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Case Report

Small Cell Variant of Osteosarcoma Tibia: A Rare Case Report with Review of Literature

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Abstract: Introduction: A rare subtype of osteosarcoma, small cell osteosarcoma has received little research that has mainly focused on histological characteristics. In our center, there are only 2 patients who were definitely diagnosed as small cell osteosarcoma within 11 years. Here, we describe a unique incidence of small cell osteosarcoma in a female patient between 17 and 35 that manifested in her right proximal tibia and hip. **Presentation of Case:** We present two cases of small cell osteosarcoma of the tibia and hip in women aged 17 and 35 years. In this case the diagnosis hard to determine, so we need a spesific immunohiystochemistry examination to establish a definite diagnosis. **Conclusion:** According to the research, which claims that small cell osteosarcoma is an uncommon variety and only makes up 1.3% of all instances of osteosarcoma, small cell osteosarcoma is a rare case. Establishing a diagnosis at our center is still difficult because it requires several examination modalities to reach a definite diagnosis. It's critical to distinguish this tumor from Ewing's sarcoma and other types of osteosarcoma in order to assess its occurrence, clinical characteristics, ideal treatment, and prognosis.
Keywords: Osteosarcoma, small cell variant.

Introduction

A high grade malignant mesenchymal tumor that affects bones is osteosarcoma. The degree of cellular atypia, location, and clinical behavior of the different variants were all recognized by the World Health Organization.[1] An uncommon variant of osteosarcoma, small cell osteosarcoma makes up about 1.3% of all osteosarcomas.[2,3] In our center (Saiful Anwar General Hospital of Malang), the number cases of osteosarcoma from 2011-August 2021 amounted to 135 cases, and patiens diagnosed with small cell osteosarcoma amounted 2 cases. Most cases of osteosarcoma occur in the 1st and 2nd decades, and based on gender, the number is almost same between men and woman.[4] Here, we present a unique instance of small cell osteosarcoma in a female patient (17 years old and 35 years old) that manifested in the right tibia and hip.

Presentation of Case

Our first patient was a 17-year-old female who arrived at the Saiful Anwar General Hospital in Malang, Indonesia, in January 2021 with the primary complaint of right knee pain. Pain has been felt for 4 months ago and getting worse within 2 months, especially at night, and now the patient is

unable to walk. Patient also complain a lump on the right knee since 4 months ago, the initial lump was small and quickly enlarged within 4 months. No past infections existed. Upon physical examination, a solitary mass measuring 37 cm in diameter was found in the right knee. The lump has a venectasy look and is painful and firm to the touch, but there is no localized increase in temperature (Figure 1).

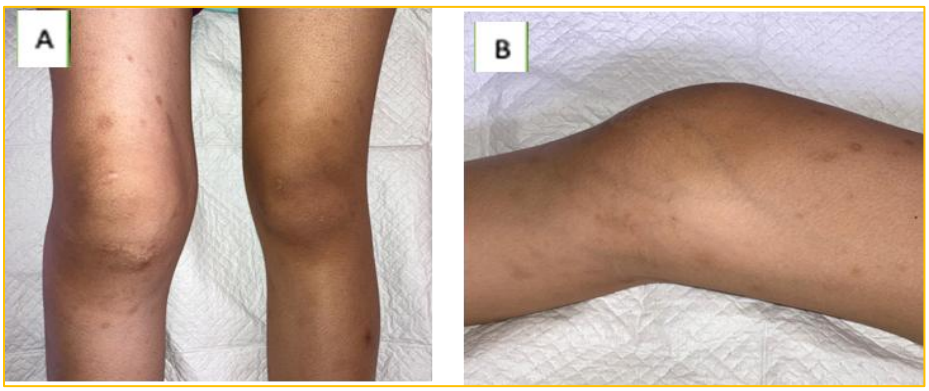

Figure 1. Clinical picture showed a mass on right knee with diameter 37 cm, hard palpable (A), and also venectasy (+) (B).

A pathological fracture on the right proximal of the tibia with periosteal response and soft tissue extension was visible on radiological x-rays. A malignant primary bone tumor in the right proximal tibia with involvement of the soft tissue in the front and deep posterior compartments of the tibia was visible during a contrast-enhanced magnetic resonance imaging (MRI) scan. From MRI, we also found involement of tibialis anterior artery with bone marrow changes, and also joint effusion on posterior right knee (Figure 2).

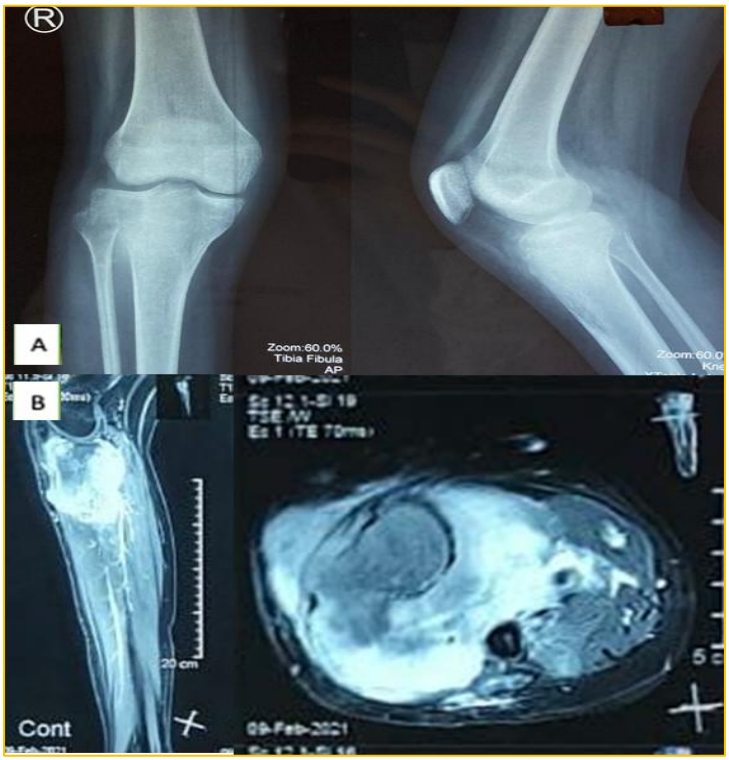

Figure 2. On the right proximal of the tibia, an X-ray of the knee revealed a pathological fracture with periosteal response and soft tissue extension (A). An appearance of a malignant primary bone tumor in the right proximal tibia was seen on an MRI with contrast, along with involvement of the tibialis anterior artery and soft tissue in the anterior and deep compartments of the tibia (B).

FNAB guiding USG of right proximal tibia has been done with an unclear conclusion of malignant small round cell tumor (Figure 3).

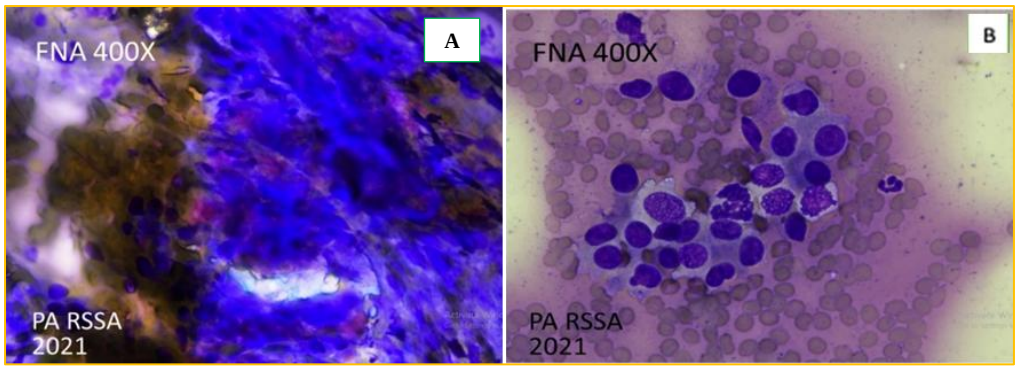

Figure 3. USG-guided FNAB of proximal tibia show of osteoid matrix with pink colour (A). Consisting of round oval cells with pleomorphic round nuclei between necrotic area (black colour), atypic mitosis, and also with faint osteoid matrix (fanta pink background)

And then an open biopsy was carried out with the result malignant small round cell tumor, suspect small cell osteosarcoma high grade with differential diagnosis of Ewing Sarcoma. (Figure 4).

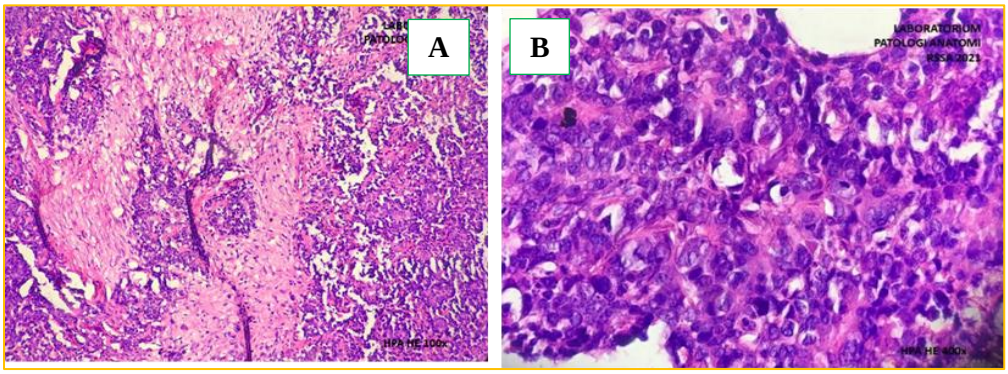

Figure 4. Open biopsy of proximal tibia shows of osteoid matrix with pink colour (A). The microscopic analysis revealed loose sheets of round to medium-sized pleomorphic tumor cells separated by connective tissue stroma. The cells exhibit mitotic activity and a sparse to moderate quantity of eosinophilic cytoplasm, along with hyperchromatic nuclei (B)

To determine a definite diagnosis, an immunohistochemistry examination (CD99, S100, Osteocalcin) (Figure 5) has been performed with the result of small cell osteosarcoma. Microscopic analysis revealed loose sheets of round to medium-sized pleomorphic tumor cells separated by connective tissue stroma. The cells' hyperchromatic nuclei are surrounded by a sparse to moderate quantity of eosinophilic cytoplasm. Malignant tumor cells are observed in tumor osteoid, which has areas of bone growth and cartilage. There are areas of necrosis and hemorrhages, enhanced mitotic activity, and tumor large cells (Figure 4). Features point to a small cell osteosarcoma variety.

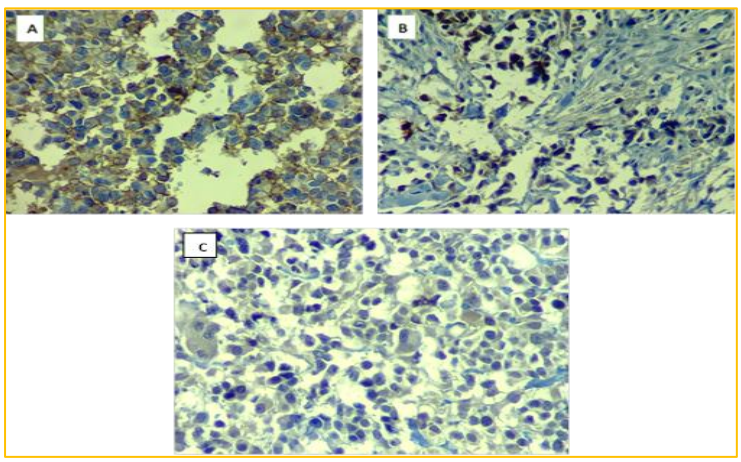

Figure 5. Microphotograph showing IHC with CD99 positive on membrane cell tumor (400x) (A), S100 positive patchy on tumor cytoplasm (400x) (B), and Osteocalcin positive on tumor cytoplasm (400x) (C).

The other case was female with complain pain and lump on the right thigh in the last 6 months ago. The lump grew rapidly in about 5 months, so the patient was unable to walk. Pain, especially at night, and weight decreased drastically. The patient had surgery after fall while drying clothes 5 years ago. From physical examination, there was a solid mass with venous venectation in the right hip with a hip circumference of 48 cm (Figure 6).

Plain radiological examination shows mixed lesions (osteolytic and osteoblastic) (Figure 7). The chemotherapy regimen was given 6 cycles with doxorubicin-cysplatin and the knee circumference decreased to 37 cm after chemotherapy. Unfortunately, in our patient, the patient still refuses surgery after chemotherapy.

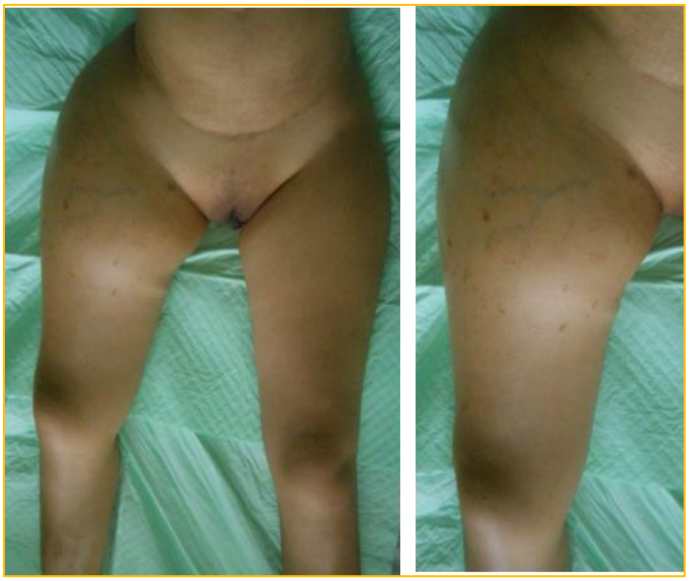

Figure 6. Clinical picture showed a mass on right hip with venectasy (+)

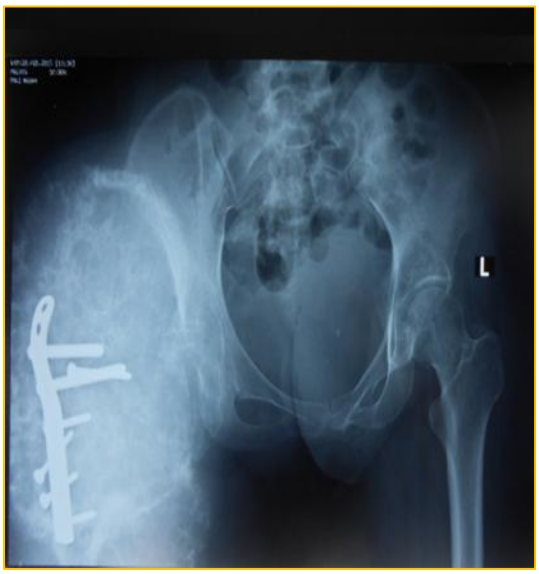

Figure 7. Plain radiograph of the hip, show mixed lesions (osteolytic and osteoblastic) with soft tissue involvement

The core biopsy result was vimentin positive diffuse in tumor, LCA: focal positive most tumor cells are negative, Ki67: high index of proliferation, so the conclusion support the diagnosis of a sarcoma with a high achievement index. An immunohistochemical analysis (CD99, S100) has been carried out to get a conclusive diagnosis and has revealed small cell osteosarcoma. The microscopic analysis revealed loose sheets of round to medium-sized pleomorphic tumor cells separated by connective tissue stroma. The cells exhibit mitotic activity and a sparse to moderate quantity of eosinophilic cytoplasm, along with hyperchromatic nuclei (Figure 8).

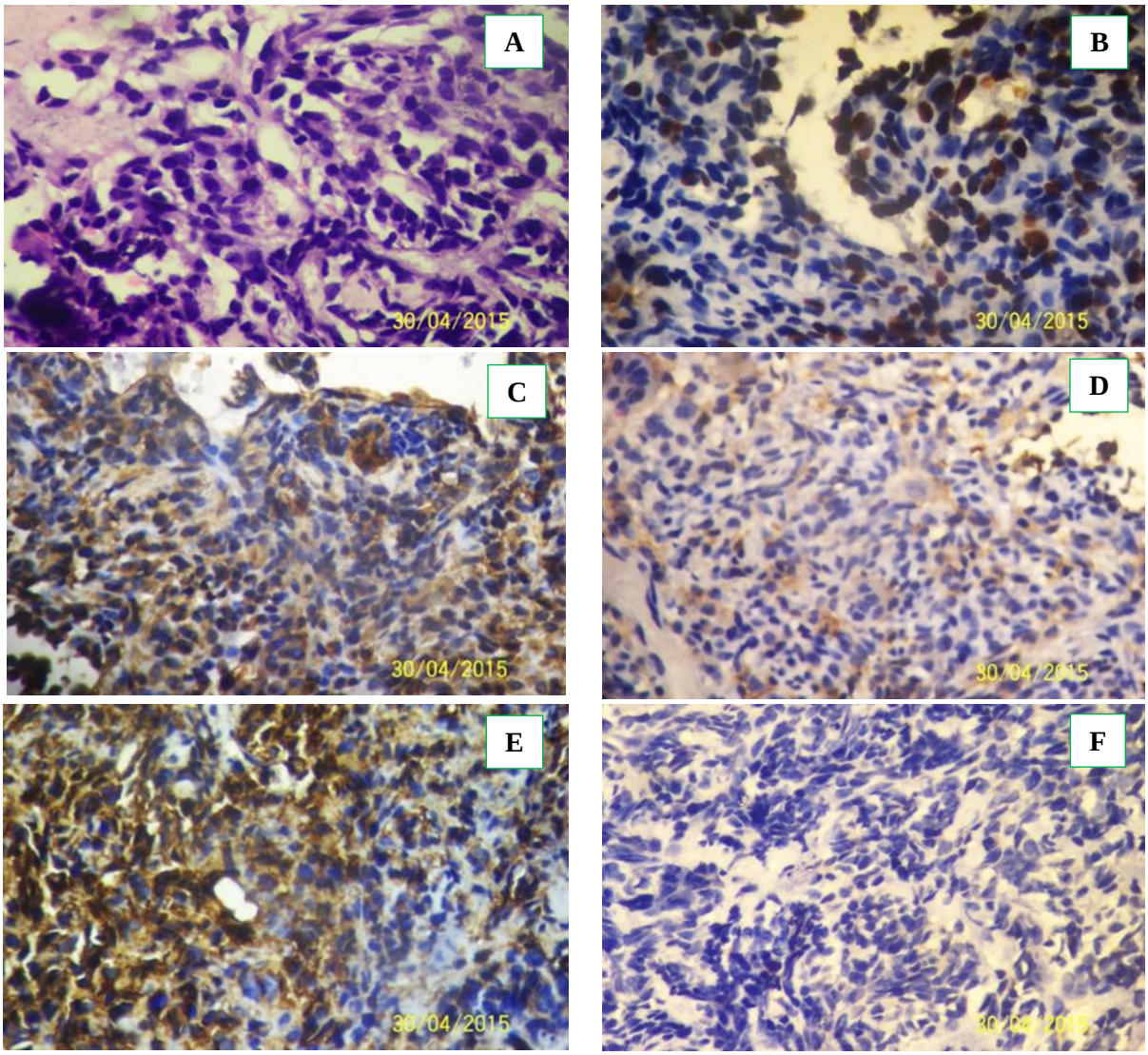

Figure 8. The microscopic analysis revealed loose sheets of round to medium-sized pleomorphic tumor cells separated by connective tissue stroma. The cells exhibit mitotic activity and a sparse to moderate quantity of eosinophilic cytoplasm, along with hyperchromatic nuclei (A). Ki 67: high index of proliferation (B), Vimentin positive diffuse in tumor (C), LCA: focal positive most tumor cells are negative (D), CD99 positive on mebran cell tumor (E), and S100 negative (F).

Discussion

In our center there are only 2 patients who were diagnosed with small cell osteosarcoma in the within 11 years. There are only 2 cases out of 135 total cases of osteosarcoma, which is 1.4% of all cases. According to the literature, tiny cell osteosarcoma is a rare variation that makes up 1.3% of all instances of osteosarcoma.[5-7] At our center, making a diagnosis can occasionally be challenging because it calls for multiple examination modalities and the histological examination's findings are still hazy due to the possibility of additional malignant small round cell tumors in the differential diagnosis. This challenge is consistent with the literature, which claims that the formation of osteoid is a hallmark feature of this tumor and changes the approach to treatment.[8] The presence of osteoid is a requirement for distinguishing small cell osteosarcoma from Ewing's sarcoma. Although reactive bone sclerosis and soft tissue mineralization can be found in Ewing's sarcoma in the form of periosteal laminated bone, mineralized tumor matrix is typically noted in small cell osteosarcoma.

However, the identification of the generated osteoid, which might again be extremely varied, is necessary for the diagnosis of small cell osteosarcoma.[9] In our center, a number of issues, including a modest lack of mineralization, the inability to distinguish between hyalinized collagen and osteoid, or even sample error, could affect the diagnosis. If there is no identifiable mineralized matrix, it can

be challenging to distinguish between Ewing's sarcoma and osteoid from the fibrin deposits that can be found between individual cells.[9] Nakajima et al. recommended making the diagnosis of Ewing's sarcoma if in doubt.[7] The other small cell tumors, including Ewing's sarcoma, should be ruled out using immunohistochemistry. In small cell osteosarcoma, CD-99 has been found to be positive. It would be preferable to rule out small cell osteosarcoma if either of these tests—LCA, S-100, EMA, SMA, factor VIII, smooth muscle acting, neuron specific enolase, and synoptophysin—reacted positively.[10] The majority of small cell osteosarcoma exhibit vimentin positivity, and a rare minority may also be muscle specific actin (HHHF-35) positive.

After the patient underwent various examinations, the patient was diagnosed with small cell osteosarcoma, and underwent preoperative chemotherapy, and planned post-chemotherapy surgery. The chemotherapy regimen was given 6 cycles with doxorubicin-cysplatin and the knee circumference decreased to 37 cm after chemotherapy. Unfortunately, in our patient, the patient still refuses surgery after chemotherapy, so we have difficulty in assessing the postoperative outcome. From literature the only treatment of this tumor is surgery.

Osteosarcomas are almost always insensitive to that treatment, although Ewing's sarcomas, which are highly radiosensitive, may need radiation for local control.[6] Pre-operative chemotherapy has no prognostic significance.[11] Post-operative chemotherapy and radiotherapy are given. Vincristine, Adriamycin, Actinomycin D, and Cyclophosphamide are the most often utilized chemotherapy drugs.[6] The 5-year survival rate for the classic osteosarcoma is 77%, whereas it is 28% for small cell osteosarcoma.[8] Overall survival rate depends on prognostic factors including tumor size, location, and histologic grade. However, a combined chemotherapy is not necessary in the absence of any evidence of any malignant cells on the surgical margins or the presence of distant metastasis. Small cell osteosarcoma was thought to have a poorer prognosis than Ewing's sarcoma and conventional osteosarcoma[9].

Conclusion

A rare case is small cell osteosarcoma. According to the research, which supports this claim, only 1.3% of cases of osteosarcoma are Small Cell Osteosarcoma, an uncommon variety. At our facility, making a diagnosis is still challenging because it takes a number of different examination modalities to make a certain diagnosis. The incidence, clinical characteristics, ideal management, and prognosis of this tumor must be distinguished from Ewing's sarcoma and from other types of osteosarcoma.

Conflicts of interest

The authors declare no conflicts of interest.

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