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Integrated Approach to Diagnosis of Bone Lesions: Study Utilizing Fine Needle Aspiration Cytology, Radiology, and Histopathology in Central India.

Chanchalesh Dahariya[1], Nancy Mourya[2], Prakriti Raj Patel[3], Puja Singh[4*], Sonali Tripathi[5]

[1] Assistant Professor, Pathology, Chhindwara Institute of Medical Sciences, Chhindwara, M.P., India
[2] Assistant Professor, Pathology, Bundelkhand Medical College, Sagar, M.P., India
[3] Senior Resident, Pathology, Bundelkhand Medical College, Sagar, M.P., India
[4] Associate Professor, Pathology, Bundelkhand Medical College, Sagar, M.P., India
[5] Assistant Professor, Anaesthesia, Chhindwara Institute of Medical Sciences, Chhindwara, M.P., India
[*] Corresponding Author

Background

Bone lesions are usually diagnosed late as the manifestation of the disease is considered generalized discomfort. To impart swift treatment diagnosing the entity rapidly is a must and foremost. This can be done by using needle aspiration. The histopathological examination requires bone to be put in preservatives which can make the bone malleable for further examination. The procedure itself requires at least a week's time. The prolonged waiting for the report is traumatic for the patient, leading to delayed treatment initiation. The present study focuses on using fine needle aspiration cytology as the diagnostic tool for evaluating bone lesions along with radiological examination. The finding is then matched with the pathological diagnosis as histopathology is the gold standard. The PPV is 77.8%, Sensitivity is 87.5%, Specificity is 75.0%, NPV is 85.7% and Overall Accuracy is 81.3%.

A total of 92 cases were identified by the orthopedics department for a period of 3 years. The findings were identical to the other studies and so we can say that FNAC can be used as a tool for fast and easy diagnosis of bone lesions.

Introduction

Improvement in health care today typically comes with the drawback of increased time and cost due to the greater complexity of the evolved procedures and/or the need for highly trained personnel to maintain and run high-priced equipment. Consequently, it comes as a pleasant surprise that fine needle aspiration is the antithesis of this trend and because of its ease of operation, it is a do-anywhere procedure. An aspiration can be performed during a routine doctor's office or clinic visit or at the patient's bedside [1]. It utilizes inexpensive equipment and can typically be performed, interpreted, and reported in a matter of minutes thereby accelerating a patient's entry into treatment.

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The diagnosis of osteoarticular lesions is based on clinical examination, roentgenographic examination, and laboratory investigations which include pathological, bacteriological, chemical, and histochemical tests [2]. Most protocols for the staging of primary malignant bone tumors require an accurate histological diagnosis. The open biopsy is almost a major surgical procedure in deep-seated lesions, such as bone. Besides this, surgical exploration has its other drawbacks, such as violation of tissue compartments, placing of a biopsy incision in an area that may interfere with the planning of subsequent surgery, risk of general or spinal anesthesia, the necessity of hospitalization, and course the cost involved in it [3].

Aims and Objectives

1. To find the accuracy of localized bone FNAC in relation to the final diagnosis made by histopathology and other diagnostic modalities.
2. To study diagnostic cytological criteria of different bone lesions.
3. To study immediate and long-term complications of FNAC procedure in patients with bone lesions.

Material and Methods

The present study is carried out after getting clearance from the institutional ethical committee. A total of 92 cases were identified from the files of inpatients of the orthopedics department. The study is a retrospective descriptive type. Preliminary information about age, sex, clinical features site of the lesion, and the radiological impression was collected. Cyto-diagnosis on light microscopy was embarked upon, all the smears were meticulously interpreted by two experienced cytopathologists.

The category of clinical-radiological presentation, along with cytological findings, confirms the nature of lesions by cytohistologic correlation. The data was collected in an MS-excel sheet and SPSS (23) was used.

The following statistical calculations were performed - Positive predictive value, negative predictive value, True positive, false positive, true negative, false negative, sensitivity, specificity, and accuracy. True-Positive: Histologically and cytologically malignant cases. True-Negative: Histologically and cytologically benign. False-Positive: Cytologically malignant, histologically benign. False-Negative: Cytologically benign, histologically malignant.

Results

The study included a retrospective evaluation of localized bone lesion FNAC and its correlation with other diagnostic methods i.e. clinical, radiological, and histological. In all the

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cases (n=92) patients with skeletal lesions were referred from the Department of Orthopaedics. FNAC was done after a clinical and radiological evaluation of the case. Out of these the needle or open biopsy for histological examination was done in a total of 20 patients. Table 1 represents the distribution of bone lesions based on Age and Sex. Based on the total diagnostic assessment there were 18 Non-neoplastic bone lesions [NNBL] cases, 29 Primary Benign Bone Tumors [PBBT] cases, 28 Primary Malignant Bone Tumors [PMBT], 6 Secondary Tumours of Bone [STB], and 11 Unsatisfactory cases. Table 2 presents the lesion distribution based on the site. We got 14 inconclusive aspirates in the present series due to inadequate diagnostic material. Out of these, the biopsy was done for 4 cases. Table 3 presents the correlation between Radiological, Cytological, and Histological findings. Figure 1 shows Chondromyxoid fibroma shows chondroid fragment fibroblast-like spindle cells in a benign myxoid background. Figure 2 is an X-ray showing the onion peel appearance. Figure 3 represents Ewing's sarcoma featuring small round malignant cells having scanty cytoplasm and irregular nuclei with dense chromatin, forming a rosette at few places.

Table 1: Distribution of bone lesions based on Age and Sex

Diagnosis	**NNBL (18)**		**PBBT (29)**		**PMBT (28)**		**SBT (6)**		**Unsatisfactory Smear (11)**		**Total N=92**
Age/Sex	M	F	M	F	M	F	M	F	M	F	**Percentage**
0-10	1	-	-	1	2	3	1	-	-	-	8 (8.7 %)
11-20	5	1	4	1	8	4	2	-	1	2	28 (30.4 %)
21-30	1	-	5	1	4	2	1	-	-	2	16 (17.4 %)
31-40	5	-	5	4	-	1	-	-	-	1	16 (17.4 %)
41-50	-	1	3	1	1	-	1	-	1	1	9 (9.8 %)
51-60	2	-	1	3	-	1	-	-	-	2	9 (9.8 %)
61-70	-	2	-	-	-	2	-	1	-	1	6 (6.5 %)
Total (%)	14	4	18	11	15	13	5	1	2	9	**92 (100 %)**
	18 (19.6 %)		**29 (31.5 %)**		**28 (30.4 %)**		**6 (6.5 %)**		**11 (12.0 %)**		

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Table 2: Distribution of bone lesions based on the Site

Type of Bone	Type of bone lesion					Total n (%)
Long Bone (62)	**NNBL (18)**	**PBBT (29)**	**PMBT (28)**	**STB (6)**	**US (11)**	
Femur (28)	4	10	9	2	3	**62 (67.4 %)**
Tibia (14)	2	4	4	2	2	
Humerus (13)	6	2	4	1	-	
Radius (6)	2	1	2	-	1	
Fibula (1)	-	-	1	-	-	
Flat Bone (17)						
Ileum (9)	-	3	4	-	2	**17 (18.5 %)**
Spine (4)	2	-	1	-	1	
Mandible (2)	-	1	-	1	-	
Ribs (1)	-	-	1	-	-	
Clavicle (1)	-	1	-	-	-	
Short Bone (13)						
Metacarpal (9)	2	5	1	-	1	**13 (14.1 %)**
Metatarsal (4)	-	2	1	-	1	

Sensitivity: (True Positive / (True Positive + False Negative)) x 100

= (7/8) x 100 = 87.5%

Specificity: (True Negative/ (True Negative + False Negative)) x 100

= (6/8) x 100 = 75.0%

Positive Predictive Value: (True Positive / (True Positive + False Positive)) x 100

= (7/9) x 100 = 77.8%

Negative Predictive Value: (False Positive/ (False Positive + True Negative)) x 100

= (6/7) x 100 = 85.7%

Accuracy: ((True Positive + False Negative) / Total number of cases) x 100

= (13/16) x 100 = 81.3%.

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Table 3: Correlation between Radiological, Cytological and Histological findings

Radiological Diagnosis	Cytological Diagnosis	Histological Diagnosis
Ewing's sarcoma (6)	Ewing's Sarcoma (6)	Ewing's Sarcoma (5)
		SCC (1)
Osteogenic sarcoma (2) GCT (2)	Osteogenic Sarcoma (2)	Osteogenic Sarcoma (1)
		GCT (1)
GCT	GCT (2)	GCT (2)
Aneurysmal bone cyst (2)	Ameloblastoma (2)	Ameloblastoma (1)
		Alveolar rhabdomyosarcoma (1)
Osteomyelitis (1)	Osteochondroma (1)	Osteochondroma (1)
Chondroblastoma (1)	Chondroblastoma (1)	Chondroblastoma (1)
Aneurysmal bone cyst (1)	Aneurysmal bone cyst (1)	Aneurysmal bone cyst (1)
Osteomyelitis	Metastasis of epithelial malignancy (1)	Papillary Digital Adenocarcinoma (1)
Bone Cyst (1)	Unsatisfactory Smear (4)	Osteogenic Sarcoma (1)
		Metastasis of renal cell carcinoma (1)
		GCT (1)
		Unsatisfactory Smear (1)

Figure 1: Chondromyxoid fibroma shows chondroid fragment fibroblast-like spindle cells in a benign myxoid background. Pap stain (100 X).

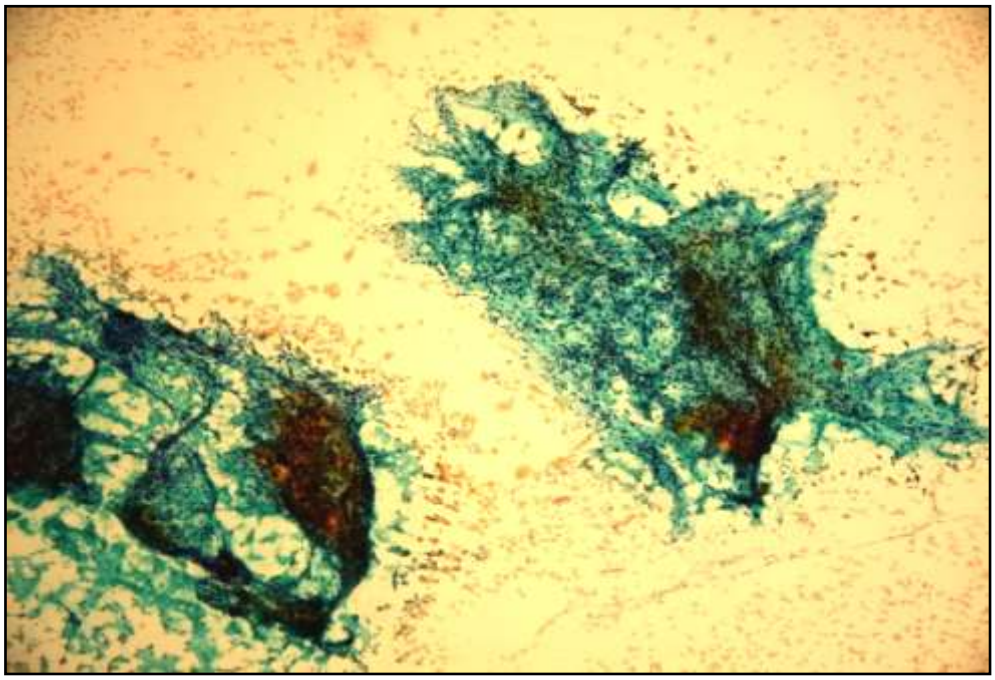

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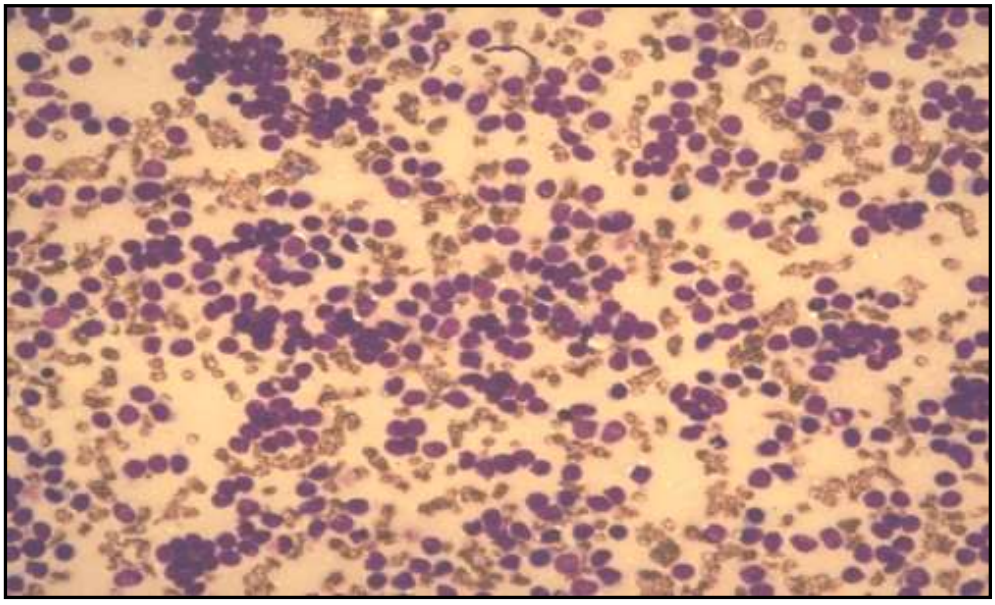
Figure 2: X-ray shows onion peel appearance

Figure 3: Ewing's sarcoma featuring small round malignant cells having scanty cytoplasm and irregular nuclei with a dense chromatin, forming rosette at few places. Geimsa stain (400 X)



Discussion

The diagnosis of bone lesions can benefit greatly from the use of FNAC (Fine-needle aspiration cytology). Numerous bone lesions, such as primary bone tumors, metastatic bone tumors, and non-neoplastic bone lesions, can be diagnosed and staged with the aid of FNAC [4].

In the late 1920s and 1930s, they demonstrated the utility of needle aspiration in the diagnosis of a large number of cases and detailed the procedure, which mirrors in large part the technique still used today. The procedure could not gain popularity at that time, due to unsubstantiated beliefs, that the acquisition of a small amount of tissue would result in difficult/less than complete interpretations and that puncturing a tumor with needles would carry a significant danger of tumor tract seeding and induction of metastatic disease [5].

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There are reports documenting the overwhelming efficacy and accuracy of this technique in the diagnosis of tumors at different body sites. The rate of inadequacy is in agreement with many other authors. Ruhs SA. et al. [6] have also demonstrated one case of inconclusive aspirate on cytology turning into metastasis of renal cell carcinoma on histopathology.

In the study by Gopal S. [7] there were 57 males and 39 females with a male-to-female ratio of 1.5:1. The male preponderance has been observed by other workers also such as Handa U. [8] (1.25:1), Aly AM. et al. [9] who recorded 22 males and 16 females with a male-to-female ratio of (1.3:1), Jorda et al. [10] found a male-to-female ratio of (1.1:1).

In the present study, maximum lesions were found in long bones (67.4%) followed by flat bones (18.5%) and then short bones (14.1%). Gopal S. [7] (64.7% cases in long bones and 35.3% cases in short bones), Aly AM. et al. [9] (64.9% cases in long bones and 35.1% cases in flat bones), Bodhireddy DS. [11] (85.7% cases in long bones and 14.3% cases in flat and short bones together), Kumar RV. [12] (65.1% cases in long bones and 34.9% cases in flat bones), Nnodu et al [13] (94.2% cases in long bones and only 4.3% cases in flat bones). In the present study, the femur was the commonest site 28/62 (45.2%) followed by the tibia 14/62 (22.6%) and humerus 13/62 (21.0%) in close succession. In the present study, FNAC of localized bone lesions revealed Non-neoplastic bone lesions (NNBL) in 19.6% of cases. Primary Benign Bone Tumours (PBBT) in 30.4% of cases, Primary Malignant Bone Tumours (PMBT) in 31.5% of cases, and Secondary Tumours of bone (STB) in 3.3% of cases.

The finding of the failure rates of Kumar RV. [12] (18.18% cases), Boomer KK. [14] (17.4% cases), and Yu GH. [15] (10.9% cases) are high. In the present study, less number of failed FNAC may be due to the fact that most of the FNACs were performed by the cytopathologists themselves. Most of the failed cases were having osteosclerotic and fibro-osseous lesions radiologically which may be the cause of dry taps and hemorrhagic inconclusive smears. Many authors have the opinion that FNAC has a limited role in diagnosing these types of sclerotic lesions [13]. However, it proves that an experienced aspirator (preferably the cytopathologist, as in our series), with correct aspiration technique and proper radiological valuation to locate the most appropriate site for needle entry may minimize the chances of inadequate material being aspirated.

In the category of non-neoplastic bone lesions, the maximum (9/18, 50.0%) cases were of chronic osteomyelitis, more or less similar to the findings of Jorda. et al. [10] (13/22, 59.1%),

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Boomer KK. et al. [14] (7/13, 53.8%), El-Khoury et al. [16] (6/26, 23.0%), and Kumar RV. [12] 38.8%.

In Primary benign bone lesions, the commonest group was Giant cell tumors comprising 13 out of 29 (44.8%) cases. This finding is also in agreement with Jorda et al. [10] (14/26, 53.8%), Boomer KK. et al. [14] (14/21, 66.7%), and Kumar RV. [12] (5/17, 24.9%).

The extremely low incidence of metastatic bone tumors in the present study, as compared to many other reports may be explained by two related facts. One is that the spinal lesions which are a common site for bone metastasis were mostly not examined in this series and secondly, any bony lesion with diagnosed malignancy of other body parts is usually considered as secondary metastasis and hence was not referred for cytological evaluation.

The clinical diagnosis in the non-neoplastic category was more or less accurate in the present study. However, in neoplastic lesions, the diagnosis was missed in 5/18 (27.8%) cases on clinical examination. Only a few studies correlated cytological diagnosis with clinical impression. Aly AM. et al. [9] got 84% and Bodhireddy DS. [11] got 67.0% of the cases consistent with clinical and radiographic findings.

In Non-neoplastic bone lesions, the correlation between all three parameters i.e. clinical, radiological, and cytological was 100%. Histological diagnosis was rarely asked in this group. Only one case was biopsied and there was an agreement between cytology and histopathology. The findings are again well correlated with other such studies like Ruhs SA. et al. [6] (97%), Handa U. [8] (99%), and Jorda et al. [10] (95%).

In Primary Benign Bone Tumours, the compliance between radiological, and cytological parameters were present in 26/28 (92.8%) of cases. In this group biopsy findings were available in 5 cases and cyto-histo agreement was obtained in 4 cases.

In Primary Malignant Bone Lesions, the correlation between radiological, cytological, and histological parameters was present in 27/29 (93.1%) of cases, well in agreement with Handa U. [8] (89%), Aly AM. et al. [9] (88.7%), Kumar RV. [12] (89.8%), Jorda et al. [10] (77%), Boomer KK. et al. [14] (83.5%) and Vangala N. et al. [16] (55%),

A total of 20 cases were identified in the present study where all three parameters radiology, cytology, and histopathology findings were present. We agree with the opinion of Handa U. [8], and Boomer KK. et al. [14] and Yu GH. [15] that for getting high diagnostic accuracy

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from cytology smears, it is essential to have a radiological opinion and the efficacy of the diagnosis by FNAC increases after cytological and radiological correlation.

Conclusions

Overall, the role of FNAC in bone lesions is to provide a rapid and accurate diagnosis, guide treatment decisions, and improve patient outcomes. However, recent advances such as genetic studies, flow cytometry, and artificial intelligence can be of great help in the coming future.

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