ABSTRACT

Background: The management of musculoskeletal neoplasms requires an accurate diagnosis, histologic type, and degree of tumor differentiation.

Aim: The present study was undertaken to compare the accuracy of fine-needle aspiration cytology (FNAC) and core needle biopsy (CNB) in the diagnosis of musculoskeletal tumors and further to compare the results with histopathological examination of surgical specimens. Grading of malignant tumors was also compared on these techniques.

Materials and Methods: This prospective study was conducted on 50 patients with musculoskeletal neoplasms. Detailed history, clinical examination, and radiological investigations were undertaken. FNAC followed by CNB were performed in each case. The tumors were categorized as benign and malignant with a definitive histotype diagnosis. For malignant neoplasms, cytologic and histologic gradings were done into three grades. The sensitivity and specificity of FNAC and CNB were compared.

Results: Of the 50 cases with musculoskeletal neoplasms, 32 (64%) were bone tumors and 18 (36%) were soft tissue tumors. The sensitivity of FNAC and CNB for categorizing bone tumors into benign and malignant was 94.7%. For soft tissue tumors, FNAC had a sensitivity of 90.9% and CNB had a sensitivity of 100%. The specificity of both the techniques, FNA and CNB for bone and soft tissue tumors was 100%. For malignant bone tumors, cytologic grade was concordant with CNB grade in 72.2% of the cases. Cytologic grade was concordant with the grade on CNB in 81.8% cases for malignant soft tissue neoplasms.

Conclusion: FNAC and CNB alleviate the need for an open biopsy in diagnosing and grading musculoskeletal neoplasms, thus facilitating appropriate therapeutic intervention.

Key words: Bone; core needle biopsy (CNB); fine-needle aspiration (FNA); histopathology; neoplasm; soft tissue

Introduction

The true frequency of musculoskeletal neoplasms is difficult to estimate because most of the benign neoplasms are not excised. The benign neoplasms are 100 times more common as compared to the malignant tumors. Sarcomas of the bone and soft tissue are relatively rare tumors and account for less than 1% of all malignant tumors.

The management of bone and soft tissue neoplasms requires a positive identification of the neoplasm, histologic type, and histologic grade for malignancy. Open biopsy has been considered as the gold standard. However, open biopsy may be associated with complications such as hematoma, subcutaneous hemorrhage, infection, and seeding of tumor cells into the surrounding tissue. Thus, a minimally invasive
procedure is desirable.[5] Core needle biopsy (CNB) has been widely accepted as a primary diagnostic technique. It is easy to perform and there is lesser chance of local complications as well as contamination of tumor cells in the surrounding tissue as compared to an open biopsy.[6,7]

Fine-needle aspiration cytology (FNAC) was first applied to bone tumors by Coley, Sharp and Ellis[6] in 1931. It has emerged as an attractive alternative to the open biopsy for preoperative diagnosis. The overall diagnostic accuracy of fine-needle aspiration (FNA) varies 62-84% in different studies.[5-11]

The combined FNAC and CNB of the musculoskeletal neoplasms permits a rapid and accurate preliminary diagnosis by combining the cytomorphological features and evaluation of tumor tissue architecture.[8] The purpose of this study was to compare the efficacy of FNAC and CNB in the diagnosis of musculoskeletal neoplasms. Further, the results were compared with the histopathological examination of surgical specimens.

Materials and Methods

This was a prospective study conducted on 50 patients with musculoskeletal neoplasms in whom both FNAC and CNB were performed. Patients with both clinically palpable and radiologically detected nonpalpable lesions were included. Patients who had received prior chemotherapy or radiotherapy were excluded from the study. Patients with clinical diagnosis of lipoma were also excluded. The study protocol was approved by the institute’s ethics committee and informed consent was obtained from all patients.

Detailed history and clinical examination were recorded in all the cases. All the patients underwent plain x-ray examination of the affected area. Other radiological investigations such as ultrasonography (USG), magnetic resonance imaging (MRI), and computed tomography (CT) scan were performed depending on the requirement. FNA followed by CNB were performed in each case. The surgical resection was performed wherever indicated.

Fine-needle aspiration

FNA was performed by the pathologist under all aseptic precautions. FNA was performed with 22-23G needle attached to a 20 mL disposable syringe fitted onto a syringe holder. In cases of bone tumors, the site for FNA was determined after correlating with the radiological findings. FNA was performed in an area of cortical breach and soft tissue extension of bony neoplasm. Two to three passes were taken in each case. A minimum of three air-dried and three wet-fixed smears were made in every case and stained with May-Grünwald-Giemsa (MGG) and hematoxylin and eosin (H and E), respectively.

Cytologic slides were categorized into benign and malignant tumors were further graded into three grades using the criteria given by Palmer et al.[12]

Core needle biopsy

CNB was performed by the orthopedic surgeon under local/regional/general anesthesia. For obtaining tissue cores, Jamshidi needle (CareFusion, 75 North Fairway Drive, Vernon Hills, IL 60061, USA) was used for both soft tissue and bone lesions. Biopsy material was fixed in 10% formal saline and processed by the paraffin embedding technique. Sections of 3-5 microns in thickness were cut and stained with hematoxylin and eosin (H and E).

The CNB sections were examined to determine the nature of neoplasm (benign/malignant) and a definitive histotype diagnosis. For malignant neoplasms, grading into three grades was done using Fédération Nationale des Centres de Lutte Contre le Cancer (FNCLCC) system where tumor differentiation, mitoses, and necrosis were taken into account.[13]

Resection specimens

The resection specimens were available in 41 (82%) cases. The specimens were fixed in 10% formal saline and representative sections were processed routinely and stained with H&E and immunohistochemical stains. For malignant neoplasms, grading was done using FNCLCC.[13] Histopathological diagnosis on resection specimens was considered as the gold standard. In nine (18%) cases where resection specimens were not available, a final histologic diagnosis reported on core biopsy specimens was taken as the gold standard.

The observations on FNA and CNB were analyzed and a comparison was drawn between both the techniques. The findings were correlated with radiological findings and the histopathology of resection specimens.

Results

Of the 50 cases with musculoskeletal neoplasms, 32 (64%) were bone tumors and 18 (36%) were soft tissue tumors. Grading was done in all malignant tumors.

Clinical profile

The age of the patients with bone tumors ranged 5-75 years (mean = 27.88 ± 16.98 years) and the maximum number
of patients was in the second decade. Seventeen (53.1%) were males and 15 (46.9%) were females. The age of the patients with soft tissue tumors ranged 13-58 years (mean = 32.06 ± 14.38 years) and the maximum number of patients was in the second and fourth decades. Eleven (61.1%) were males and seven (38.9%) were females. The size of the tumors varied 1.0-20.0 cm (mean = 5.61 ± 4.05 cm) in the maximum dimension.

Radiological findings
X-ray was performed in all the 50 cases, MRI in 19 cases, and CT scan in 6 cases. In case of bone tumors, 15 (46.9%) benign and 17 (53.1%) malignant diagnoses were rendered. Among soft tissue tumors, six (33.3%) cases were benign and 12 (66.7%) cases were malignant on imaging.

Pathological findings
Fine-needle aspiration and core needle biopsy
Among the 32 bone tumors, 14 (43.7%) were benign [Figures 1a-d] and 18 (56.3%) were malignant [Figures 1e and f] both on FNAC and CNB. Out of 18 soft tissue tumors, 8 (44.4%) were benign and 10 (55.6%) were malignant on cytology, whereas on CNB, 7 (38.9%) were benign and 11 (61.1%) were malignant. Specific diagnoses given on FNA and CNB are shown in Table 1.

Bony tumors
Of the 32 cases of bone tumors, curettage/surgical resection was available in 12 benign and 13 malignant cases [Table 2]. On correlation, there was one false negative case of well-differentiated chondrosarcoma, which was diagnosed as chondroma on FNAC and CNB. There was no false positive case. There were three cases, which were diagnosed as osteosarcoma on surgical resection, out of which two were correctly diagnosed as osteosarcoma on cytology and one was labeled as sarcoma, not otherwise specified (NOS). In another case, diagnosis of benign chondroid neoplasm was rendered, which on histopathology was chondromyxoid fibroma. The sensitivity and specificity were 94.7% and 100%, respectively.

| Table 1: Diagnosis rendered on FNAC and CNB in bone and soft tissue lesions (n = 50) |
|---|---|---|---|
| **Bone lesions (32)** | **Soft tissue lesions (18)** |
| **FNAC† diagnosis** | **CNB‡ diagnosis** | **FNAC diagnosis** | **CNB diagnosis** |
| Benign (14) | Giant cell tumor (9) | Giant cell tumor (9) | Benign fibrous lesion (4) |
| | Chondroblastoma (1) | Chondroblastoma (1) | GCT tendon sheath (2) |
| | Enchondroma (1) | Enchondroma (1) | Neurofibroma (1) |
| | Giant cell-rich lesion (1) | Aneurysmal bone cyst (1) | Benign fibrous histiocyto (1) |
| | Chondroma (1) | Chondroma (1) | Malignant (10) |
| | Benign chondroid neoplasm (1) | Chondromyxoid fibroma (1) | Synovial sarcoma (3) |
| | Malignant (18) | Malignant (18) | Spindle cell sarcoma (1) |
| | Ewing’s sarcoma (9) | Ewing’s sarcoma (9) | Sarcoma, NOS§ (1) |
| | Osteosarcoma (3) | Osteosarcoma (3) | Malignant (10) |
| | Sarcoma, NOS (2) | Osteosarcoma (2) | Synovial sarcoma (3) |
| | Metastatic carcinoma deposits (2) | Metastatic carcinoma deposits (2) | Synovial sarcoma (1) |
| | Chondrosarcoma (1) | Chondrosarcoma (1) | Malignant fibrous histiocyto (1) |
| | Chordoma (1) | Chordoma (1) | Malignant peripheral nerve sheath tumor (1) |

†FNAC: Fine-needle aspiration cytology, ‡CNB: Core needle biopsy, GCT: Giant cell tumor, §NOS: Not otherwise specified

Figure 1: Giant cell tumor: (a) Aspirate showing cohesive stromal cells with osteoclast-like giant cells (H and E, ×200) (b) Biopsy showing uniformly distributed giant cells (H and E, ×200). Chondromyxoid fibroma: (c) Aspirate showing cellular tumor with spindle shaped cells in a myxoid matrix (H and E, ×200); (d) Lobules of chondromyxoid matrix separated by cellular spindle cell stroma on biopsy (H and E, ×100). Osteosarcoma: (e) Aspirate showing pleomorphic cells with multinucleate tumor cells and intercellular osteoid (MGG, ×400); (f) Biopsy showing tumor cells laying down osteoid (H and E, ×200).
### Table 2: Correlation of FNAC and CNB diagnosis with excision diagnosis in bone and soft tissue lesions \((n = 41)\)

| Type of Lesion                  | FNAC Diagnosis | CNB Diagnosis | Excision Diagnosis |
|--------------------------------|----------------|---------------|--------------------|
| Bone lesions \((n = 25)\)      |                |               |                    |
| Aneurysmal bone cyst \((1)\)   |                |               |                    |
| Giant cell tumor \((9)\)       |                |               |                    |
| Giant cell-rich lesion \((1)\) |                |               |                    |
| Giant cell tumor \((5)\)       |                |               |                    |
| Giant cell tumor \((4)\)       |                |               |                    |
| Chondroblastoma \((1)\)        |                |               |                    |
| Chondrogenic sarcoma \((1)\)   |                |               |                    |
| Chondroma \((1)\)              |                |               |                    |
| Malignant peripheral nerve sheath tumor \((3)\) | | | |
| Soft tissue lesions \((n = 16)\) |                |               |                    |
| Benign fibrous lesion \((4)\)  |                |               |                    |
| Benign fibrous histiocytoma \((1)\) | | | |
| Synovial sarcoma \((1)\)       |                |               |                    |
| Benign fibrous histiocytoma \((3)\) | | | |
| Malignant fibrous histiocytoma \((1)\) | | | |
| Pleomorphic sarcoma \((1)\)    |                |               |                    |
| Pleomorphic sarcoma \((1)\)    |                |               |                    |
| Pleomorphic sarcoma \((1)\)    |                |               |                    |
| Pleomorphic rhabdomyosarcoma \((1)\) | | | |
| Chondrosarcoma \((1)\)         |                |               |                    |
| Chondroma \((1)\)              |                |               |                    |
| Malignant peripheral nerve sheath tumor \((3)\) | | | |

†FNAC: Fine-needle aspiration cytology, ‡CNB: Core needle biopsy

### Table 3: Comparative analysis of FNAC and CNB in bone and soft tissue lesions

| Category             | Bone lesions \((n = 32)\) | Soft tissue lesions \((n = 18)\) |
|----------------------|-----------------------------|-----------------------------------|
|                      | FNAC†                       | CNB‡                            |
|                      | FNAC†                       | CNB‡                            |
| Benign tumors        | 14                         | 14                                |
| Malignant tumors     | 18                         | 18                                |
| Sensitivity (%)      | 94.7                       | 94.7                             |
| Specificity (%)      | 100                        | 100                               |
| Accuracy for grading | 72.2                       | 86.4                             |

†FNAC: Fine-needle aspiration cytology, ‡CNB: Core needle biopsy

### Soft tissue tumors

Among 18 soft tissue tumors, surgical resection was available in 16 cases. Surgery was performed in five cases of benign tumors, which were larger than 2.5 cm and 11 malignant cases. There was a single false negative case of malignant peripheral nerve sheath tumor (MPNST) diagnosed as neurofibroma on cytology. There were no false positive cases. The sensitivity and specificity of cytological diagnosis was 90.9% and 100%, respectively.

### Comparison of fine-needle aspiration cytology and core needle biopsy with final histopathologic diagnosis

Table 2 enumerates specific FNA and CNB diagnosis, along with histopathologic diagnosis on surgical resection. As there was no false positive case, the specificity of both the techniques was 100%. The overall sensitivity of CNB (96.6%) was slightly higher than FNAC (93.3%) for the diagnosis of benign and malignant lesions.

### Comparison of cytological and histological gradings

The grading was performed in all cases labeled as malignant, which included 28 on cytology, 29 on CNB, and 24 on excision. For bone tumors, cytologic grade was concordant with CNB grade in 13 cases (72.2%). CNB grade was concordant with grade on excision in 11 cases (84.6%). For soft tissue tumors, cytologic grade was correct in eight (72.7%) cases. CNB grade was concordant with grade on excision in nine (81.8%) cases.

### Discussion

The management of bone and soft tissue tumors requires high diagnostic accuracy, as the protocol for treating benign and malignant lesions is entirely different. Early correct diagnosis leads to an increase in the possibility of improving the patient’s prognosis and success of the salvage of the tumor-affected limb.[13-15] Currently, there are three methods available, which can provide the required diagnosis for subsequent therapy: FNAC, percutaneous CNB, and open surgical biopsies. In the literature, there is a paucity of in labeling a lesion benign and malignant on both FNAC and CNB [Table 3].
studies, which compare the diagnostic accuracy of FNAC and 
CNB in musculoskeletal tumors.[5,11]

Compared to an open biopsy, both CNB and FNA are less 
invasive, cause fewer potential complications, and are less 
expensive.[8,16,17] With FNA, it is easy to sample material from 
different parts of large tumors, as compared with biopsies. 
FNA smears are well-suited for rapid staining and quick 
preliminary diagnosis.[11] However, tumor tissue architecture 
is evaluated much more accurately in CNB samples, and 
adequate tissue for ancillary diagnostics is obtained more 
often by CNB than by FNA.

**Bone tumors**

In the present study, 32 bone tumors considered neoplastic 
radiologically were evaluated by FNAC and CNB. The age range of 
patients was 5-75 years with a peak in the second decade 
of life. Our results are in congruence with another study 
where most of the patients were in the second decade.[6] A 
slight male preponderance was seen in the current study that 
was in conjunction with other studies.[6,18] The most common 
presenting complaint in our study was swelling followed by 
pain and fever, which coincided with other reports in the 
literature.[6,19] The most frequently affected bones were around 
the knee joint in 36.3% of the cases, upper end of the tibia in 
18.2% of the cases, and lower end of the femur in 15.2% cases, 
which coincided with the study by Wahane et al.[6]

Diagnosis by aspiration depends on the yield of diagnostic 
material and experience in the interpretation of cytological 
smears. Most initial series have reported difficulty in 
obtaining adequate diagnostic material from bony swellings, 
especially from lesions surrounded by intact cortical bone 
or sparsely cellular lesions rich in calcified stroma.[5,8,19,20] 
In the present study, a 22-23G needle was found to yield 
satisfactory results. An adequate aspirate mainly depends 
on the bore of the needle, the number of needle punctures, 
and the experience of the aspirator.

On cytologic examination, the categorization of tumors into 
benign and malignant had sensitivity and specificity of 94.7% 
and 100%, respectively. The diagnostic accuracy was found 
to be 96.8%. The other studies reported in the literature 
have given varied results with diagnostic accuracy ranging 
62.7-95.7%.[5,11,18,19,21,22]

Giant cell tumor was the most common benign tumor and 
all the cases were accurately diagnosed on FNA and CNB. 
One case diagnosed as giant cell-rich lesion on cytology 
was reported as aneurysmal bone cyst on subsequent 
histopathological examination. In two cases of osteosarcoma, 
which did not demonstrate any osteoid material on 
cytoplogic smears, diagnosis of sarcoma, NOS was given. 
However, diagnosis of osteosarcoma was made on CNB 
where well-visualized osteoid was demonstrable, along with 
pleomorphic malignant cells. In the absence of demonstrable 
osteoid on aspirate material, diagnosing osteosarcoma on 
FNAC is a challenge.[6,23]

Cartilaginous tumors are a frequent source of error in 
distinguishing between benign and malignant neoplasms. As 
on histopathology, it is difficult to differentiate chondroma 
from a well-differentiated chondrosarcoma. In the present 
study, the only false negative case was of well-differentiated 
chondrosarcoma reported as chondroma both on FNA and 
CNB due to lack of atypia. The literature also mentions that 
it is extremely difficult to make a diagnosis of low-grade 
chondrosarcoma on cytology or CNB alone.[6,19,24]

**Soft tissue tumors**

The present study included 18 cases of soft tissue tumors. 
The age of patients ranged 13-58 years with a mean of 
32.06 ± 14.38 years. The literature mentions a slight 
predilection of soft tissue lesions for males, as also seen in the 
current study.[25] The most common presenting complaint was 
swelling followed by pain and fever, which were commensurate 
with other reports.[5,25] The most common site involved was 
the thigh followed by the gluteal region. Extremities were the 
most common site reported in other studies.[9,25]

In the current study, the sensitivity and specificity of FNAC for 
categorization into benign and malignant soft tissue tumors 
was 90.9% and 100%, respectively. The diagnostic accuracy 
was 94.4%. There was one false negative result on cytology. 
The various studies in the literature have given sensitivity 
ranging from as low as 65% to as high as 100%. [5,11,25-27]

Synovial sarcoma was the most common malignant soft tissue 
tumor in the current study. Cytology correctly identified all but 
one case of synovial sarcoma where a diagnosis of spindle cell 
sarcoma was suggested on FNA. It was labeled as monophasic 
synovial sarcoma on CNB. Diagnosing monophasic variant 
of synovial sarcoma is difficult on cytology and not all cases of 
synovial sarcoma can be accurately diagnosed.[27,28] There was 
one false negative case of MPNST reported as neurofibroma on 
cytology. Such a problem is usually faced in low grade tumors 
with no significant atypia, mitotic activity, and lacking necrosis.

Malignant fibrous histiocytoma (MFH) is the most common 
soft tissue sarcoma in adults and the elderly.[13] In our study, in 
one case of MFH, a diagnosis of sarcoma, NOS was rendered 
where the FNA smears were sparsely cellular and composed
of a few singly scattered pleomorphic tumor cells. This problem was faced by other researchers where a diagnosis of pleomorphic sarcoma was suggested in most of the cases.\[^{27}\]

The grading of bone tumors on FNA was correct in 72.2% cases in the current study. CNB was able to identify the accurate grade in 84.6% of the cases when compared with final excision, which was close to 87% as reported in another study.\[^{11}\]

For soft tissue tumors, the correct cytologic grade on FNAC was assigned in 72.7% cases, which was commensurate with other reports.\[^{11,12,29}\]

However, CNB grade was concordant with the grade on excision in 81.8% cases. Yang \etal\[^{11}\] reported a diagnostic accuracy of 83% for histologic grading on CNB.

In the present study among a total of 50 musculoskeletal tumors, cytological examination was able to categorize 48 tumors correctly into benign and malignant, giving a sensitivity of 94.7% and 90.9% for bone and soft tissue tumors, respectively. Sensitivity ranging 83-100% has been reported on FNAC.\[^{7,18,19,21,25-27,30}\]

The specificity of both the techniques, FNA and CNB was 100%.

Hence, the present study has established that FNA and CNB can alleviate the need for an open biopsy in many cases of musculoskeletal neoplasms. Even a satisfactory subcategorization of the tumors can be done, which facilitates appropriate therapeutic intervention.

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**Conflicts of interest**
There are no conflicts of interest.

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