International Journal of Pathology; 2005; 3(2): 57-64

Spectrum of Bone Lesions Diagnosed on Fine Needle Aspiration Cytology

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Objective: The objective of this study was to determine the spectrum and morphological features of various bone pathologies as observed on fine needle aspiration cytology.
Study Design: It was a descriptive study.
Setting: Pathology Department of Pakistan Institute of Medical Sciences, Islamabad.
Duration: The study was carried out from 01.04.04 to 31.03.05.
Subjects: The total number of cases was 50, selected through convenience non-probability sampling.
Methods: The data was entered in the proforma. A criterion was set for examining each slide, which included cellularity of the smear, pattern (if any), cell type, cellular atypia, background and salient microscopic features. Cellularity was graded as 0, +, ++, +++. Patterns included discohesive cells, clusters and sheets, mixed and others. Cells were typed as mesenchymal, epithelial, inflammatory, fibrohistiocytic, neuroectodermal and others. Atypia graded as nil, mild, moderate and marked while the background was labeled as clear, amorphous, chondromyxoid and hemorrhagic. Cytomorphologically, 7 groups of bone pathologies were identified. All the data was analyzed using computer software SPSS version 10 and descriptive statistics applied.
Results: There were 66% males and 34% females in our study. The most frequent age group was between 0-10 years. The most frequent group of bone pathologies in our study was inflammatory (32%), followed by fibrohistiocytic and synovial group (22%), primary malignant osseous tumors (18%), metastatic (12%), plasma cell dyscrasias (8%), primary benign tumors of bone (6%), and miscellaneous group (2%).
Conclusion: Our study of 50 cases of pathological osseous lesions carried out in Pathology Department of Pakistan Institute of Medical Sciences proves that FNAC is very useful diagnostic technique which can easily replace the need for biopsy.
Key words: Bone, Lesions, Spectrum, Fine needle aspiration cytology.

Introduction

FNAC has distinct advantages over open biopsy as it is safe, simple, highly economical and relatively painless procedure which can be performed in office, at bed side and in out patient department. It provides reasonably accurate pre-op diagnosis in vast majority of cases.[1]

Bone, like any organ system of the body, can be afflicted with a number of generalized and localized pathologies. Any workup of a bony lesion should begin with proper history, physical examination and a good set of plain films. The biopsy should be the final staging procedure. FNAC though widely applied in the diagnosis of tumors in almost all other sites, has been slow to gain popularity in diagnosis of bone tumors. This is largely due to the impression that it is difficult

or impossible to obtain diagnostic material from bone lesions with a fine needle. However, the pathological lesions such as inflammation, cysts, neoplasia, haemorrhage and malformations usually soften the bone permitting easy penetration of the bone by the needle. Cytologic assessment with clinical and radiographic findings, together with the experience of cytopathologist can yield almost the same diagnostic accuracy as histopathology of subsequent open biopsies in majority of lesions[2]. Also FNAC material can be sent for other studies i.e. immunohistochemistry, electron microscopy, cytogenetics, microbiological analysis etc. as and when required. Easy retrieval of diagnostic material for successful cytomorphologic and microbiologic assessment makes FNAC the procedure of choice in diagnosis of bony lesions.[3]

Objective:

The objective of this study was to determine the spectrum and morphological features of various bone pathologies as observed on fine needle aspiration cytology.

Materials and Methods

This study was carried out at the Pathology department of Pakistan Institute of Medical Sciences, Islamabad from 01.04.04 to 31.03.05. It was a descriptive study. The total number of cases included in this study was 50 and they were selected through convenience non- probability sampling. Patients of both sexes and all age groups, suffering from either localized or generalized bony lesions and in whom plain radiographs were done were selected. Patients in whom history was not available and those with traumatic fractures were excluded from the study.

In all the cases FNAC was performed using either a 23 or 24 gauge needle. A minimum of 3 passes was made per patient. The material was checked for adequacy by asking the patients to wait for a little while. Slides were stained. In cases of

inadequacy, more passes were made. The smears were fixed in alcohol and slides stained with eosin and hematoxylin.

The slides were viewed under light microscope. A criterion was set for examining each slide, which included cellularity of the smear, pattern (if any), cell type, cellular atypia, background and salient microscopic features.

Cellularity of the smears was graded into 4 groups depending on the number of cell clusters i.e. 0 if not even a single cell cluster was seen, (+) if 1-6 clusters were present, (++) if 7-10 clusters were present and (+++) if more than 10 clusters were present.

The patterns included scattered/discohesive cells, clusters and sheets, mixed (including both discohesive cells and clusters and sheets) and others (papillae, cords, glands etc). The cells were typed as mesenchymal, epithelial, inflammatory, fibrohistiocytic, neuroectodermal and others.

Atypia was evaluated on the basis of hypercellularity of the smear, overlapping, loss of polarity, aniso and poikilocytosis, hyperchromasia, prominent nucleoli, nuclear membrane breaks, chromatin pattern, high N/C ratio, mitosis and necrosis. We graded atypia into nil, mild, moderate and marked (Table. 1) based on standard criteria for dysplasias, well recognized in various tissues.[4, 5, 6, 7]

Table 1: Criterion of Grading Cellular Atypia

Morphological Features	Mild Atypia	Moderate Atypia	Marked Atypia
• N/C ratio.	• High with nucleus occupying less than half the area of the cell.	• High. Nucleus occupies between one half to two third of the total size of the cell.	• N/C ratio very high with the nucleus occupying at least two-thirds of the total area of the cell.
• Nuclear hyperchromasia.	• Present.	• Present.	• Present.
• Chromatin pattern.	• Abnormal	• Abnormal, > than in mild atypia.	• Abnormal, > than in moderate atypia.
• Nuclear membrane.	• Irregular.	• Irregular.	• Irregular with grooves and indentations.
• Multinucleation.	• May be seen.	• Multiple abnormal nuclei.	• Multiple abnormal nuclei.
• Cytoplasm.	• Reduced.	• Reduced.	• Reduced.
• Nucleoli.	• Absent or inconspicuous.	• Absent or inconspicuous.	• Absent or present.
• Others.			• Bizarre forms.

Background was labeled as clear, amorphous, chondromyxoid and hemorrhagic.

On the basis of cytomorphology the bone lesions were divided into 7 groups. These included (I) fibrohistiocytic and synovial group, (II) inflammatory (osteomyelitis), (III) primary benign tumors, (IV) primary malignant tumors of bone, (V) plasma cell dyscrasias, (VI) metastatic tumors and (VII) miscellaneous lesions. The trainee and the supervisor made the final diagnosis after correlating FNAC findings with radiography. All the slides were

reassessed later. All the data was entered into SPSS version 10.0. Descriptive statistics, that is mean, range and standard deviation were applied to numerical data like age while frequencies were calculated for categorical data like clinical features, cellularity of smears, patterns of smears, cellular atypia, background of smears, groups of bone pathologies as well as individual bony lesions. The data was presented as tables and graphs including pie and bar graphs.

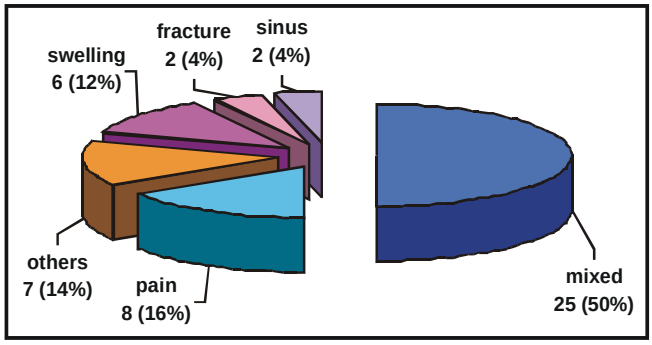
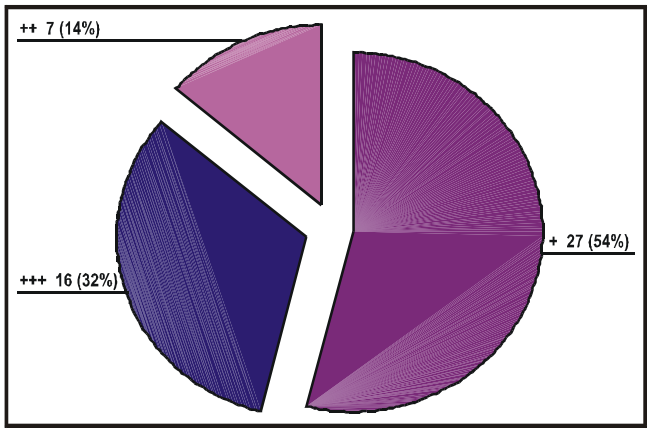


Fig. 1: Graphical Presentation of Various Clinical Features



+ -------- 1-6 Clusters
++ ------- 7-10 Clusters
+++ ------ > 10 Clusters

Fig. 2: Frequencies of Cellularity of Smears

Results

There were 50 patients in this study. There were 33 (66%) males and 17 (34 %) females. Age ranged from 5 months to 70 years, mean was 25.090 years and Standard Deviation was 21.802. The most frequent age group (18 patients, 36%) was 0-10 years, followed by 11-20 years (12 patients, 24%). The most frequent clinical presentation was mixed that included both pain and swelling that is in 25 (50%) patients (Figure: 1). Figure: 2 shows that 27 (54%) smears had (+) cellularity, i.e.; 1-6 clusters. 07 (14%) had (++) cellularity, i.e.; 7-10 clusters and 16 (32%) had (+++) cellularity, i.e.; more than 10 clusters. The

Table 2: Patterns of Smears

	Frequency	Percent
Discohesive/scattered	18	36.0
Clusters/sheets	12	24.0
Mixed	16	32.0
Others	4	8.0
Total	50	100.0

Table 3: Frequencies of Cellular Atypia

	Frequency	Percent
Nil	30	60.0
*Mild	1	2.0
*Moderate	12	24.0
*Marked	7	14.0
Total	50	100.0

- *Please refer to Table 1 for the criterion / key used to grade cellular atypia.*

paucicellular smears were mostly encountered in sclerotic bony lesions.

The patterns were variable and ranged from scattered, discohesive cells to clusters, sheets, papillae, cords, glands and even mixed patterns. The various patterns and their frequencies are shown in Table: 2.

The cells were typed as mesenchymal, epithelial, inflammatory, fibrohistiocytic, neuroectodermal and others. 16 (32%) smears had predominantly inflammatory cells, 11 (22%) smears had mesenchymal cells, 10 (20%) had fibrohistiocytic cells, 4 (8%) had plasma cells, 4 (8%) had epithelial cells, 3 (6%) showed neuroectodermal cells, 1(2%) had physaliferous cells and 1 (2%) showed synovial cells.

Atypia, where present was graded as nil, mild, moderate and marked on the basis of criteria already discussed in material and methods. Table: 3 show frequencies of smears on the basis of cell atypia.

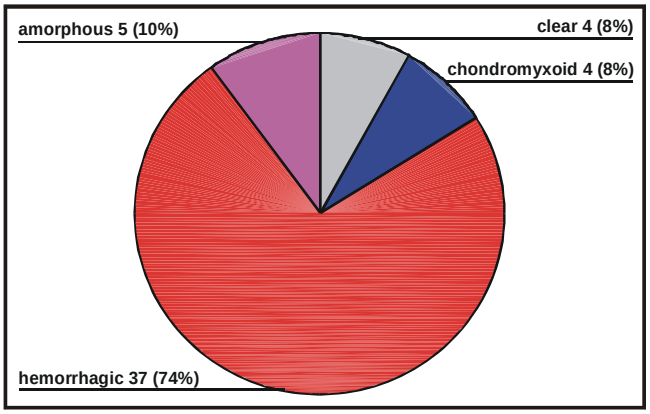


Fig. 3: Frequencies of Background of Smears

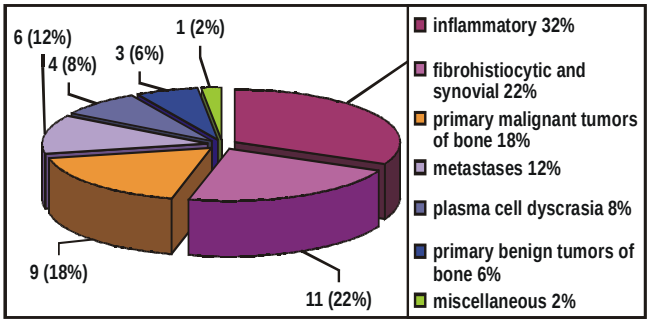


Fig. 4: Frequencies of Various Groups of Bone

Pathologies

In most of the cases i.e. 37 the background was hemorrhagic. 5 had amorphous, 4 had chondromyxoid and 4 had clear background. (Figure: 3)

On the basis of cytomorphology, the various bone lesions were divided into 7 groups: I- Fibrohistiocytic and Synovial, II- Inflammatory (Osteomyelitis), III- Primary benign tumors, IV- Primary malignant osseous tumors, V-Plasma cell dyscrasias, VI- Metastatic and VII- Miscellaneous. Group I included 11 cases, group II, 16 cases, group III, 3 cases, group IV, 9 cases, group V, 4 cases, group VI, 6 cases and group VII, 1 case. Their distribution is further elaborated by Figure: 4. The individual diagnoses are given in Table. 4.

Discussion

In our study of 50 cases, the various bone pathologies were seen. (Table. 4)

Nanda et al[8] in their study on 55 malignant bone tumors, found that there were 12 (22%) cases of metastatic tumor, 12 (22%) of giant cell tumor, 10 (18%) of Ewing's sarcoma, 7(13%) of osteosarcoma, 7 (13%) of multiple myeloma, 3 (5%) of chordoma, 3 (5%) of chondrosarcoma, and 1 (2%) of fibrosarcoma. Wedin et al[9] in their study on 110 cases of unknown skeletal lesions found 80 (73%) cases of metastatic carcinoma, 16 (14%) cases of multiple myeloma and 14 (13%) cases of lymphoma. The higher incidence of metastatic carcinoma in their series is due to their selection bias as most authors feel that FNAC's primary utilization is in metastatic carcinomas. In another study carried out by Agarwal et al [10] on 226 cases of bone tumors, 136 were malignant and 72 benign. In remaining 18 cases, cytohistopathologic examination revealed no bony lesion. GCT (32%) and Ewing's sarcoma were the most common tumors in this series. In another study by Mondal et al[11], CT-guided FNAC of 112 cases of vertebral lesions revealed 61 cases of metastatic tumor, 24 of tuberculosis, 6 plasmacytomas, 6 giant cell lesions, 3 eosinophilic granulomas 3 chordomas, 2 ewing's sarcomas, 2 Hodgkin's disease, 1 chondrosarcoma and 4 cases with no definite diagnosis.

Fibrohistiocytic and Synovial group was characterized by highly variable manifestation of marked potential of differentiation of fibrohistiocytic and synovial cells in various directions. In our study, this group comprised of 11 cases: 4 aneurysmal bone cysts, 3 simple bone cysts, 3 giant cell tumors, and

one markedly reactive synovial cell hyperplasia. The

Table 4: Frequencies of Various Bone Pathologies as Diagnosed on FNAC

	Frequency	Percent
Acute suppurative osteomyelitis	2	4.0
Chondrosarcoma	1	2.0
Chronic granulomatous inflammation suggestive of tuberculosis	5	10.0
Chronic osteomyelitis	9	18.0
Consistent with aneurysmal bone cyst	4	8.0
Chordoma	1	2.0
Enchondroma	1	2.0
Giant cell tumor	3	6.0
Metastatic rhabdomyosarcoma	1	2.0
Multiple myeloma	2	4.0
Osteosarcoma	5	10.0
Plasmacytoma	2	4.0
Simple bone cyst	3	6.0
Reactive synovial cell hyperplasia	1	2.0
Metastatic anaplastic carcinoma of thyroid	1	2.0
Metastatic adenocarcinoma	1	2.0
Metastatic papillary carcinoma of thyroid	1	2.0
Metastatic papillary transitional cell carcinoma, high grade type	1	2.0
Metastatic pleomorphic sarcoma	1	2.0
Osteoid osteoma	1	2.0
Primitive neuroectodermal tumor of infancy (melanotic prognoma)	1	2.0
Ewing's sarcoma	2	4.0
Chondromyxoid fibroma	1	2.0
Total	50	100.0

smears from simple and aneurysmal bone cysts revealed clusters of fibroblasts, hemosiderin-laden macrophages, foci of osteoid and thin capillaries with entrapped RBCS. Background was hemorrhagic. Our observations were consistent with the reported findings.[12] In Giant cell tumors (GCT) double cell

population of mononucleated tumor cells and multinucleated giant cells (osteoclasts) was seen.

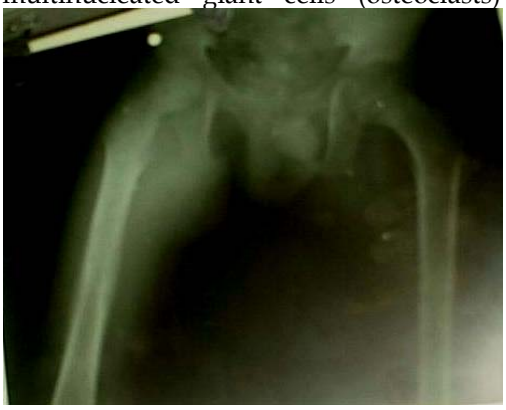


Fig. 5 A: X-ray Pelvis: Mottled Lucencies with Wide Zone of Transition at Metadiaphysis of Right Femur

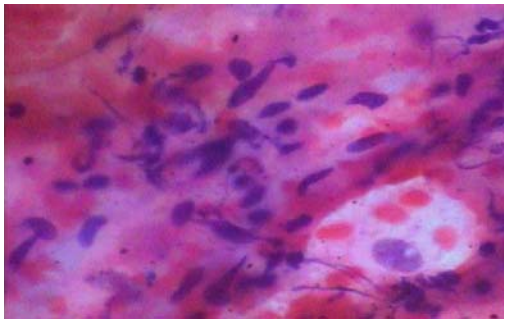
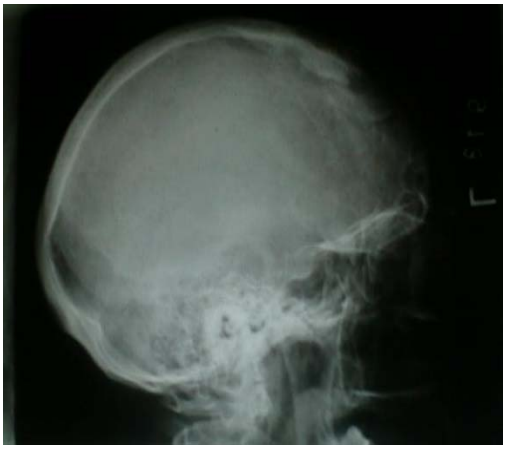


Fig. 5 B: Chronic Granulomatous Inflammation Suggestive of Tuberculosis. Showing Few Epitheloid Cells. H & E (x 400).



Sneige et al.[13], had sensitivity of 83.3% and specificity of 100% in GCT.

Fig. 6 A: X-ray Skull (Lateral View): Lytic Lesion in Left Frontal Region with Complete Destruction of Inner and Outer Tables

Osteomyelitis was seen in 9 cases, 5 of chronic granulomatous inflammation suggestive of tuberculosis and 2 of acute suppurative osteomyelitis. Several authors[3] have emphasized upon the use of FNAC in the diagnosis of tuberculosis of bone. FNAC material obtained could be sent for microbiological assessment. We frequently encounter neutrophils, sometimes numerous, in early and recurrent tuberculosis. In such cases a high index of suspicion and careful examination of all the slides is mandatory
for the diagnosis.

Primary Benign Tumors of Bone had paucicellular smears; diagnosis was still possible on the basis of cytomorphology and radiographic picture. In case of chondromyxoid fibroma the diagnosis was made on the basis of plump looking chondrocytes and a slightly chondromyxoid background.

Primary Malignant Tumors of Bone included 5 cases of osteosarcoma, 2 of ewing's sarcoma, 1 of chondrosarcoma and 1 of chordoma. Nanda et al[8] in their study on 55 malignant tumors found 7 osteosarcomas, 3 chondrosarcomas, 10 ewing's sarcoma, 3 chordoma and 1 fibrosarcoma. In another study[14] (n=140), FNAC accurately subtyped various sarcomas as skeletal osteosarcomas, pediatric small blue cell tumors, synovial sarcoma and skeletal chondrosarcoma.

White et al[15] concluded that with well-preserved cellular aspirates cytologic criteria can identify the sarcoma cells and if the clinicoradiological data is also compatible with osteosarcoma, the atypical cells can be classified as consistent with osteosarcoma. However, if the clinicoradiological data is not typical of osteosarcoma, the cytologic examination can still establish the presence of malignancy and suggest a differential diagnosis. Both White et al [15] and Walaas et al. [16] in their studies found a significant limitation of FNA being the inability of the procedure to accurately and reliably establish the presence of osteoid. The probable explanation for this limitation is that dense nature of osteoid resist the suction created during aspiration and that when osteoid is aspirated, the small disrupted fragments lack the characteristic lattice-work architecture recognized in histologic section. White et al.[15] in their study identified osteoid in only 16 out of 51 aspirates. However, they have recommended that if osseous matrix is noted on radiograph and clinical history is compatible with osteosarcoma, a diagnosis of sarcoma consistent with osteosarcoma still maybe rendered.

In our study, demonstrable osteoid matrix was seen in only 2 out of 5 cases of osteosarcoma. White et al.[15] have concluded that FNAC is useful in the diagnosis of osteosarcoma except the lesions having predominantly thick, dense, osteoblastic stroma yielding paucicellular smears. In our study, however, adequate material for diagnosis was obtained in all 5 cases of osteosarcoma as we did not encounter osteosarcoma with heavily osteoblastic component.

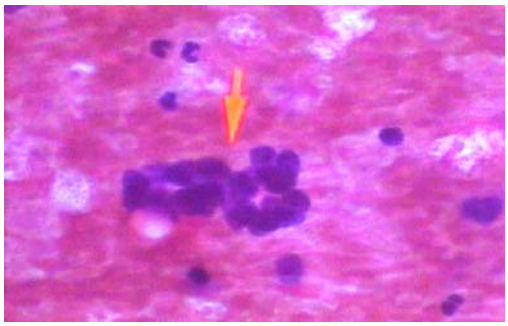


Fig. 6 B: Metastatic Adenocarcinoma. Showing Gland Formation (Arrow). H & E (x 400)

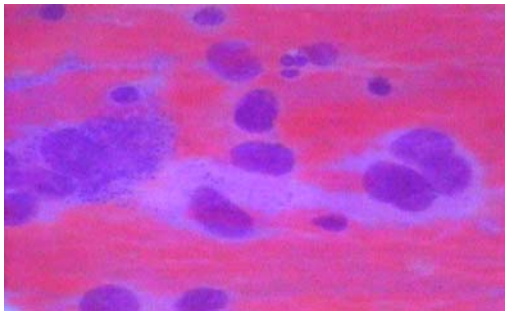


Fig. 7: Chondrosarcoma. Showing Polygonal Cells having Pleomorphic, Hyperchromatic Nuclei in a Chondromyxoid Background.

H & E (x 1000).

Soderlund et al [17], in a retrospective study of 52 cases were able to correctly diagnose 32/33 cases of typical osteosarcoma and 6/19 cases of atypical osteosarcoma, cytologically. They have concluded from their study that open biopsy can be obviated in typical high-grade osteosarcoma.

According to Koh JS[18] and Rangdaeng S [19], FNAC has a limited role in the diagnosis of chondroid neoplasms especially in cases where the clinicoradiologic data is atypical. FNA, with immunohistochemistry can distinguish chondrosarcoma from other chondromyxoid tumors like chordomas and metastases of mucous producing carcinomas. Kabukcuoglu et al[2] in their study of 38 bone lesions that were malignant clinicoradiologically, had the greatest diagnostic difficulty in differentiating chondrosarcoma from other chondroid tumors.

There were 2 cases of Ewing's sarcoma in our study. In a series of 71 cases of Ewing's sarcoma Mondal[20] et al found the diagnostic accuracy of FNAC to be 100%.

In our series of 50 cases there was 1 case of chordoma. Waalas et al[21] in their study of 17 cases concluded that a preoperative diagnosis of chordoma could be reached by FNAC provided the findings are carefully evaluated in relation to clinical and roentgenographic findings.

In our study there were 2 cases of multiple myeloma and 2 of plasmacytoma. Nanda [8] and Wedin[9] in their studies found the frequencies of multiple myeloma as 30% (n=110) and 14% (n=55) respectively. Soderlund et al.[22] in their study of 40 cases of multiple myeloma and 43 cases of lymphoma had a conclusive diagnosis in all myeloma cases and in 41/43 lymphoma cases using fine needle aspiration cytology. In vast majority of patients with lytic bone lesions there is already a diffuse infiltration of the marrow by plasma cells. FNA of the osteolytic lesions may thus obviate the need of bone marrow biopsy in at least a proportion of the cases.

In our study there were 6 cases of metastatic bone disease. In studies carried out by Nanda [8] and Wedin[9], metastatic lesions were the most frequent.

We had a case of melanotic prognoma (primitive neuroectodermal tumor of infancy) presented in a 6 months old child as swelling of maxilla since birth. The smears were hypercellular showing two types of cells: first were small round cells having round uniform nuclei and second were larger cells having moderate amount of eosinophilic cytoplasm with abundant melanin pigment and uniform looking nuclei.

Conclusion

Our study of 50 cases of pathological osseous lesions carried out in Pathology Department of Pakistan Institute of Medical Sciences proves that FNAC is very useful diagnostic technique which can easily replace the need for biopsy.

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