclerotic margins (A) with scalloped edges (B).

Table-1: Site of involvement of various bones.

Site:	No. of cases
Tibia	16
Fibula	4
Humerus	4
Ileum	3
1st Metatarsal	3
Big toe	2
Calcaneum	2
Mandible	1
Thumb	1

The most common site of involvement was tibia in 16(44.4%) (Table), and the main presenting symptom was pain in 30(83.3%) and/or swelling in 6(16.6%).

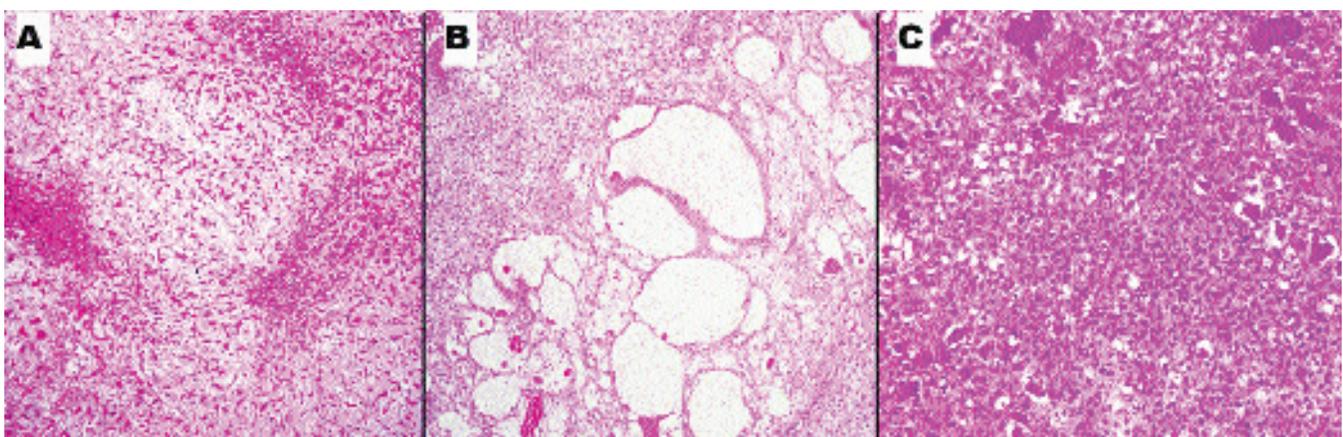


Figure-2: Photomicrograph of chondromyxoid fibroma. Lobulations are appreciated with increased cellularity (A), foci of cystic degeneration (B) and extensive calcifications (C). (Hematoxylin and Eosin stain (H&E), 20X).

Plain radiographs were available for 26(72.2%) patients, computed tomography (CT) scan in 14(39%) and magnetic resonance imaging (MRI) in 4(11.1%) patients and these revealed no foci of soft tissue involvement.

Bizarre large atypical cells were seen in 14(38.9%) cases and osteoid formation in 2(5.5%), leading to extreme difficulty in diagnosis. Calcifications were identified in 13(36%) cases, giant cells in 12(33%). And foci of cystic degeneration in 4(11.1%).

Treatment options included wide resection and marginal excision in 22(61%) cases, intra-lesional curettage in 14(39%), followed by bone graft or cement in 10(71%) of these 14.

The mean \pm SD, follow-up was 48.8 ± 40.2 months (range: 8-152 months). Follow-up details were available only for 19(53%) patients. Among them, recurrence occurred in 7(36.8%) patients. No functional loss developed after surgical treatment, but 3(16%) patients developed wound-site infection.

Discussion

CMF is a rare and benign bone tumour. Its aetiology is not completely understood and various chromosomal anomalies and immunological factors have been proposed. Recent studies have revealed clonal abnormalities of chromosome 6.⁴ The physis cartilage has been thought of as a tissue of origin. It usually affects patients under the age of 30, as exhibited in our study too where the mean age was only 20.9 years even though overall age range was quite wide (6-51 years).

As described in literature, its development is more aggressive in children, hence, correlating with the histopathological features seen in our series, with reactive bone formation and osteoid formation along with bizarre atypical cells were more common in cases in children. Recurrences are also more frequent in children. However, we observed recurrences in both adult and younger cases. We observed that CMF occurred in all age groups, but they were more common in children and adolescents. It is generally seen in the metaphysis of long bones, coordinating with our observation too, with two-third cases having affected long bones; the most common site being proximal and distal tibia. It is rarely located entirely in the diaphysis. In literature it has been observed that most frequently involved bone is tibia, and the other bones affected include flat bones, facial bones, and bones of the hand and foot. It has also been shown that CMF is a bit more frequent in men than in women,^{6,7} but we found that

males were much more frequently involved than females (61% vs. 39%).

The most important clinical feature is pain,⁸ which was present in 83% of our cases, overlapping with swelling in most cases, making the swelling/mass the second most common clinical complaint. In the remaining 17%, it revealed clinically as a swelling which was tender on palpation.

In terms of diagnosis, chondrosarcoma, chondroblastoma, fibrous dysplasia, non-ossifying fibroma, giant cell tumour, aneurysmal bone cyst and simple bone cyst are options. Radiologically, soap bubble or trabeculated appearance is a frequent observation. We also came across such findings with soap bubble appearance and sclerosed margins being the most common one (Figure-1). The cortex was expanded and there was no periosteal reaction. Calcification and intra-lesional opacities are rare.

In addition to plain X-rays, CT was available for our review in 14 patients, and MRI in 4 patients. However, no soft tissue involvement was seen.

Especially when it is seen in old patients or when it develops in unexpected locations, CMF can be mistaken for malignancy, especially chondrosarcoma.⁹⁻¹¹ Our experience also revealed that clinical differentials included a high-grade sarcoma or chondrosarcoma when the Iliac bone was involved. Chondromyxoid sarcoma may rarely show malignant transformation, but we did not observe this and no malignant transformation was identified histologically or clinically with metastasis).

In literature few cases have been described in which the preoperative histopathological diagnosis was made by means of Trucut biopsy.¹¹⁻¹³ However, in all of our patients, CMF diagnosis was postoperatively made through histopathological examination and the tissue sent was either the fragmented curettage specimen or excisional biopsy.

Most of the gross specimen included in this study were fragmented in nature, so that a circumscribed with sharp outer borders and lobulated centre was observed in only few cases where excision was done in its entirety. The curetted or excised tissue was firm and had a distinct glistening appearance and a bluish-white tinge.

CMF can be confused with a malignant tumour because of its potential for recurrence and occasional nuclear atypia.^{13,14} In the World Health Organisation (WHO)

Classification of Bone and Soft Tissue Tumours 2002, CMF was defined as a "benign tumour characterised by lobules of spindle- or stellate-shaped cells with abundant myxoid or chondroid intercellular material."^{2,10,11}

The worrying histological features, such as scattered nuclear atypia, which are noted occasionally, together with alarming clinical behaviour of multiple recurrences and radiological or microscopic soft tissue extension, may lead to a misdiagnosis of chondrosarcoma.¹⁵⁻¹⁷ This can result in erroneous over-treatment of radical resection or amputation. However, in line with literature, our study also showed that CMF is a benign disease with indolent clinical course despite its local recurrences.

Microscopically, majority of CMF cases comprised myxochondroid and myxohyaline lobules with increased peripheral cellularity. The three components embodying CMF (chondroid, the myxoid and the fibrous tissue) were seen in all the specimens (Figure 2), though with varying proportions.¹⁷⁻¹⁹ The chondromyxoid component comprised stellate cells having hyperchromatic nuclei with mostly inconspicuous nucleoli. But some cases had cells with prominent nucleoli. On occasion, mild to moderate nuclear atypia was noted and giant cells were also observed. Foci of calcifications were also present in few cases, and erroneously, 2 cases had osteoid formation, rendering diagnosis difficult. Rare mitotic figures were identified in 2 cases, but necrosis was not seen in any of the cases. Cystic spaces were also identified in the stroma in a number of cases (Figure-2). On the application of immunohistochemistry, myofibroblastic, myochondroblastic and chondrocytic differentiation was seen in CMF on the basis of variable immune-staining for actin and S100 protein.

Two cases showed chondroblastoma-like areas and 3 more cases revealed calcifications.

The microscopic differential diagnosis of CMF includes myxoid chondrosarcoma, chondroblastic osteosarcomas, chondroblastomas, and fibrous dysplasia.^{20,21} Chondrosarcomas show more uniformity than CMF, with the absence of giant cells at the lobules' periphery and the lobules are much large with myxoid ground substance. Mature hyaline cartilage is more commonly seen in chondrosarcomas.^{12,22} Again, as no osteoid formation is seen in CMF, it is difficult to differentiate it from chondroblastic osteosarcoma on small biopsies because of focal atypia. However, it is easier on large/excisional biopsies. Chondroblastomas, unlike CMF, are epiphyseal, making the clinical differentiation

easier. It may locate rarely on epiphysis and may be confused with chondroblastoma or giant cell tumour.²³

Surgical treatment of the patients who were treated at our hospital comprised "extended intra-lesional curettage". Traditionally, excision has also been employed as treatment of choice. Phenol lavage was also used and at certain locations bone grafts were used according to structural stability of the bone. The phenol lavage and bone grafting was associated with decreased chances of recurrence compared to cases where it was not used. No confounding factors influencing chances of recurrence e.g. microscopic incompleteness of resection, played a role because in all such cases, the tumour was completely removed.

Conclusions

The absence of typical diagnostic features in every case, and the predisposition for recurrence may advocate a malignant tumour diagnosis. Though rare, the CMF diagnosis should be kept in mind by orthopedic surgeons, radiologists and pathologists.

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