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Chondromyxoid Fibroma-Like Osteosarcoma in a 16-Year-Old: A Rare Case Report

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ABSTRACT

Introduction: Chondromyxoid fibroma-like osteosarcoma (CMF-like OS) is a rare subtype of osteosarcoma that exhibits low-grade histological features but high-grade aggressive behaviour. It shares overlapping characteristics with other benign and malignant bone lesions, often complicating diagnosis and management.

Case Presentation: We report a case of a 16-year-old male presenting with a painful, progressively enlarging mass on the proximal tibia over three years. Initial imaging suggested a giant cell tumor or aneurysmal bone cyst. Histopathological examination revealed proliferative stellate and spindle cells in a chondromyxoid stroma, with cellular atypia and osteoid matrix areas. Immunohistochemical analysis showed positive staining for MDM2, S-100, and low P53. Based on clinical, radiologic, and histologic findings, CMF-like OS was diagnosed. The patient was started on neoadjuvant chemotherapy with plans for surgical resection.

Discussion: CMF-like OS is often misdiagnosed due to its resemblance to benign lesions such as chondromyxoid fibroma. Unlike benign lesions, CMF-like OS exhibits aggressive features, including osteoid production and potential for metastasis. Radiologic findings, though non-specific, may indicate malignancy when there is cortical destruction and soft tissue extension. Histological and immunohistochemical analyses are essential for distinguishing CMF-like OS from other bone tumors.

Conclusion: CMF-like OS is a diagnostic challenge requiring meticulous histologic and immunohistochemical evaluation alongside clinical and radiologic correlation. Early diagnosis and prompt treatment are crucial, but further research is needed to establish definitive management guidelines and improve prognosis for this rare entity.

Keywords: aggressive bone malignancy, chondromyxoid fibroma-like osteosarcoma, chondromyxoid stroma, neoadjuvant chemotherapy, osteosarcoma subtype, tumor diagnosis

INTRODUCTION

Osteosarcoma (OS) is the most prevalent bone malignancy in children and adolescents. OS, as a primary malignant bone tumor, has a bimodal age of distribution. It is associated with a p53 tumor suppressor gene mutation and occurs mostly in long bones (i.e., proximal or distal femur and proximal tibia or humerus).[1,2] OS is differentiated into various subtypes according to their degree of differentiation, location, and histological findings.[2] One of the rarest subtypes of OS is the chondromyxoid fibroma-like (CMF-like

OS), which falls under the conventional variant of OS with low-grade histological properties.[3] Despite its low-grade features, CMF-like OS shows high-grade, aggressive behaviour. CMF-like OS is a hypocellular tumor with chondromyxoid stroma and unremarkable osteoid. It differs from chondromyxoid fibroma (CMF) because the cellular atypia, aggressiveness, and osteoid matrix are more prominent in CMF-like OS.[2-4] Due to its similar characteristics to other bone lesions and commonly misdiagnosed as other bone tumors, the prognosis of patients presenting with the disease is poor.[5] From our knowledge, Indonesia has not reported cases of CMF-like OS in literature, so this may be the first of its kind.

CASE PRESENTATION

A 16-year-old male patient was admitted to the orthopaedics department of our hospital with a chief complaint of a painful lump on his right knee. According to the patient, the lump initially was as big as a chicken egg but gradually grew bigger over three years, reaching the size of a baseball. The lump was painful and worsened with movements, but I felt better with rest. He had no difficulty walking, no previous history of trauma or operative procedures done on his knee, and did not experience any weight loss or any other systemic symptoms. The patient's family tried to treat the lump traditionally by massaging it on five separate occasions.

General physical examination yielded no significant findings and showed stable vital signs, except a visual analogue score of 2-3 out of 10, along with Traube space dullness. Physical examination of the right knee showed a single, fixed, solid mass with a distinct border that was tender and warm on palpation, with no venectation. The range of motion of the right knee was limited due to pain with active knee extension and flexion between 5-120°. The circumference of the right knee was 39 cm, while the left side was 32 cm.

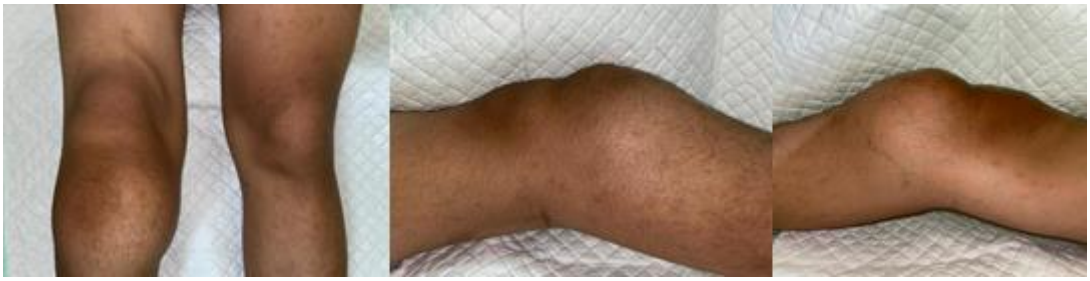

Figure 1. Clinical views of the right ankle

The serum analysis of this patient's lactate dehydrogenase (LDH) and alkaline phosphatase (ALP) are within normal values. X-ray of the right knee shows a relatively well-demarcated, geographic, osteolytic lesion on the 1/3rd proximal tibia, which initially was thought to have been either a giant cell tumor or an aneurysmal bone cyst. There are no obvious periosteal reactions such as Codman's triangle, sunburst appearance, or onion skin appearance. Further magnetic resonance imaging (MRI) examination concluded an aggressive primary bone tumor on the proximal 1/3rd epiphyseal up to the diaphyseal plate of the tibia, accompanied by bone marrow oedema, implying high-grade surface osteosarcoma with a differential diagnosis of chondrosarcoma.

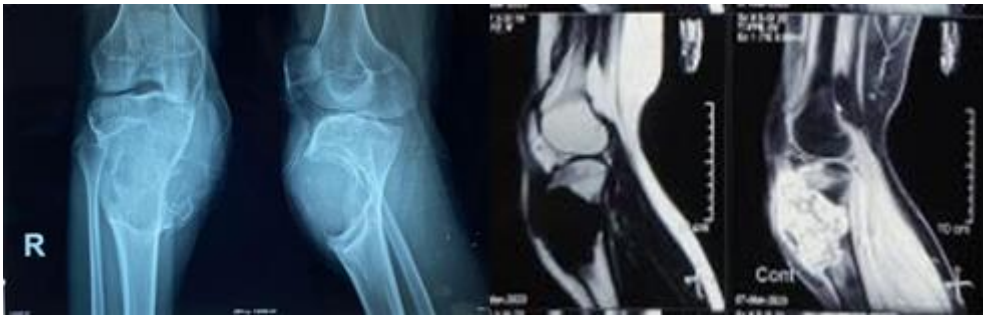

Figure 2. Left: Antero-posterior X-ray views of the right knee. Right: MRI of the right knee shows a solid lobulated heterogeneous mass with classification areas, destroying corticomedullary regions and extending up to the tibialis anterior muscle and right tibiofemoral joint.

Fine needle aspiration biopsy (FNAB) was done on the proximal tibia. It resulted in clusters of oval-shaped cells with pleomorphic nuclei, some with eccentric nuclei, and polynuclear cells. Surrounding the cells are osteoid and chondroid matrix. Diagnosis of high-grade- conventional osteosarcoma was made, with suspicion towards the chondroblastic type. Afterward, a core needle biopsy was done on our patient, and the samples obtained were taken for the frozen section. Histopathological images of the samples showed proliferative spindle and stellate-shaped cells with irregularly arranged nuclei and eosinophilic cytoplasm. There were chondromyxoid areas, 16 mitotic cells per 10 high-power fields, and atypical cells in areas of hypercellularity. Some areas of the cells and tissue are arranged in lobules separated by septa. The immunohistochemical analysis yielded positive for MDM2 (on chondromyxoid areas), SMA, S-100 (on chondromyxoid areas), and P53 (<5%) staining and negative SAT B2 staining. The histopathological results were more suggestive of a CMF. Still, after further discussion during the clinical pathologic conference, the working diagnosis of chondromyxoid cell fibroma-like osteosarcoma was made, and a consult was made with the paediatrics department to start chemotherapy for the patient.

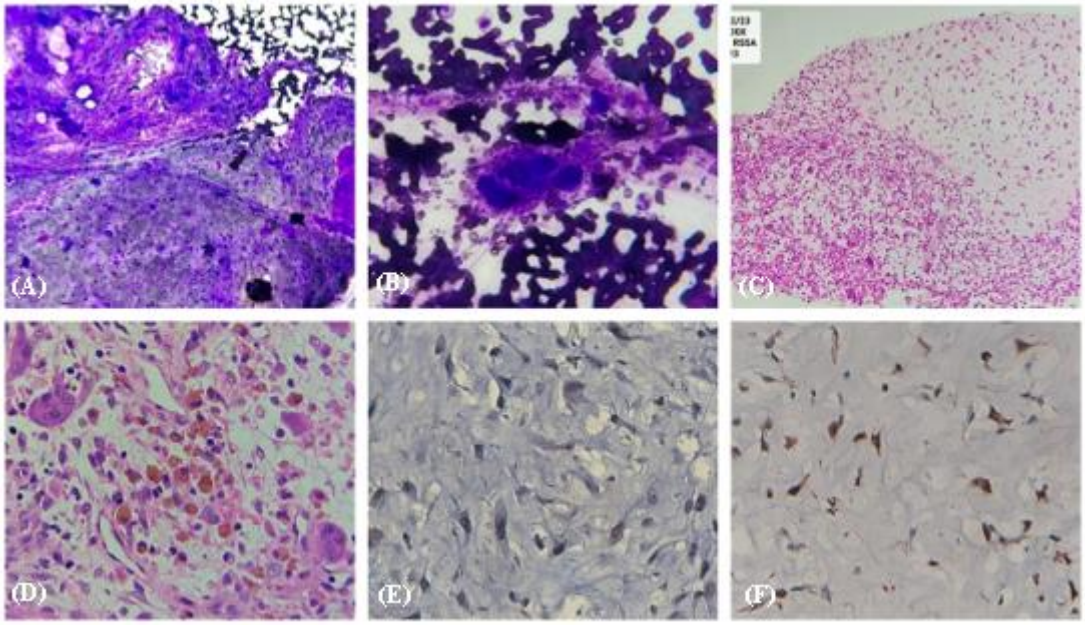

Figure 3. Histopathological findings. A and B: Samples from fine needle aspiration biopsy. C and D: Hematoxylin-eosin staining of samples. E: P53 immunohistochemistry staining. F: S100 immunohistochemistry staining.

DISCUSSION

Osteosarcoma is the most common pediatric malignancy of the bone. It can arise as a primary bone tumor (de novo) or secondary bone tumor (due to previous bone pathology).[1,2] According to the World Health Organization (WHO)'s 5th edition of The Classification of Tumors of Bone,[6] osteosarcomas are classified into low-grade central osteosarcoma, conventional osteosarcoma, telangiectatic osteosarcoma, small cell osteosarcoma, parosteal osteosarcoma, periosteal osteosarcoma, high-grade surface osteosarcoma, and secondary osteosarcoma.

Some refer to CMF-like OS as a subtype of conventional OS, considered a high-grade central OS, based on its biological and morphological properties.[2] Contrary to that, Mirra et al. (1989) first defined CMF-like OS as one of the four low-grade primary central OS variants: osteoblastoma-like, fibrous dysplasia-like, and non-ossifying fibroma-like. Even though it holds low-grade features, CMF-like OS is prone to metastasis and has a poor prognosis.[3]

Cases of CMF-like OS are scarcely documented, even more so in paediatrics, with only very few case reports describing 13-month-old, 9-year-old, and 13- and 17-year-old patients. [2,3,5-7] Our patient's age falls under that range. The tumor presents itself in various locations, atypical of other conventional osteosarcoma cases. Although some pediatric CMF-like OS cases, likewise ours, show the tumor presenting in the distal femur and proximal tibia, [3,6] other cases report the tumors being found on the craniofacial region, thoracic bones, phalanx, and rarely on short and flat bones. [4-7] Painful or painless swelling or mass that grows over time on the involved region is the main symptom experienced by CMF-like OS patients. Some literature suggests that serum LDH and ALP values may hold prognostic significance, with elevated ALP indicating less disease-free survival and elevated LDH indicative of metastasis. [1,8] Fortunately, in our patients, both values remain normal. However, it is still unclear whether LDH and ALP values are significant in CMF-like OS cases.

Radiologic features of CMF-like OS are not specific; it is possible that from radiologic imaging alone, CMF-like OS may be mistaken for other bone tumors. The tumor may present as an osteolytic, osteogenic, or expansive lesion, with or without calcified segments, and could include cortical destruction and bone marrow oedema.[4] Unlike benign CMF, radiologic findings of CMF-like OS of our patient show soft tissue extension, hence, highly suggestive of being malignant.

Through cytopathologic analysis, the patient was initially misdiagnosed with chondroblastic osteosarcoma. According to the WHO, histological features of chondroblastic osteosarcoma are dominated by the chondroid matrix, but osteoid matrix, or a combination of both, occurs in some cases. [9,10] It is of utmost importance that more detailed tests are needed to differentiate CMF-like OS from other lesions. CMF-like OS and CMF have similar histologic features. Both may feature stellate-shaped cells on a myxoid background, but cellular atypia and mitotic figures are less commonly found in CMF. [1,2] Furthermore, osteoid matrix on histological findings and local aggressiveness are more characteristic of osteosarcoma.

Immunohistochemistry cells of CMF-like OS are positive for vimentin, osteopontin, and osteonectin. Contrary to this case report, S-100 proteins are usually negative in CMF-like OS (so are SOX9, P53, CD34) but positive in CMF. [3-5] Despite positive S-100 and P53 in our patient, it is important to consider that clinically, as well as further radiologic and other histologic findings, the final diagnosis was CMF-like OS. Positive MDM2 may also be significant as it is positive in low-grade osteosarcomas.

As of today, there are no specific guidelines that display the specific treatment of CMF-like OS, but generally, doxorubicin, cisplatin, iphosphamide, and methotrexate are first-line chemotherapeutic agents for

osteosarcoma treatment. Neoadjuvant chemotherapy is usually given in combination to prevent resistance and increase the chances of tumor necrosis. After being re-evaluated for chemotherapy response in 8-12 weeks, if the tumor is resectable, resection and reconstruction are performed. The five-year survival of patients with osteosarcoma who undergo chemotherapy combined with surgery is around 60%. [11,12]

Although it is unclear how chemotherapy and surgery affect the survival rate of patients with CMF-like OS, only one case report reported a 97% tumor response to chemotherapy, showing a low risk of recurrence and a better 5-year survival rate. The patient in the said case received doxorubicin, cisplatin, and, eventually, a high dose of methotrexate. Other cases have mentioned doxorubicin-cisplatin and adriamycin-cisplatin combinations, with some undergoing radiotherapy. Regardless of the treatment, the efficacy of chemotherapy and surgery in treating CMF-like OS is still questionable, with one of the best possible outcomes out of all the cases being a disease-free survival of up to 39 months.2-5,13 [2-5,13]

CONCLUSION

The diagnosis of chondromyxoid fibroma-like osteosarcoma is tricky. It holds many similar clinical, radiological, and histologic traits with other benign or malignant tumors of the bone, such as chondromyxoid fibroma, chondroblastic osteosarcoma, and chondroblastoma. Diagnosing this rare disease requires intricate histological and immunohistochemical considerations and detailed clinical and radiological findings.

Declaration by Authors

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