ORIGINAL ARTICLE

Percutaneous Needle Biopsy-An Assertive Tool In The Diagnosis of Bone Tumors in Under Developed Countries

S Mahboob Hasan, Shamshad Ahmad, Kafil Akhtar, Jaseem Hasan,
Mazhar Abbas*, Ibne Ahmad**

Abstract

Our study on 106 cases of bone tumors aims at correlating the clinical, radiological and cytological findings of benign and malignant tumors of bone and evaluating the usefulness of percutaneous biopsy as a diagnostic tool in underdeveloped countries. Giant cell lesions were the most common benign tumor, 42 cases (84%) and giant cell tumor was the most common giant cell lesion in our study, 27 (64.3%). Round cell tumor appeared to be the most common malignant tumor of bone, 20 cases (35.7%). Osteosarcoma represented 15 cases (14.2%) of all bone tumors and 26.8% of all malignant bone tumors in our study. Final histopathological diagnosis was available only in 54 cases. Out of which 53 cases showed concordance with previous cytological diagnosis. Only a single case of chondrosarcoma was misdiagnosed as chondroma on FNAC (false negative). The sensitivity and specificity of FNAC was 96.0% and 100% respectively while positive predictive value and negative predictive values were 100% and 96.7% respectively. The diagnostic accuracy in our study was 98.1%.

Key Words

Percutaneous Needle Biopsy, Bone Tumors, FNAC, Under-Developed Countries

Introduction

The treatment of tumors has become so highly specialized that oncologists now insist on a definite diagnosis of the type of tumor before initiating therapy. In this regard aspiration biopsy is considered to be a simple, safe and reliable technique and it's possible to reach an accurate diagnosis for most patients within 24 hours (1). Fine needle aspiration biopsy helps to diagnose not only primary lesions but can also has used to confirm recurrences or metastases from distant sites (2).Despite the increased availability of sophisticated methods of evaluation such as computerized tomography, magnetic resonance imaging, ultrasonography and scanning with radioisotopes, percutaneous needle biopsy especially in the form of fine needle aspiration remains the ultimate diagnostic technique for evaluating neoplasms in under developed countries like ours. Our study aims at correlating the clinical, radiological and cytological findings of benign and malignant tumors of bone and evaluating the usefulness of percutaneous biopsy as a diagnostic tool.

Material and Methods

The present prospective study was conducted on 106 cases of bone tumors attending the inpatients and outpatients departments of Orthopaedics and Pathology at Jawaharlal Medical College Hospital, AMU, Aligarh. With the help of radiographs, the superficial and deeply located lesions were localized and aspirated with 20-22G needle. Most of the aspirations were done blindly without any radiological guidance, but computed tomographic guidance was utilized for most of vertebral lesions. Smears were fixed in 95% ethyl alcohol and stained by Haematoxylin and Eosin and Papanicolaou stains. Special stains and immunostains were employed wherever necessary.

Results

Out of 106 cases, 50 were benign and 56 malignant. Age of the cases ranged from 1½ years to 75 years. The maximum number of both benign tumors (20) and malignant tumors (22) belonged to the second decade of life. Giant cell lesions were the most common benign tumor, 42 cases (84%). Most of the giant cell lesions, 29 cases (69%) were seen between 11-30 years. Round cell tumor, 20 cases (35.7%) constituted the commonest malignant bone tumor, followed by osteosarcoma and metastatic tumors, 15 cases (14.2%) each. 15 cases (75%) of all round cell tumors occurred between 0-20

From the Deptt. of Pathology, *Orthopaedic & **Radiodiagnosis, JNMC, Aligarh Muslim University, Aligarh -UP India
Correspondence to : Dr. Kafil Akhtar, Lecturer, Department of Pathology, Jawaharlal Nehru Medical College, Aligarh Muslim University, Aligarh -UP

years age group and 9 cases (60%) of osteosarcoma occurred in the second decade of life. Maximum number of metastatic lesions, 8 cases (53.3%) occurred in the 41-60 years age group.

Male to female ratio of 1.9: 1. Tibia was the most frequently involved site of bone tumors (26 cases), followed by femur (22 cases) and humerus (11 cases). Vertebrae were involved in 7 cases while multiple bones were affected in 6 cases. Giant cell tumor was the most common giant cell lesion in our study, 27 (64.3%), with a male preponderance (M: F ratio = 1.5: 1). Tibia was the most commonly affected bone (13 cases), followed by femur (7 cases). Sixteen out of the 27 cases provided a final histopathological diagnosis, whereas in rest of the cases, the diagnosis was made after correlating clinical, radiological and cytological findings where smears showed mononuclear spindle cells in sheets as well as singly, along with many large osteoclastic giant cells having 20-40 uniform nuclei without any atypia.

Cystic lesions constituted 7 cases; where cytology revealed haemorrhagic smears with cystic macrophages, few multi-nucleated giant cells and osteoblasts. Histopathology was performed in 5 cases; when a diagnosis of aneurysmal bone cyst was confirmed. There were 4 cases of fibrous dysplasia;with final histopathological diagnosis was possible in 3 cases where sections showed narrow curved bony trabeculae interspersed with fibrous tissue of variable cellularity.

Chondromyxoid fibroma constituted 4 cases with a female preponderance. Osteochondroma constituted 5 cases; with humerus being the most common bone involved. Histopathological examination was done in 4 cases where sections showed thick cartilaginous cap without atypia and underlying bony trabeculae. Two cases of chondroma was diagnosed on FNA; one in a 40-year old male involving the first metatarsal and other in iliac blade of a 22 year old female. Round cell tumor appeared to be the most common malignant tumor of bone, 20 cases (35.7%). The most common involved bone was tibia (4 cases), followed by femur and calcaneum (3 cases each), fibula and pelvic bone (2 cases each). One case each occurred in the radius, rib, great toe, sacrum and calvarium. Out of 20 cases of round cell tumors, 17 were diagnosed as Ewing's sarcoma. FNA smears showed clusters of monomorphic cells with round to oval basophilic nucleus, opened up chromatin, scanty cytoplasm with cytoplasmic vacuolations. Pseudorosette formation were seen at places (*Fig 1*). Out of 17 cases, final histopathological diagnosis was available in 5 cases, where sections showed sheets of small round tumor cells separated by fibrocollagenous stroma.There were 3 cases of small round cell tumor diagnosed cytologically, and were kept under differential diagnosis of Ewing's Sarcoma and Primitive neuroectodermal tumor (PNET) on histopathology. The bones involved were tibia, calcaneum and ribs (1 case each); Cytohistological findings showed dissociate pattern of small round cells with increased nucleocytoplasmic ratio, finely granular chromatin and cytoplasmic blebs with interspersed spindle cells. Immunohistochemistry confirmed the diagnosis of PNET with positivity of tumor cells for vimentin (*Fig 2*) synaptophysin and S-100 but Leucocyte Common Antigen (LCA) was negative.

Osteosarcoma represented 15 cases (14.2%) of all bone tumors and 26.8% of all malignant bone tumors in our study. Femur was affected in 6 cases, tibia in 4 cases and fibula in 5 cases. There were 3 cases of chondrosarcoma; with 1 case each in humerus, metatarsal and ulna have been observed. Histopathological evaluation was done in all the 3 cases. A single case diagnoased cytologically as chondroma was confirmed as chondrosarcoma, with histological sections revealing variably sized lobules of irregularly distributed chondrocytes with plump and enlarged nucleus separated by thin fibrous septae and permeating the soft tissue.There were 2 cases of plasma cell myeloma, with lesions in skull bone and vertebra. A single case of lymphoma with lesion at L4 and L5 vertebra was encountered in a 22 year old female. MRI showed destructive pathology involving L4 and L5 vertebra with compression of thecal sac and the nerve roots. Cytologically hemorrhagic aspirate showed varied lymphoid population of cells; few with atypical features. Histopathologically sections showed sheets and cords of cells with round to oval nuclei and indistinct cytoplasmic outline. Tumor cells were negative for PAS stain, but were immunoreactive for LCA.There were 15 cases (14.2%) of metastatic bone tumors; with femur being the commonest bone involved 8 cases, followed by humerus 3 cases, vertebrae 2 cases and sternum and pelvic bone, 1 case each. Primary sites were detected in 13 cases but in 2 cases primary sites remained unknown.

In 6 cases, lung appeared to be the primary site. In all the cases, X-rays, ultrasonographic and CT findings along with aspiration of primary site confirmed the diagnosis. Out of the 6 cases, histopathological findings were present in 2 cases; with one case each of adenocarcinoma and squamous cell carcinoma. CECT thorax showed a soft tissue mass in the right upper lobe.Two male patients aged 75 years and 50 years developed lesions involving the sternum and pelvic bone respectively; with fine needle aspiration from the former from both kidney and sternum showed morphology of renal cell carcinoma, with isolated sheets of polygonal tumor cells with abundant vacuolated

Table I. Correlation of Clinical, Radiological and Cytological Diagnosis of Bone Tumors

Lesions	No. of cases	Clinical diagnosis	Radiological diagnosis	Cytological diagnosis
Giant cell lesion	42	37	40	42
Round cell tumor	20	16	19	20
Osteosarcoma	15	12	12	15
Osteochondroma	05	05	05	03
Chondrosarcoma	03	02	02	02
Chondroma	02	02	02	02
Plasma cell myeloma	02	02	02	02
Lymphoma	01	01	01	01
Metastatic lesions	15	15	15	15

Table 2. Correlation Between Cytological and Histological Diagnosis

Lesions	**FNAC**	**Histopathology**	**Histopathology**		
			Concordant	**Discordant**	**Not available**
Giant cell lesion	42	25	25	-	17
Round cell tumor	20	08	08	-	12
Osteosarcoma	15	09	09	-	06
Osteochondroma	05	04	04	-	01
Chondrosarcoma	03	03	02	01	-
Chondroma	02	01	01	-	01
Chondromyxoid fibroma	04	01	01	-	03
Lymphoma	01	01	01	-	-
Metastatic lesions	15	03	03	-	12

Fig 1. Ewing's Sarcoma: Smear Shows Large Pale Cells With Vacuolated Cytoplasm & Small Dark cells with Scanty Cytoplasm with Rosette Formation (H & E x 400)

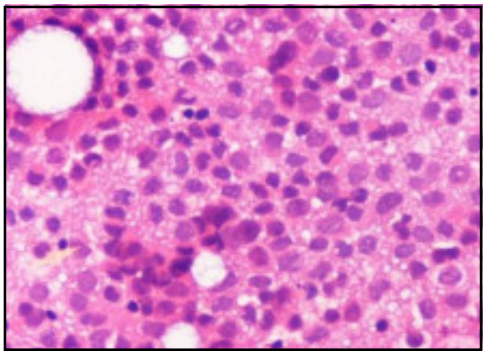
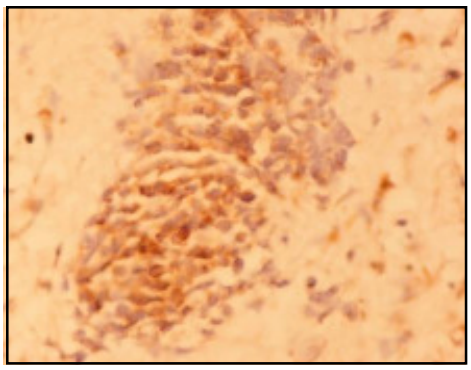


Fig 2. PNET: Tumor Cells Show Positivity for Vimentin (Immunostain-Vimentin x 400)



cytoplasm and nucleoli in some nuclei. In the latter case, USG findings were suggestive of left sided renal cell carcinoma with metastasis around left iliac blade.

There was a single case of a 30 year old female of papillary carcinoma of thyroid who presented upper femur showed lytic, expansile metaphyseal lesion of femur with pathological fracture of neck of femur. Cytologically hemorrhagic smears showed aggregates of epithelial cells with nuclear overlapping, uniformly enlarged round to oval nuclei with intranuclear inclusion in few cells. A 55 year old lady with lump in the left breast presented pathological fracture of the neck of femur was detected. FNA smears from fracture sites showed occasional small clusters of partially degenerated cells and few atypical cells. Histologically, section showed sheets of tumor cells with round to oval hyperchromatic, pleomorphic nuclei bearing prominent nucleoli with areas of necrosis and confirmed the diagnosis of carcinoma breast. In three cases cytological diagnosis of metastatic adenocarcinoma was made with pain at the involved site of first lumber vertebrae, femur and humerus. Primary site was not detected in 2 cases; both males, aged 30 years and 75 years, who had lytic lesions in multiple bones and cytological smears in both cases showed malignant cell population which were not native to the bone. Out of 42 cases of giant cell lesions diagnosed by cytology, concurrent clinical and radiological diagnosis was present in 37 and 40 cases respectively. Two cases of aggressive giant cell tumor were diagnosed as osteosarcoma both clinically and radiologically.

Twelve cases of osteosarcoma were diagnosed accurately after correlation of clinical, radiological and cytological findings. One case each of giant cell rich osteosarcoma, chondroblastic osteosarcoma and periosteal osteosarcoma was diagnosed as giant cell tumor, chondrosarcoma and osteoid osteoma respectively both clinically and radiologically (*Table I*). In one case round cell tumor was diagnosed as osteosarcoma both on clinical and radiological background while in another case a diagnosis of tubercular osteomyelitis was made on clinical background. In two other cases round cell tumor was diagnosed as soft tissue tumor (fibrosarcoma and liposarcoma) clinically. Out of 3 cases of chondrosarcoma, a single case was diagnosed as osteosarcoma both clinically and radiologically.Out of 106 cases of bone tumors diagnosed by FNAC, final histopathological diagnosis was available only in 54 cases. Of these 54 cases, 53 cases showed concordance with previous cytological diagnosis. Only a single case of chondrosarcoma was misdiagnosed as chondroma on FNAC (false negative) (*Table 2*).The sensitivity and specificity of FNAC was 96.0% and 100% respectively while positive predictive value and negative predictive values were 100% and 96.7% respectively. The diagnostic accuracy in our study was 98.1%.

Discussion

Out of 106 cases of bone tumors, 47.2% cases were benign and 52.8% were malignant. The patients were aged between 1½ years and 75 years with majority of the cases, 39.6% in the 2nd decade of life. Agarwal S *et al* (3) and Sherwani *et al* (4) have reported age incidences of 1 - 74 years and 6 - 80 years respectively in their studies. The maximum number of both benign (40%) and primary malignant tumor (53.6%) occurred in the 2nd decade while most of the metastatic tumors (53.3%) occurred in the 5th and 6th decades. Quite similarly Agarwal S *et al* (3) have reported occurrence of majority of metastatic tumors in 5th and 6th decades of life. Males out numbered females with a ratio of 1.9: 1 with the exception of osteochondroma and chondromyxoid fibroma; a finding consistent with reports of Pai *et al* (5) . But a female predominance was reported by El Khoury *et al* (1).Tibia appeared to be the most common site for primary bone tumors, 26 cases, followed by femur, 18 cases and humerus 8 cases. Overall long bones of extremities were most common site for bone tumors. Kreichbergs A *et al* (6) and Agarwal PK *et al* (7) have also reported same site of involvement. In our study giant cell tumor appeared to be the most common bone tumor, 25.5% cases; a finding consistent with that reported by Pai *et al* (5). The most common site of involvement was upper end of tibia, 13 cases and lower end of femur, 7 cases; with the remaining cases seen in miscellaneous bones. But Pai *et al* (5) reported lower end of radius, 6 cases and lower end of femur, 5 cases as the most common site of giant cell tumor. Out of 27 cases, final histopathological diagnosis was available in 16 cases all of which showed concordance with previous FNA diagnosis, suggesting 100% diagnostic accuracy of FNAC in diagnosing giant cell tumor (GCT); a finding consistent with that reported by Kumar *et al* (8). In rest 11 cases where histopathological evaluation was not done, the diagnosis of GCT was made after correlating clinical, radiological and cytological findings. Seven cases of cystic lesions were observed by us, all of which yielded haemorhagic smears; with occasional cyst macrophages and osteoblasts, thus a diagnosis consistent with cystic bone lesion was made after clinical and radiological correlation. Ayala and Zornosa (9) also faced similar problems with cystic lesions.Osteosarcoma represented 15 cases (14.2%) of all bone tumors in our study which was consistent with the findings of Pai *et al* (5) 14.5%; but was slightly greater than those observed by Sherwani *et al* (4), who reported 8% incidence of osteosarcoma.

Metaphyseal region of femur was the most common affected site of osteosarcoma, a finding similar to that observed by Sherwani *et al* (4). We studied 15 cases of osteosarcoma where cytology revealed pleomorphic and occasional bizarre looking cells with amorphous eosinophilic osteoid like material in 11 cases. 3 cases of chondroblastic osteosarcoma and a single case of giant cell rich osteosarcoma was also observed. Out of 15 cases, histopathological evaluation was done in 9 cases and all showed concordance with previous cytological diagnosis, thus a diagnostic accuracy of 100% was obtained; a finding consistent with Xiaonjing *et al* (10) who reported accuracy of 92.3% and 100 respectively. But our findings were better than figures of 85.7% and 84.6% as reported by Pai *et al* (5). Round cell tumor was the second most common bone tumor, represented 18.9% of all tumors; a finding consistent with Agarwal and Wahal (11), who reported 15.9% cases. Small round cell tumors of bone comprise a histologic group of lesions including Ewing's sarcoma, myeloma, lymphoma and metastatic lesions from neuroblastoma, rhabdomyosarcoma and retinoblastom (12). The treatment varies significantly for various round cell tumors, so it's a real challenge to the diagnostic skill of cytopathologist to correctly diagnose these tumors by FNA cytology. Although it is possible to reach to a correct diagnosis after clinico-radiological and cytopathological correlation, in many cases diagnosis also requires immunohistochemistry, cytogenetics and electron microscopy. In our study 3 cases were diagnosed as PNET after immunohistochemical examination which showed positivity for vimentin, synaptophysin and S-100 but, were negative for LCA. Ewings Sarcoma accounted for 16.0% of all tumors; a finding consistent with Nanda *et al* (13), who reported 18.1% and 12.6% cases respectively in their study. Out of 20 cases of round cell tumors, histopathological evaluation was done in 8 cases, and all these cases showed concordance with the cytological diagnosis.

Chondrosarcoma accounted for 3 cases, 2.8% of all bone tumors in our study. The typical location of chordoma in the sacrococcygeal and spheno-occipital region is essential for differentiation from chondrosarcoma. Though cytological features of chordoma and chondrosarcoma may overlap, but presence of physaliferous cells is characteristics. Histopathological evaluation was done in all the 3 cases of chondrosarcoma with cytohistological concordance seen in 2 cases only. In the third case, a cytological diagnosis of chondroma was made, which turned out to be chondrosarcoma on histopathological evalution. This was the only false negative case in our study. Nanda *et al* (13) have reported similar findings in their study probably due to scanty material obtained by aspiration because of hardness of cartilaginous tumors. In our study metastatic tumor accounted for 14.2% of all bone tumors. Most common primary site for metastatic bone lesions were carcinoma lung 6 cases, followed by metastatic adenocarcinoma from GIT, 3 cases, renal cell carcinoma 2 cases, and 1 case each of carcinoma thyroid and breast. Mondal and Ray (2) in their study reported most common primary site as follicular carcinoma thyroid followed by breast and lung whereas Sherwani *et al* (4) reported adenocarcinoma as the most common metastatic lesion in the bone. We obtained diagnostic accuracy of 98.1%, sensitivity, specificity; positive and negative predictive value as 96.0%, 100%, 100% and 96.7% respectively; a finding consistent with Agarwal PK *et al* (7)

Conclusion

Diagnostic methods like immunostains combined with increased clinical expertise and FNA cytology could reduce the need for open biopsy of bone tumors, without jeopardizing the diagnostic accuracy.

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