

**ORIGINAL ARTICLE**

Fine Needle Aspiration Cytology in the Management of Tumors and Tumor like Lesions of Bone

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Abstract

FNAC should be considered as the part of routine preliminary investigation of orthopaedic patients presenting with musculoskeletal tumorous lesions. A total of 110 cases were screened cytologically in the background of clinical, radiological findings and biochemical tests. Primary malignant tumor formed the major entity accounting for 56% of the cases, while benign tumors comprised 8% only. Overall success rate of needle aspiration cytology in diagnosing tumors and tumor like lesions was 92%. Giant cell tumors of bone was the most common malignant lesion observed in 15 cases (30%), followed by Ewing's Sarcoma in 5 cases (10%). Cytologic diagnosis was completely compatible with the final histopathologic diagnosis in 82.3% of cases.

Key words

Fine Needle Aspiration Cytology, Benign and Malignant Bone Lesions.

Introduction

Aspiration cytology has proven in recent years to be a very convenient and reliable method for the rapid diagnosis of bone lesions(1). The usual mode of presentation in a neoplastic bone lesions is pain, altered function and a palpable mass, at times accompanied by pathological fracture. Initially a bone lesion is identified on the basis of history and radiological examination but often the clinician fails to pinpoint the diagnosis.

Application of techniques like high resolution bone scanning and CT-guided biopsy and cytology have extended the non-invasive techniques of approach in diagnosis; but in third world countries like ours, where such facilities are minimal and large proportion of patients belong to rural areas, aspiration cytology provides a simple, quick and easy method of diagnosis.

This study was carried out to evaluate the role of needle aspiration cytology as well as to correlate the cytological findings of aspirate smears with those of clinical, radiological, biochemical and histopathological parameters.

Material and Methods

One hundred and ten cases of bone lesions, attending the outpatients and inpatients wards of Orthopaedic Department of J.N. Medical College Hospital were included in the study. The cases were thoroughly interrogated, clinically examined and relevant investigations done. The most probable diagnosis in the first instance was based upon clinical and radiological findings. They were then subjected to needle aspiration biopsy.

With clinical and radiological background and by aspiration biopsy, 60 cases were diagnosed as inflammatory bone lesions while 50 cases were suspected as tumors and tumor like lesions of bone. These 50 cases were studied in detail clinically and radiologically. Routine blood and urine examination along with serological tests like serum acid and alkaline phosphatase, serum calcium and phosphorous were performed. Smears obtained by fine needle aspiration cytology with 18-22G needle were fixed in 95% ethyl alcohol for Papanicolaou and

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Haematoxylin & Eosin staining, and 80% methyl alcohol for May-Grunwald-Giemsa staining. Incisional and excisional biopsy specimens were fixed in 10% formal saline, cut into 2-3 mm thick sections, and decalcified in 3-5% nitric acid solution; paraffin embedded and finally stained with Haematoxylin & Eosin. Special stains like Van-Gieson, Reticulin and P.A.S. done whenever required.

Results

The total number of aspirations were carried out in 110 orthopaedic cases. 60 cases were inflammatory and 50 cases were tumors and tumor like lesions of bone, which included 4 cases of benign, 28 cases of primary malignant tumors, 11 cases of tumor like lesions and 7 cases of metastatic lesions in bone. The study included patients from 6 years to 80 years of age, majority were young adults. Incidence of neoplastic lesions was more common in second and third decades of life i.e. 32%. A male predominance was observed in both benign and malignant tumors, the ratio of male to female being 1.63: 1. It was observed that the maximum number of primary lesions (76%) were detected in the long bone of extremities; the femur, tibia, fibula and humerus being the most frequently affected sites. Metastatic lesions commonly affected the humerus and pelvic bones. The clinical diagnosis, relevant biochemical findings and radiological picture of lesions were taken into consideration prior to and during cytological interpretations. The cytological observations which led to conclusive diagnosis, and the cases which could be confirmed by histopathological examination are discussed below:

Osteochondroma : (Two cases) Male patients aged 11 years and 10 years presented with bony swelling of right scapula and left humerus of 1 year and 3 months duration respectively which on radiological examination showed sessile bony swellings. Aspiration cytology failed to provide adequate material for diagnosis. Tumor on excision showed a sessile growth. Histopathological examination revealed a center of mature lamellar bone covered by a cartilaginous cap and a thin layer of fibrous periosteum, with mononuclear and vacuolated chondrocytes. All these features together clinched the diagnosis of benign tumor, osteochondroma.

Chondroblastoma : (Two cases) 14 and 18 years females presented with pain and tenderness at medial

condyle right femur of 8 months duration with no past history of trauma. X-ray showed a small osteolytic lesions in medial condyle of femur in the first while the second showed metaphyseal extension. In the first case, clinicoradiological diagnosis was suggested as chondroblastoma, while in the other a bone cyst in the lower end of femur. Aspiration cytology material in the first case was inadequate for diagnosis, while the other case was diagnosed as giant cell containing lesion as osteoclasts type giant cells were seen in a haemorrhagic and inflammatory background. Histopathology revealed tumor composed of immature small chondrocytes, having single round to polygonal nuclei with scattered multinucleated giant cells and islands of chondroid matrix.

Osteogenic Sarcoma : (Four cases) All the patients in the age group of 15-25 years were consistent cytologically with the clinicoradiological diagnosis, who presented with pain and swelling since 4-6 months at the involved bony site. Two of the cases had a history of trauma to the right thigh and knee joint. Radiological examination revealed osteolytic lesions with irregular thickening of cortex at the junction of middle and upper 1/3rd of femur and soft tissue around it.

Smears on needle aspiration were highly cellular with large, pleomorphic cells and hyperchromatic nuclei with coarsely stippled chromatin and large nucleoli. 3 cases were labelled chondroblastic osteogenic sarcoma because of the presence of ring chondroblasts (immature type) with cartilage fragments; one of which showed presence of microfilaria (Fig-1). One case was diagnosed as small cell variant of osteogenic sarcoma on the basis on small round cells with hyperchromatic nuclei with giant cells and osteoid.

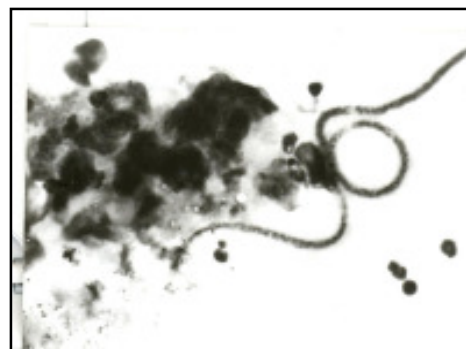


Fig-1: Osteosarcoma: Smear showing group of malignant cells with microfilaria. H & E stain x 500.



Chondrosarcoma : (Two cases) Males aged 70 years and 80 years were consistent cytologically with the clinico-radiological diagnosis. One patient presented with fungating swelling right upper thigh with purulent discharge and pathological fracture with inability to walk. Other patient presented with firm, non-tender swelling over the chest extending from manubrium sterni to the body of sternum.

Radiological examination in first case showed osteosclerotic growth at upper end of right femur with calcific mottling and pathological fracture of trochanter. Other case showed homogenous swelling arising from the manubrio-sternal joint.

Cytological examination revealed a small group of isolated stubby undifferentiated spindle cells of mesenchymal origin with few differentiated cartilage cells in the first case, which was designated as mesenchymal chondrosarcoma. Smears of other case showed enlarged bizarre mononuclear and binucleated cells with finely vacuolated cytoplasm, diagnosed as poorly differentiated chondrosarcoma.

Giant cell tumor : (Fifteen cases) Comprised maximum number of cases with pain or swelling or both with or without tenderness, cytologically consistent with clinical and radiological diagnosis. Majority of patients were in the 2nd and 3rd decade, with male to female ratio being 1.5 : 1.

Radiological findings were common in all, i.e. osteolytic lesions in the proximal or distal end of long bones of extremities. One of the cases showed osteolytic lesions in skull, femur and tibia of right side with X-ray chest showing radio-opaque shadows. Cortex of the affected site of bone was thinned out in majority of cases.

Needle aspiration and imprint smears showed small round to fusiform stromal cells, occasional binucleated cells and fair number of multinucleated giant cells with 15-100 nuclei. Excisional biopsy could be done in only six cases. Sections showed the presence of multinucleated giant cells and stroma with varying amount of vascularity.

Ewing's Sarcoma : (Five cases) three were females of age 6 years, 15 years and 28 years and 2 were males aged 14 year and 20 years. Four of them presented with painful swelling and one with fungating growth over ventral aspect of left forearm.

Radiological examination revealed osteolytic lesions in all with soft tissue extension in four cases. On cytology, monomorphous population of small cells with round to oval nuclei and scanty cytoplasm, in poorly cohesive clusters including rosette like structures were seen. Cytologically these cases were diagnosed as round cell sarcoma consistent with Ewing's sarcoma (Fig-2). All were advised radiotherapy and responded well.

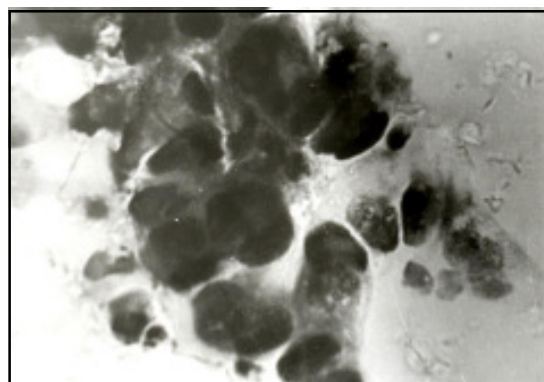


Fig-2: Ewing's Sarcoma: Smear showing large round cells arranged in rosette. H & E stain x 500.

Tumor Like Lesions

Fibrous Dysplasia : (Three cases) A 22 year male with swelling and pain lower end of right femur for 8 months duration, on radiology revealed multiloculated osteolytic lesion with pathological fracture. The other 2 cases were females aged 22 and 28 years with pain and swelling at upper end of left femur and around left ankle for approximately 1 year respectively. Two were clinically diagnosed as fibrous dysplasia and the third as giant cell tumor of lower end of tibia. Cytology was successful to give early morphological diagnosis of fibro-osseous lesion. Smears showed bits of fibrous tissue, small groups of spindle cells, calcified material and an occasional multinucleated giant cells.

Histopathology revealed characteristic features of fibrous dysplasia i.e. spindle celled fibrous tissue with osseous metaplasia.

Aneurysmal Bone Cyst : (One case) 10 year male with swelling and tenderness of proximal end of left humerus, with history of recurrent fractures following trivial injury was clinically diagnosed as simple bone cyst.

Radiological examination revealed characteristic expansile, eccentric, well-circumscribed zone of



rarefaction which appeared as a blow out lesion of bone. Cytological examination showed heavily blood stained smears with fusiform and round cells with few osteoclast giant cells and scattered osteoblasts.

Histopathology confirmed the diagnosis which grossly, showed multiloculated cavities filled with blood. On section, large blood filled spaces of various size, separated by fibrous tissue septae, containing few multinucleated giant cells, foci of osteoid and immature bones were seen.

Brown tumor of Hyperparathyroidism : (One Case) Male aged 22 years presented with tender swelling lower end of right forearm for 6 months. X-ray revealed a radiolucent cavity in lower end of right ulna with breach in medial cortex and clinically diagnosed as giant cell tumor.

Cytological smears showed numerous giant cells with lesser number of nuclei and sheets of oval, spindle shaped cells, diagnosed as giant cell containing lesion, but histopathology confirmed the diagnosis which showed cystic cavity lined by fibrous tissue and osteoclast giant cells with extensive patchy osteoblastic activity with biochemical tests of raised levels of serum calcium and alkaline phosphatase.

Metastatic Lesions : (Seven cases)

(i) **Metastatic Renal Cell Carcinoma** (One case) : A 60 year male with complete paraplegia for 6 months with a left clavicular swelling on X-ray showed pathological fracture of clavicle, collapse of T-7 vertebra and osteolytic lesions in parietal region of skull. On cytology large tumor cells with abundant pale vacuolated cytoplasm, eccentric nuclei and prominent nucleoli were seen, the case cytodiagnosed as metastatic renal cell carcinoma.

Metastatic Follicular Carcinoma Thyroid : (One case) A 52 year female with swelling and inability to move the right arm with a goitrous swelling in neck for last 16 years, on X-ray showed osteolytic lesions with pathological fracture of right humerus.

Aspiration smears from neck swelling showed evidence of follicular carcinoma. Smears from bony lesion showed small groups of tumor cells with anisonucleosis and prominent nucleoli with tendency to follicle formation. This case was diagnosed as metastatic carcinoma with follicular differentiation.

(ii) **Metastatic Bronchogenic Carcinoma** (One case). A 55 years male with hemoptysis, chronic cough with expectoration and swelling in supratrochanteric region which radiographically showed osteolytic lesion in iliac bone.

On aspiration biopsy, smears showed sheets of pleomorphic and hyperchromatic cells with well-defined cytoplasm and evidence of keratin. This case was diagnosed as metastatic squamous cell carcinoma. On further investigation of the patient, X-ray chest showed radio-opaque shadow on right lung. Thus a diagnosis of bronchogenic carcinoma with iliac bone metastasis was ascertained.

(iii) **Metastatic Adenocarcinoma** (Four cases) : Two males aged 60 and 65 years with swelling in right and left upper arms around 9 and 11 months duration with palpable liver in first case. X-ray showed pathological fracture with osteolytic lesions which on aspiration showed groups of hyperchromatic mucus secreting malignant cells with eccentric nuclei and diagnosed as metastatic adenocarcinoma. Source of primary tumor could not be identified in both the cases.

There were 2 cases of metastatic papillary adenocarcinoma. One was 50 years female with pain in left hip and upper thigh which revealed osteolytic lesions with pathological fracture right neck of femur radiographically. Skull X-ray also showed osteolytic lesion. Clinical diagnosis of multiple myeloma was made but urine was negative for Bence Jones protein. Another female aged 65 years with pain and swelling in lower third of right arm for 9 months duration showed osteolytic areas with fracture in lower third of right humerus, on X-ray.

Smears from both the cases showed malignant columnar cells with basally placed hyperchromatic nuclei arranged in papillary structures, and diagnosed as metastatic papillary adenocarcinoma.

Out of the total 50 neoplastic cases, cytological examination proved to be successful with adequate material for diagnosis in 46 cases i.e., 92%; while in 4 cases inadequate material and inconclusive smears were the reasons of failure. Cytological examination was successful in giving a definite diagnosis in 82.3% of cases (Table-1). Most of primary malignant tumors exhibited 100% overall diagnostic accuracy (Table-2).



Table-1

Cyto-histological correlation in major groups of neoplastic cases

Final diagnosis	Total No. of Cases	Compatible (%)	Partially Compatible (%)	Incompatible (%)
Benign tumor	01	-	1 (100)	-
Malignant tumors	07	6 (85.8)	1 (14.2)	-
Tumor like lesion	09	8 (88.8)	-	1 (11.2)
Total	17	14 (82.3)	2 (11.7)	1 (5.8)

Table-2

No. of positive aspirations with clinico-cytological and Cyto-histological correlation

Final diagnosis	Total No. of Cases	Positive Cytology	Cytohistologically Consistent	Clinicohistologically Consistent	Diagnostic Accuracy (%)
Osteochondroma	2	-	-	-	-
Chondroblastoma	2	1	1	-	50
Osteosarcoma	4	4	-	4	100
Chondrosarcoma	2	2	-	2	100
Ewing's Sarcoma	5	5	-	5	100
Giant cell tumor	15	15	6	9	100
Brown tumor of hyperparathyroidism	1	1	1	-	100
Fibrous dysplasia	3	3	2	1	100
Aneurysmal bone cyst	1	1	1	-	100
Metastatic tumor	7	7	-	7	100

Discussion

Tumors of bone are difficult to diagnose because of their rarity and unsurpassed ability to present in disguise. Hence these should be diagnosed with caution by a skilled pathologist taking the help of combined clinical and radiological investigations. Therefore in the present study great care has been taken to give the cytodiagnosis of bone lesions after gathering thorough information about the clinical and radiological features.

El Khoury *et al.* (1) suggested that needle aspiration biopsy can be used as a substitute for open surgical biopsy, but at the same time they pointed out that cytodiagnosis of malignant bone tumors was a real challenge, required

experience and should not be regarded as a substitute for histological examination.

In the present study 50 cases of tumors and tumor like lesions of bone were included, of which 4 were benign, 28 primary malignant tumor, 7 metastatic tumors and 11 cases were of tumor like lesions. Primary malignant lesion formed the commonest group of neoplasms, accounted 56% while benign lesions were only 8% while metastatic lesions were observed in 14% and tumor like lesions in 22% of the cases. Others workers like Ayala *et al.* (2) and Xiojing *et al.* (3) have reported a little higher incidence of primary tumors i.e. 64% and 76% respectively.

The overall success rate in obtaining sufficient material for diagnosis was 92% in our study, which is similar to 93% as reported by Murray *et al.* (4). The failure rate was only 8% in our work, which is comparable to findings to Coley *et al.* (5) of 9.31%.

The cytodiagnostic accuracy in primary bone tumors was 90.7% in the present study which is comparable to the work of De Santos *et al.* of 83.5% (6). The diagnostic accuracy in the metastatic lesions was 100% in our study which is exactly the same as reported by Mittal *et al.* (7).

Only 4 cases of benign tumors, i.e., 2 cases each of osteochondroma and chondroblastoma were recorded. The provisional diagnosis in osteochondroma was made radiologically and confirmed histologically. Aspiration failed to provide any material but it was positive in one of the two cases of chondroblastoma. Histopathologically both were diagnosed as chondroblastoma. The failure rate of aspiration cytology was mainly due to the fact that tumor was hard and fibrous and safely guarded by thick cortex, leading to difficulty in piercing the needle.

All the four cases of osteogenic sarcoma diagnosed provisionally, belonged to the classical age group of 15-25 years. Out of these one showed the presence of microfilaria along with sheets of malignant cells. The diagnostic accuracy was 100% which was in conformity with finding of Layfield *et al.* (8), who also reported 100% accuracy in 9 cases studied by them.



Two cases of chondrosarcoma provisionally diagnosed clinico-radiologically showed characteristic cytological findings; similar to as observed by Hajdu *et al.* (9).

Giant cell tumor of bone constituted the maximum number of cases i.e. 15. These were clinico-radiologically suggested as giant cell tumor, but cytologically 13 could be confirmed as G.C.T. while two of these after histology were diagnosed as fibro-osseous lesions.

All the 5 cases of Ewing's Sarcoma involved the long bones, with no classical radiological findings, but the cytodiagnosis of round cell sarcoma consistent with Ewing's sarcoma was made. The cytodiagnostic accuracy of 100% was in conformity with Ayala *et al.* (2).

Among the eleven cases of tumor like lesions of bone, the case of hyperparathyroid osteodystrophy was suggested on the basis of increased serum calcium and alkaline phosphatase and presence of giant cells cytologically. The presence of red blood cells with a few giant cells was suggestive of aneurysmal bone cyst, which was confirmed on histopathology. The three cases of fibrous dysplasia were cytodiagnosed correctly as fibro-osseous lesion, later confirmed as fibrous dysplasia on histopathology.

The seven cases of metastatic lesions belonged to the 5th, 6th and 7th decades of life. All could be diagnosed correctly. Cytological findings were characteristic, therefore cytodiagnostic accuracy was 100%, same as reported by Mittal *et al.* (7).

Out of the 46 cytologically positive cases, only 17 cases were subjected to histopathological examination. A cytohistological correlative study showed complete compatibility in 85.8% of primary malignant tumor and 88.8% in tumor and tumor like lesions of bone. The overall diagnostic accuracy was found to be 93% which is comparable to findings of Murphy *et al.* (10) who reported diagnostic accuracy of 94% each.

FNAC can be useful in the preoperative assessment of bone tumors especially where other diagnostic modalities are unavailable. The accuracy of specific cytological diagnosis (87.8%) and incorrect in (12.2%) has been reported by Nnodu *et al.* (11) in accordance to

our study. FNAC has also emerged as a cost effective tool for initial diagnosis for both neoplastic and non-neoplastic lesions of the bone (12).

Conclusion

Fine needle aspiration cytology can no more be regarded as screening procedure but it can play a pivotal role in the surgical decision making, as a rapid, easy, cost effective and non-traumatic maneuver which can be carried out as an outpatient department procedure. But it never can be substituted for histopathological examination of such cases where cytodiagnosis is debatable.

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