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Chondromyxoid Fibroma of Phalanges

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Abstract

Chondromyxoid fibroma (CMF) is a rare, benign metaphyseal bone tumour characterised by a combination of chondroid, myxoid, and fibrous elements, which can affect any bone at any age, without a gender predilection. We report the case of CMF in a 47-year-old lady who presented with swelling of the left little finger to a tertiary care hospital at Kolkata, India, in May 2024. Imaging showed presence of a lobulated lesion arising from the middle phalanx of the left little finger, extending to involve the base of the distal phalanx. Fine needle aspiration cytology of the lesion was indicative of a moderately cellular myxoid lesion. Histopathology remains crucial for diagnosis, which revealed a lobulated tumour with zones of spindle to stellate cells, associated with abundant myxoid and chondroid matrix in the intercellular areas. Treatment involves complete local excision with tumor free margins, as recurrence can occur with local curettage.

Keywords: Bone Neoplasm; Cartilage; Chondromyxoid Fibroma.

Introduction

Chondromyxoid fibroma (CMF) is a rare benign bone tumour of chondrogenic origin. The incidence accounts for less than 1% of all histologically confirmed primary bone tumours. CMF typically occurs in the metaphysis of long bones, with the distal femur and proximal tibia being common sites. While it is more prevalent in younger individuals, older patients

may present with involvement of flat bones.[1, 2] Initially recognised as a distinct entity by Jaffe and Lichtenstein, CMF is both locally aggressive and benign. Clinically and radiologically, it can closely mimic chondrosarcoma, making accurate diagnosis arduous.[3] Cytopathological evaluation may be challenging, but is a useful initial investigation in conjunction with clinical and radiological inputs.[4] In the 2020 WHO classification of Bone Tumours, CMF is now categorised as a benign chondrogenic tumour, whereas it was previously considered as intermediate locally aggressive tumour.[5] Although the exact cause remains unclear, the glutamate receptor GRM1 gene fusion, leading to promoter swapping and GRM1 upregulation, has been implicated in CMF. [6] Analysing the index case alongside the existing literature on CMF involving the phalanx will enhance our understanding of this rare condition.

Case Report

A 47-year-old lady was referred to a tertiary care hospital, at Kolkata, India in May 2024, with a two-year history of swelling in her left little finger. Over the past three months, she had experienced intermittent, vague pain and restricted movement. There was no history of trauma or signs of infection. Physical examination revealed an eccentric swelling, approximately 2 x 1 cm in size, located on the radial aspect of the distal left little finger. The overlying skin appeared normal. The lesion was fixed, tender, firm, and the overlying tendons felt free. Fine needle aspiration cytology showed ill-defined fragments of myxoid stroma with oval to spindle-shaped cells having bipolar to stellate cytoplasmic processes, scattered singly alongside a few multinucleated giant cells against a haemorrhagic background (Figure 1A and 1B). A provisional diagnosis of an “Unclassified myxoid lesion” was offered. An X-ray of the little finger revealed an osteolytic, radiolucent, eccentric lesion in the metaphysis at the extensor aspect of the radial border of the middle phalanx and the proximal part of the distal phalanx of the left fifth finger (Figure 2A). Magnetic resonance imaging (MRI) showed a well-defined lobulated lesion involving the middle phalanx, arising from the underlying bone with the adjoining distal phalanx showing pressure changes (Figure 2B). The lesion appeared isointense on T1 and heterogeneously hyperintense on T2/Proton-density weighted fat suppressed (PDFS)/Short tau inversion recovery (STIR) sequences. She underwent local excision of the lesion through a curved incision which was given over the dorsal aspect of the middle phalanx. Following reflection of the skin, the extensor tendon was identified and retracted to expose the lesion. Intra-operatively the lesion was seen to be arising from the middle phalanx, while abutting the base of the distal phalanx with no evidence of infiltration.

The lesion was excised with curettage of underlying bone of the middle phalanx. The specimen measured 2 x 1 cm. The outer surface was smooth, and the cut surface revealed a grey-white, lobulated, heterogeneous lesion that felt gritty on cutting (Figure 3A). Haematoxylin and eosin stained sections revealed a lobulated lesion with central bony trabeculae and marrow spaces, extending into variously sized lobules composed of chondromyxoid stroma (Figure 3B). These lobules exhibited peripheral hypercellular areas and inner hypocellular regions (Figure 3C). The cellularity mainly consisted of stellate to spindle cells with bland chromatin and pale eosinophilic cytoplasmic processes (Figure 3D). Grungy calcification was observed in some areas, along with a few peripherally located multinucleated giant cells (Figure 3E). There was no evidence of nuclear pleomorphism, necrosis, or mitosis. Alcian blue stain highlighted the acidic ground substance of the stroma. Immunohistochemistry with S100p (Clone Beta EP-32, Ready to use, Pathnsitu) showed patchy nucleocytoplasmic expression in some of the stellate to spindle-shaped stromal cells (Figure 3F). A diagnosis of 'Chondromyxoid fibroma of the left little finger' was made. The patient is currently on a three-month follow-up schedule for the past 9 months with no signs of recurrence.

The authors retain an informed written consent for publication by the patient and the manuscript is in accordance with the Institutional Ethics committee requirements.

Discussion

Chondromyxoid fibroma is a rare tumour of the bone of chondrogenic origin accounting for less than 1% of all bone tumours and less than 2% of all benign bone tumours. It is more commonly seen in long tubular bones around the knees, most frequently the proximal tibia. [1,2,5] Involvement of bones of hands is extremely rare. The diagnosis is difficult and often requires clinico-radiological correlation with histopathological diagnosis; but as Jaffe emphasized, "its recognition is of some importance in that pathologically it may be mistaken for sarcoma and, as such, treated more radically than is necessary."[2] A literature search using MeSH terms 'Chondromyxoid fibroma', and 'Phalanx' revealed a total of 13 cases of CMF (Table 1). Of these 7 involved phalanges of foot and 7 (including the index case) involved the phalanges of hand. CMF of phalanges shows a female preponderance. The age range was from 8 to 53 years, with the second and third decades being more commonly involved. Clinical diagnosis is challenging and misdiagnosis is not uncommon because of inconstant array of symptoms presented by patients of CMF.[3] Pain and swelling are the most consistent

complains with or without mild to moderate tenderness, restriction of movement and may sometimes present as pressure symptoms like carpal tunnel syndrome or with neuro-vascular deficit. [1, 4, 5] Khan and Bandopadhyay reported a case of CMF of middle phalanx of left hand misdiagnosed as Spina Ventosa who was worked up with initial clinico-radiological diagnosis of tubercular dactylitis.[7] Clinical misdiagnosis of CMF as chondrosarcoma is also well documented.[2, 8] The differential diagnosis of CMF includes chondrosarcoma, chondroblastoma, fibrous dysplasia, non-ossifying fibroma, giant cell tumour, aneurysmal bone cyst and simple bone cysts.[3,5,9] On radiology, CMF is likely if there is focal bone lesion showing geographic bone destruction, a sclerotic rim, lobulated margins, and septation.[3, 9] On MRI, chondromyxoid fibroma features a peripheral intermediate signal band and central hyperintense signal on T2-weighted images, generally corresponding to the peripheral nodular enhancement and central non-enhancing portion on contrast-enhanced T1-weighted images, respectively. [3] Because CMF is a clinico-radiological mimicker of many other bone lesions, a histopathological confirmation of biopsied specimen is mainstay of diagnosis. Fine needle aspiration cytology reveals presence of spindle or stellate cells embedded in chondroid matrix, essentially without hyaline material, presence of which should raise suspicion of enchondroma or low-grade chondrosarcoma.[4] Grossly, the lesion has a white lobulated appearance with a heterogeneous cut-surface. The histopathological features comprise of the lesion almost always arranged in lobules, which may be prominent (macro lobular) or somewhat indistinct (micro lobular).[1, 5] On hematoxylin and eosin-stained sections, these lobules are seen to be composed of chondromyxoid stroma having peripheral hypercellular areas and inner hypocellular areas. The cellularity is predominantly composed of stellate to spindle cells having bland chromatin and pale eosinophilic cytoplasm. Calcification may be present along with osteoclastic giant cells.[1, 5] Bizarre nuclei have been reported without mitosis in some cases, which is likely to be a degenerative change in long standing cases.[7, 8, 10] Bony permeation is not uncommon.[11] The lack of infiltrative margins and preservation of zonation pattern is vital to differentiate CMF from the more sinister chondrosarcoma.[2] Chondroblastoma will have characteristic peri-cellular chicken wire calcification which is absent in CMF. Fibrous dysplasia and ossifying fibroma are medullary lesions having typical fibrous stroma associated with presence of woven bone and calcification respectively, which are absent in CMF.[3] Giant cell tumor, and aneurysmal bone cysts will have a greater number of osteoclastic giant cells scattered evenly and along vascular spaces respectively.[3, 5, 9] Simple bone cyst will have a simple epithelial lining making it distinct.[3, 5] Based on careful patient selection, treatment options include curettage with or without cementation, wide local

excision and en-block resection. Approximately 9-15% cases show recurrence following local resection.[5] Recurrence is least with en-bloc resection; however, this results in subsequent functional deficit as well as cosmetic concerns; while curettage alone has been reported as showing relatively high rates of recurrence of up to 80%.[12] Among the phalangeal CMF, 2 cases managed by curettage showed recurrence.[13, 14] The exact cause of CMF pathogenesis is not known. Study by Nord et al, provides substantial evidence that aberrant glutamate signalling leads to development of CMF and shows that direct targeting of Glutamate metabotropic receptor 1 (GRM1) is a necessary and highly specific driver event for CMF development. The glutamate receptor gene GRM1 recombines with several partner genes through promoter swapping and gene fusion events leading to GRM1 upregulation which is implicated in chondromyxoid fibroma pathogenesis.[6] No known syndromic association of CMF has been reported till date and co-existence as part of other pathological process is little known. No malignant conversion of CMF has been reported in literature. Reports of malignancy seen in a case of CMF if any have been attributed to instances wherein a chondrosarcoma was initially misdiagnosed as a chondromyxoid fibroma. [7, 8]

Conclusion

We present a rare case of chondromyxoid fibroma involving phalanges of the hand. CMF is known to affect any bone of body but involvement of phalanges is extremely rare. It is often misdiagnosed clinically because of its rare occurrence and overlap of symptomatology with other bone tumours in which case histopathological examination remains the mainstay of diagnosis. Treatment options include local resection, wide local excision with free margins and en-bloc removal. Recurrence rate is higher in treatment with local curettage and en-block resection is considered the treatment of choice. A careful clinico-radiological evaluation of patients with histopathological confirmation will lead to correct, timely diagnosis and comprehensive treatment in cases of CMF.

Authors' Contribution

SF conducted the cytopathological evaluation of the case. The surgery was performed by VKP and VPS. LSK and MGM handled the histopathological workup. The manuscript was prepared by LSK and MGM and subsequently reviewed and amended by SF, VKP and VPS. All authors approved the final version of the manuscript.

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229 **Table 1**: Comparison of available literature reporting chondromyxoid fibroma of phalanx.

S. NO	Author	Year	Age	Gender	Site	Size	Nuclear pleomorphism on histology	Treatment	Follow-up	Recurrence
1	Gupta SC et al [15]	1979	Not available	Not available	Phalanx of toe	Not available	Absent	Not available	Not available	Not available
2	Anderson W J et al [16]	1986	Not available	Female	Proximal phalanx of left ring finger	Not available	Absent	Curettage	42 months	No recurrence
3	Zillmer DA et al [13]	1989	3rd decade	Not available	Phalanx of hand	Not available	Absent	Curettage	Not available	Recurrence present
4	Zillmer DA et al [13]	1989	3rd decade	Not available	Phalanx of foot	Not available	Absent	Curettage	Not available	No recurrence
5	Bahk et al[8]	1998	19	Male	Distal phalanx of great toe	4 cm	Present	Disarticulated at interphalangeal joint	2 years	No recurrence
6	Kim YS et al [10]	1998	53	Female	Distal phalanx of left great toe	3 cm	Present	Disarticulation at metatarsophalangeal joint	Not available	Not available
7	Yamamoto T et al [17]	2000	Not available	Not available	Middle phalanx of index finger	Not available	Absent	Not available	Not available	Not available
8	Atalar H et al [18]	2007	8	Male	Phalanx of great toe	Not available	Absent	Curettage	46 months	No recurrence
9	Daghfous M et al [14]	2007	Not available	Not available	Phalanx of thumb	Not available	Absent	Curettage	9 months	Recurrence
10	Stotcavage RL et al [19]	2009	29	Female	Metacarpophalangeal joint of right ring finger	Not available	Absent	Curettage and synovectomy	15 months	No recurrence
11	Bill Chang K et al [20]	2010	40	Female	Distal phalanx of great toe	2.3 cm	Absent	Amputation at the level of base of proximal phalanx	6 years	NO recurrence
12	Khan Kalyan et al [7]	2012	21	Male	Middle phalanx of left middle finger	Not available	Present	Curettage	2 months	No recurrence
13	Vasudeva N et al [11]	2020	11	Female	Distal phalanx of great toe	Not available	Absent	Curettage	6 months	No recurrence
14	Present case	2024	47	Female	Middle phalanx of left fifth finger	2 cm	Absent	Curettage	6 months	No recurrence

230

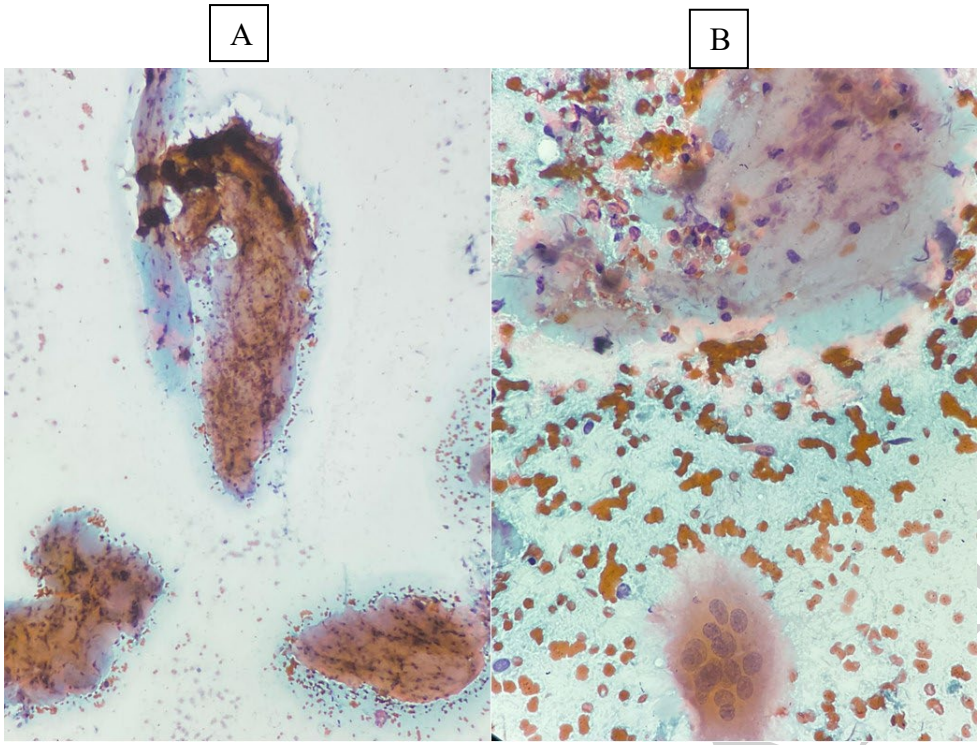

Figure 1: Papanicolau stained aspirate smears (A 100x magnification, B 400x magnication) show ill-defined moderately cellular fragments of myxoid stroma with oval to spindle-shaped cells having bipolar to stellate cytoplasmic processes, scattered alongside a multinucleated giant cell against a haemorrhagic background.

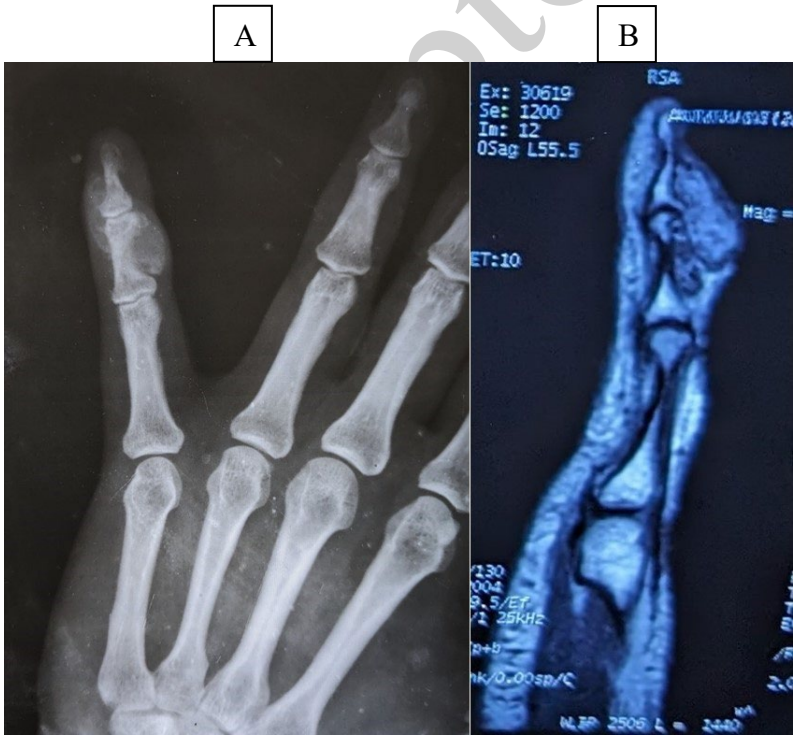

Figure 2: A: Radiograph (dorso-ventral view) shows a osteolytic, radiolucent, eccentric lesion in the metaphysis at the extensor aspect of the radial border of the middle phalanx and

the proximal part of the distal phalanx of the left fifth finger. **B**: MRI (lateral view) shows a well-defined lobulated lesion involving the middle phalanx of the distal phalanx, arising from the underlying bone with the distal phalanx showing pressure changes.

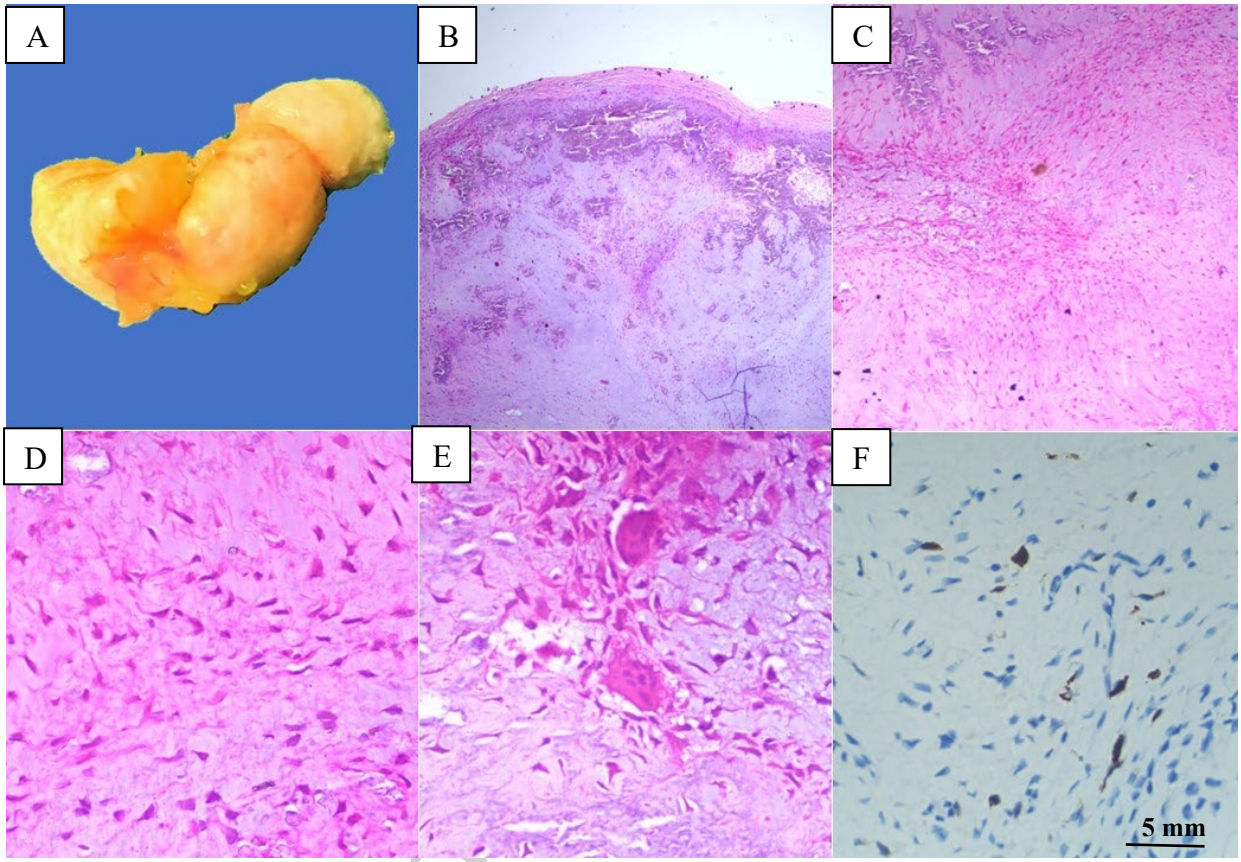

Figure 3: **A**: Excised specimen with a lobulated appearance and smooth surface. **B**: Hematoxylin and eosin stain (Magnification 40x) An encapsulated lobulated lesion. **C**: Hematoxylin and eosin stain (Magnification 100x) Peripheral hypercellularity with central hypocellularity. **D**: Hematoxylin and eosin stain (Magnification 400x) Spindle to stellate shaped cells in a myxoid stroma. **E**: Hematoxylin and eosin stain (Magnification 400x) Multinucleated giant cells in the periphery. **F**: Immunohistochemistry with S100p (Clone Beta EP-32, Ready to use, *Pathnsitu)* with nucleocytoplasmic expression in few spindle cells.