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Case Report

Osteosarcoma: a fluid cytologic diagnosis

Mitila T., Lakshmi Priya Asokan*, Vimal Chander

Department of Pathology, Saveetha Medical College, Chennai, Tamil Nadu, India

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***Correspondence:**
Dr. Lakshmi Priya Asokan,
E-mail: lakshmipriya2702@gmail.com

ABSTRACT

Osteosarcoma is the most common malignant bone tumor characterized by the formation of disorganized immature bone or osteoid tissue from mesenchymal tumor cells. It most commonly occurs in the appendicular skeleton involving the metaphysis of long bones. It is the third most common cancer in adolescence with an annual incidence of 5.6 cases per million children under the age of 15 years. Giant cell-rich osteosarcoma (GCRO) is an exceedingly rare histological variant of conventional primary osteosarcoma. It constitutes about 1%-3% of all osteosarcomas. A 20-year-old male presented with the complaints of pain and swelling over the right knee. Examination revealed a tender 15×10×8 cm swelling palpable on the distal femur. Radiological investigations showed features suggesting right femoral osteosarcoma in the meta-epiphyseal region. A core needle biopsy from the lesion was performed and 15 ml of fluid obtained from the biopsy site was sent for cytological examination, which showed features suggestive of osteosarcoma. Biopsy showed features of osteosarcoma probably of giant cell rich type confirming the fluid cytology findings. Cell block preparation also revealed giant cell predominance. Osteosarcoma is a bone tumor found in areas of rapid bone turnover, most commonly the distal femur and proximal tibia of adolescent patients. Cytology plays a vital role in diagnosing bone tumors, being a rapid, easy, and minimally invasive outpatient department procedure. Histopathology, since it gives a complete architectural pattern of tissue, remains the gold standard diagnostic tool.

Keywords: Osteosarcoma, Fluid, Cytology, Giant cell rich

INTRODUCTION

Osteosarcoma (OS) is the most common primary high-grade sarcoma of the skeleton. It has a bimodal age distribution, with most cases developing between the ages of 14 and 18 years and a second smaller peak in older adults.[1] The annual incidence rate is about 4.4 cases per 1 million population, showing a male predominance (1.3:1).[1] It usually occurs in the appendicular skeleton involving the metaphysis of long bones, most commonly the distal femur and proximal tibia of adolescent patients.[1-3]

In long bones, the tumor is usually metaphyseal (90%), infrequently in the diaphysis (9%), or rarely in the epiphysis.[1] It may occasionally be an incidental finding, but usually presents with local pain, swelling, or pathological fracture.[2] Radiologic examination shows classic lytic or blastic lesions, with periosteal reaction, and bone destruction. Histopathological examination serves as a gold standard diagnostic tool.[2] Osteosarcoma is subdivided histopathologically into osteoblastic, chondroblastic, or fibroblastic, depending on the cellular atypia and the type of the extracellular matrix, produced by the tumor cells.[3,4,5] In most cases, the presence of malignant osteoid matrix among malignant cells is pathognomonic of osteosarcoma.[2]

Giant cell-rich osteosarcoma (GCRO), an extremely rare histologic variant, constituting about 1%-3% of conventional osteosarcoma, shows numerous osteoclast-like giant cells and variable amount of tumor osteoid.[4,5] Neoadjuvant chemotherapy along with conventional surgery, mostly limb salvage treatment, effectively improves the survival rate.[2,3] Here, we present a rare case of diagnosis made by fluid cytology.

CASE REPORT

A 20-year-old male presented to the orthopedic OPD with complaints of swelling over the right knee for 6 months. The patient had a history of trauma a month back, since when he developed pain in the right knee and the swelling increased in size remarkably during the last 1 month. There was no history of fever, loss of sensation. Grossly no deformity was seen. Examination revealed a 15×10×8 cm swelling on the right distal femur and overlying skin appeared mildly erythematous. The swelling was warm and tender on palpation. There was restriction of movement of the knee joint.

Biochemical investigations were normal but with elevated alkaline phosphatase level of 130 IU/l. Radiological investigations showed an ill-defined heterogenous lesion arising from the posterior aspect of distal femur metaphysis with soft tissue extension involving the posterior compartment of the distal thigh and proximal leg, displacing the neurovascular bundle on MRI (Figure 1). PET-CT showed features consistent with right femoral osteosarcoma with ipsilateral ilio-inguinal lymph nodal spread and no obvious distant metastases.

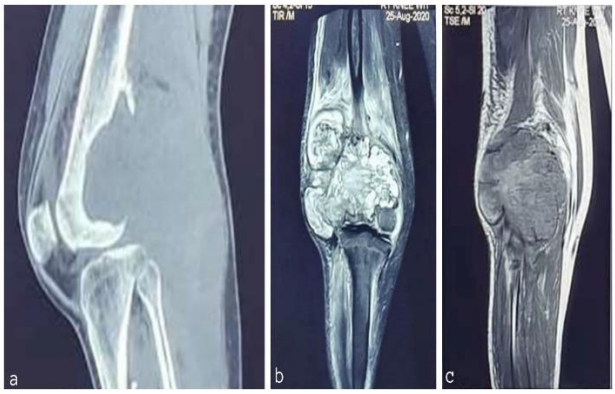

Figure 1: (a) CT image showing a posterior osteolytic lesion in the meta-epiphyseal region of right femur with a wide zone of transition and a large soft tissue compartment; and (b and c): MRI images showing an ill-defined heterogeneously enhancing lesion arising from the posterior aspect of distal femur metaphysis involving the posterior compartment of distal thigh and proximal leg.

A core needle biopsy from the lesion was performed, and 15 ml of reddish-colored fluid obtained from the biopsy site was sent for cytological examination to the department of pathology. Cell block preparation was also done. Microscopic examination of the fluid aspirated revealed highly cellular smears. Few tumour cells were seen surrounding occasional osteoid-like material. Tumor giant cells with markedly pleomorphic nuclei were seen. Scattered osteoclastic giant cells were also seen in a background of abundant hemorrhage. A diagnosis of osteosarcoma was made from the fluid cytologic examination (Figure 2).

Cell block preparation was done, and microscopic examination confirmed the features of osteosarcoma, showing predominance of giant cells. Gross examination of the core needle biopsy specimen showed multiple grey-white soft tissue fragments, on aggregate measuring 3×3×2 cm. Core needle biopsy microscopy showed tumor cells, high mitotic rate, with osteoid matrix, hemorrhage, and necrosis, confirming the diagnosis of osteosarcoma, probably giant cell-rich type (Figure 3).

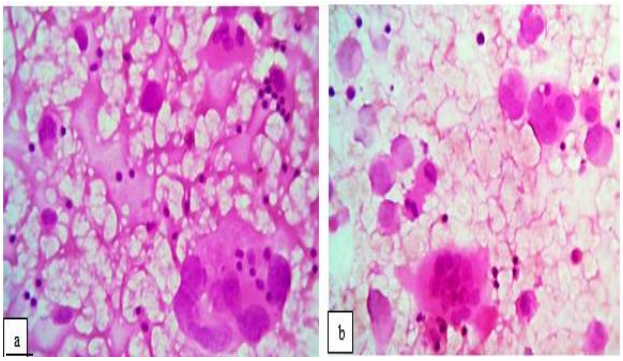

Figure 2: Fluid cytology (a) tumor cells surrounding occasional osteoid-like material with bizarre nuclei; and (b) tumor giant cells scattered osteoclastic giant cells and abnormal mitosis.

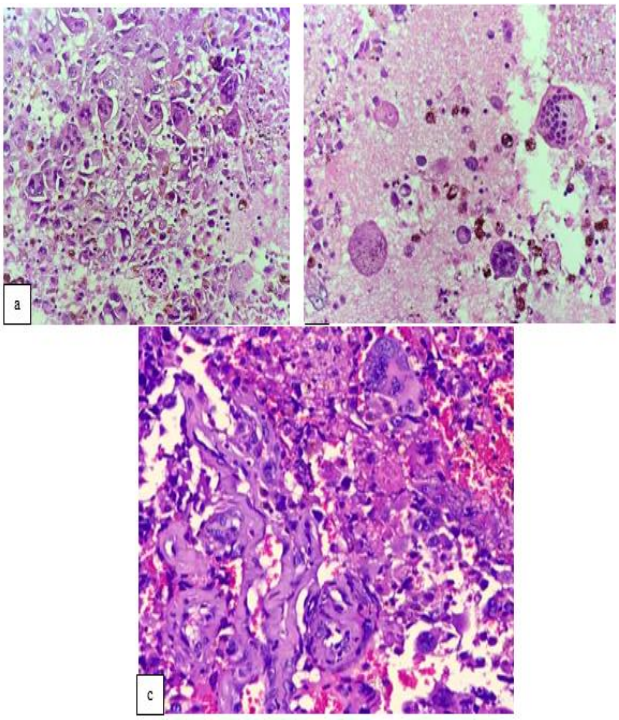

Figure 3: (a) Cell block- high cellularity with numerous tumor giant cells and osteoclast giant cells with mitotic figures; (b) cell block- higher magnification of tumor cells; and (c) biopsy- tumor giant cells, abnormal mitosis, osteoid matrix, and abundant hemorrhage.

DISCUSSION

Osteosarcoma is the most common malignant bone tumor characterized by the formation of disorganized immature bone or osteoid tissue from mesenchymal tumour cells. It involves the long bones of the extremities, most commonly in the distal femur (30%), followed by the proximal tibia (15%) and the proximal humerus (15%), i.e., sites of the most proliferative growth. Diagnosis by core needle biopsy is usually confirmatory. Osteosarcoma can be histologically classified as conventional osteosarcoma, low-grade intramedullary osteosarcoma, high-grade surface osteosarcoma, telangiectatic osteosarcoma, parosteal osteosarcoma, and periosteal osteosarcoma. Conventional osteosarcoma is the most common type with an aggressive characteristic, predominantly occurring in the meta-diaphysis of the long bone.[1-3,5]

Giant cell rich osteosarcoma is an uncommon variant of osteosarcoma which was first described by Bathurst in 1986 under the term "osteoclast-rich osteosarcoma". This variant is characterized by an abundance of osteoclastic giant cells and a lack of tumor osteoid.[2,4,5] It mimics giant cell tumor (GCT) histologically and radiologically, especially when it occurs in an epiphyseal location, making it hard to differentiate them.[2]

Cytological examination of fluids can be used to distinguish between benign, reactive conditions and malignancies. Proper screening and scrutiny of cellular features helps distinguish benign from malignant cellular.[6] Cytological smears have a few disadvantages, diagnostic yield may be low, owing to cellular overlapping, delaying artifact, suboptimal processing, preparatory cytotechnique and leaving behind useful material. This residual material can be very useful in increasing diagnostic yield by the cell block method, which can be used as adjuncts to smear for establishing a more definitive cytopathological diagnosis.[6]

Cell block technique was done by Bahrenburg nearly a century ago, it has been used routinely for processing fluids.[6] It is a simple, cost-effective preparation. It increases the sensitivity of detecting malignancies and can reduce false-positive interpretations. This technique can be used as adjuncts to smear for establishing a more definitive cytopathological diagnosis, providing the best milieu for morphological interpretation, with less background staining.[6] The main advantages of cellblock technique are preservation of tissue architecture and multiple sections from the same material can be obtained for special stains.[7] In a study by Santwani et al, a new method of cell block preparation by using 10% alcohol-acetic acid formalin as fixative was used to identify the sensitivity of the diagnosis in comparison with the conventional smear (CS) study.[6] Malignant osteoid matrix can be seen as a dense extracellular glassy to waxy hyaline material. It stains green-blue in a Papanicolaou stain, more easily appreciated in Romanowsky stains such as Giemsa stain and Diff-Quick stain. It stains pink to bluish in cellblock sections depending on the extent of mineralization.[8]

Biopsies are considered the gold standard for evaluation of bone tumors.[9] But there are risks associated with biopsy procedure like compartmental violation, tumor seeding, infection and occasionally fracture, which can be avoided by use of fine needle aspiration cytology (FNAC).[9] FNAC is a minimally invasive technique for evaluating both primary as well as secondary bone lesions. It has a diagnostic yield is comparable to biopsies, when used selectively in cases with soft tissue extension, cortical breach, or pathological fracture. Gupta et al[9] studied 41 cases and the most characteristic features included the presence of scattered as well as loose clusters of pleomorphic osteoblasts, multinucleated osteoclastic giant cells and acellular eosinophilic osteoid. Cellular smears with numerous pleomorphic malignant cells, bizarre cells, tumor giant cells, abnormal mitoses, and the typical wispy pink osteoid material along with suggestive clinico-radiologic findings.[9,11] This tumor mimics giant cell tumor but the features like relative paucicellularity with hemodilution, predominance of multinucleated giant cells and scattered mononuclear cells which were considered bland, attachment of osteoclastic giant cells to the periphery of stromal cell clusters, spindle- and ovoid-shaped nuclei without atypia, absence of typical lacy osteoid, and misinterpretation of metachromatic osteoid material as fibro-collagenous stromal material, helps to distinguish the two.[9,11,12]

CONCLUSION

Giant cell rich osteosarcoma is difficult to diagnose because its histological and radiological features mimic a benign giant cell tumor. Although the diagnosis is confirmed by the histopathological findings of biopsy, this case presents a rare scenario of fluid from the swelling revealing the tumor diagnosis. Cytologic evaluation may help in arriving at the correct diagnosis if the smears and cellblock sections are carefully examined for certain helpful cytomorphologic features, particularly osteoid matrix.

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