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Diagnostic Dilemmas in Cytodiagnosis of Primary Osteogenic Sarcoma

Authors

Vandna Yadav[1], Sonal Bhati[2], Aruna Pancharia[3], Vinod Kumar[4], Abhay Deshmukh[5]

[1]Senior Resident, Pathology, RNT Medical College Udaipur

[2]MD Pathology, Senior Demonstrator at RNT Medical College, Udaipur

[3]MD Pathology, Assistant Professor at Geetanjali Hospital and Medical College Udaipur

[4]Postgraduate 2nd year at RNT Medical College Udaipur

[5]MD Pathology, Blood Bank Officer at Mahatma Gandhi Institute of Medical Sciences Sewagram, Wardha, Maharashtra

ABSTRACT

Introduction: *FNA is not gaining acceptance worldwide by clinicians for diagnosis of primary bone tumors. Osteogenic sarcoma is one of the most common primary malignant bone tumors and predominantly affects children and young adults.*

Aims and Objectives*: The aim of this study was to identify the different cytomorphological features which enable correct diagnosis and to identify the common pitfalls which occur in cytodiagnosis of osteogenic sarcoma.*

Materials and Methods: *A total of 19 cases of histologically confirmed osteogenic sarcoma were retrieved from the records of Pathology department from 2008-2013. Previous cytology smears of these cases were reviewed to determine the usefulness of cytology in diagnosing osteogenic sarcoma. Cases were reviewed for clinical, radiologic, cytologic and histologic features.*

Results: *Of the 19 histologically proven cases of osteosarcoma, fine needle aspirates had been reported as: osteogenic sarcoma (n=5), suspicious of osteogenic sarcoma (n=6) and high grade pleomorphic sarcoma (n=3). The discrepant diagnoses were: de-differentiated chondrosarcoma, chondroblastoma, benign cartilaginous tumor and acute inflammatory lesion (one case each). One case was reported as inconclusive due to non-representative smears. The main reasons for discrepancy were: abundance of chondroid matrix, absence of osteoid, super-added infection and non-representative sampling.*

Conclusion: *Insufficient sampling and regional variations in the morphology of osteogenic sarcoma can cause difficulties in cytodiagnosis. Multiple aspirates from different sites of the lesion are recommended for diagnostic sampling. Cytomorphological smears must always be read in conjunction with clinical and radiological data.*

INTRODUCTION

Histopathology on tumor material obtained through open biopsy is considered the golden standard in the diagnosis of bone tumors. However, it remains an in-patient procedure requiring regional or general anesthesia. Moreover, it entails a risk of compartmental violation, tumor seeding, infection and occasionally fracture.[1] Osteogenic sarcoma (OS) is 2nd most common bone tumor after plasmacytoma, affecting people in 2nd decade of life with a male to female ratio of 2:1. These lesions involve metphysis of long bones with bone destruction and cause painful swelling.[2]

As Osteosarcoma is treated with preoperative multidrug chemotherapy in combination with radical surgical excision. A reliable diagnosis is required for preoperative multidrug chemotherapy. Fine-needle aspiration (FNA) and cytologic examination is a sensitive and cost-effective method that is being used increasingly in the diagnosis, staging and management of osteosarcoma.[3] Fine-needle aspiration cytology (FNAC) is an established cost-effective diagnostic tool, but osseous lesions often pose to be diagnostic challenge at FNAC. The main criticism against FNAB is the anticipated difficulty in sampling representative cell material from bone tumors because of tumor heterogeneity.[1]

FNAC of bone lesions has its own advantages of being a simple, safe, inexpensive, quick outpatient procedure, does not require hospitalization or general anesthesia, allows preliminary diagnosis within 15–20 min of aspiration with very less possibility of seeding of tumor cells. In addition, FNAC can be safely performed in difficult sites such as the vertebrae or the pelvis.[4]

AIMS AND OBJECTIVES

- The aim of the study was to identify the different cytomorphological features which enable correct diagnosis of OS.
- To identify the common pitfalls which occur in cytodiagnosis of OS.

MATERIAL AND METHODS

Retrospective analysis of cytology smears of 19 cases of histologically proven OS reported from 2008-2013 at Mahatama Gandhi institute of Medical Sciences, sevagram, Maharashtra was performed. FNAC was done using 22-25 bore long needles and in each case minimum two passes were given. In all cases, the smears were air-dried and wet-fixed in 95% ethanol and stained with Giemsa and Papanicolaou stains, respectively. The smears were reviewed for cytomorphologic characteristics, including cellularity, presence of tissue fragments and/or single cells, cellular shapes, presence of osteoid, necrosis, cellular pleomorphism, nuclear characters and mitotic figures, Cases were reviewed for demographic, clinical, radiologic, cytologic and histologic features.

RESULTS

Patient Demographics, Clinical and Radiologic Findings:

There were 4 females and 15 males. Mean age was 22 (Age range 6–47) years. Clinically 15 cases presented with painful swelling and difficulty in walking. Two cases presented with pain after minor trauma and 2 cases came with pathological fracture. Bony lesions were observed in proximal tibia (5), proximal femur (4), distal femur (3), distal tibia (3), shoulder (3) and one case involved chest wall.

When reviewed for radiological findings, 14 cases were reported as Osteogenic sarcoma or features suggestive of same (osteolytic lesion, perosteal reaction, sunburst appearance).

The 19 histologically proven cases of OS were reported on FNA as: OS (5), suspicious of OS (6), high grade pleomorphic sarcoma (3), dedifferentiated chondrosarcoma (1), chondroblastoma (1), benign cartilaginous tumor (1), inconclusive (1) and acute inflammatory lesion (1). (Table no. 1)

Table no.-1

Age/Sex	Site	Radiologic findings	FNA Diagnosis	Histologic Diagnosis
31/M	Right ankle (Distal tibia)	MRI-? Multicentric Ewing's sarcoma	Benign cartilaginous tumor	Chondroblastic OS
26/M	Left knee (Proximal tibia)	X-Ray: Osteolytic lesion with sunburst and periosteal reaction	Giant cell rich OS	OS with predominant fibroblastic areas and giant cells
18/M	Left upper thigh (Proximal femur)	MRI-? OS	OS	OS
22/M	Left leg (Distal tibia)	X-Ray: Osteolytic lesion in lower end of left tibia	Chondroblastic OS	Chondroblastic OS
9/M	Right thigh (proximal femur)	X-Ray: Osteolytic lesion proximal femur with periosteal reaction	Low cellular smears. Highly suspicious of OS	OS with necrosis and focal calcification
17/F	Right shoulder	MRI right shoulder joint - ? OS ? Ewing's sarcoma	OS	Chondroblastic OS
11/F	Right thigh (Proximal femur)	X-Ray: Osteomyelitis right femur	Acute inflammatory exudate. No malignant cells seen	OS
16/M	Left knee (Distal femur)	X-Ray: Osteolytic lesion	Suspect fibroblastic variant of OS	OS with chondroid and fibroblastic areas
47/M	Left knee (proximal tibia)	NA	Suspect high grade surface OS	OS
21/M	Left shoulder	X-Ray: Bony swelling, osteolytic lesion, pathological fracture shaft left humerus	Features are suggestive of pleomorphic sarcoma	OS
28/F	Left distal tibia	X-Ray: Osteolytic lesion of left distal tibia	Suspect OS, fibroblastic variant	Chondroblastic OS
6/F	Chest swelling- left side	NA	High grade pleomorphic sarcoma	OS
52/M	Left knee (proximal tibia)	X-Ray: Osteolytic lesion left proximal tibia	Suspect dedifferentiated chondrosarcoma	OS
30/M	Left knee (distal femur)	MRI: Ossifying lesion	Suspect periosteal OS	Periosteal OS
18/M	Right thigh (Proximal femur)	X-Ray: ? OS left distal femur	Pleomorphic sarcoma, most probably OS	Chondroblastic OS
17/M	Left knee (proximal tibia)	X-Ray: Osteolytic lesion	Suspect high gradepleomrphic sarcoma	OSwithreactive osteoclastic cells
16/M	Right shoulder	X-Ray: Perosteal reaction seen	Chondroblastoma	Chondroblastic OS
14/M	Left knee(distal femur)	X-Ray: Osteolytic lesion	Giant cell rich osteosarcoma	OS - Giant cell rich type
24/F	Left proximal tibia	X-Ray: Multiple osteolytic lesions in proximal third of left tibia	Non representaive hemorrhagic smears	Chondroblastic osteogenic sarcoma

Cytopathologic Features

Smears from cases diagnosed as OS or suspicious of OS revealed cellular specimen with blood, necrosis and pleomorphic cells. Nuclei were hyperchromatic. Bi and multinucleated cells were also noted. Osteoid matrix was obvious in these cases.

Three cases were reported as high grade pleomorphic sarcoma. Smears of these cases were cellular having necrosis, blood, spindled pleomorphic cells and multinucleated cells but there was no osteiod matrix.

Due to superimposed infection one case was diagnosed as acute inflammatory lesion and aspirate from another case was non representative.

Discussion

FNA is an accurate and cost-effective tool for the initial diagnosis of primary osteosarcoma with a sensitivity of 65% and accuracy of 95%.[3,5,6,7,8,]

- We wrongly diagnosed 5 cases on FNA as de-differentiated chondrosarcoma, chondroblastoma, benign cartilaginous tumor, acute inflammatory lesion and inconclusive.

Details on discordant cases:

Case no. 1 was diagnosed as benign cartilaginous tumor on FNA and final histopathologic diagnosis was Chondroblastic OS. Smears were reviewed and have shown low cellularity with abundance of chondroid material and absence of osteoid. Also while reporting, Imaging study findings were not available.

In case no. 13, though osteolytic lesions were seen on x-ray, on FNA picture was variable, with few areas suggestive of low garde chondrosarcoma and at places presence of pleomorphic spindled cells embedded in myxoid matrix. But osteoid was absent altogether.

In case no. 17, x-ray have shown perosteal reaction, on FNA there was abundance of giant cells with calcification and round to oval cells. No osteoid matrix was appreciated. Cellular pleomorphism was also not obvious. Histopathologically it was diagnosed as chondroblastic OS.

- Diagnosis of OS on cytology is difficult because of regional variations in a tumor's morphology and FNAC may not sample all areas. It is not always possible to obtain sufficient material for diagnosis.[5,9] Nowadays, medical imaging is an integral part in the pathological assessment of bone lesions as well as for localizing the area to be aspirated but in our study all the FNA were done directly without USG/CT guidance. So there were chances of missing the exact lesion. It's difficult to aspirate bone and most of the times smears are hemorrhagic, which obscure the exact cellular details. Sampling errors of FNAC are due to low cellularity, inadequate sampling and copious cystic/bloody/ necrotic material.[10] So aspiration from multiple areas is recommended in bony lesions to maximize chances of sampling different areas of these heterogenous lesions.[11] Adequacy of the aspirate plays an important role in early and correct diagnoses, which in turn depends on the site, characteristics, histological grade of the tumor and adequacy of the clinical and radiologic data.[12]

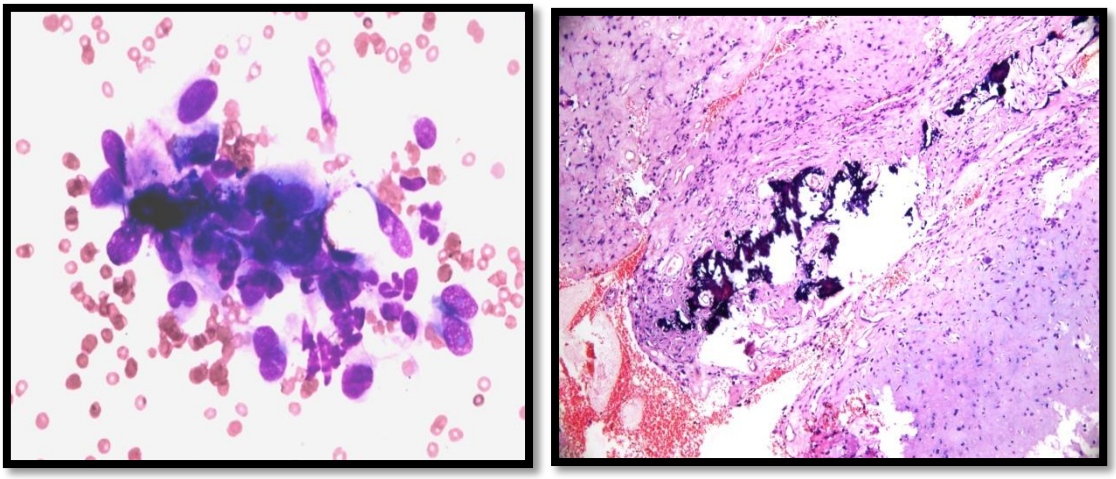
In most cases aspirated material was sufficient for diagnosis. In few (5) cases we were able to correctly diagnose the variant of OS.

Many studies have shown that osteoid is not always aspirated in FNA[2] and in our study, like many other studies,[7,9] presence of osteoid was considered one of the essential criteria for diagnosing OS.

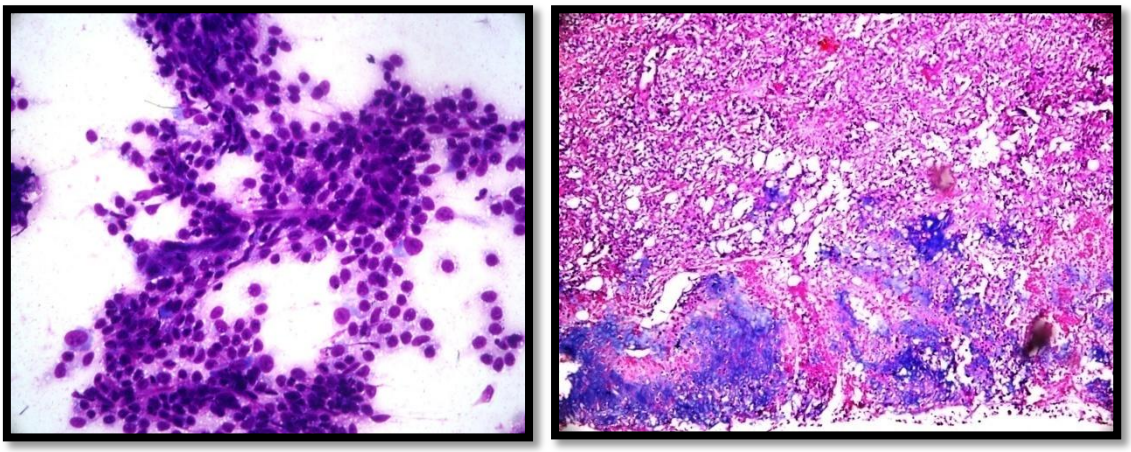
Conclusions

- Regional variations in morphology of a tumour cause difficulties in cytodiagnosis.
- Multiple passes and preferably guided FNAs yield better cellularity comparative-ely.
- However when smears are viewed with clinical and radiologic correlation, the diagnostic accuracy of FNAC can be improved.
- When sampling is adequate and the clinico-radiologic findings are available, FNAC of bone lesions is a highly accurate and diagnostic technique.

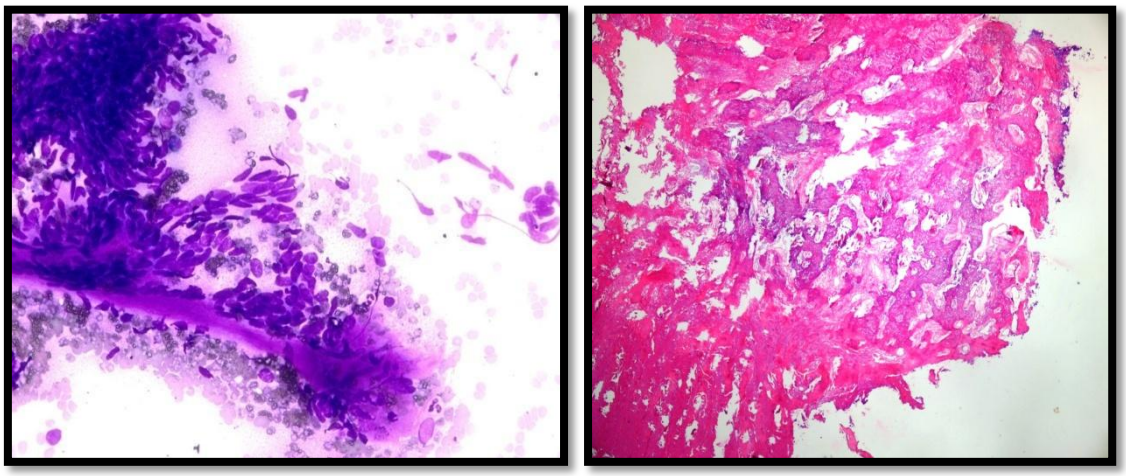
Considering the overall advantages and cost-analysis, FNAC may be suggested as the initial method of choice for evaluation of bone lesions in most clinical settings.



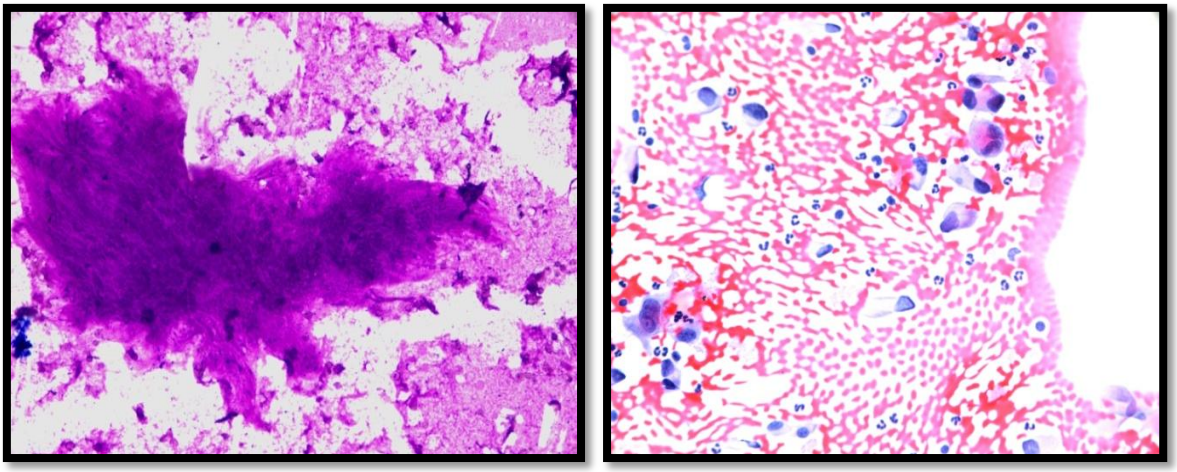
FNAC (1a): Dedifferentiated Chondrosarcoma. **Biopsy (1b):** Osteogenic Sarcoma.



FNAC (2a): Chondroblastoma. **Biopsy (2b):** Chondroblastic OS.



FNAC (3a)- Pleomorphic sarcoma **Biopsy (3b)-** OS.



FNAC (4a and b): OS

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