RESEARCH ARTICLE

Critical Evaluation of Fine Needle Aspiration Cytology as a Diagnostic Technique in Bone Tumors and Tumor-like Lesions

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Abstract

Background: Though open surgical biopsy is the procedure of choice for the diagnosis of bone tumors, many disadvantages are associated with this approach. The present study was undertaken to evaluate the role of fine needle aspiration cytology (FNAC) as a diagnostic tool in cases of bony tumors and tumor-like lesions which may be conducted in centers where facilities for surgical biopsies are inadequate. Methods: The study population consisted of 51 cases presenting with a skeletal mass. After clinical evaluation, radiological correlation was done to assess the nature and extent of each lesion. Fine needle aspiration was performed aseptically and smears were prepared. Patients subsequently underwent open surgical biopsy and tissue samples were obtained for histopathological examination. Standard statistical methods were applied for analysis of data. Results: Adequate material was not obtained even after repeated aspiration in seven cases, six of which were benign. Among the remaining 44 cases, diagnosis of malignancy was correctly provided in 28 (93.3%) out of 30 cases and categorical diagnosis in 20 (66.67%) . Interpretation of cytology was more difficult in cases of benign and tumor-like lesions, with a categorical opinion only possible in seven (50%) cases. Statistical analysis showed FNAC with malignant tumors to have high sensitivity (93.3%), specificity (92.9%) and positive predictive value of 96.6%, whereas the negative predictive value was 86.7%. Conclusion: FNAC should be included in the diagnostic workup of a skeletal tumor because of its simplicity and reliability. However, a definitive pathologic diagnosis heavily depends on compatible clinical and radiologic features which can only be accomplished by teamwork. The cytological technique applied in this study could detect many bone tumors and tumor-like conditions and appears particularly suitable as a diagnostic technique for rural regions of India as other developing countries.

Keywords: Fine needle aspiration cytology - bone tumors and tumor-like lesions - diagnostic sensitivity

Asian Pacific J Cancer Prev, **13**, 3031-3035

Introduction

Fine needle aspiration cytology (FNAC) has established itself as a diagnostic modality in various visceral and soft tissue lesions. However its usage in the diagnosis of different bony lesions has not received much attention. Open surgical biopsy is considered as the procedure of choice for obtaining diagnostic tissue sampling of bone tumors (Kreicbergs et al., 1996). Apart from being an inpatient procedure and cost, other disadvantages of this procedure is disruption of compartments, contamination of surrounding tissues, risk of infection, hematoma and pathological fracture (Mankin et al., 1982). Fine needle aspiration is easier to perform, kinder to the patient, and less invasive than a large core needle biopsy or an open biopsy (Bommer et al., 1997). However FNAC has not been widely applied in the diagnosis of bone masses. This could be due to technical problems, the morphological heterogenesity of bone tumors and anticipated difficulty in obtaining adequate tissue material chiefly due to limited experience (Kreicbergs et al., 1996). With the development of neoadjuvant chemotherapy and new orthopedic surgical techniques like salvage limb procedures to treat primary malignant bone neoplasms, there has been an enhancement of the role of FNAC in the management metastatic as well as primary malignant bone tumors (Jorda et al., 2000). In many instances this technique provides a definitive pathologic diagnosis. FNAC may be a great diagnostic aid in rural regions of India and other countries where facilities for surgical biopsies are insufficient.

The present study was undertaken to assess the role of FNAC in the evaluation of various bone tumor and tumorlike lesion and to assess its reliability as a replacement diagnostic tool for core needle or open surgical biopsy

Materials and Methods

The present was conducted among patients presented with skeletal masses in the Department of Orthopedics of Institute of Post Graduate Medical Education and Research (IPGME&R) and Department of Pathology, ESI PGIMSR,

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Manicktala, Kolkata, India over a duration of one year. A detailed history was taken followed by thorough clinical examination including duration, site, number, size, extent and consistency of the lesion. Radiological correlation (with x-ray plate, CT Scan, MRI study and whole body scan etc. as applicable) was done to assess the nature and extent of the lesion. Aspiration was done asceptically by using 10 or 20 cc syringe and 20 to 22 gauge needle. Smears were prepared over glass slides. Leishman Giemsa (LG) stain was done in air dried smears and Hematoxyline & Eosin (H&E) stain was done after fixing smears in 95% alcohol. Afterwards, a tissue sample from the lesion was obtained either by core needle biopsy or an open biopsy for histopathological examination. Tissues were fixed in 10% formalin, paraffin blocks were prepared and sections were studied using H&E stain. In some cases special stains like Periodic acid Schiff (PAS), reticulin ZN stain were done.

Lesions were categorized as benign, low grade / tumorlike lesion and malignant neoplasm. Standard statistical methods were applied for analysis of data to evaluate the significance of FNAC as a diagnostic modality.

Results

51 cases of different skeletal tumors and tumorlike lesions were included in the study having age range between 10 to 78 years. Male accounted for 33 cases and 18 patients were female. Chief presenting features were swelling, pain, pathological fracture and constitutional symptoms.

The most common site of skeletal lesion was femur (11 cases, 21.6%) followed by tibia and humerus (9 cases each, 17.6%). Uncommon locations were rib, scapula, Skull, small bones of finger and talus (Table 1).

Histological examination of lesions surgically resected specimen revealed primary tumor of bone and tumorlike lesions in 45 cases (88.24%). Overall malignant neoplasm accounted for 31 cases (60.78%). Osteosarcoma was the commonest primary tumor (11 cases, 21.6%) followed by giant cell tumor (8 cases, 15.7%) and Ewing's sarcoma (4 cases, 7.8%). Among six cases of secondary tumors, metastasis from ductal carcinoma of breast accounted for 3 cases (5.9%). Simple bone cyst and aneurismal bone cyst accounted for 8 cases of 12 non -malignant primary bony lesions (66.67%). Among the six metastatic tumor, ductal carcinoma of breast accounted for three cases (Table 1). The diagnostic material was adequately obtained in 44 cases (86.3%) sometimes on repeated attempts. In seven cases (13.7%) adequate cytological material was not obtained (Table 1). Simple bone cyst and aneurysmal bone cyst accounted for 4 cases where aspirates mostly consisted of blood due to significant vascularity of such lesion. In osteoid osteoma, the sclerotic peripheral area prevented collection of adequate tissue material. In one case of osteosarcoma, the lesion could not be reached as the cortical bone was not destroyed by the tumor. Hence cases where diagnostic material could not be obtained were mostly benign in nature.

Bony tumors at first were classified in the cytological smear as positive for malignancy or negative (benign/ low grade lesion) and subsequently categorical diagnosis (Figure 1, 2) was offered (Table 2). Among 30 malignant neoplasms where sufficient diagnostic material were obtained, false negative reporting of malignancy accounted for two cases (6.67%) and no false positive diagnosis was rendered. The diagnostic accuracy of FNAC diagnosis was 93.34% in cases of malignant neoplasms, 92.86% in benign condition (overall 93.1%). Categorical opinion was accurate in 20 cases (66.67%).One case of low grade chondrosarcoma was reported as benign

Table 1. Sites of the Bony Lesions and Types of Bone Tumors: Tumor like Lesions Encountered in the Study Group

	Number (percent)	
Sites of the bony lesions		
Femur	11	(21.6)
Tibia	9	(17.6)
Humerus	9	(17.6)
Vertebral column	4	(7.8)
Radius	4	(7.8)
Fibula	2	(3.9)
Ulna	2	(3.9)
Hip bone	2	(3.9)
Metacarpal	2	(3.9)
Rib	1	(2.0)
Scapula	1	(2.0)
Skull	1	(2.0)
Proximal phalanx of thumb	1	(2.0)
Metatarsal	1	(2.0)
Talus	1	(2.0)
Total	51	
Tumors and tumorlike lesions encountered in the study group		
Primary bone tumor (N=45)		
Malignant neoplasm (N=25)		
Osteosarcoma	11	(21.6)
Ewing's sarcoma	4	(7.8)
Chondrosarcoma	3	(5.9)
Fibrosarcoma	2	(3.9)
Malignant fibrous histiocytoma	2	(3.9)
Solitary myeloma	2	(3.9)
Synovial sarcoma	1	(2.0)
Benign tumor, low grade and tumorlike lesions (N=20)		
Giant cell tumor	8	(15.7)
Simple bone cyst	4	(7.8)
Aneurysmal bone cyst	4	(7.8)
Osteochondroma	1	(2.0)
Osteoid osteoma	1	(2.0)
Chondroblastoma	1	(2.0)
Chondroma	1	(2.0)
Secondary (metastatic) tumor (N=6)		
Ductal carcinoma of breast	3	(5.9)
Carcinoma of Prostate	2	(3.9)
Adenocarcinoma of colon	1	(2.0)
Total	51	
Showing cases where adequate diagnostic material could not be obtained		
Osteosarcoma	1	
Simple bone cyst	3	
Aneurysmal bone cyst	2	
Osteoid osteoma	1	
Total	7	

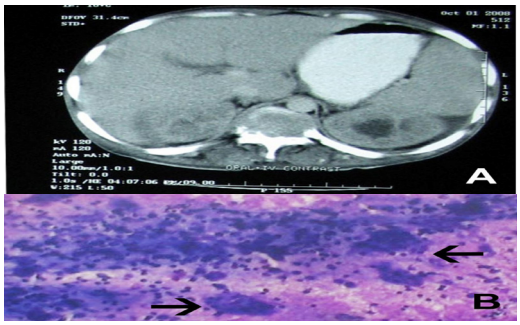

Figure 1. A) CT Scan of Abdomen Showing a Bone Tumor Destroying Body and Posterior Elements of L2 vertebra. B) FNAC of the Tumor Showing Numerous Osteoclastic Giant Cells (arrows) and Mononuclear Stromal Cells in a Case of Giant Cell Tumor of Spine (Leishman Giemsa x100).

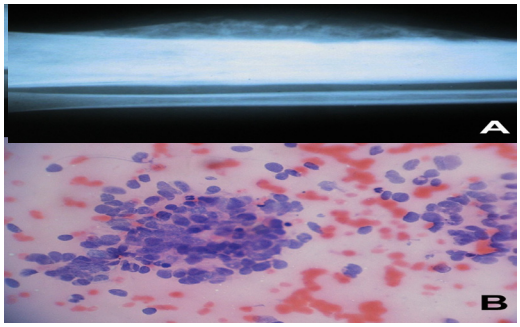

Figure 2. A) Bony Lesion Originating from the Diaphysis of Tibia. B) FNAC Smear Showing a Mixture of Cell Clusters and Dissociated Cells. Atypical cells are forming rosette-like structures indicating Ewing's sarcoma (Leishman Giemsa x100).

Table 2. Accuracy of Cytological Diagnosis where Adequate Cytological Material was Obtained (N=44)

Type of tumor	Correct cytological classification (Benign/ low grade /Malignant)	Appropriate categorical diagnosis
Malignant neoplasm (N=30)		
Osteosarcoma (N=10)	9	5
Chondrosarcoma (N=3)	2	2
Ewing's sarcoma (N=4)	4	3
Other sarcomas (N=5)	5	2
Solitary myeloma (N=2)	2	2
Metastatic tumor (N=6)	6	6
Total	28 (93.34%)	20 (66.67%)
Benign, low grade and tumorlike lesions (N=14)		
Giant cell tumor (N=8)	7	5
Simple bone cyst (N=1)	1	0
Aneurysmal bone cyst (N=2)	2	1
Other tumors (N=3)	3	1
Total	13 (92.86%)	7 (50%)

cartilageneous tumor and two cases of osteosarcoma reported only necrotic material and inflammatory lesion in the smear. However in both occasions, surgical biopsy resolved the discrepancy between clinical /radiologic and cytologic opinion. Among the secondary tumor (N=6), appropriate nature of malignancy and categorical opinion was accurate in all cases. Among 20 benign tumors, low grade and tumorlike lesions, adequate cytological material for evaluation was obtained in 14 cases. False positive diagnosis was rendered in one case of giant cell tumor as low grade sarcoma due to cytological atypia and absence of giant cells in smears.

We have statistically evaluated FNAC as a diagnostic tool for bone tumor and tumorlike lesion. We have excluded cases where the test were inconclusive due to inadequate aspiration (n=7). Among the rest 44 cases, FNAC have a high sensitivity (93.33%), specificity (92.86%) and predictive value positive of a positive test (96.55%) in the diagnosis of malignant bony tumor (Table 3). FNAC also have a low rate of false positives (7.14%) and false negatives (6.67%) results.

Discussion

The use of fine needle aspiration for the diagnosis of lesions musculoskeletal system was noted as early as the 1930s (Coley et al., 1931). However its use was mostly limited to the diagnosis of metastatic malignancies to bone and assumed a less important tool the diagnosis of primary neoplasms (Layfield, 2009).

Recognition of FNAC as a diagnostic tool for bony lesion has been largely hindered by the inability to obtain adequate smears. The rate of inadequate aspirates varies and may be as high as 33% (Layfield et al., 1987; Dollahite et al., 1989). Another recent study has reported a failure in 12 out of 66 (18.2%) cases (Handa et al., 2005). Most of the diagnostic discrepancies occur due to sampling error and lack of clinicoradiologic correlation. In the present study adequate cytological material was not obtained in only seven cases (13.7%). The failure rate is comparable to the rate for open or cutting core needle biopsies (Mankin et al., 1982; Ayala et al., 1989). The high rate of adequacy in sampling is due to repeated attempt of aspiration in difficult cases, clinicoradiologic correlation to determine the suitable area of aspiration and presence of a cytopathologist during the FNAC sampling procedure. Aspirated material cannot be presumed as optimal unless the cytologic findings correlate with the clinicoradiologic picture.

Among 30 malignant neoplasms where sufficient

Table 3. Showing the Evaluation of FNAC as a Diagnostic Tool where Adequate Diagnostic Material was Obtained (N=44).

Diagnosed as malignant	Diagnosed as benign / tumorlike lesions non-neoplastic		False positive	False negative
Malignant neoplasm (N=30)	28	2	0	3
Benign, low grade and tumorlike lesions (N=14)	1	13	1	6

	Sensitivity	Specificity	Predictive value	
			Positive test	Negative test
FNAC as screening test	93.33%	92.86%	96.55%	86.67%

diagnostic material was obtained, only two cases reported as negative for malignancy. Overall rate of accuracy was 93.1%, which is higher than the study of Kreicbergs et al. 1996 (80%) but comparable to study of Bommer et al. 1997 (97.1%) and Wahane et al. 2007 (90.5%). FNAC was found to have a high sensitivity (93.33%) and specificity (92.86%) as a diagnostic procedure for malignant bone tumors in the present study. In the study by Nnodu et al. 2006, sensitivity and specificity of diagnosing malignancy by FNAC were 95% and 94% respectively. The fact that only one false positive diagnosis of malignancy was rendered is also encouraging. Categorical opinion was accurate in two third of cases, which is lower than the study of Jorda et al. 2000 (75%). The correct categorical diagnosis was rendered in two cases each of chondrosarcoma and multiple myeloma, most cases of giant cell tumor and Ewing's sarcoma. The observation was similar to Wahane et al. 2007 where authors able to differentiate between round cell tumors like Ewing's sarcoma and myeloma, among giant cell-rich lesions of bone and benign and malignant chondroid bone tumors.

In the present study the most challenging bony lesion was consisting of tumorlike, benign, and low grade lesions. Out of seven cases where diagnostic material was inadequate, six were from this group. Compactness of the stroma and vascularity contributed to low cellular yield and blood mixed aspiration respectively, resulting in failure of adequate aspiration. There was high false negative (30%) cytologic diagnosis. In one case, false positive diagnosis of malignancy was rendered in GCT, where failure to obtain osteoclastic giant cells in smears together with high cellularity and atypical stromal cells contributed to improper cytologic diagnosis. In case of chondroid neoplasm, close resemblance of chondroid cells in benign chondroma and low grade chondrosarcoma contributed to the false positive diagnosis. Concomitantly we have successfully categorized two cases of chondrosarcoma based on cytological and radiological features. Dodd, 2006 has reported a diagnostic accuracy of FNA in 67% (18/27 cases) in cases of primary chondrosarcoma and 86% (6/7 cases) in recurrent or metastatic lesions. Similar diagnostic difficulties has been reported by other studies (Kreicbergs et al., 1996; Jorda et al., 2000). It must be emphasized that discrimination between low grade chondrosarcoma and enchondroma is not possible on the basis of cytology alone (Sanerkin, 1980; Layfield et al., 1987).

Correct cytological classification of osteosarcoma was done in 90% cases in the present study while categorical diagnosis was done in 50% cases which are comparable to other studies (White et al., 1988; Walaas and Kindblom, 1990). In a study of 40 cases, conclusive cytological opinion of osteosarcoma /high grade sarcoma was possible in 26 (65%) cases (Dodd et al., 2002). 18 of these patient underwent neoadjuvant therapy and/or resection based exclusively on the FNA interpretation. Neoadjuvent chemotherapy has become standard treatment for osteosarcoma (Bielack et al., 2009) and therefore FNAC is an appropriate diagnostic method in such lesion.

In the present study, all cases of Ewing's sarcoma were correctly classified. Klijanienko et al. 2012 from Institut Curie, Paris, has reported a correct cytological diagnosis of "malignant" in all cases and accurate classification in 92% cases of primary Ewing sarcomas/ peripheral neuroectodermal tumors. The precision of results offered by FNAC in Ewing sarcoma makes a highly reliable procedure in the diagnosis of such tumor (Akhtar et al., 1985). All metastatic tumors in this study were appropriately categorized. Correct diagnosis of metastatic lesion by FNAC aids in the appropriate management of such lesion (Jorda et al., 2000).

All cases of bone lesions must be evaluated in correlation with clinical and radiological features. A combination of conventional radiography and FNAC is of a great value in cases bone lesions as it can reduce risk of false diagnosis to around 1% (Söderlund et al., 2004)

Cost effectiveness of FNAC in primary bony lesions where a definite cytological diagnosis was yielded, has been calculated in one study. The expense of FNAC was found to be about 38.5% cheaper compared to cases where surgical biopsy alone used in the diagnosis as per records of three medical centers (Layfield et al., 2010). This observation is significant in countries like India where a significant financial savings is possible in the patient care service.

We emphasize that FNAC should be considered as a diagnostic tool in the initial workup of skeletal tumors and related lesions as the procedure is simple, economic, and reliable. The results are obtained quickly and if necessary repeated aspirations can be performed. FNAC of bony masses have a high diagnostic accuracy especially when sampling is adequate. If radiologic information is not compatible or diagnostic material is insufficient, a definitive pathologic opinion should never be delivered. Therefore orthopedic surgeons and Pathologists must work together to augment the diagnostic efficacy of this procedure. Cytological technique that has been applied in this study can detect both primary and metastatic tumors as well as many benign tumor and tumorlike conditions of bone which is particularly suitable as a diagnostic modality for rural regions of India as well as in other countries where facilities for surgical biopsies are scarce as well as having limited financial funds.

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