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(CASE REPORT)

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Diagnostic challenge of clear cell chondrosarcoma at proximal tibia: A case report

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Abstract

Introduction: Clear cell chondrosarcoma (CCC) is a rare neoplasm originating from the epiphyseal cartilage. The ratio of males is higher, which peaks in the third and fourth decades. Common locations are the proximal femur and humerus, in this case in the proximal tibia. There is often misdiagnosis clinically and radiologically in CCC, generally diagnosed as a giant cell tumor (GCT) because it grows slowly and has the same location as GCT. Radiological findings suggest GCT, and MRI suggests an aggressive primary bone tumor. On a fine needle aspiration biopsy examination, the distribution of osteoclast-type multinucleated giant cells and atypical round oval cells was found, concluding that GCT cells were atypical. Confirmation of the diagnosis is required by histopathology and immunohistochemistry.

Case Presentation: Histopathology showed hyaline cartilage tissue containing atypical chondrocytes with proliferating large round cells, partially centrally located oval nuclei with clear cytoplasm, and suspected CCC. Furthermore, immunohistochemical examination showed positive S100 expression, so the diagnosis of CCC could be established.

Conclusion: Clear cell chondrosarcoma (CCC) is a rare but important bone tumor that can be easily misdiagnosed as a giant cell tumor (GCT) due to its similar clinical presentation and radiological features. Accurate diagnosis relies on a combination of histopathology and immunohistochemistry, particularly the identification of S100 expression. This case highlights the importance of considering CCC in the differential diagnosis of epiphyseal bone tumors, especially when conventional imaging findings suggest a benign tumor, to ensure proper management and treatment.

Keywords: Fine Needle Aspiration Biopsy; Clear Cell Chondrosarcoma; Bone Tumor

1. Introduction

Clear cell chondrosarcoma (CCC) is a rare malignancy of the epiphyseal cartilage. The ratio of males is higher, with a peak in the third to fifth decade. The most common location for CCC is the femoral and humeral heads. The microscopic characteristic of CCC is the presence of many cells with clear cytoplasm. The lesion is often found in diameters of 2 to 13 centimeters, containing soft but gritty material, sometimes with cystic areas. The gross appearance of hyaline cartilage can be focal or absent. Radiological findings of CCC are well-defined, purely lytic lesions in the epiphysis of a long bone that may extend to metaphysis with a sclerotic rim may be present [1,2]. In CCC histopathology, the appearance of the tumor included a lobular pattern with large and round nuclei cells that were exposed in the center with clear cytoplasm [2]. The main sign of CCC in immunohistochemistry is a positive staining in S100 [1].

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The diagnosis of CCC is often delayed due to slow tumor growth. This is a clinical diagnosis problem which is often misinterpreted as a non-malignant tumor. Radiologically, CCC often showed cystic changes, suggesting cystic bone lesions. Even with histology evaluation, there is still a gap for errors in diagnosing CCC. Prominent hemorrhage-like conditions have been observed to make it difficult to differentiate with aneurysmal bone cysts [2]. The differential diagnosis of CCC, are giant cell tumor (GCT) and chondroblastoma due to its overlapping epiphyseal predilection [3]. Other differential diagnoses such as osteosarcoma and clear cell renal cell carcinoma also need to be considered [4].

2. Case Report

2.1. Clinical Findings

A 45-year-old male came with a chief complaint of pain in his lower right leg since a year ago without decreasing weight. Only did small lumps appear at first but grow in size over time within one year. The patient's walking ability has been affected by the worsening pain, especially at night, for one month. There is no prior history of trauma, fever, or family history of the same complaint, and any medication was never received before. Physical examination presented vital signs at normal range and no history of other lumps on the body. At the proximal tibia presented a single mass, oval, fixed, and tender. There is no sign of venous dilation, ulcer, and warmness. A limited range of motion is also observed when the patient was asked to move. The diameter of the right leg with the tumor is longer than the left leg.

2.2. Radiological Findings

X-ray was performed in one-third proximal right knee AP lateral. Well-delineated osteolytic lesions suggesting a benign tumor were found in Figure 1. From the location and characteristics of the tumor, the conclusion of the X-ray has suspected a giant cell tumor. In addition, a Chest X-ray was also done and found no metastasis in Figure 2. For further evaluation, an MRI examination suggested an aggressive primary bone tumor with bleeding components and soft tissue involvement in Figure 3a and 3b. The conclusion of the MRI examinations was suspected as osteosarcoma, therefore FNAB was performed for further evaluation.

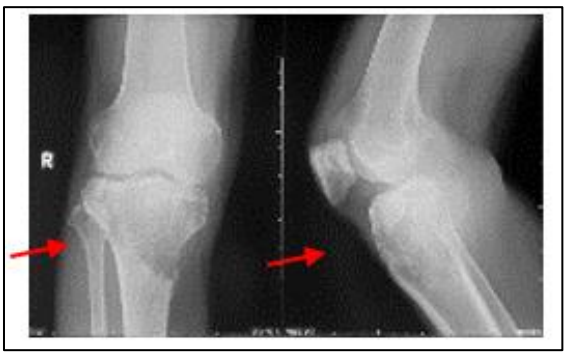

Figure 1 AP and lateral knee X-ray with a benign characteristic primary bone tumor in the proximal one-third of the right tibia, suspected giant cell tumor

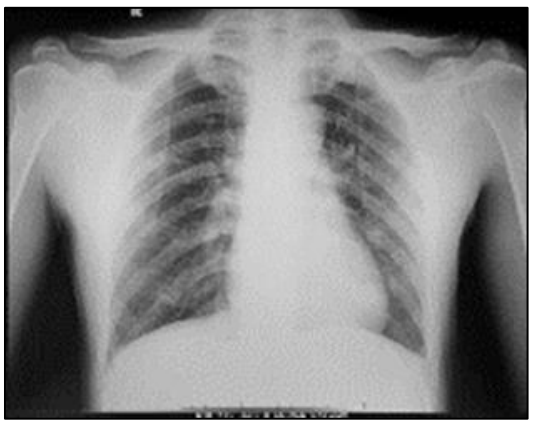

Figure 2 Chest X-ray with no metastasis.

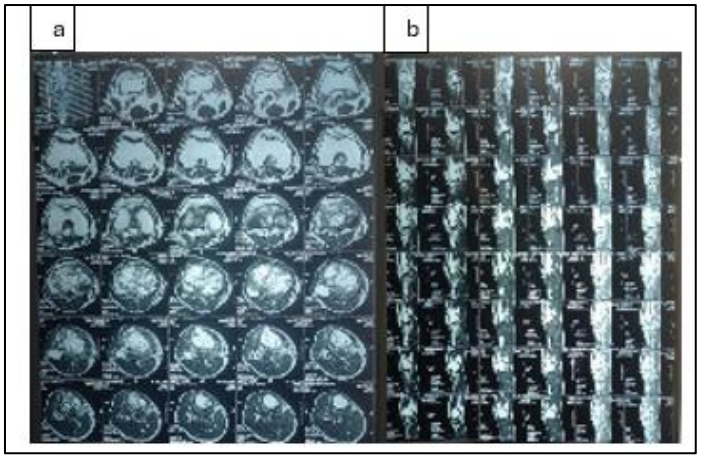

Figure 3ab MRI of the Right Proximal Tibia

2.3. Cytologic Findings

The cytological smear consists of dispersed and clustered round to polygonal large cells atypical looking in Figure 4. Tumor cells have a hyperchromatic round oval nucleus with clear cytoplasm. One of the tumor cells appears a dispersed multinucleated giant cell osteoclast type with an oval vesicular nucleus in Figure 5 From the cytological findings, concluded a Giant Cell containing tumor suspected GCT (Giant Cell Tumor) of bone with atypical cells with the differential diagnosis of giant cell-rich osteosarcoma and malignant GCT. For further examination, histopathology was suggested from open biopsy specimens and followed by immunohistochemistry examination.

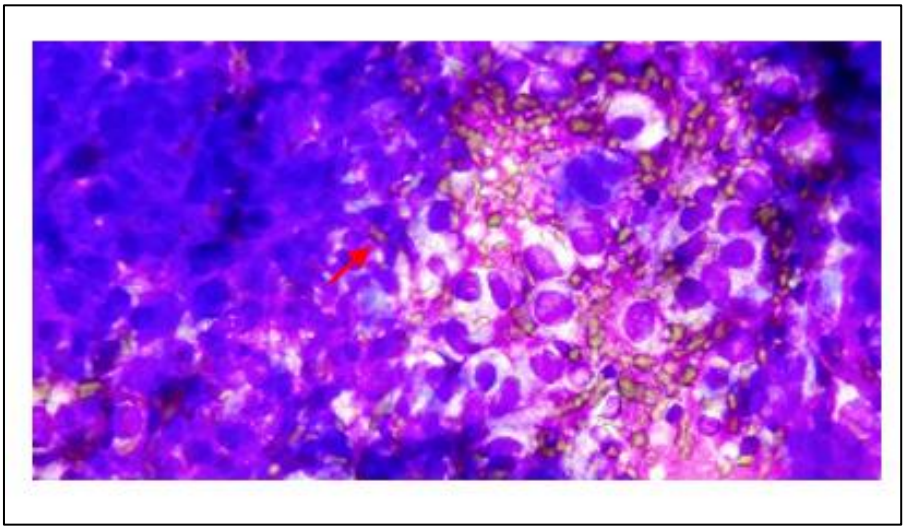

Figure 4 Dispersed and clustered of round to polygonal large cells atypical looking. Hyperchromatic round oval nucleus with clear cytoplasm tumor cell

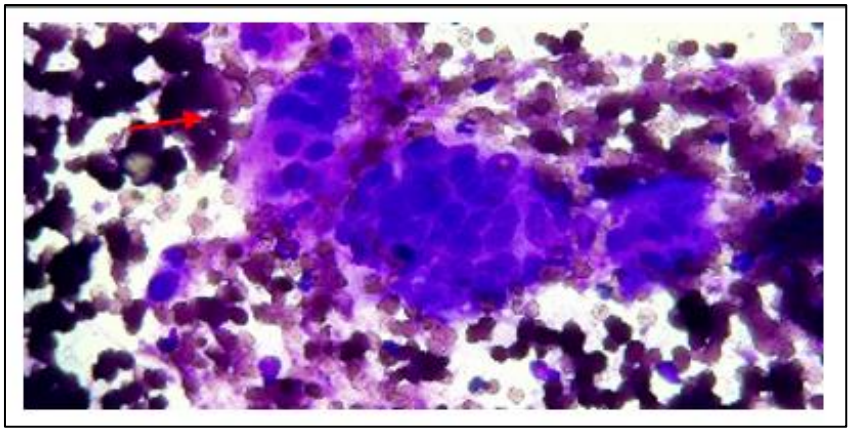

Figure 5 A dispersed multinucleated giant cell osteoclast type with oval vesicular nucleus found in cytology smear

2.4. Histologic Findings

On histopathological examination, the results of an open biopsy found pieces of tumor tissue consisting of hyaline cartilage tissue containing atypical chondrocytes in Figure 6and pieces of tumor tissue consisting of proliferation of large round cells with central round oval nuclei with clear cytoplasm in Figure 7. Between the tumor cells, there are immature woven bone trabeculae and scattered osteoclast-type multinucleated giant cells in Figure 8.

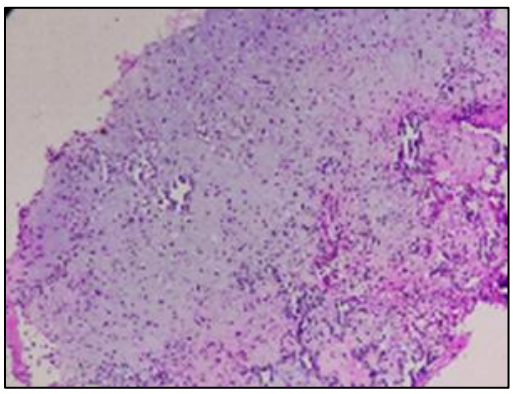

Figure 6 Hyaline cartilage components in the tumor, adjacent to the clear cells component

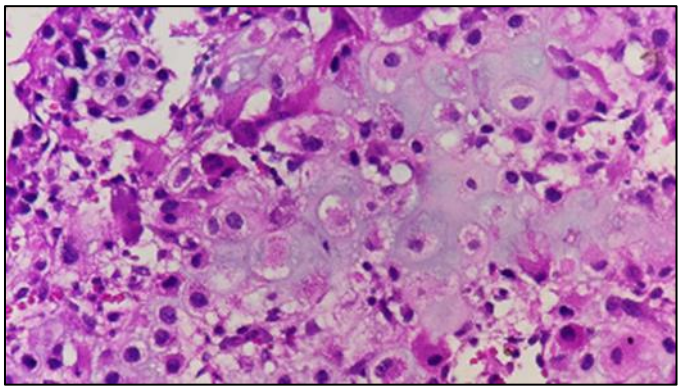

Figure 7 Round cells with round-oval nuclei, clear cytoplasm and scattered multinucleated giant cell osteoclast-type between tumor cells

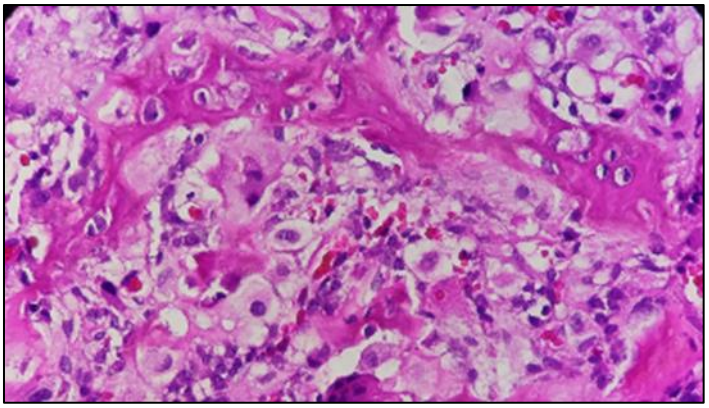

Figure 8 Woven bone trabeculae between tumor cells

2.5. Immunohistochemistry Findings

In this case, immunohistochemistry was done with antibody cytokeratin, osteocalcin, and S100. The expression of CK is negative in Figure 9. Expression of osteocalcin in Figure 10 and S100 in Figure 11 both are positive. S100 positively stained both at the cytoplasm and nuclei of tumor cells. Osteocalcin positively stains the cytoplasm of osteoblast surrounding woven bone trabeculae. Based on the histopathology and immunohistochemistry, this case diagnosed as Clear Cell Chondrosarcoma and planned for megaprosthesis implantation.

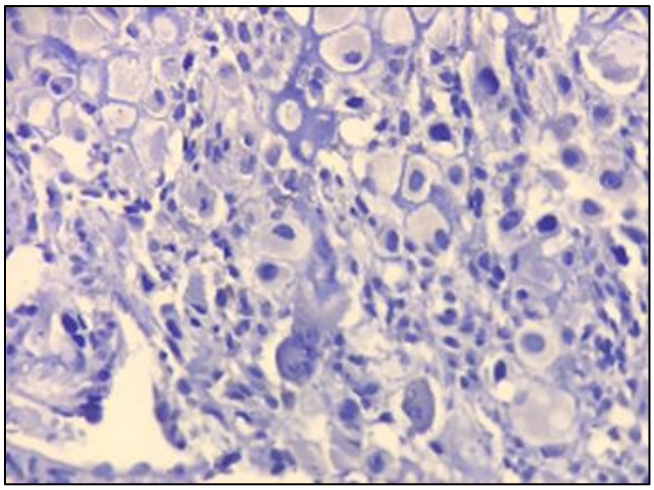

Figure 9 Negative for Cytokeratin 400 x

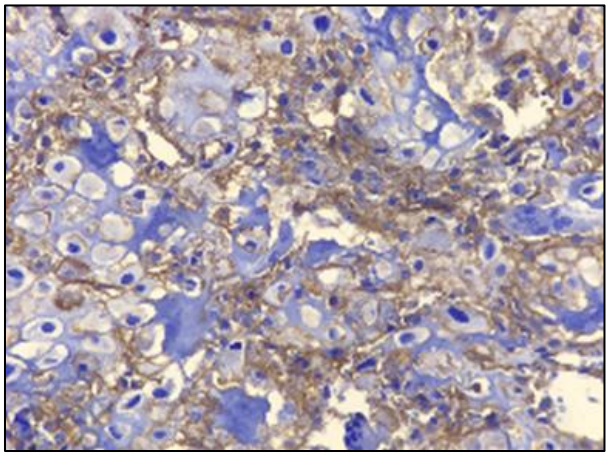

Figure 10 Positive for Osteocalcin 400 x

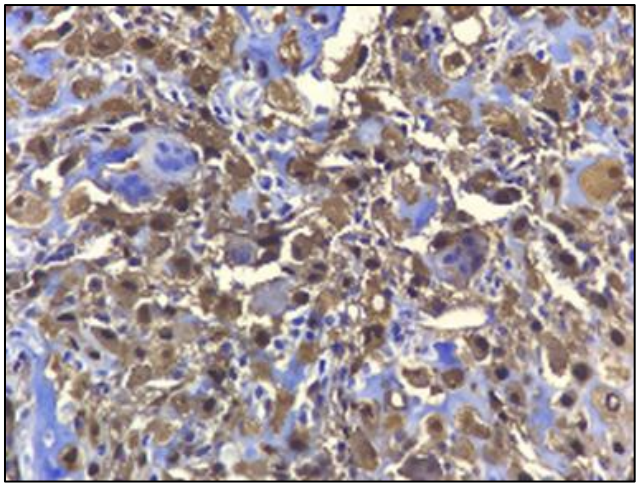

Figure 11 Positive for S100 400 x

2.6. Histopathology of Tumor Resection

A wide excision procedure was performed on a mass proximal to the tibia with a size of 12 x 8 cm. Followed by the installation of megaprosthesis. The results of the histopathological examination of the surgical specimen showed a CCC with a malignant cell-free distal end of the resection. Malignant cell invasion was found 6 mm from the posterior edge. On the superior edge, malignant cell infiltration was seen between the skeletal muscle tissue and 5 mm from the operative margin. No malignant invasive cells were found on the proximal fibular biopsy examination.

3. Discussion

Based on clinical findings, it is possible to suggest this patient's condition as a benign tumor. There is no red flag sign of cancer like the history of unexplained weight loss and fast-growing mass [5]. Based on the epidemiological findings. There is conformity between epidemiological data of CCC and patient history which males have a higher prevalence with a peak age in the third to fifth decade. The most common location of CCC is in the head of the femur and humerus, but in this case is in the proximal tibia [1]. The long tumor growth in this patient (1 year), the patient's age in the fourth decade, and the location of the tumor which is located in the knee area (proximal tibia) caused this case to be initially diagnosed as a suspect GCT of bone. Tumor growth occurred quite a long time in this patient (1 year), the patient's age in the fourth decade and the location of the tumor which is located in the knee area (proximal to the tibia) caused this case to be initially diagnosed as a suspect GCT of bone. In GCT, the prevalence of women is higher. GCT was suspected because the most common location are also in the distal femur, proximal tibia, and distal radius with the peak age range in the third decade to fourth decade [1,6,7].

X-ray examination concluded that the mass was a giant cell tumor. This is due to the position in the epiphysis of proximal tibia, a common location for GCT. Also, the osteolytic lesion has a well-defined margin and doesn't show any invasion to the nearby tissue, referring to a benign tumor like GCT. These benign features of GCT, also owned by CCC make it overlapping even though CCC is a malignant condition [1]. Radiographically, CCC looks like a benign tumor with characteristics like osteolytic lesions accompanied by well-defined margins and minimal cortical disruption [7]. For this reason, CCC cases sometimes can be misdiagnosed as a benign condition. It is important to consider CCC as one of the differential diagnoses especially when the mass appears in the epiphyseal of the head of the femur, humerus, and tibia [1,7]. Based on radiological examination, the differential diagnoses of CCC are osteomyelitis, GCT, and chondroblastoma [3,8,9]. Osteomyelitis and GCT can be excluded by examining the radiologic and clinical features. However for chondroblastoma differentiation from CCC, clinical presentation, radiology feature, and patient demographic presentation are not sufficient enough. Therefore, FNAB and Histopathological examination are important [8]. Other differential diagnosis that can be excluded by X-ray examination is conventional chondrosarcoma. In contrast to (CCC, conventional chondrosarcoma does not typically arise from the epiphyseal region [4].

MRI examination suspecting osteosarcoma because of soft tissue involvement. MRI result also showed iso- to hyperintensity on T1- and T2- weighted images. These results are not aligned with CCC because the common CCC results in MRI show low signal intensity in T1W1 [1].

FNAB examination results showed giant cells containing tumor-suspected GCT with atypical cells. GCT is suspected because there is a multinucleated giant cell osteoclast type and a cluster of round to oval stromal cells. A differential diagnosis was given giant cell-rich osteosarcoma and malignant GCT because there was a distribution of large round and polygonal cells with atypical nuclei. From the FNAB examination, it does not refer to CCC because there is no chondroid matrix [4]. Another characteristic of CCC is a low-grade tumor with clear cells, nucleus located on central or paracentral, and showed as a single or small group of cell [10]. Based on FNAB result, it is recommended to do histopathological examination from open biopsy followed by immunohistochemistry.

Histopathological results found hyaline cartilage tissue containing atypical chondrocytes with the proliferation of large round cells with round oval nuclei and clear cytoplasm, among these are immature woven bone trabeculae and scattered multinucleated giant cells of the osteoclast type [7,4]. According to WHO, CCC consists of lobules of cells with pale, well-defined cytoplasm with large round nuclei that are slightly atypical [1]. In CCC, hyaline cartilage can also be found which looks blue-gray or white when exposed to light. Appearances of giant cells, chondroid matrix, and benign reactive woven bone may also be found [11]. GCT cells consist of moderately vascularized stroma with mononuclear cells of short, single, and oval monotone. The cytoplasm is indistinctly demarcated and surrounded by multinucleated giant cell osteoclast types. In contrast to CCC, which has low mitosis, GCT cells are mitotically active, which is often considered as malignancy [7,4]. Differential diagnosis that can be excluded through histopathology are chondroblastoma and conventional chondrosarcoma (CSA). CCC have clear cells which are large cells with clear cytoplasm. Chondroblastoma and CSA do not have this characteristic. Apart from that, chondroblastoma cells have a nuclear groove, whereas CCC lacks this characteristic. CSA also does not contain osteoclast-type multinucleated giant cells and metaplastic bone formation [4].

Even though histopathology confirmed CCC, immunohistochemistry was also done to exclude differential diagnoses like osteosarcoma and metastatic clear cell renal cells. Osteosarcoma can be excluded because an osteoid matrix with a lace-like pattern is not found. Additionally, osteocalcin, even though it stains positively, only targets the osteoblasts surrounding trabeculae, not the tumor cells themselves [4]. In metastatic clear cell renal cell carcinoma, Cytokeratin should be positive, while in this case, it was negative. CD10 can also be used to differentiate renal cell carcinoma from CCC if it also expressed CK [12]. Expression of CK (AE1/AE3, CK18, CK7, CK 8, CK20) can happen in some cases of CCC [1,13]. Osteosarcoma was excluded because osteocalcin expression in this case only stained the osteoblasts surrounding the trabeculae, not the tumor cells. The diagnosis of CCC is confirmed by a strong positive of S100 in the nuclei and cytoplasm of tumor cells [1].

4. Conclusion

In summary, it is necessary to consider the diagnosis of CCC in patients with bone tumors in the epiphyseal of the proximal tibia with the radiological findings showed well-delineated osteolytic lesions accompanied by minimal cortical disruption and pathology examination showed clear cells with multinucleated giant cell osteoclast type.

Compliance with ethical standards

Acknowledgments

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Disclosure of conflict of interest

The authors affirm that there are no conflicts of interest regarding the conduct, results, or publication of this study.

Statement of ethical approval

The data used in this study were obtained from medical records approved by the Ethics Committee of Dr. Saiful Anwar General Hospital.

Statement of informed consent

Informed consent was obtained from all individual participants included in the study.

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