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Chondromyxoid fibroma of bone

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Abstract Chondromyxoid fibroma is a benign, although potentially aggressive tumor, with a cartilage-like matrix, accounting for approximately 1% of all bone tumors. It usually affects the metaphyseal region of long bones of patients in their first or second decade of life. An additional peak of incidence has been observed between 50 and 70 years of age. Three cases are presented here: 10-, 13-, and 52-year-old patients, with lesions in the proximal tibia, the proximal humerus, and the proximal femur, respectively. The literature is reviewed in terms of clinical behavior, diagnostic procedures, prognostic factors, treatment, and outcome. Preferred treatment is complete local excision with tumor-free margins. Intralesional curettage with or without local adjuvants shows a local recurrence rate of approximately 25%. Radiation therapy may be useful in nonresectable cases but bears the well documented risk of radiation-induced malignancies.

Introduction

Chondromyxoid fibroma is the least commonly occurring bone tumor, accounting for approximately 1% of all biopsied primary bone tumors [7, 32]. It has a cartilage-like matrix composed of chondroid, fibrous, and myxoid areas in varying proportions. Since 1948, when Jaffe and Lichtenstein first recognized this tumor as a distinct entity, and one which should be differentiated from chondrosarcoma [15], approximately 500 cases have been reported. It usually affects the metaphyseal region of the long bones in children and young adults, particularly near the growth plate of the proximal tibia [31]. Although it is a benign tumor, recurrence after intralesional treatment may range from 10% to 80% [10, 11, 27, 28, 32]. We present three cases of chondromyxoid fibroma involving the proximal humerus, femur, and tibia observed in our clinic between 1980 and 1996.

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Case reports

Case 1

A 13-year-old girl was admitted to our hospital with a 2-month history of a progressive and slightly painful swelling of the left proximal humerus. She was previously healthy, and additional signs of illness could not be found. Physical examination showed a tender swelling of the proximal lateral humerus with pain on pressure.

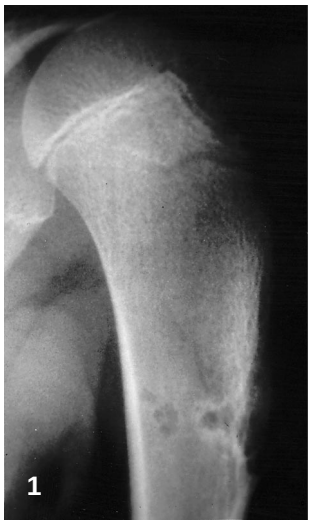
The plain films showed an eccentric lucency at the proximal metaphysis of the left humerus (Fig. 1). The lesion had distended, thinned, and partially destroyed the cortex, as seen on computed tomography (CT) scans (Fig. 2). Angiography showed a poorly vascularized lesion with no tumor blush (Fig. 3).

The presumptive radiological diagnosis was chondromyxoid fibroma (CMF). In order to rule out a chondrosarcoma, which is exceedingly uncommon in childhood, a biopsy was performed. Histological examination confirmed the diagnosis of CMF (Fig. 4). A subsequent en bloc resection with interpositioning of a pelvic bone transplant was carried out, resulting in recurrence-free healing with unimpaired function 3 years after surgery (Fig. 5).

Case 2

A 52-year-old woman with a 12-month history of pain in the right hip had a circumscribed osteolytic area in the right intertrochanteric region (Fig. 6). Clinical examination revealed localized pressure pain. A soft-tissue extension was excluded with magnetic resonance imaging (MRI). Further examinations, including a CT scan of the thorax and abdomen, showed no primary lesion. An intramedullary chondrosarcoma was suspected, and an incisional biopsy was performed.

After the diagnosis of CMF, the patient was informed about the benign but potentially aggressive nature of the tumor, but she refused any further treatment. At the last follow-up 3 years after biopsy, the situation was unchanged.



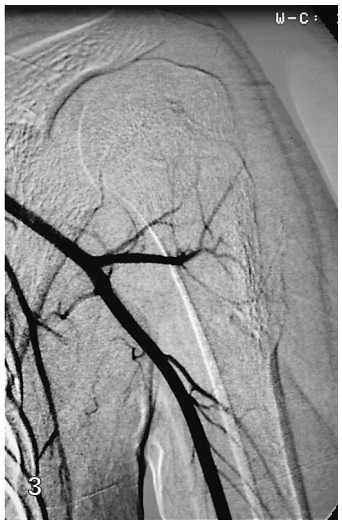


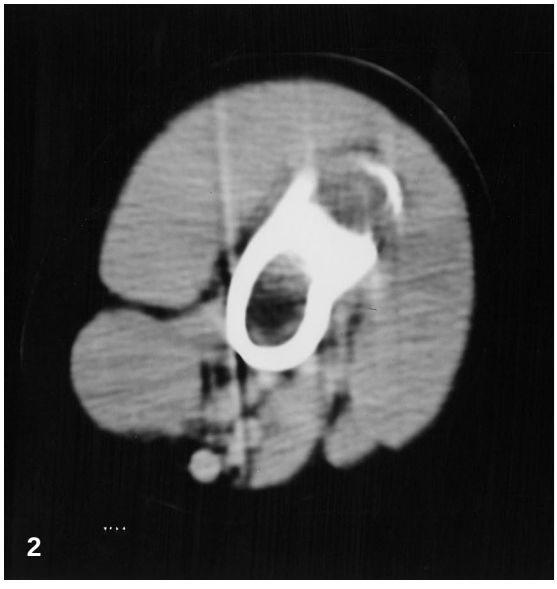
Fig. 1 A 13-year-old girl with chondromyxoid fibroma (CMF). The plain film shows an eccentric lucency with several small underlying satellite lesions, which are distinct from the main lesion in the proximal metaphysis of the humerus. In addition to a Codman triangle, there is thinning and bulging of the cortex. The lesion itself does not invade the epiphyseal line

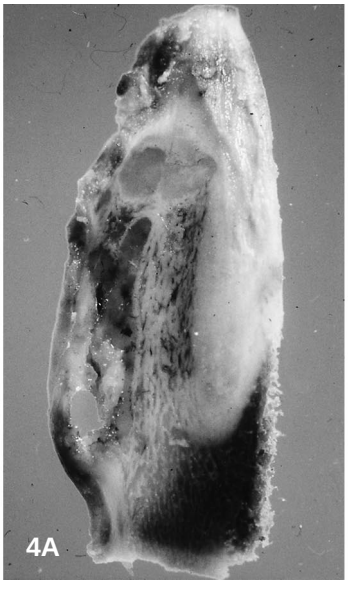
Fig. 2 In the same patient as Fig. 1, apart from a sclerotic rim, computed tomography (CT) shows a partially disrupted cortex and newly formed bone

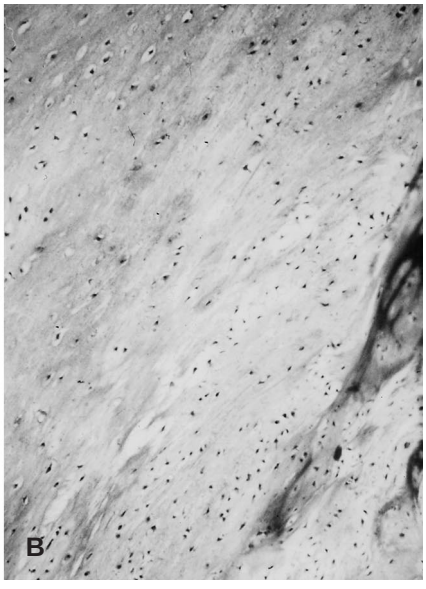
Fig. 3 Angiogram of the left shoulder girdle demonstrates no abnormal tumor vessels or tumor blush

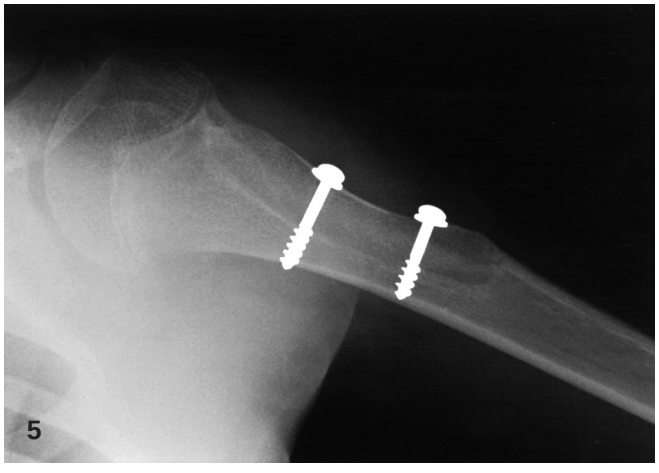
Fig. 4 **A** Macroscopic aspect of the resected specimen shows the eccentric tumor with several small satellite-like nodules at the periphery. **B** Histologic overview of the tumor shows a fibrochondroid matrix with embedded chondroid cells without atypia (H & E, original magnification × 100)

Fig. 5 Two years after resection, an incorporated pelvic bone graft without any sign of recurrence is visible on the plain film









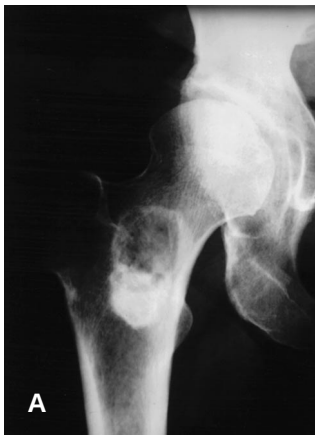
Case 3

A 10-year-old boy was admitted to our hospital with a 2-month history of progressive swelling of the right proximal lateral tibia. The patient and his parents attributed this swelling to a sport trauma which had occurred a few days prior to the onset of symptoms. The examination revealed an otherwise healthy boy with a firm tumor adherent to the proximal tibia, with no signs of pain. The plain films demonstrated a large, eccentric, radiolucent lesion in the proximal tibia-metaphysis (Fig. 7). The well-defined internal margin of the tumor was scalloped and outlined by a narrow rim of sclerotic bone adjacent to the marrow cavity. The external surface showed a thinned cortex and a blown-up shell of newly formed, partially absent periosteal bone. Three-dimensional surface reconstruction confirmed the web-like appearance of the outer surface (Fig. 8). MRI revealed the exact soft-tissue expansion of this well-structured lesion (Fig. 9).

From the typical clinical and radiological findings, a CMF was suspected, and a subsequent incisional biopsy (Fig. 10) confirmed this diagnosis. The marginal resection was accomplished by adjuvant phenolization. Today the patient is still tumor-free, with unimpaired leg function 12 months after surgery.

Discussion

Chondromyxoid fibroma is a benign but aggressive tumor occurring primarily in the first and second decades of life [42], but can appear as early as 3 years and as late as 79



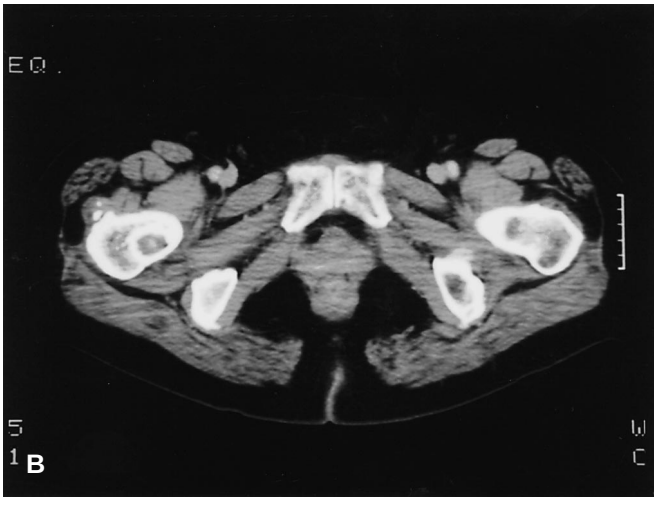


Fig. 6 A, B A 52-year-old woman with CMF. The anteroposterior view demonstrated an eccentric, metadiaphyseal lesion with a sclerotic rim and pseudotrabeculation. This pattern classifies the lesion as Lodwick I A

years of age. Eighty percent of patients are younger than 36 years of age [12], but a second peak in the fifth, sixth, or seventh decades is observed [11, 30, 42], fitting in well with our own experience. There is no relationship between sex and CMF. Clinically, the main symptoms are pain, swelling or tenderness, and pressure. Duration of symptoms may range from weeks (often in younger patients) to even years (in adults) [8, 42]. An associated pathologic fracture occurs in approximately 5% of cases [12]. The most common site of the tumor is the metaphysis adjacent to the epiphyseal growth plate. This is consistent with the hypothesis that the tumor arises from remnants of cartilage at these sites [27]. Epiphyseal involvement is very uncommon [37]. In rare cases with predominantly cortical involvement, CMF may arise from apophyseal cartilage cells, as found near the tibial tuberosity [31]. CMF has a predilection for the long bones, with lesions of the tibia and femur accounting for approximately 50% of the 356 cases described by Wilson et al. in a literature review (1991) [41]. The typical radiographic pattern includes an expansile ovoid lesion with a radiolucent center [13]. Well-defined sclerotic margins, septations, and a bulging, thinned, overlying cortex are frequent findings (Fig. 7). In contrast, juxtacortical CMF lesions are rare, with only five cases reported up to 1985 [6]. Geographic bone destruction in conjunction with clinical findings should raise suspicion of CMF [26, 41]. Distinguishing the lesion from an aneurysmal bone cyst (ABC) may be difficult. In rare cases, CMF does not produce bone expansion but may cause an unusually thick, dense rim of reactive bone around the central lucency, as seen in our patient no. 2 [25, 40]. To our knowledge, the type of lesion seen in patient no. 1, with its eccentric bubbly appearance and concomitant separate smaller nodules, has not yet been reported.

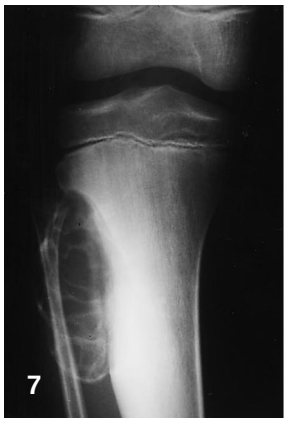
Angiographically, CMF is usually avascular and has a benign appearance (Fig. 3) [1]. On MRI, depending on the varying amounts of myxoid and cartilage tissue, the center of the tumor is hyperintense on T2-weighted spin-echo images and STIR sequences. Along with the typical lobulated pattern, the images are distinctive of a tumor of cartilaginous origin. The highly vascularized connective tissue at the border of the lesion accounts for a rim of moderate to high signal enhancement on T1-weighted images after gadolinium-diethylene triamine penta-acetic acid (Gd-DTPA) (Fig. 9). Planning the extent of resection with MRI demonstrating soft tissue or bone marrow not seen on the plain radiographs may result in a reduction of the recurrence rate [2, 24, 34].

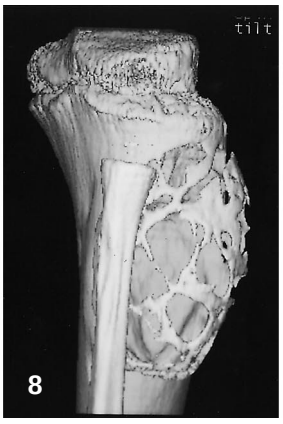
The typical aspects of chondroid, fibrous, and myxoid tissues are not present in each histological specimen. Therefore, a small biopsy could lead to a false-negative diagnosis. The tissue changes in two ways: areas with large numbers of cells with loose connective tissue stroma are penetrated by lobulated areas of chondroid material (Fig. 4 B), and occasionally as in our patient no. 2, extended cystic and hemorrhagic degeneration.

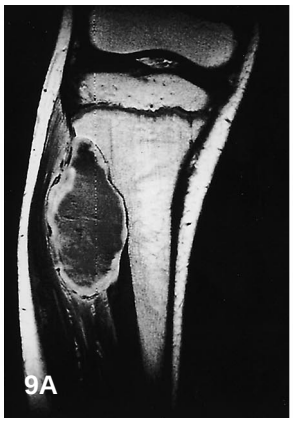
Dahlin stressed that increased numbers of cell nuclei at the periphery of the chondroid lobules with plump hyperchromatic nuclei are characteristic of CMF [7]. Agreeing that this is a common finding, Mirra did not designate this as a diagnostic feature [23]. Focal calcifications [16], as found in our second case, occurred in approximately 25% of the 76 cases seen by Rahimi et al. [27]. Newly formed peripheral osteoid and bone may be misinterpreted as osteosarcoma. Chondroid elements, including multinucleated and polymorphic cartilage cells, may dominate the histological pattern and lead to the misdiagnosis of chondrosarcoma.

Radiological differential diagnoses include an ABC (with typical vascular patterns) [7] or a nonossifying fibroma. The occurrence of an ABC in a CMF is rare but possible.

Treatment in most of the reported cases consists of intralesional curettage. Excision with or without bone grafting is often performed and advocated by many investigators [7, 10, 27, 30]. In exceptionally rare cases, especially recurring tumors, an amputation was found to be necessary despite the tumor's benign nature [39]. Initially, curettage alone was considered an adequate treatment because the lesion did not tend to recur, but as Jaffe and Lichtenstein found, "even with incomplete removal, spontaneous regression of the remnants followed" [15, 19]. Rahimi reported in his series 6 recurrent cases among 15 patients treated by curettage alone; in 1 case recurrence







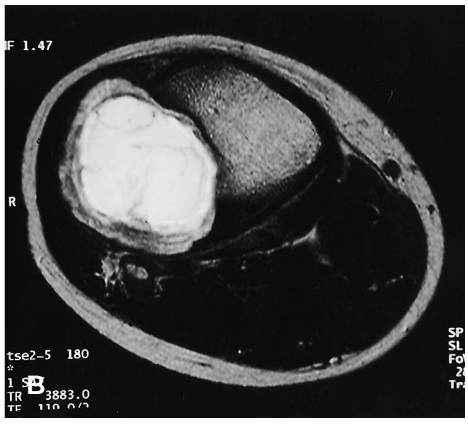
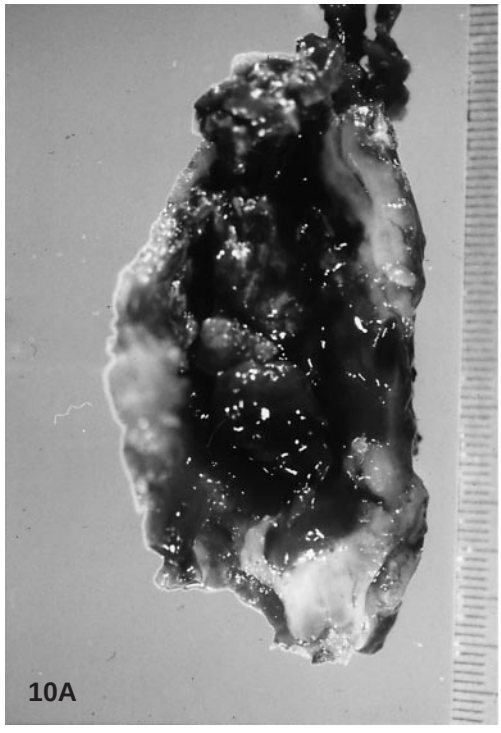


Fig. 7 A 10-year-old boy with CMF. This radiograph shows the typical site and appearance of the lesion in the upper metaphysis of the tibia. According to Lodwick, the lytic pattern classifies as I C

Fig. 8 The 3D surface reconstruction of the same patient reveals the web-like character of the outer surface due to partly interrupted, newly formed bone. The tumor itself is well below the epiphyseal line

Fig. 9 A, B On MRI, the lesion has a well-structured appearance. The coronal T1-weighted image after gadolinium-diethylene triamine penta-acetic acid (Gd-DTPA) (**A**) shows a hypointense tumor surrounded by a border of tissue with moderate to high enhancement. The axial T2-weighted image (**B**) exhibits a hyperintense, lobulated center. This corresponds to the histopathological structure of myxoid material and richly vascularized connective tissue



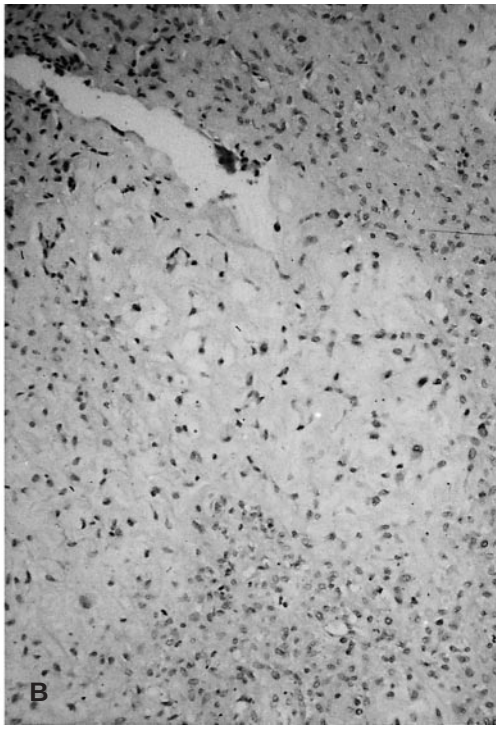


Fig. 10 **A** Macroscopic aspect of the resected specimen revealing a centrally located myxoid tumor mass, consistent with the MRI findings. **B** Histologic overview of the lesion showing a mixture of hypocellular regions with myxoid tumor tissue and more cellular areas (H & E, original magnification × 100)

was reported 9 years following surgery [27]. Various combinations of local adjuvants did not stop recurrence. In 6 other cases of tumor excision or en bloc resection, no recurrence was found. In conclusion, the recurrence rate is lower with resection using wide margins, although this may not always be possible in certain anatomical regions [9, 20, 21, 32].

Age seems to have a significant influence on the recurrence rate [17, 28]. In the Mayo Clinic group, 11 out of 14 tumor recurrencies developed in patients who were younger than 15 years of age [27]. In a detailed report from Zillmer and Dorfman, 7 out of 8 recurrences occurred in patients 20 years of age and younger [42]. There is only one study reporting recurrences independent of the patient's age [11]. Correlating these findings with the histological pattern, tumors that contain mostly myxoid areas and have large nuclei are found more often in younger patients. These cases are most likely to develop recurrences after curettage [29]. No prognostic histological characteristics could be identified in two studies [11, 32]. The recurrence rate after thorough curettage has been estimated at approximately 25% [7, 26, 35].

In cases of recurrence, soft-tissue extension of the tumor is not rare, presumably because of the displacement of tumor cells during surgery [18, 27]. In a review of the literature, 4 cases of soft-tissue recurrence of CMF without a bone lesion could be found [36], one of them arising 19 years after the initial treatment [22].

Radiation therapy has been used only in exceptional cases. In an unresectable iliac tumor [27], radiation alone led to no change in tumor size in an 8-year follow-up period. Considering patient no. 2, one should be aware of

the possible spontaneous arrest of tumor growth. Benson and Bass reported a case of CMF in the cervical area being free of recurrence 15 months after radiation [4]. Radiation therapy, however, is not recommended for tumors amenable to limb-sparing surgical procedures, because of two case reports of radiation-induced malignancies [7, 42].

Malignant transformation of CMF to chondrosarcoma has been suggested in several cases [14, 19, 33, 38]. However, none of those cases were sufficiently documented to be able to exclude a misdiagnosis. Also, 8 of 21 cases of presumed CMF reported by Aegerter and Kirkpatrick [3], with partial features of chondrosarcoma but without metastasis, may on critical review be classified primarily as sarcomas [5]. Accordingly, primary malignant CMF has been rejected [18, 28, 30, 32]. In two large reviews, well-documented distant metastases have not been found [10, 27], although Kyriakos noted a tumor thrombus in a small artery in a case of soft-tissue recurrence of CMF [18].

In summary, CMF is a rare tumor, showing distinctive radiological patterns in most cases. When occurring in unusual locations or in older patients, the fatal misdiagnosis of chondrosarcoma may be made. The preferred treatment, where possible, is an en bloc excision with tumor-free margins. Intralesional curettage, although possible, carries a 25% risk of recurrence even with the use of local adjuvants. Despite the benign nature of the tumor, its local aggressiveness should not be underestimated. Amputation must be considered, particularly in cases of local recurrence with soft-tissue involvement in critical areas. Radiation therapy might be useful for local tumor control but should be avoided because of the risk of radiation-induced malignancies.

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