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Correlation of cytological and histopathological findings in bone lesions: A cross-sectional study

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Abstract

Introduction: Bone lesions represent a diverse group of pathological conditions, including developmental, reactive, infectious, benign, and malignant processes. The age-adjusted incidence rate for all bone and joint cancers is 0.9 per 100,000 persons annually. Globally, the incidence of bone lesions varies based on factors such as geographical location, age, and gender distribution. The aim of the study was to study the sensitivity, specificity, positive predictive value, and negative predictive value of FNAC in bone lesions, comparison of cytological findings to histopathological findings; and identify the accuracy of FNAC in bone lesions.

Material and methods: The study was carried out at a tertiary care centre department of pathology Rohilkhand medical college for the duration of 1 year. A total of 52 bone lesions were analysed. Bone biopsy and FNAC was performed after detailed clinical and radiological examination. The aspirates were air dried, stained by the Leishman Giemsa stain method and examined microscopically. Histology was performed on patients who had subsequent surgical biopsy. These were then correlated with the cytology reports.

Result: Mean age affected was 33 years. Male-female ratio was 1.7:1. Out of total 52 cases of bone tumors and tumor like lesions, maximum was osteogenic tumors followed by chondrogenic tumour. Osteosarcoma (08) and giant cell tumour(10), were the most common primary malignant bone tumour & primary benign bone tumor respectively. The most common bone affected was femur (14; 27.0%), followed by tibia (10; 19.2%).

Sensitivity and specificity of FNAC as a diagnostic modality were 85.71% and 95.83% respectively. The positive predictive value was 96% and the negative predictive value was 85.19%. Cohen kappa value of 0.81 was obtained in this study which showed substantial agreement between the cytological and histopathological impression.

Conclusion: FNAC plays a very crucial role in diagnosing and early intervention and treating any ailment. Bone FNAC also is beneficial for identifying the treatment modality. It should be used on regular basis for bone lesions.

Keywords: Benign tumors; Fine Needle Aspiration Cytology; Histopathology; Malignant tumors

1. Introduction

Bone tumors accounts for 0.9% of all cancers.[1] Compared to primary bone malignancies; bone metastases are substantially more prevalent. Bone tumours have a low incidence compared to cancers of other tissues. However, they have a pervasive impact on the patient and carry a significant rate of mortality worldwide.[2-5]

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Bone lesions can be divided into three parts non neoplastic, benign and malignant. Bone tumours are categorized into "primary tumours" that originate in the bone, and "secondary tumours or metastases" which arise in other body organs and involve the bone. The primary tumours are further classified into benign and malignant lesions. The bulk of primary bone tumours are benign and non-symptomatic.

Accurate incidence of primary bone tumours remains unknown because most benign lesions are not biopsied for histopathological analysis.[6] The rarity, and histologic diversity of tumour types make the identification of benign and malignant soft tissue and bone neoplasms a difficult field of surgical pathology.[7] Cytological techniques, especially Fine Needle Aspiration Cytology (FNAC),have gained prominence as minimally invasive tools in the evaluation of bone lesions. This technique is particularly advantageous in settings where resources are limited or where patients are not compliant for more invasive procedures due to comorbidities.

While FNAC is a valuable initial diagnostic modality, its findings must often be corroborated with histopathological examination to ensure accuracy. Despite the widespread use of FNAC in the assessment of bone lesions, there remains a knowledge gap regarding the correlation between cytological and histopathological findings, while previous studies have explored this relationship, inconsistencies and limitations exist, particularly in terms of sample size, diversity of lesion types and methodological rigor.

A comprehensive understanding of the concordance between cytological and histopathological findings is crucial for optimizing the diagnostic workup of bone lesions and minimizing unnecessary invasive procedures.

Our cross – sectional study aimed to address the research gap by investigating the correlation between cytological and histopathological findings in diverse cohort of bone lesions. By comparing the diagnostic accuracy and limitations of FNAC with the gold standard of histopathology, we were able to provide valuable insights into the clinical utility of FNAC in the initial evaluation of bone lesions.

2. Methodology

The study was conducted in Department of Pathology in collaboration with Department of Orthopaedics, Rohilkhand Medical College & Hospital, Bareilly. It Included all cytological and biopsy specimens of bone lesions received in department in one year duration. 52 cases were subjected to FNAC as well as biopsy during this period. Preliminary information about age sex clinical feature site of lesion was collected. Cytodiagnosis on light microscopy was embarked on ; all the smears were meticulously interpreted by two cytopathologist. Specimens preserved in 10% formalin were obtained from the orthopaedic department. Fine needle aspiration of the bone tumor was conducted at the bedside at the Orthopedics department.

All had undergone evaluation using plain radiography, fine needle aspiration, biopsy, and, when necessary, computed tomography (CT) and magnetic resonance imaging (MRI) for suspected primary bone tumors. The information was gathered using a unique performa made just for the study. It was turned into a master chart and then analyzed statistically.

3. Result

The study includes evaluation of localized bone lesion FNAC and its correlation with histopathological findings. During the study period, all the cases of localized bone lesions of patients with skeletal lesions were referred from the department of orthopaedics. FNAC was done after clinical evaluation. The needle or open biopsy for histopathological examination was also done for all the cases. Patients were followed up for post FNAC complications. Based on total diagnostic assessment, the final diagnosis was: Non-neoplastic bone lesions [NNBL] (8 cases), primary benign bone tumors [PPBT] (16 cases), primary malignant bone tumors [PMBT] (21 cases), secondary tumors of bone [STS] (7 cases), and no unsatisfactory smears were reported (Figure 1).

The various lesions diagnosed on cytological examination under the 4 major categories of Non neoplastic bone lesion [NNBL;6], primary benign bone tumours [PBBT;21], primary malignant bone tumours [PMBT;21], secondary tumours of bone (4). Out of 52 cases, the cytohistopathological correlation was observed in 47 cases. The majority of cases of osteosarcoma, giant cell tumor and Ewing's sarcoma were observed with cytohistopathological correlation. Out of 8 non-neoplastic bone lesions, most common lesions were chronic osteomyelitis, 6 correlated with FNAC.

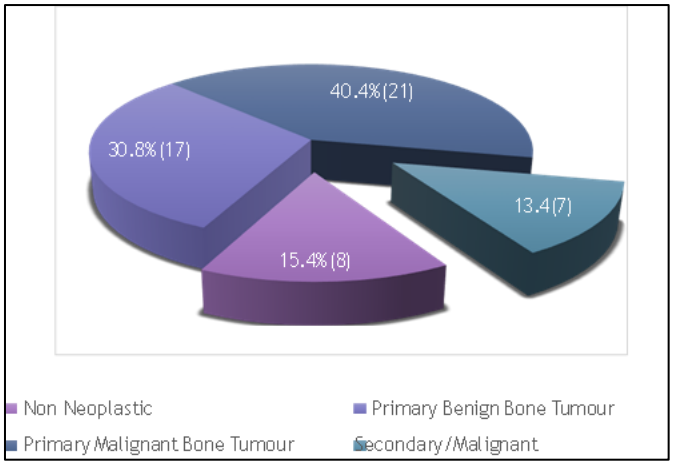

Figure 1 Graphical Presentation of the Histological Impression Of Bone Lesions

The age group affected ranged from 11-90 years. Males (53.8%) were affected more than females (46.2%) with M:F ratio of 1.7:1.

Table 1 Comparison of cytological versus histological diagnosis -confusion matrix

		Final diagnosis		**Total**
		Malignant	**Benign**	
FNAC diagnosis	**Malignant**	24(TP)	1(FP)	25
	Benign	4(FN)	23(TN)	27
	Total	28	24	52

The final diagnosis shows 28 malignant and 24 benign cases. Of the 52 total cases, 24 malignant cases were correctly identified (true positives, TP), while 1 benign case was incorrectly classified as malignant (false positive, FP). Additionally, 23 benign cases were correctly identified (true negatives, TN), and 4 malignant cases were missed (false negatives, FN). This highlights a high accuracy in detecting malignant cases with some misclassification of benign cases.

The diagnostic test demonstrates high sensitivity (85.71%) and specificity (95.83%), indicating strong ability to correctly identify both true positives and true negatives. The positive predictive value is excellent at 96% while the negative predictive value is lower at 85.19%. Overall accuracy 90.38% is with confidence intervals confirming reliable performance across all metrics.

Table 2 Analysis of discordant cases

Cyto-Histopathological Correlation			
False Negative(N=4)			
S. No.	**Cytological Diagnosis**	**Histopathological Diagnosis**	**Comment**
1.	Spindle Cell Lesion	Conventional osteosarcoma	Only spindle like cells seen on cytology: no osteoid or diagnostic cells were seen.
2.	Giant Cell Lesion	Giant cell rich osteosarcoma	Might be a sampling error since lesion was deep seated
3.	Giant Cell Lesion	Chondroblastic osteosarcoma	Osteosarcoma is heterogenous lesion, sampling error lead to misinterpretation

4.	Necrotic Bone Lesion	Metastatsic carcinoma	Scant necrotic material, radiograph unavailable prior to interpretating FNA
False Positive (N=1)			
S.No	**Cytological Diagnosis**	**Histopathological Diagnosis**	**Comment**
1.	Suspicious Atypical Cells	Aneurysmal bone cyst	Overinterpretation of cells showing reactive changes.

Out of 27 benign bone lesions reported on cytology, 23 correlated with it on histopathology. Out of 25 malignant bone lesions reported on cytology 24 correlated on histopathology. 5 cases showed discordance.

4. Discussion

The primary aim of this study is to evaluate the correlation between cytological and histopathological findings in bone lesions through a cross-sectional analysis. By systematically comparing the results obtained from Fine-Needle Aspiration Cytology (FNAC) with those from definitive histopathological examinations, study aims to assess how effectively cytological methods can differentiate between malignant, benign, non-neoplastic, and secondary bone lesions, thereby establishing FNAC as a viable preliminary diagnostic tool in clinical settings.

A total of 52 patients were recruited in the past 1 year, who fit the inclusion criteria. The youngest was 1 year old and the oldest was 90 years old, the age group with the majority of bone lesions was found in the second decade of life (11-20) followed by (21-30) years of age group, The gender distribution in our study, with a slight male predominance (53.8% males vs. 46.2% females), aligns with the findings of Kethireddy *et al* [8] who also reported a higher incidence of bone lesions in males

We encountered 4 false positive cases in our study, summarised in table 2 which comprised of 52 cases, showed discordance in 5 cases, of which 4 were false negative while one was false positive. It was found that maximum cases of false negative diagnosis were of osteosarcoma (3/4). One false positive case found was that of aneurysmal bone cyst.

Coming to first discrepant case, (FIG 2 & 3) it was found that an osteolytic lesion involving metaphyseal-diaphyseal region of in a 20-year-old was diagnosed as spindle cell lesion on cytology. The smears were paucicellular showing wavy spindly cells with mild atypia. However, no chondroblasts, osteoid, matrix or atypical mitotic figures were noted, even on review. Subsequent histopathology showed a conventional osteosarcoma with osteoid formation and spindling at the periphery. Coupled with their inherently challenging microscopic nature, ranging from benign to borderline to malignant, and their generally heterogeneous composition, spindle cell tumors can be a source of diagnostic comparison.[9]

Two cases were misinterpreted as giant cell lesion on cytopathology that turned out to be giant cell rich osteosarcoma on histopathology & conventional osteosarcoma. one case was of 18 yr/male with lesion in epi-metaphyseal region of tibia. Other case was of 20yr/m with lytic lesion in meta diaphyseal region of femur.

In the first case, the cytology smear was cellular and contained numerous dispersed osteoclastic giant cells within haemorrhagic material. In one case, focally pinkish matrix material was seen that raised suspicion but even on reviewing the smears significant nuclear pleomorphism was not evident, so it was assumed that better differentiated area was aspirated.

When radiography is available at the same time and cases are appropriately selected for aspiration, cytology can be utilized as a tool to determine treatment. For a precise cytologic diagnosis, cases exhibiting extensive soft tissue expansion, cortical thinning, and cortical breach provide enough diagnostic information. Because musculoskeletal neoplasms are only aspirated and reported by a small number of cytopathology facilities worldwide, there is a greater likelihood that these tumors may be misdiagnosed by cytopathologists with less expertise.

One of the most difficult tasks was correctly identifying osteoid and differentiating it from stromal matrix. The malignant osteoid could not be correctly identified by a single morphological trait. This challenge has also been acknowledged in earlier research, where the authors noted that osteoid detection rates range from 10% to 60%.[10,11]Furthermore, it is

undeniable that the presence of typical or suggestive clinico-radiological features facilitates the process of correctly diagnosing tissue in both cytology smears and histopathological sections.

According to our study the frequent misunderstanding of OS as a giant cell tumor on cytology was a significant flaw in the current investigation due to following relative paucicellularity with haemodilution, smears displaying mostly multinucleated giant cells and very few mononuclear cells, which were deemed bland, absence of notable atypia to indicate a malignant nature, misinterpretation of metachromatic osteoid material as fibro-collagenous stromal material.[12]

A pelvic metastatic carcinoma in 18 yr female was misinterpreted by FNAC necrotic material. On review the case showed scant necrotic material and few histiocytes and should have been considered non diagnostic. Even radiographic findings were not available. Prior research has effectively demonstrated the elevated diagnostic precision of FNAC of bone in identifying metastatic lesions. This case should have been deemed non diagnostic due to the limited amount of cytological material in a myxoid background that was observed during review. Erroneous cytologic interpretation, along with lack of clinic radiologic correlation, was the reason for error in the case.[13]

Considering the one false positive case we encountered in our study (FIG 4 & 5) It was a case of 14-year-old male with a lytic lesion on D4 vertebrae of bone with history of backache and fall few months back. The smears were paucicellular with few atypical cells showing hyperchromatic nuclei. Since the patient has a history of fracture and clinical diagnosis was not supporting our cytological diagnosis, additional needle biopsy was performed before signing out cytology report. Needle biopsy revealed dilated variable sized vascular spaces lined by fibroblasts with mildly pleomorphic nuclei. Occasional Giant cells gave an impression of aneurysmal bone cyst. Cause of the overinterpretation of cells might be presence of reactive cells showing proliferative or reactive changes.[14]

4.1. Discordant case 1

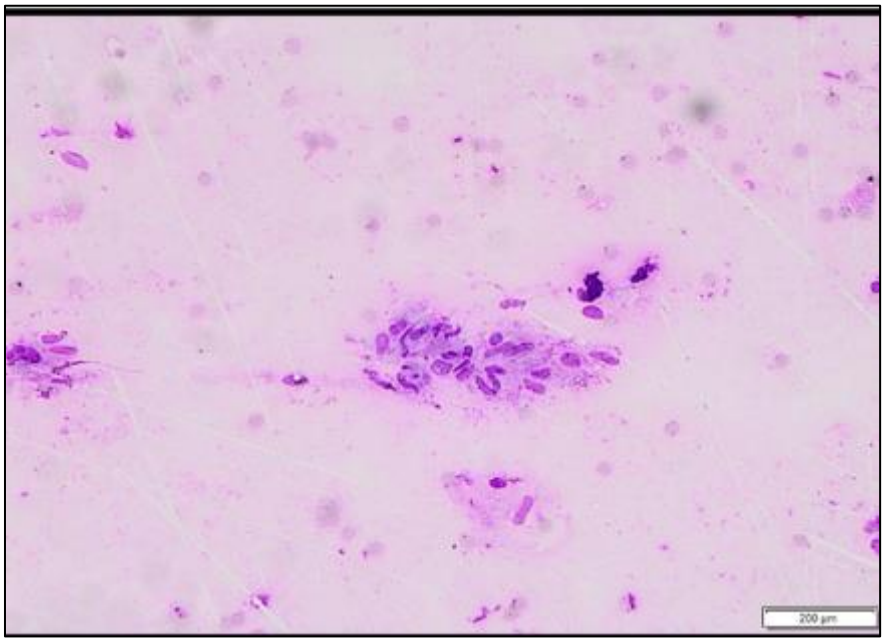

Figure 2 Spindle cell benign lesion (100X)-Cytology showing few spindle cells in cluster showing no atypical features

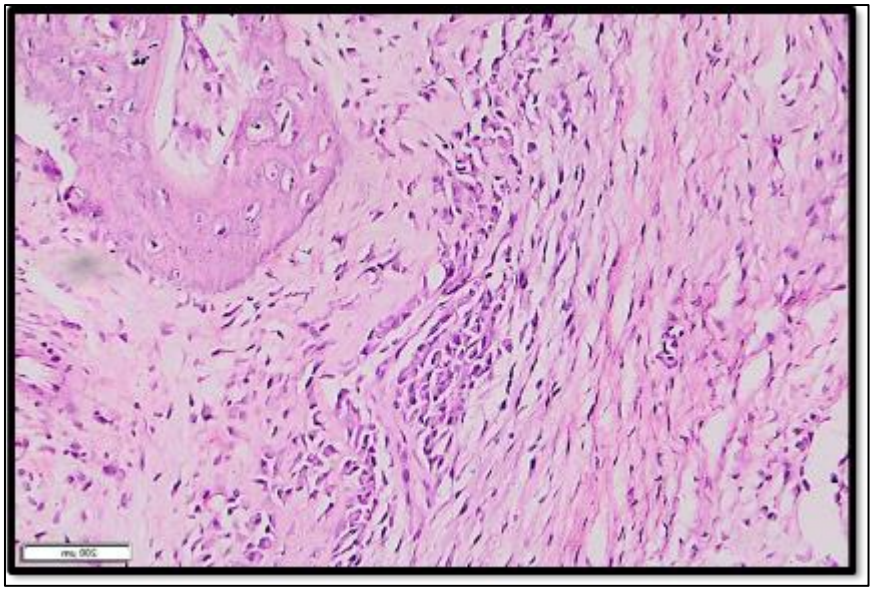

Figure 3 Conventional osteosarcoma (100X)- Histopathology showing atypical cells showing pleomorphism, fibrous tissue and osteoid

4.2. Discordant case 2

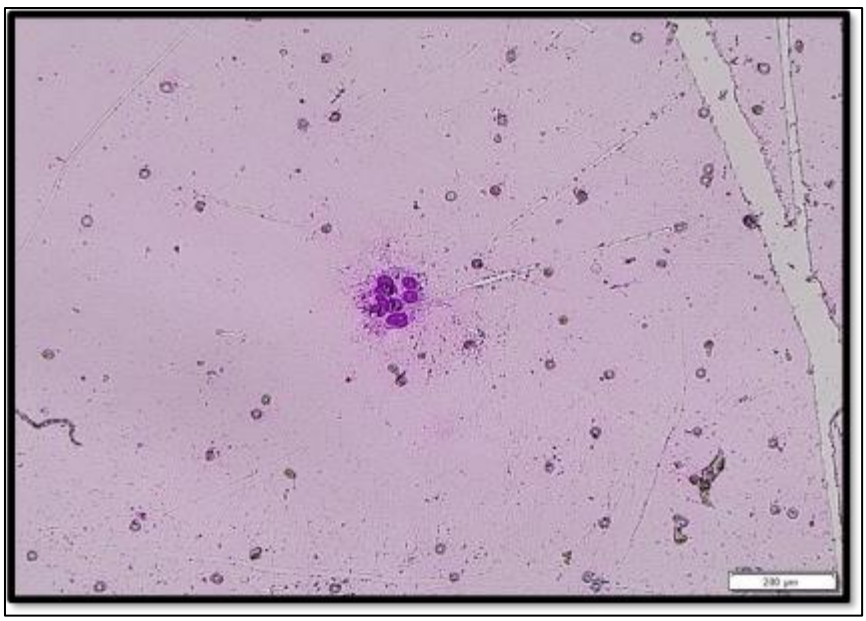

Figure 4 Suspicious atypical cells (100X)- Paucicellular smear showing few atypical cells, also showing degenerative changes against haemorrhagic and proteinaceous background

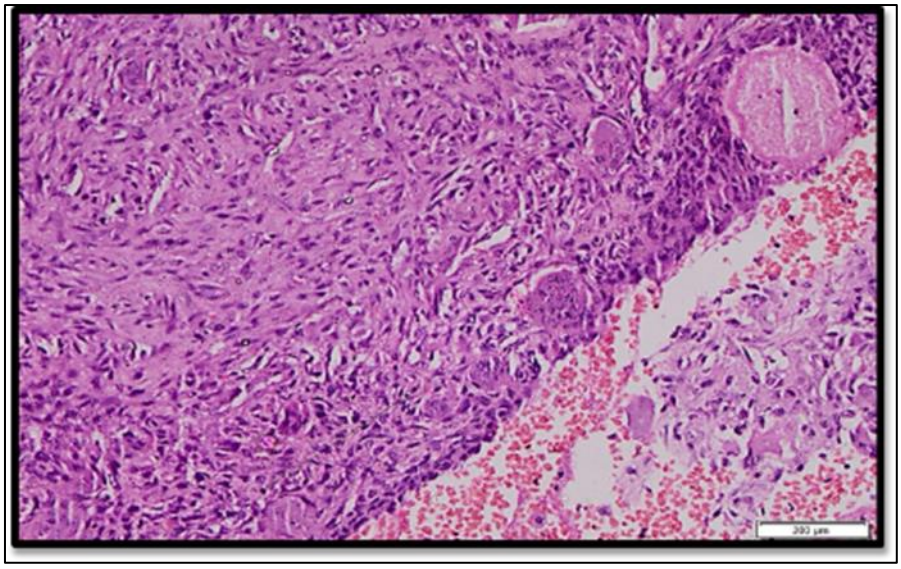

Figure 5 ABC (aneurysmal bone cyst) (100X)- Section shows haemorrhagic area, with surrounding fibrous tissue, osteoclastic giant cell and focal necrotic area. Few cells showing atypia due to reparative changes at the periphery

5. Conclusion

The study underscores the importance of a multidisciplinary approach, combining cytological, histopathological, and radiological assessments to achieve comprehensive and accurate diagnoses. As healthcare continues to advance, the adoption of minimally invasive and cost-effective diagnostic tools like FNAC will be pivotal in enhancing the efficiency and effectiveness of bone lesion evaluations, ultimately contributing to better patient care and management in the realm of bone pathology.

Compliance with ethical standards

Disclosure of conflict of interest

No conflict of interest to be disclosed.

Statement of informed consent

Informed consent was obtained from all individual participants included in the study.

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