Original Article

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Fine Needle Aspiration Cytological Study of Bone Tumors and Tumor-like Lesions: A Review of Cases with Cytological-histopathological Correlation

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Abstract

Introduction: Fine needle aspiration cytology (FNAC) is a highly effective primary diagnostic method adopted worldwide to establish diagnosis.

Materials and Methods: About 9 years retrospective study on 202 cases of bone tumors and tumor-like lesions aims at investigates the diagnostic utility of FNAC.

Results: Out of 202 cases, 12.37% were non-neoplastic lesions, 30.19% were benign tumors, and 57.42% were malignant tumors. Osteosarcoma represented 24.75%, giant cell tumor represented 20.29%, and granulomatous osteomyelitis represented 6.93% of all bony lesions in our study.

Conclusion: The overall sensitivity was 96.66%, the specificity was 95.23%, positive predictive value was 97.75%, and diagnostic accuracy was 96.92%. Our data supports prior studies in the literature in showing that FNAC can be a valuable method for diagnosing these lesions.

Key words: Benign tumors, Fine needle aspiration cytology, Histopathology, Malignant tumors

INTRODUCTION

Primary bone tumors, both benign and malignant, are rare. Primary malignant bone tumors are uncommon, constituting only 0.2% of all neoplasms; however, in children (<15 years) malignant bone tumors account for approximately 5% of all malignancies.[1] Their incidence is only 0.8 in 100,000 people per year.[2] Clinical-radiological-pathological correlation is essential to the proper evaluation of chondrogenic/osteogenic lesions. Tumor-like lesions of bone are lesions having the appearance of a neoplasm and clinical behavior of non-neoplastic lesions. Their significance lies in the fact that they are very common, and their radiological appearance mimics true bone tumors including malignant lesions. Martin and Ellis first applied fine needle aspiration (FNA) technique to the diagnosis of bone lesions in 1930.[3] Since then, several published series have yielded overall accuracy values ranging from 51% to 100%.[4] Fine needle aspiration cytology (FNAC) is a minimally invasive and highly effective primary diagnostic method practiced worldwide for accurate diagnosis of various pathological lesions.

The aims of this study were to investigate the utility of FNA in the diagnosis of bone lesions from a tertiary medical center.

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MATERIALS AND METHODS

Out of 22,870 FNAC were performed during a period from January 2007 to December 2015 (9 years) of all patients attending Regional Cancer Research Center and Department of Orthopedics of the Pt. J. N. M. Medical College and associated Dr. B. R. A. M. Hospital, Raipur, Chhattisgarh. 202 cases of bone lesions were retrospectively retrieved.

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FNA cytological smears of bony lesions cases stained with May-Grònwald-Giemsa stain, hematoxylin and eosin (H and E) stain and paraffin wax blocks with histopathology slides stained by hematoxylin and eosin (H and E). Histopathological slides were retrieved only 143 (70.79%) cases, and radiological finding was retrieved 90% cases. The clinical data of these cases will be retrieved from medical records. We had selected those cases that fulfill following criteria.

Inclusion Criteria

The patient complains with palpable bony mass lesion, bony pain, and pathological fracture of all age and both gender.

Exclusion Criteria

Patients had previous diagnosed case receiving therapy, recurrence of lesion and bone marrow aspiration.

RESULTS

Overall, long bones of extremities were the most common site for bone tumors. Tibia appeared to be the most common site for primary bone tumors 58%, followed by femur 20%, and humerus 12%. Other sites 10% were ribs, spine (dorsal, lumber, cervical), maxilla, mastoid, mandible, clavicle, metatarsal, metacarpal, skull, pelvic, pubic bone, and iliac crest.

The age ranges from 6 to 80 years, male to female ratio of 1.9:1 with a male preponderance in our study. Of all non-neoplastic lesions, the youngest patient was 11 years male and the oldest was 60 years female both were reported as an inflammatory lesion. The peak age was 21-30 years of benign tumors, whereas 10-20 years of malignant tumors. Of all cases of benign tumors, the youngest patient was a 17 years male reported as ameloblastoma and the oldest was a 80 years old female reported as giant cell tumor. In our study, of all cases of malignant tumors, two youngest was a 6-years-old male reported as Langerhan's cell histiocytosis and another case was reported as osteosarcoma, whereas the oldest was a 79-years-old female reported as metastatic carcinoma.

The most of the patients were complaint palpable bony mass and bony pain (80%), followed by pathological fracture (20%).

Out of 202 cases, the radiological correlation was reported 80% and cytohistopathological correlation were observed 65.84% cases. The majority of cases of osteosarcoma, giant cell tumor and metastatic tumor were observed clinic-radiological and cytohistopathological correlation.

Out of 25 (12.37%) non-neoplastic bone lesions, most common lesions were granulomatous osteomyelitis 14 (6.93%), biopsy were available of 4 lesions and 100% correlated with FNAC, only two cases showed positivity for Zheel–Nelson stain of acid-fast bacilli, followed by chronic osteomyelitis 9 (4.45%) biopsy were available of 6 lesions and 100% correlated, rhinosporidiosis 2 (0.99%) biopsy were available one lesion and correlate 100% which showed positivity for periodic acid Schiff stain (Table 1).

Out of 61 (30.19%) benign bone lesions, giant cell tumor 41 (20.29%) was the most common diagnosis, biopsy were available 30, 25 were correlated with cytology but three were turned out to be osteosarcoma and two were turned out to be giant cell tumor, smears were highly hemorrhagic and obscured the large part of smear, only few osteoclastic giant cells were seen along with some mesenchymal element. 4 (1.98%) cases of chondroblastoma biopsy were available in 2 cases where correlated with FNAC.

About 100% cytohistopathological correlation observed in benign tumors such as osteochondroma three (1.48%) cases, aneurysmal bone cyst 3 (1.48%) cases, ameloblastoma 2 (0.99%) cases, fibrous dysplasia 1 (0.49%) case, osteoid osteoma 1 (0.49%), neurofibroma 1 (0.49%), and enchondroma 1(0.49%) case (Table 2).

Out of 116 (57.42%) malignant bone lesions, osteosarcoma 50 (24.75%) was the most common diagnosis, biopsy were available 40 cases, 38 were correlated with cytology but 2 were turned out to be giant cell tumor, on review it was found paucicellular smears and lack of clinico-radiological correlation was the reason for misdiagnosis. Ewing's/PNET 21 (10.39%) was the second most common diagnosis, biopsy were available 18 cases, 16 were correlated with cytology but two were turned out osteosarcoma histologically. The sampling and interpretative error was the reason for this misinterpretation.

Around 100% cytohistopathological correlation observed in malignant tumors such as metastatic tumor 20 (9.9%), chondrosarcoma 10 (4.95%), chordoma 1 (0.49%), and Langerhan's cell histiocytosis 1 (0.49%) with multisystem involvement and confirmed by immunohistochemistry examination which showed positivity for S-100.

Multiple myeloma represented 2 (0.99%) cases, biopsy available and 100% correlated to cytology and one case showed positivity for M band on serum electrophoresis another case showed leukemic blood picture with >30% blasts. Leukemia represented 2 (0.99%) cases; biopsy was available of a single case and 100% correlated to cytology.

Malignant fibrous histiocytomas (MFH), fibrosarcoma, other sarcoma represented 8 (3.96%)of all bony lesion were

histologically confirmed, one case of 24-years-old male presented with the swelling in the shoulder, radiologically both lytic lesion and soft tissue mass was noted. This case was reported as pleomorphic sarcoma of MFH on cytology but high-grade osteosarcoma on histopathology. This case emphasize on the importance of radiologically guided FNAC in the case of bony lesion having large soft tissue swelling causing difficulty in aspiration from deep-seated bony lesions (Table 3).

The overall sensitivity was 96.66%, the specificity was 95.23%, positive predictive value 97.75% and efficiency of the study was 96.92%. 100% efficiency was observed of metastatic tumors (Figures 1-3).

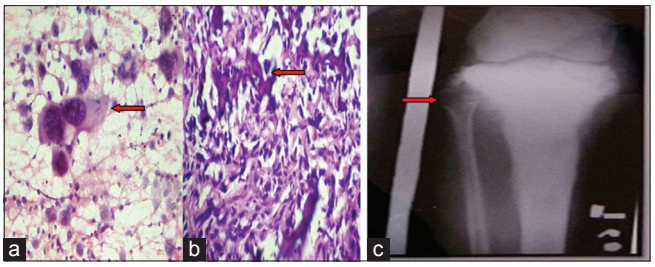

Figure 2: Osteogenic sarcoma (a) cytological smear showing hyperchromatic, pleomorphic tumors cells that produce osteoid (H and E, ×400), (b) follow-up Histopathology revealing the fibroblastic spindle cell portion of the neoplasm with osteoid (H and E, ×100), (c) corresponding radiological finding of proximal end of tibia and fibula showing a mixed radiodence/ radiolucent lesion with irregular surface contour

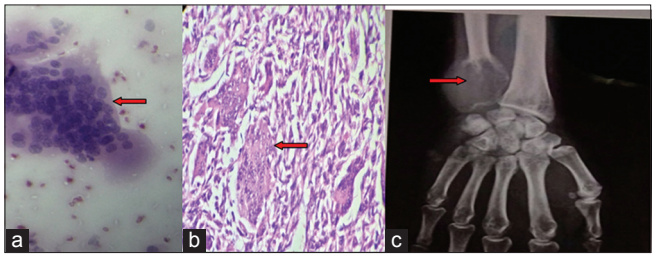

Figure 1: Giant cell tumors (a) cytological smear showing mixture of mononuclear cells with giant cell (H and E, ×100), (b) follow-up histopathology revealing same (H and E, ×100), (c) corresponding radiological finding of distal ulna showing the purely lytic nature of the lesions, its extension to the articular surface

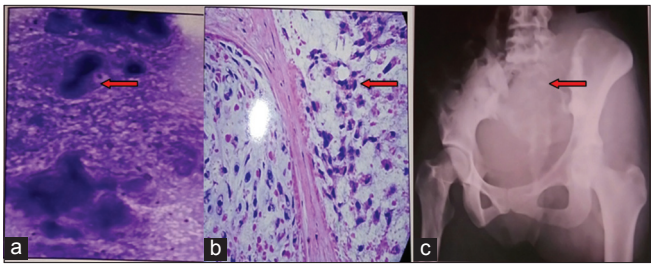

Figure 3: Chondrosarcoma. (a) cyotological smear showing chondroid matrix with vaculated clear cells (May-Grunewald-Giemsa ×100), (b) follow-up histopathological finding of the same (H and E, ×100), (c) corresponding radiological finding of pelvic bone showing lytic destructive lesion and soft tissue extension

Table 1: FNAC and histopathological diagnosis of non-neoplastic bone lesions

Cytological diagnosis	Number of cases (%)	Biopsy available	Histological diagnosis concordance	Histological diagnosis disconcordance
Granulomatous osteomyelitis (tubercular)	14 (6.93)	4	4	0
Chronic osteomyelitis	9 (4.45)	6	6	0
Rhinosporidiosis	2 (0.99)	1	1	0
Total	25 (12.37)	11	11	0

FNAC: Fine needle aspiration cytology

Table 2: FNAC and histopathological diagnosis of benign bone tumors

Cytological diagnosis	Number of cases (%)	Biopsy available	Histological diagnosis concordance	Histological diagnosis disconcordance
GCT	41 (20.29)	30	25	3 Osteosarcoma 2 aneurysmal bone cyst
Chondroblastoma	4 (1.98)	2	2	
Osteochondroma	3 (1.48)	3	3	
Aneurysmal bone cyst	3 (1.48)	2	2	
Ameloblastoma	2 (0.99)	2	2	
Fibrous dysplasia	1 (0.49)	1	1	
Osteoid osteoma	1 (0.49)	1	1	
Neurofibroma	1 (0.49)	1	1	
Enchondroma	1 (0.49)	1	1	
Intra osseous ganglion	2 (0.99)	0	0	
Simple bone cyst	2 (0.99)	0	0	
Total	61 (30.19)	43	38	5

GCT: Giant cell tumors, FNAC: Fine needle aspiration cytology

Table 3: FNAC and histopathological diagnosis of malignant bone tumors

Cytological diagnosis	Number of cases (%)	Biopsy available	Histopathological concordance	Histopathological disconcordance
Osteosarcoma	50 (24.75)	40	38	2 GCT
Ewing's sarcoma/PNET	21 (10.39)	18	16	2 osteosarcoma
Metastatic	20 (9.9)	12	12	
Chondrosarcoma	10 (4.95)	8	8	
MFH, fibrosarcoma other sarcoma	8 (3.96)	6	5	1 high grade osteosarcoma
Langerhan's cell histiocytosis	1 (0.49)	1	1	
Chordoma	1 (0.49)	1	1	
Myeloma	2 (0.99)	1	1	
Lymphoma	1 (0.49)	1	1	
Leukemia	2 (0.99)	1	1	
Total	116 (57.42)	89	84	5

FNAC: Fine needle aspiration cytology, MFH: Malignant fibrous histiocytomas, PNET: Primitive neuroectodermal tumor

DISCUSSION

In our study, total duration of period was 9-year, nearby duration of period was observed by Wedin *et al.* 2000[5] (8 years), but Treaba *et al.* 2002[6] were observed prolong duration.

In our study, male:female ratio was 1.9:1 with male predominant. Similarly, male: female ratio of 1.9:1 was observed in the study of Hasan *et al.* 2012.[7]

In our study, the age of cases ranged from 6 to 80 years. Similarly by Nnodu 2006[8] observed from 4 to 76 years and by Goyal *et al.* 2015[9] observed from 2.5 to 76 years. Age of cases ranged from 1.5 to 75 years in the study of Hasan *et al.* 2012.[7]

In our study, a total number of 202 cases were reviewed. Similarly, by Agrawal *et al.* 2000[10] included 226 cases. But by Khalbuss *et al.* 2010[11] reviewed the highest number of cases 1114. Ramdass *et al.* 2015,[12] by Goyal *et al.* 2015[9] and by Pathur 2013[13] were included less number of cases in their study.

In our study, granulomatous osteomyelitis/tubercular osteomyelitis and chronic osteomyelitis were reported 6.99 and 4.45%, respectively, Similarly by Brischetto *et al.* 2016,[14] by Goyal *et al.* 2015,[9] and by Korjodkar *et al.* 2012[15] reported in their study.

In our study, rhinosporidiosis was observed 0.99%, bony involvement was also reported by Amritanand *et al.* 2008[16] and by Mankannavar and Chavan 2001.[17]

In our study, tumor-like lesions was reported such as simple bone cyst 0.99%, aneurysmal bone cyst 1.49% intraosseous ganglion 0.99% and fibrous dysplasia 0.49%. Similar lesions were reported very higher, by Puthur 2013,[13] 37.83%, 18.91%, 5.4% and 12.16%, respectively. By Goyal *et al.* 2015[9] were reported 37.14% of cysts and by Ramdass *et al.* 2015[12] was reported 4.76% of bone cyst. Aneurysmal bone cyst accounted of 7.1% by Rajani *et al.* 2014.[18]

In our study, a total number of benign tumors were observed 30.19%, but others study was slightly higher, by Ramdass *et al.* 2015[12] and by Khalbuss *et al.* 2010[11] were observed 43% and 45.5%, respectively.

Benign tumorss consists of Giant cell tumor, osteochondroma, osteoid osteoma and neurofibroma were observed 20.29%, 1.49% and both 0.49%, respectively. By Ramdass *et al.* 2015[12] observed frequency of similar bone tumor 4.76%, 12.69%, 3.17% and 1.58%, respectively. Giant cell lesions accounted of 42 cases by Hasan *et al.* 2012.[7] Giant cell tumor 7.1%, osteochondroma 2.3%, and osteoblastoma 2.3% were accounted by Rajani *et al.* 2014.[18] Ameloblastoma was observed 1% in the present study but by Goyal *et al.* 2015[9] reported 7.1%. Chondroblastoma accounted for 2% cases, of all bone tumors in our study. Krishnappa *et al.* 2016[19] reported two cases of chondroblastoma. Rajani *et al.* 2014[18] accounted for 2.3% and Khabuss *et al.* 2010[11] accounted for one case in their study.

In our study, a total number of malignant tumors were observed 57.42% cases, by Ramdass *et al* 2015[12] was observed 19%, by Khalbuss *et al* 2010[11] was observed 47%. A maximum number of 71.4% malignant tumors was observed by Rajani *et al* 2014.[18] Nearby 52.8% malignant tumors were observed by Hasan *et al* 2012.[7]

Primary malignant tumors were composed of osteosarcoma, chondrosarcoma, fibrosarcoma/MFH and myeloma 24.75%, 4.95%, 3.96% and 0.99% respectively in our study. By Ramdass *et al.* 2015[12] observed 11.11%, 1.58%, both 3.17% respectively. MFH accounted 8% by Khalbuss *et al.* 2010.[11] Osteosarcoma accounted by Nnodu 2006[8] and Arora *et al.* 2012,[20] 16.66% and 34.2%, respectively. Osteosarcoma 11.9%, chondrosarcoma 9.5%, Ewings sarcoma 14.2% and myeloma 2.3% accounted by Rajani

et al. 2014.[18] By Wedin *et al* 2000[5] observed 3.57% of myeloma and by Soderland 2004[21] reported 8.52% of combined myeloma and lymphoma. Lymphoma reported 0.5% of our study, Similarly, cases observed by Goyal *et al.* 2015[9] of 2.38% and 1 case observed by Hasan *et al* 2012[7] and two cases observed by Yadav *et al.* 2014.[22] Leukemia reported 0.99% in our study, whereas combined cases of lymphoma and leukemia accountd 27% by Khalbuss *et al.* 2010.[11]

Ewings sarcoma accounted 10.49% in our study. By Khalbuss *et al.* 2010,[11] Arora *et al.* 2012[20] and by Sherwani *et al.* 2015[23] accounted 11%, 19.3% and 10%, respectively.

Chondrosarcoma accounted 4.95% in our study. By Khalbuss *et al.* 2010,[11] Arora *et al.* 2012[20] and by Ramdass 2015[12] accounted 8.5%, 27.2% and 1.58%, respectively.

Metastatic carcinoma accounted 9.9% in our study such as renal cell carcinoma, adenocarcinoma, follicular carcinoma of thyroid, metaplastic carcinoma of breast, and undifferenciated carcinoma. By Handa *et al.* 2005[24] reported 9.09%, the most common malignant tumors observed same as reported in our study. Ramdass *et al.* 2015[12] accounted 30% cases for metastatic tumors, whereas by Goyal *et al.* 2015[9] reported 4.76%. A maximum number of metastatic carcinoma 50% reviewed by Khalbuss *et al.* 2010.[11]

Soft tissue sarcoma reported 3.96% in our study. Similarly, this tumor had been reported by Vincenzi *et al.* 2013[25] and Debeer *et al.* 2007.[26]

Chordoma was observed 0.49% in our study, similar study was observed by Rao *et al.* 2005[27] and three cases were reported by Khalbuss *et al.* 2010.[11]

Langerhans cell histiocytosis was observed 0.49% in our study, similarly by Aricò *et al.* 2013[28] was observed multisystem involvement of cases and case was also observed by Khalbuss *et al.* 2010[11] in their study.

Overall diagnostic accuracy was reported sensitivity, specificity, positive predictive value and diagnostic accuracy as 96.66%, 95.23%, 97.75% and 96.92% in our study. Sensitivity, specificity as 96%, 98%, respectively, quoted by Khalbuss *et al.* 2010.[11] Sensitivity, specificity, positive predictive value and diagnostic accuracy as 96%, 100%, 100% and 98.1% quoted by Hasan *et al.* 2012.[7]

CONCLUSION

In this study, it reviews large series of bone FNAC in a tertiary medical center with an active orthopedic oncology group and regional cancer research center. FNA cytology is being used as a diagnostic modality for initial diagnoses because of its simplicity, low morbidity, cost effectiveness, and ability to issue rapid diagnoses that can facilitate clinical decision making.

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