 DOI: 10.5958/2394-6792.2016.00108.3

Role of fine needle aspiration cytology in diagnosis of various giant cell lesions of bone and its Histopathological correlation

Mohammad Jaseem Hassan[1,*], Sabina Khan[2], Nihal Ahmad[3], Kafil Akhter[4]

[1,2,3]Hamdard Institute of Medical Sciences & Research, Jamia Hamdard, New Delhi, [4]Dept. of Pathology, JN Medical College, Aligarh Muslim University, Aligarh, Uttar Pradesh

***Corresponding Author:**
Email: jaseemamu@gmail.com

Abstract

Introduction: Correct diagnosis is a matter of supreme importance because the treatment varies in different types of musculoskeletal tumors and in conditions simulating these tumors. Because of limited presence of literature for cytological diagnosis of giant cell lesions of the bone, we conducted this study to assess the reliability of Fine needle aspiration cytology in diagnosis of giant cell lesion of the bone and correlating our findings with final histopathological diagnosis.

Method: The superficial and deeply located bone lesions were localized with the help of radiographs. For aspiration of superficial lesions 22-23 gauge needles was used along with 10 ml disposable syringe, while for deeply located lesion 20 gauge needles was used. The cytological smears were then stained by May Grunwald Giemsa and Hematoxylin and eosin stain.

Result: During the period of one and half years, cytological diagnosis of giant cell lesions was made in 27 cases on FNAC. The mean age of the patient was 21.7 years with male to female ratio of 1.25:1. Maximum number of cases (18/27 cases) was encountered in 11-30 year age group. Tibia was the most common bone involved (12 cases) followed by femur and humerus (5 cases each). On final histopathological evaluation various giant cell lesions consist of 16 cases of Giant cell tumor, 5 cases of aneurysmal bone cyst and 3 cases each of Fibrous dysplasia and Chondromyxoid fibroma.

Conclusion: Despite limited literature we wish to recommend fine needle aspiration cytology as initial tool for differentiation of various giant cell lesions especially in conjunction with clinical and radiological findings.

Keywords: ABC, Bone tumors, FNAC, Giant cell lesions, GCT

Introduction

While dealing with problems of musculoskeletal lesions, correct diagnosis is a matter of supreme importance because the treatment varies in different types of tumors and in conditions simulating tumors. Though the open biopsy is considered as the gold standard for obtaining diagnostic tissue in connective tissue tumors, it can be difficult to perform and hazardous to the patient. Inappropriate biopsy technique causes problems in patient management leading to adverse patient outcomes.[1,2] Recently fine needle aspiration cytology (FNAC) became the recommended procedures at a number of medical centers because of the relative ease, safety and cost effectiveness of this technique. FNAC has advantages over open biopsy in that this technique is less painful, results in fewer complications and usually does not require general anaesthesia or hospitalization. It can be done as an outpatient procedure saving the time and expense of hospitalization and it is possible to reach an accurate diagnosis within 24 hours.[3] A multidisciplinary approach including clinical, radiological and FNAC is required to overcome the problems in early diagnosis of bone tumors.[4]

Other than giant cell tumor (GCT) of bone, the giant cell lesions of bone includes various entities like nonossifying fibroma, metaphyseal fibrous defect, chondromyxoid fibroma, chondroblastoma, solitary bone cysts, aneurysmal bone cyst, Brown tumor of hyperparathyroidism, Osteoid osteoma and Osteoblastoma etc.[5] Histopathologically the spatial relationship between the giant cells and stromal cells is used to differentiate giant cell tumor with these variants. In giant cell tumor, the giant cells are distributed regularly and uniformly, whereas in giant cell tumor like lesions there are foci containing numerous giant cells separated by large areas completely lacking giant cells.[5]

Because of paucity of literature available for cytological diagnosis of giant cell lesions of the bone, we conducted this study to assess the reliability of FNAC in diagnosis of giant cell lesion of the bone and correlating our findings with final histopathological diagnosis.

Material and Method

The superficial and deeply located bone lesions were localized with the help of radiographs. For aspiration of superficial lesions 22-23 gauge needles was used along 10 ml disposable syringe, while for deeply located lesion 20 gauge needles was used. The air dried smears were stained by May Grunwald Giemsa (MGG) stain, while for Hematoxylin and eosin (H&E) stain, smears were fixed in 95% alcohol. For histopathological evaluation, bones were decalcified and Paraffin sections were then prepared from the tissue block after fixation in 10% formal saline, dehydration, clearing, impregnation and embedding in paraffin. Sections were made 3-4 micron thick on rotary microtome and stained with H&E.

Result

During the period of one and half years, cytological diagnosis of giant cell lesions was made in 27 cases on FNAC. The mean age of the patient was 21.7 years (age range 7-60 years) with male to female (M:F) ratio of 1.25:1. Maximum number of cases (18/27 cases) was encountered in 11-30 year age group (70.37%). Tibia was the most common bone involved (12 cases) followed by 5 cases each of femur and humerus (Table 1). On final histopathological evaluation various giant cell lesions consist of 16 cases of GCT, 5 cases of aneurysmal bone cyst (ABC) and 3 cases each of Fibrous dysplasia and Chondromyxoid fibroma.

Table 1: Involvement of bones by different Giant cell lesions of the bone

Giant cell lesions	Femur	Tibia	Humerus	Radius	Ulna	Metacarpal	Total
Giant cell tumor M:F=1.28:1	05	08	01	01	01	-	16
Aneurysmal bone cyst M:F=1.5:1	-	02	02	01	-	-	05
Fibrous dysplasia M:F=2:1	-	01	01	01	-	-	03
Chondromyxoid Fibroma M:F=1:2	-	01	01	-	-	01	03
Total	05	12	05	03	01	01	27

Giant cell tumor (16/27 cases) was the most common giant cell lesion in our study (59.25%). It was present in the age group of 7-45 years (mean age=23.66 years) with M:F ratio of 1.28:1. Tibia was the most commonly affected bone (8 cases) followed by 5 cases in femur and one case each in humerus, radius and ulna. Clinically majority of the patients were presented with swelling and pain of the affected part with few patients complaining of difficulty in using the involved limb. Radiological findings showed lytic, expansile lesion in the epiphysis of bone without any new bone formation (Fig. 1A). FNAC smears were moderately to highly cellular and showed mononuclear spindle cells in sheets, as well as singly, along with many large osteoclastic giant cells having 20-40 uniform nuclei in a hemorrhagic background. The mononuclear cells had moderate amount of dense cytoplasm and oval basophilic nuclei with well dispersed chromatin. There was no nuclear atypia (Fig. 1B). In majority of the cases the typical X-ray finding of lytic, expansile lesion in the epiphysis of long bone without periosteal reaction leads to provisional diagnosis of GCT, which is augmented by presence of mononuclear stromal cells and osteoclastic giant cell on cytology. Histopathological sections showed oval to spindle shaped stromal cells along with more or less uniform distribution of multinucleated osteoclastic giant cells (Fig. 1C & 1D). In some cases giant cells were arranged typically in the periphery of stromal cells. All of our cases confirmed histologically. Fig. 2 shows typical presence of giant cells at the periphery of stromal cells on cytological smears (Fig. 2A, B, C) and presence of giant cells and stromal cells on histological examination (Fig. 2D).

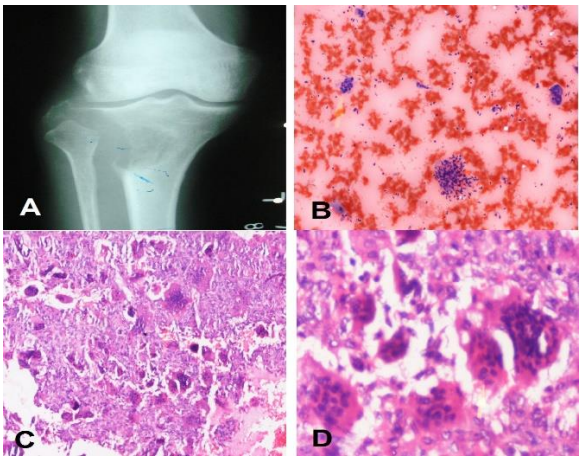

Fig. 1: Giant cell tumor- (A) Radiograph: AP view of knee shows an eccentric lytic lesion in the epiphyseal region of tibia with erosion of overlying cortex. (B) Cytology: Smear shows mononuclear cells and osteoclastic giant cells in a hemorrhagic background (H&E ×100). (C) Histopathology: Section shows uniform distribution of mononuclear stromal cells and osteoclastic giant cells (H&E ×100). (D) Histopathology: Section shows mononuclear stromal cells and osteoclastic giant cells (H&E ×400)

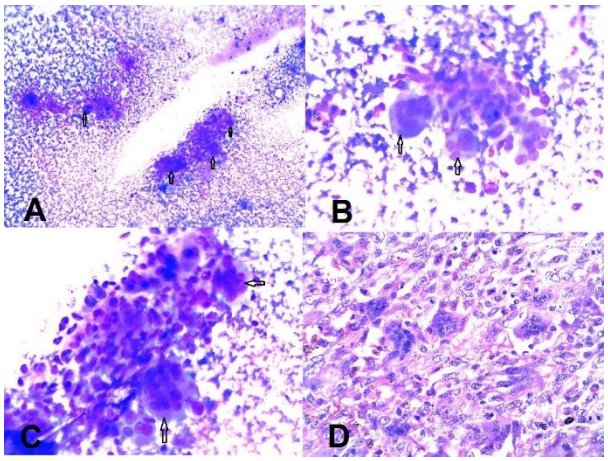

Fig. 2: Giant cell tumor- (A, B, C) Cytology: smears show typical presence of giant cells (arrow) at the periphery of stromal cells. (A, Giemsa x100, B & C, Giemsa x400). Histopathology: Section shows mononuclear stromal cells and osteoclastic giant cells (H&E ×400)

Out of 27 cases of giant cell lesions of bone diagnosed cytologically, a diagnosis of cystic bone lesion was rendered in 5 cases (18.51%), all of which confirmed to be aneurysmal bone cyst histologically. These lesions were present in the age range of 7 years to 60 years (average age= 20.5 years) with M:F ratio of 1.5:1. Most common bone affected was humerus and tibia (2 cases each). Most of the patients presented with swelling and pain in the affected part. Radiological Findings showed eccentric expansile lytic lesion in the metaphyseal region of bone with erosion of the cortex (Fig. 3A). By presence of eccentric expansile lytic lesion, a provisional diagnosis of cystic lesion of bone was made in majority of the cases. Cytologically low cellularity hemorrhagic smears were usually obtained. These smears as well as cytospin smears of fluid obtained on FNAC showed cyst macrophages, few osteoblasts, few multinucleated giant cells and hemosiderin laden macrophages (Fig. 3B). After correlating clinical, radiological and cytological findings, a diagnosis of cystic bone lesion was made in all cases. On histopathological examination sections showed large spaces of variable size filled with blood, separated by fibrous tissue and containing few osteoclastic giant cells (Fig. 3C).

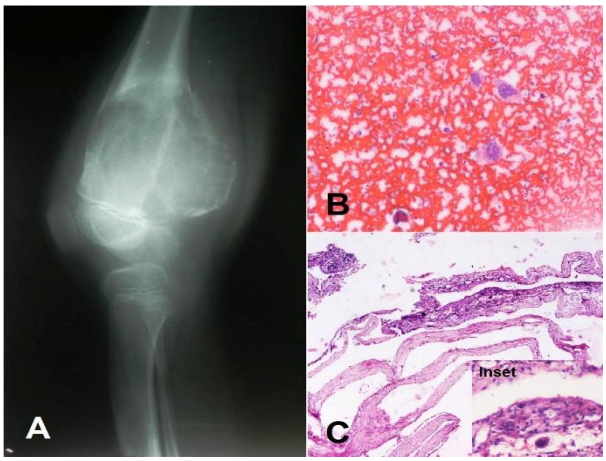

Fig. 3: Aneurysmal bone cyst- (A) Radiograph: AP view of knee region showing an expansile lytic lesion in the metaphyseal region of femur with a narrow zone of transition. (B) Cytology: Low cellularity hemorrhagic smears showing few osteoblasts and multinucleated giant cells (H&Ex100) (C) Histopathology: Section shows variable sized vascular spaces with infiltrate of multinucleated giant cells in the periphery. (H&E ×40) [Inset, H&Ex400]

The diagnosis of fibrous dysplasia was made in 3 cases (11.11%). The mean age of presentation was 19.3 years (age range =12-28 years) with M:F ratio of 1.5:1. One case each occurred in humerus, radius and tibia. Most of the patients clinically presented with pain at the involved site. Radiological findings showed an expansile lytic lesion in the diaphysis of long bone with pathological fracture (Fig. 4A). Cytological smears showed scattered osteoclastic giant cells and small clusters of osteoblasts along with clusters of spindle cells, few inflammatory cells and bony matrix. Histopathological sections of all three cases showed narrow, curved bony trabeculae interspersed with fibrous tissue of variable cellularity (Fig. 4B).

Fig. 4: Fibrous Dysplasia – (A) Radiograph: AP view of arm shows an expansile lytic lesion in the diaphyseal region of humerus with a pathological fracture. (B) Histopathology: Section shows eosinophilic curved trabeculae of woven bone in a

loosely textured connective tissue. Bone trabeculae are not rimmed by osteoblasts. (H&E ×400)

Three cases of chondromyxoid fibroma were diagnosed out of 27 cases of giant cell lesions (11.11%). The mean age of presentation was 14.3 years (age range = 10-25 years) with M:F ratio of 1:2. One case each involved the humerus, tibia and metacarpal. Clinically all patients presented with swelling of involved part. X-ray showed well defined, lytic lesion of the involved bone. Cytologically hemorrhagic smears showed large number of chondroid matrix along with chondroblasts and fragments of spindle shaped cells. Some giant cells were also seen along with few bare nuclei (Fig. 5). The radiological finding of well defined lytic lesion with typical presence of chodroblasts, spindle shaped cells and giant cells in a chondroid matrix on cytology leads to provisional diagnosis of chondromyxoid fibroma. Histopathological sections of all three cases showed distinct (low power) lobulation. On enhanced magnification the lobules were formed by spindle cells arranged loosely in a myxoid, focally chondroid matrix. The lobules were encased by peripheral hyper cellular zones of spindle to ovoid cells, small multinucleated giant cells were also seen.

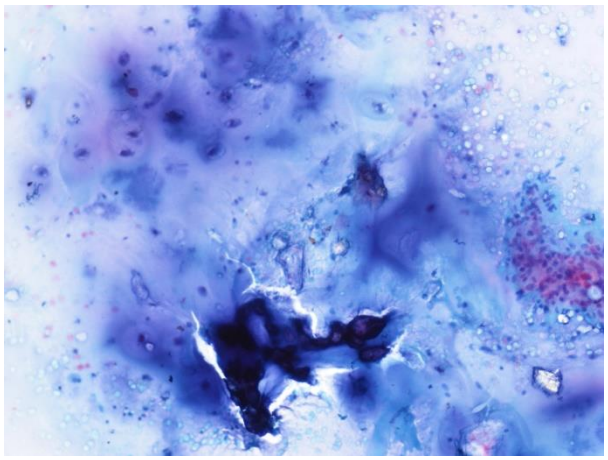

Fig. 5: Chondromyxoid fibroma- Smear shows fragments of chondrocytes with a cluster of spindle cells in a Chondromyxoid background. (H&E ×100)

Discussion

Although open biopsy is considered as gold standard for the diagnosis of bone tumors, it require the process of decalcification, thereby delaying diagnosis and treatment planning. FNAC is of great importance because the needle can reach deeper areas of skeleton that are otherwise accessible only by open operation and multiple specimens can be obtained without increased morbidity. Hence it is important to recognize FNAC as a bed side method for early diagnosis of bone tumors. Despite of advancement in imaging techniques with availability of modern diagnostic equipments like ultrasonography, computed tomography, magnetic resonance imaging and radioisotope scan, FNAC is still the ultimate diagnostic technique for evaluating bone tumors especially in underdeveloped countries. The radiological findings are of utmost importance in initial diagnosis of musculoskeletal tumors. The clinical and roentgenographic evidences together enable us to make a correct diagnosis in most of the cases. Because of diversity of giant cell lesions of bone, it is often not possible to reach at accurate diagnosis, however in majority of the cases we were able to reach at correct diagnosis after correlating cytological features with clinical and radiological findings. In India for the first time in 1983, Agarwal and Wahal evaluated the role of needle aspiration biopsy for diagnosis of primary tumors of bone and joints.[6]

In this study out of 27 cases of giant cell lesions of the bone, a final diagnosis of GCT of bone was rendered in 16 cases (59.2%). GCT as most common benign tumor of bone was also reported by Agarwal PK et al (80.64%), Sherwani et al (62.5%), Agarwal S et al (83.33%) and Pai et al (84%) in their study.[6,7,8,9] Agarwal PK et al correctly diagnosed 40 cases of GCT on cytology out of 45 adequate smears.[6] Khan et al diagnosed GCT in 11 cases out of 13 cases with reported sensitivity of 92.4% and specificity of 88.4%, while Nnodu et al reported 19 cases of GCT in their aspiration cytological study of bone tumors.[10,11] Aly AM et al diagnosed 5 cases of GCT of bone with histological confirmation in 4 cases.[12] Jain M et al diagnosed 4 cases of GCT at unusual sites by cytology.[13] In our study Tibia was the most common bone involved by GCT (8 cases) followed by femur (5 cases). Similarly the commonest involvement of Tibia (16cases) followed by femur (13 cases) was also reported by Aggarwal PK et al.[6] Pai et al (2002) reported lower end of radius (6 cases) and lower end of femur (5 cases) as most common site of GCT.[9] In all these studies clinical and radiological findings in conjunction with cytology played an important role in establishing the final diagnosis of GCT of bone. Majority of the patients were presented with swelling and pain of the affected part and radiologically showed expansile lytic lesion at epiphysis or epiphysio-metaphysis of long bones. Cytologically smears showed mononuclear spindle cells dispersed singly as well as present in clusters along with dispersed osteoclastic giant cells with typical presence of giant cells at the periphery of stromal cells in some cases.

In this study 5 cases of ABC was diagnosed cytologically with average age of 20.7 years and M:F ratio of 1.5:1. Agarwal PK et al also reported 4 cases of ABC diagnosed on cytology, while Aly Am et al diagnosed 3 cases of ABC on FNAC.[6,12] Khan et al and sherwani et al reported 1 case each of ABC in their study.[7,10] In all these cases typical X-ray finding in the form of expansile lytic lesion of bone in conjunction with presence of hemorrhagic fluid on FNAC and finding of giant cells, osteoblasts and hemosiderin laden macrophages on cytological smears leads to diagnosis of

ABC of bone. Fibrous dysplasia was diagnosed in 3 cases with mean age of 19.3 years and M:F ratio of 1.5:1. Sherwani et al also reported 3 cases of Fibrous dysplasia, while Nnodu et al reported 2 cases of Fibrous dysplasia on cytology with histopathological confirmation in one case.[7,11] X-ray finding of expansile lytic lesion in the diaphysis of long bone with pathological fracture and cytological finding of scattered osteoclastic giant cells, small clusters of osteoblasts along with clusters of spindle cells, few inflammatory cells and bony matrix leads to diagnosis of fibrous dysplasia in our study, which later on confirmed by histopathology. 3 cases of chondromyxoid fibroma was diagnosed with mean age group of 14.3 years and M:F ratio of 1:2. X-ray showed well defined, lytic lesion of the involved bone and cytologically smears showed large number of chondroid matrix along with chondroblasts and fragments of spindle shaped cells and few giant cells in a hemorrhagic background. Histopathology confirms the cytological diagnosis of chondromyxoid fibroma.

Conclusion

Although the literature regarding the cytological differentiation of various giant cell lesions of the bone on FNAC is limited but still we wish to recommend this method as initial tool for differentiation of various giant cell lesions especially in conjunction with clinical and radiological findings.

References

1. Mankin HJ, Lange TA, Spanier SS: The hazards of biopsy in patients with malignant primary bone and soft tissue tumors. J Bone Joint Surg Am 1982;64:1121-1127.
2. Simon MA: Current concept review-biopsy of musculoskeletal tumors. J Bone Joint Surg Am 1982;64:1253-1257.
3. EI Khoury GY, Terepka RH, Mickelson MR, Rainville KL, Zaleski MS: Fine needle aspiration biopsy of bone. J Bone Joint Surg 1983;65:522–525.
4. Pai MR, Coimbatore RV, Naik R, Lugade M: Role of Fine needle aspiration cytology in the diagnosis of bone tumors. J Cytol 2002;19:33–39.
5. Rosai J. 2005. Bone and joints. In Rosai and Ackerman's Surgical Pathology, 9th ed(vol 2). Mosby, Missouri, 2005: p2171.
6. Agarwal PK, Wahal KM: Cytopathologic study of primary tumors of bone and joints. Acta Cytol 1983;27:23–27.
7. Sherwani R, Akhtar K, Abrari A, Sherwani K, Goel S, Zaheer S: Fine needle aspiration cytology in the management of tumors and tumor like Lesions of Bone. JK Science 2006;8:151-156.
8. Agarwal S, Agarwal T, Agarwal R, Agarwal PK, Jain UK: Fine needle aspiration of bone tumors. Cancer Detect Prev 2000;24:602-609.
9. Pai MR, Coimbatore RV, Naik R, Lugade M: Role of Fine needle aspiration cytology in the diagnosis of bone tumors. J Cytol 2002;19:33–39.
10. Khan AR, Mir BA: FNAC- Giant cell tumor of bone a study of 13 cases (part III). J K Practitioner 2003;10:236-238.
11. Nnodu OE, Giwa SO, Samuel U Eyesan SU, Abdulkareem FB: Fine needle aspiration cytology of bone tumours- the experiencefrom the National Orthopaedic and Lagos University Teaching Hospitals, Lagos, Nigeria. CytoJournal 2006;3:16.
12. Aly AM, Shaaban HM, Abou-Sinna I: Accuracy of fine needle aspiration cytology in the diagnosis of bone lesions with radiological assistance: Experience from the National Cancer Institute, Cairo University, Egypt. The Egyptian Journal of Radiology and Nuclear Medicine 2014;45:127–135.
13. Jain M, Aiyer HM, Singh M, Narula M: Fine-needle aspiration diagnosis of giant cell tumour of bone presenting at unusual sites. Diagn Cytopathol. 2002;27:375-8.