103 case to case compare of Core Needle biopsy results with open biopsy one in skeletal tumor

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Abstract: We compared Core Needle biopsy results with open biopsy one in skeletal tumors to assess related factors that affect core needle biopsy accuracy. Between 2008 and 2011, 103 patients (54 males and 44 females) with skeletal lesions with an average age of 33 years (ranging between 6 to 74) were performed biopsies. Initially needle biopsy was performed, followed by an open biopsy in the same anesthetic procedure. Two pathologists, with experience in musculoskeletal lesions, examined the specimens. The needle biopsies were reported as definitive diagnosis, suspicious for malignancy, indefinite diagnosis and inadequate specimens. The histological results of open biopsies were used as the reference standard. In our study, the diagnostic sensitivity for conventional open biopsy was 100%. The diagnostic sensitivity of core needle biopsy in diagnosis of malignancy and tumor typing were 93.2 %(96 of 103) and 77.6% (80 out of 103) respectively. Diagnostic accuracy of Core Needle Biopsies is 64.4 % (26 out of 38), 83% (54 of 65) and 100% (10 out of 10) for benign tumors, malignant tumors and metastatic tumors respectively. Needle biopsy is suggested an appropriate and effective alternative to open biopsy for diagnosis of skeletal tumors. Careful clinical and radiographic evaluation and close cooperation of an orthopedic surgeon, a radiologist and a pathologist would improve the outcome..
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1. Introduction

After accurate clinical, radiographic and paraclinical evaluations of bone lesions, correct histological diagnosis is necessary before deciding a therapeutic strategy. Open biopsy and needle biopsy are two conventional means for histological diagnosis. Fine needle aspiration provides only cytological material without tissue, which is not adequate for bone tumor diagnosis [1]. Open biopsy, on the other hand, provides sufficient material for accurate diagnosis. In some cases open biopsy leads to spreading tumor cells into the surrounding tissues, local relapse or metastasis, which would compromise limb salvage and even have a negative effect on overall survival [2]. Local complications after open biopsy have been reported up to 17.3%. In 4.5% to 8.5% of those patients the prognosis were adversely affected [3, 4]. This was not considered important in the past, because the most malignant bone tumors were treated by amputation. The first case of needle biopsy of musculoskeletal lesions was reported by Coley in 1931 [5]. Needle biopsy is an easy procedure and can be performed out-patient. Complications after needle biopsy, especially tumor cell, are less than those in open biopsy [6-8]. Except for a case of osteosarcoma reported by Davies et al [9], there has been no report of tumor recurrence caused by a needle biopsy. Radiation and chemotherapy may necessary to administer immediately after confirmation of pathological diagnosis. An advantage of core needle biopsy (CNB) is that with definitive diagnosis, chemotherapy or radiation therapy can be started the day after biopsy [10, 11]. In contrast, the literature

indicates that a delay (of even up to 3 weeks) may be required after surgical biopsy to allow wound healing and prevention of infection and bleeding before commencing treatment [10]. However, there are concerns about obtaining adequate tissue for histological diagnosis [12]. The purpose of this study was to evaluate the diagnostic value of core needle biopsy in different types of bone tumors, adequacy of tissue and complication of needle biopsy.

2. Material and Methods

Between 2008 and 2011, 103 biopsies from the skeletal lesions were performed. The research committee of our institute approved the study. The patients include 54 males and 44 females with an average age of 33 years (rang between 6 to 74). Patients with previous surgical experience were excluded. The routine method of biopsy in our department was open biopsy. In our study, before doing the open biopsy, in one anesthetic procedure, we performed needle biopsy for all the patients. Core needle biopsy was performed with Jamshidi needle biopsy under general anesthesia which consists of a distally tapering trocar, with a diameter varying from 2 to 4mm and a length of 10cm, and a stylet and a probe. Distal taper prevents specimen from sliding out or being crushed. The only contraindication for a needle biopsy was a bleeding diasthesis. The biopsy track was along the surgical approach and in a way which is shortest to lesion. All the biopsies were performed by two orthopedic surgeons experienced in musculoskeletal lesions who were in charge of further treatment. 34% of biopsies were performed by the guide of fluoroscopy; others were accurately determined according to the plane radiographies, CT scans and MRI imagines. On the basis of Jim S. Wu et al study, which suggests obtaining a minimum of three specimens in bone lesions for prevention of inadequate sample [13], at least three biopsy samples were obtained at different tumor sites.

All specimens were fixed in 10% formaldehyde and were routinely processed for hematoxylin and eosin staining. Two pathologists with experience in musculoskeletal lesions examined the specimens. If needed, special staining was performed in cases to confirm the diagnosis. All the data including clinical and radiological information were available for the pathologists to be used in accurate diagnose. At first, the pathologist examined the needle biopsy and confirmed the diagnosis and then the open biopsy was diagnosed. The needle biopsies were reported as definitive diagnosis, suspicious for malignancy, indefinite diagnosis and inadequate specimens. In inadequate specimens there is not sufficient tumoral tissue for diagnosing. The indefinite specimens are small pieces of tumoral tissue without diagnostic features and suspicious for malignancy specimens there include tumoral tissue with features highly suspicious for malignancy but not definite for such a diagnosis. The histological results of open biopsies were used as the reference standard. Distribution of the bone lesions which undergone biopsy is shown in table-I. The final histological diagnosis of the bone lesions after open biopsies is shown in table-II. We used SPSS ver.17 for descriptive and statistical analysis. We used the X^2 or Fisher exact test for categorical variables. A p-value of less than 0.05 was deemed to be significant. Diagnostic sensitivity is the number of biopsies that result in a diagnosis divided by the total number of biopsies performed. A specimen was considered to be diagnostic when a distinct pathologic diagnosis could be rendered from the needle biopsy tissue compared with the open biopsy.

Table-1: Distribution of the bone lesions in extremities

		Frequency	Percent
Lower extremity	pelvis	20	19.4
	Proximal femur	7	6.8
	shaft femur	5	4.9
	distal femur	25	24.4
	Proximal tibia	12	11.7
	shaft tibia	7	6.8
	distal tibia	2	1.9
	fibula	3	2.9
Upper extremity	scapula	6	5.8
	Proximal homerus	11	10.7
	Proximal ulna	1	1
	distal radius	1	1
	hand	3	2.9
	Total	103	100

3. Results

A total of 103 consecutive CNBs were performed (56 male and 67 female). The average age for the patients was 33 (range between 6 to 74). Each patient was tried for one lesion and 3 to 6 CNBs for macroscopic and microscopic evaluations performed. The sites and numbers of the bone lesions biopsies are shown in table-1and Table-2. 69 lesions (67%) were malignant and 34 (33%) were benign. The most common bone lesion site was distal femur (25 lesions). 34% of biopsies were performed under guide of fluoroscopy and 66 % performed anatomically. In 103 patients, 99 (96.1%) of samples were diagnosed as adequate. Inadequate samples

included: 2 eosinophilic granelomes, an osteoid ostoma and an aneurismal bone. In analysis of 103 sample series, differentiation between benign and malignant was possible in 96 (93. 2%) lesions.

Table-2: The final histological diagnosis of the bone lesions after open biopsies

	Frequency	Percent
Osteosarcoma	28	27.2
Ewing sarcoma	10	9.7
Metastases	10	9.7
Lymphoma	7	6.8
Chondrosarcoma	5	4.9
Plasma cell myeloma	4	3.9
Sinovial sarcoma	3	2.9
MFH	2	1.9
Liposarcoma	1	1
Giant cell tumor	8	7.8
Osteochondroma	5	4.9
UBC	3	2.9
ABC	3	2.9
EG	3	2.9
Chondroblastoma	2	1.9
Hemangioma	1	1
Fibroma	1	1
Chondromixoidfibroma	1	1
Chondroma	1	1
Tomoral calcinosis	1	1
Mixofibroma	1	1
TB	2	1.9
Osteonecrosis	1	1
Total	103	100

Of 99 lesions in which adequate tissue material was obtained, definitive diagnosis was possible in 83 (83. 8%). 16 of 99 patients with adequate samples did not have an accurate diagnosis (table-3). In our study, two eosinophilic granoloma were diagnosed as bone lesions with calcified particles in CNBs (inadequate for diagnosis). There were 2 of 28 osteosarcomas from which one was detected as fibroblastic tissue (non-diagnostic) and diagnosed as intermedullary low-grade osteosarcoma in open biopsy and the other one was an unknown tumor with chondroid particles (non-diagnostic). The later one seemed finally compatible with osteosarcoma. 3 of 7 non Hodgkin's lymphoma showed no accurate diagnosis. 3 of 5 low-grade chondrosarcoma were diagnosed as well differentiated chondroid tumors. Among 5 sessile osteochonromas, 4 lesions were diagnosed benign tumors with chondroid cells. One of 3 synovial sarcomas were diagnosed as non-diagnostic lesion. 2 of 3 cases, with ABC, were diagnosed as benign lesions with giant calls (suspicious) and a piece of normal bone in CNBs (inadequate for diagnosis). The other samples which were not diagnosed accurately included Boney hemangioma (non-malignant lesion), osteoidostoma (sclerotic lesion with chronic inflammation) and MFH with invasion to bone (low grade Sarcoma). It is important that all the needle biopsies with specific tumor diagnosis were compatible with open biopsies. According to 72 patients ultimately need further surgery; the diagnostic sensitivity for conventional open biopsy was 100%. The diagnostic sensitivity of core needle biopsy (CNB) in diagnosis of malignancy and definite tumor diagnosis were 90.9% (90 of 99) and 83.8% (83 of 99). Diagnostic sensitivity for malignant and benign tumors were 64.7 % (22 of 34) and 84% (58 of 69) respectively (p=14.9%). Diagnostic sensitivity for metastatic tumors was 100 % (10 of 10).

Tumor	**Needle biopsy diagnosis**	**Needle biopsy category**	**cases**
Eosinophilic granoloma	bone lesions with calsified particles in CNBs (inadequate for diagnosis)	inadequate	2
Osteosarcoma	fibroblastic tissue	Non-diagnostic	1
	unknown tumor with chondroid particles	Non-diagnostic	1
Non hogkins lymphoma		Non-diagnostic	3
Low-grade chondrosarcoma	well differentiated chondroid tumor	Non-diagnostic	3
Sessile osteochonromas	benign tumors with chondroid cells	suspicious	4
Synovial sarcomas		Non-diagnostic	1
ABC	benign lesions with giant calls	suspicious	1
	a piece of normal bone	inadequate	1
Boney hemangioma	non-malignant lesion	suspicious	1
Osteoidostoma	sclerotic lesion with chronic inflammation	inadequate	1
MFH with invasion to bone	low grade Sarcoma	suspicious	1

4. Discussions

Open biopsy is the diagnostic standard to which other biopsy techniques must be compared [14]. In our study, the accuracy of open biopsies is 100%. It is comparable to other studies [15, 16]; However, Yao et al study declined if open biopsies perform in cases CNBs were in doubt, the open biopsy accuracy would be decreased as low as 72% [17]. The complications resulted from needle biopsies occur at rates ranging from 0 to 1.1% [4, 18]. In our study because of performance of CNBs and open biopsies in one anesthetic procedure, we could not define the exact rate of core needle biopsy complication. Some studies have shown that core needle biopsy of bone lesions are more accurate than those of soft tissue lesions [18, 19]. The more specific manifestation of bone tumors on radiographs may narrow the deferential diagnosis for the pathologist [13]; on the other hand, in most of these studies, bone lesions included a large number of metastatic tumors, which usually lead to higher accuracy [16, 20]. The explanation for this is that because of the homogenous nature biopsies of metastatic tumors, they are more likely to contain diagnostic tumor cells. However, by the use of new imaging technique, recent researchers [17, 21, 22] have found no significant difference in diagnostic accuracy for biopsies performed in bone versus soft-tissue lesions.

In this study, inadequate material for diagnosis was obtained in 3.9% (4 of 103) of cases. This rate is comparable with those in previous reports [4, 11, 23] .The majority of them showed only necrosis, fibrosis, blood component or intact bone. An accurate pathological result was achieved in 83.8% (83 of 99) of the CNBs trials. These results are comparable to previous similar studies. Yao et al [17] reported an accuracy of 73% (41 of 56) in bone lesions; Jim S. Wu et al 77 %(68 of 88) [13], Mitsuyoshi et al [22] 85% (77 of 91), Pramesh et al [ ] 89% (121 of 136), Ki-Sun Sung et al 89% (122 of 137)[25]. Dupuy et al [26] reported a higher accuracy of 93% (164 of 176 procedures) when assessing core needle biopsies of skeletal neoplasms. Mankin et al [4] reported an accuracy rate for CNBs of musculoskeletal tumors of 60% (51 of 85 procedures), Tehranzadeh et al [26] 72% (87 of 120), Hau et al [27] 74% (192 of 258), Ayala and Zornosa [28] 78.6% (140 of 178) and Skrzynski et al [29] 84% (52 of 62). Needle samples of metastatic tumors have been reported the highest probability of achieving a diagnostic result [30]. The accuracy of CNBs for metastatic lesions in our study was 100% (10 of 10).

The accuracy of CNBs was 84% and 64.7% in malignant and benign lesions respectively. Our results are equal to the previous similar studies. Hau et al [27] and Ayala and Zornosa [28] found similar differences with an accurate diagnosis in 90% and 83% of malignant tumors and in 80% and 64% of benign tumors, respectively. Hyun-Joon Shin et al [30] found a statistically significant difference (P=0.008) in the ability of CNB to provide an accurate diagnosis in the primary malignant tumors (92%, 34/37) compared to the primary benign tumors (65%, 22/34). Jim S. Wu et al 13 study indicated same results. The diagnostic accuracy of skeletal tumors was considerably affected by histological type. We found tumors with lower diagnostic accuracy were usually made of heterogenic cells. In our study, these tumors included synovial sarcomas, haemangiomas, fibrosteosarcoma and schwannomas. Synovial sarcoma is a heterogenic tumor and for diagnosis of this tumor an examination of structural tissue is necessary; because it is a biphasic tumor and the shape of cells are not characteristic. This probably explains the lower diagnostic accuracy observed for these tumors in our study. When synovial sarcoma is suspected, Ki-Sun Sung et al suggest that FISH analysis could improve the diagnostic accuracy of core needle biopsy [25]. Another tumor that we found to have lower diagnostic accuracy was haemangioma. It is because of heterogenous nature of these tumors which make it difficult to determine the tissue architecture of a whole tumor by needle biopsy [13] and it is important to pay attention to all the cross-sectional tumor slides for diagnose of heterogenous tumors. Multiple samples from different sites of the lesions may minimize the risk of misdiagnosis in such cases [22]. In our study some tumors such as low-grade chondrosarcoma, low-grade MFH with invasion to bone and intermedullary low-grade fibroblastic osteosarcoma were low grade sarcomas which are difficult to recognize from their benign type; Additionally, We could not diagnosis three non Hodgkin's lymphoma from chronic inflammation. A number of tumors show special macroscopic structures that make CNBs challenges. Examples of those lesions in our study were sessile osteochonromas and ABCs. In this study, we could not diagnose one osteoid ostoma; sclerotic lesions often require a cutting needle or drill to breach the cortex and reactive bone which may destroy the samples [13]. In two tiny eosinophilic granoloma, adequate tumoral lesion could not be achieved. There were limitations in our study. One limitation was that the numbers of specimens taken from different biopsies were not equal. Another limitation was that patients with spinal lesions were not included in this

study, as spinal biopsies are performed by our interventional neurosurgeons. The other limitation was that we did not consider the tumor size in each lesion and because of performance of needle biopsy before open biopsies and in one anesthetic procedure it is impossible to estimate the CNBs complication rate.

The diagnostic outcome of core needle biopsy for musculoskeletal tumors is principally dependent on tumor type. Needle biopsy is challenges in heterogeneous structures. MRI may help to exclude such tumors unsuitable for needle biopsy. Moreover, an orthopedic surgeon, a radiologist and a pathologist should cooperate closely with each other for best outcome. It should be assigned that due to an obvious discrepancy between the clinico-radiologic diagnosis and the core needle histopathology, the diagnosis needs to be confirmed with an open biopsy. If the needle biopsy shows a specific tumor diagnosis, it would be strongly compatible with open biopsies.

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