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Image-guided percutaneous biopsy of intramedullary lytic bone lesions: utility of aspirated blood clots

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Abstract The diagnostic value of aspirating blood clots while performing percutaneous biopsy of intramedullary lytic bone lesions was assessed. This was a retrospective analysis of 400 patients with intramedullary lytic bone lesions who underwent image-guided needle biopsy. The nature of the specimens obtained was noted from the histopathology records. In 83 (20.8%) of the 400 patients, the specimen obtained was either blood clot only or essentially blood clot with only tiny fragments of bone or soft tissue. Lesional tissue was present on needle biopsy specimens in 65 (78.3%) of the 83 cases, while in 18 (21.7%) cases no lesional tissue was obtained. In 24 of the 83 cases, there was no surgical histological diagnosis available. In the 59 cases where surgical histological diagnosis was available for comparison, the diagnostic accuracy for needle biopsy was 73%. Percutaneous biopsy provided the diagnosis allowing appropriate further management in 62 cases, for an overall diagnostic yield of 75%. The results of our study show a sufficiently good diagnostic value in obtaining blood clots as to necessitate routine attempts at obtaining such material while performing percutaneous biopsy of intramedullary lytic bone lesions.

Keywords Lytic · Diagnostic yield · Clots · Biopsy · Bone lesions

Introduction

Image-guided percutaneous needle biopsy of suspected bone tumours is cheaper, less invasive, and has a lower complication rate compared with open biopsy and is becoming the favoured technique for the diagnosis of suspected bone tumours before execution of definitive management [1]. It is important that these biopsy techniques provide sufficient and appropriate material so that an accurate histopathological diagnosis can be made, thereby avoiding mismanagement. It is recommended that they are performed in centres where definitive surgical management will be undertaken [2, 3]. One study looking exclusively at the diagnostic accuracy of percutaneous biopsy of sclerotic bone lesions reported high positive and negative predictive values [4]. Lytic lesions are reported to have a higher diagnostic yield than sclerotic lesions and biopsy of an extraosseous soft tissue component provides higher diagnostic yield than bone sampling [5, 6]. Intramedullary lytic bone lesions form a large subset of bone lesions that are biopsied under image guidance and may or may not be associated with extraosseous soft tissue components.

Percutaneous biopsy of intramedullary lytic lesions that do not have a soft tissue component may only yield blood clots. The literature is divided on the diagnostic utility of aspirated blood clots, with some authors reporting that such tissue is of little or no diagnostic value [7], and others suggesting a high diagnostic value to these blood clots in achieving diagnosis [8]. We undertook a retrospective study

to assess the diagnostic value of obtaining a specimen that is only or essentially blood clot, while performing needle biopsy on intramedullary, lytic bone lesions.

Materials and methods

A search of the database of the Bone Tumour Unit revealed 400 patients with intramedullary lytic bone lesions who had undergone image-guided percutaneous needle biopsy using fluoroscopy, computed tomography (CT) or ultrasound (US) over a 6-year period between 1998 and 2004. The age range was from 3 to 93 years. Following consultation with the surgical team, a decision was made by the radiologist to biopsy the lesion under fluoroscopic, CT or US guidance after review of available imaging. Lesions biopsied under US guidance included those with large extraosseous soft tissue components, whilst lesions biopsied under fluoroscopic guidance were those that were purely intramedullary or with very little extraosseous soft tissue components. However, the majority of lesions were biopsied under CT guidance. Lesions with extraosseous soft tissue components were biopsied with either a 14G Tru-Cut needle or a 14G Temno needle and those without extraosseous soft tissue components requiring bone sampling were biopsied with an 11 G or a 13 G Jamshidi needle. All biopsies were performed by experienced consultant musculoskeletal radiologists or by a senior radiology trainee under direct consultant supervision, after obtaining full informed consent from the patient. Biopsies were performed through small stab incisions using an aseptic technique and following local anaesthesia for adults and general anaesthesia for children aged 16 years and under. Between two and four passes were made, depending on the quality of the specimens obtained. When a Jamshidi needle was used to biopsy the intramedullary component of a lytic bone lesion, a 20-ml syringe was routinely used to obtain a medullary aspirate. On average, where clots were obtainable on such aspiration, approximately 5–10 ml of blood clot was obtained and sent in a separate container to the laboratory. In general, the specimen consisted of soft tissue cores and fragments when biopsies were performed with Temno and Tru-Cut needles. In the case of biopsies performed with Jamshidi needles, the specimen consisted of a combination of either bone cores only, bone cores and blood clots or blood clots only. The exact nature of the specimen obtained for all 400 cases that underwent needle biopsy were documented from descriptions of the same on histopathology records. The histological results from the needle biopsy were divided into three categories based on a previously described system [9]:

Category 1:
A definitive diagnosis could be made by the histopathologist, with the aid of various immunohistochemical techniques, with a high degree of certainty.

Category 2:
A definitive diagnosis could not be made, but a narrow differential diagnosis could be suggested, allowing further management; for example, an osteoclast-rich lesion without evidence of malignancy in which the differential would include a giant-cell tumour (GCT) of bone and an aneurysmal bone cyst (ABC).

Category 3:
Insufficient material was available to the histopathologist to allow a diagnosis to be made with any degree of certainty.

We examined the diagnostic value of obtaining specimens that were essentially blood clots by comparing the needle biopsy and surgical histology results. In the Category 1 and 2 diagnoses group, surgical histological results were available to compare with when the patient went on to have a definitive surgical procedure. In the Category 3 diagnosis group, surgical histology was available primarily because the patients had a surgical procedure to establish the diagnosis; subsequently, some of them went on to have a definitive procedure. A Category 2 diagnosis was considered as matching with the surgical histology, if the final diagnosis was suggested in the initial narrow list of differential diagnoses on the percutaneous biopsy specimens. A Category 2 diagnosis was considered a mismatch, if the final surgical histology diagnosis was not mentioned in the initial histological differential diagnosis from the needle biopsy specimen. The pathologist had access to data such as age and sex of the patient, location of the lesion and relevant imaging findings. After the histological diagnoses from the needle biopsy specimens were available, each case was discussed at the multidisciplinary bone tumour meeting attended by the surgeon, oncologist, radiologist and the pathologist of the Bone Tumour Unit. Where necessary, the pathologist used the information from imaging findings, before giving a final report on the needle biopsy specimens.

The calculation of diagnostic accuracy and diagnostic yield was made using the following definitions that have been used in previous published studies in the literature [5, 6, 9]:

- True-positive result (TP): the needle biopsy provided lesional tissue and a correct diagnosis.
- True-negative result (TN): the needle biopsy produced no lesional tissue and no pathological lesion was present.
- False-positive result (FP): the needle biopsy provided lesional tissue which was diagnosed as pathological, when no pathological lesion was present.
- False-negative result (FN): the needle biopsy produced no lesional tissue, but pathological lesion was present, or there was a mismatch in the diagnosis between the needle biopsy and the surgical histology.
- Diagnostic Accuracy $= 100\% \times (\mathrm{TP} + \mathrm{TN}) \div (\mathrm{All\ results})$

– Diagnostic Yield = 100% × (Total no. of TP results ÷ Total no. of biopsies performed)

Only cases with surgical histology were used in calculation of diagnostic accuracy [9]. While calculating the diagnostic accuracy, we included as true-positives, results in which needle biopsy results were correct with regards to malignancy but not necessarily with regards to exact histological features (reasonable match); i.e. appropriate further management could be instituted based on the result without any harm done [10]. Any needle biopsy that resulted in incorrect histological features that could potentially prompt inappropriate management was considered as false-negative, even if no harm was actually done [10].

While calculating diagnostic yield, all cases where needle biopsy provided a diagnosis allowing further appropriate management were included as true-positives in the numerator [5]. This included needle biopsy results reasonably matching with surgical histology and Category 1 and 2 diagnoses without surgical histology, but which allowed appropriate further management. No Category 3 diagnosis was included in the numerator while calculating diagnostic yield.

Approval from the local Ethics Committee was not required for this retrospective study, as data and information used neither revealed patient identity nor breeched patient confidentiality.

Results

There were a total of 400 patients with intramedullary lytic bone lesions who had biopsies using CT (n=325), US (n=26) or fluoroscopic guidance (n=49). In 83 (20.8%) of the 400 patients, the specimen was essentially or only blood clots. Lesional tissue was seen on needle biopsy specimens in 65 (78.3%) of the 83 cases. In 37 (56.9%) of these 65 cases, a Category 1 diagnosis was made. Twenty-two (33.8%) of these 37 cases had surgical histology for comparison and matched in all cases (Table 1). In 15 (23.1%) of the 37 cases, no surgical procedure was performed (Table 2).

In 28 (43.1%) of the 65 cases where lesional tissue was seen on needle biopsy specimens, a Category 2 diagnosis was made. In 23 (82.1%) of these 28 cases, surgical histological diagnosis was available for comparison, with mismatch occurring in only five cases (Tables 3 and 4). The diagnoses in five (17.9%) of the 28 cases where needle biopsy diagnoses was Category 2, but no surgical procedure was performed, were all benign and are summarised in Table 5.

In 18 (21.7%) of 83 cases, a Category 3 needle biopsy diagnosis was obtained; i.e. no lesional tissue was present. In 14 (77.8%) of these 18 cases, surgical histological diagnosis was available and there were no malignant diagnoses on surgical histology (Table 6). In four (21.1%) of the 18 cases there was no histological diagnosis available. In three of these four cases, follow-up information was available and these lesions were all presumed to be benign. In one of these three cases, there was a lytic lesion in the body of the talus and subsequent radiological review suggested avascular necrosis of the talus. In another patient, a lytic lesion in the distal humerus was deduced to be a focus of eosinophilic granuloma taking into account the clinical and radiological information available, with the patient asymptomatic at 2-years follow-up and showing radiographic evidence of resolution. In the third patient, a lytic lesion in the distal tibial metaphysis demonstrated callus formation on imaging follow-up with resolution of clinical symptoms of pain by 6 months follow-up; this was assumed to be fracture with callus formation. In one 6-year old patient with a lytic distal humeral lesion, no lesional tissue was obtained and no surgical procedure was performed; however no further follow-up information

Table 1 Category 1 diagnosis in 22 cases with surgical histology

Diagnosis	No. of cases
Giant-cell tumour	10
Aneurysmal bone cyst	4
Chondroblastoma	3
Benign fibrous histiocytoma	2
Metastasis	2
Grade 2 chondrosarcoma	1

Table 2 Category 1 diagnosis in 15 cases without surgical histology

Diagnosis	No. of cases
Ewing sarcoma	1
Plasmacytoma	1
Aneurysmal bone cyst	1
Osteomyelitis	3
Metastasis	5
Sub-chondral cyst	1
Paget's osteosarcoma	1
Fibrous dysplasia	1
Chondromyxoid fibroma	1

Table 3 Category 2 diagnosis in 18 cases with matching surgical histology

Diagnosis	No. of cases
Benign fibrous histiocytoma	3
Aneurysmal bone cyst	3
Simple bone cyst	1
Fibrous dysplasia	1
Chondroblastoma	1
Giant-cell tumour	9

Table 4 Diagnosis in five patients in whom there was mismatch between Category 2 diagnosis and surgical histology results

Needle biopsy diagnosis	Surgical histology diagnosis
Aneurysmal bone cyst	Giant cell tumour
Post-traumatic focus	Fibrous dysplasia
Aneurysmal bone cyst	Epithelioid haemangioma
Benign fibrous histiocytoma	Fibrous dysplasia
Infection	Pigmented villonodular synovitis

was available. In the cases where no surgical procedure was performed, it was either because the patient was managed conservatively or the patient declined operative treatment.

Calculation of diagnostic accuracy

Surgical histological diagnosis was not available to compare with the needle biopsy diagnosis in 24 of the 83 cases. Of the 59 cases, where surgical histological diagnoses were available, there were 42 TP results (22 Category 1, 20 Category 2 diagnoses). In five Category 2 diagnoses where there was diagnostic mismatch (Table 4), there was no case where a malignant diagnosis was missed or a benign lesion was diagnosed as malignant. Two of the cases in Table 4, wherein a diagnosis of ABC was revised to GCT and benign fibrous histiocytoma was revised to fibrous dysplasia following surgical histology, were considered as TP results while calculating diagnostic accuracy, as further management does not change with the revised diagnosis. None of these five mismatches led to actual clinical mismanagement. One case with Category 3 diagnosis (Table 6) wherein no evidence of neoplasia was seen on both needle biopsy and surgical histology was considered as a TN result. The overall diagnostic accuracy calculated was 73%.

Calculation of diagnostic yield

Percutaneous needle biopsy provided diagnosis allowing further appropriate management in 62 cases (all the 37 Category 1 diagnoses, 25 Category 2 diagnoses) for a diagnostic yield of 75% (62/83 biopsies). The Category 2 diagnoses included were 18 with matching surgical histology (Table 3), two cases which were not absolutely concordant with surgical histology but did not change management (ABC to GCT and benign fibrous histiocytoma to fibrous dysplasia, Table 4), two cases in Table 5 (florid inflammation and non-specific fibroconnective tissue) where no neoplastic cells were seen on needle biopsy and no adverse features were noted on imaging and clinical follow-up and three cases of benign osteoclast rich lesion in Table 5 (in these three cases the pathologist was confident of a benign diagnosis but unsure of exact type of histology, and the patients were managed conservatively).

Table 5 Category 2 diagnosis in five cases with only needle biopsy diagnosis

Diagnosis	No. of cases
Florid inflammation	1
Benign osteoclast-rich lesion	3
Non-specific fibro-connective tissue	1

Table 6 Surgical histology diagnosis in 14 patients with Category 3 diagnosis

Surgical histology diagnosis	No. of cases
Fibrous dysplasia	2
Active bone resorption, no neoplasia	1
Aneurysmal bone cyst	5
Simple bone cyst	2
Chondromyxoid fibroma	1
Benign fibrous histiocytoma	1
Giant-cell tumour	2

Discussion

Although lytic bone lesions are reported to have higher diagnostic yield on needle biopsy compared with sclerotic lesions, there are also diagnostic problems with needle biopsy of lytic bone lesions [11]. “Cystic” bone lesions that principally contain areas of necrosis and blood within them present difficulties not only in obtaining diagnostic material at needle biopsy but also in making the distinction between benignity and malignancy in the needle biopsy specimens and in arriving at the exact histological diagnosis on needle biopsy material [7, 11, 12]. In intramedullary lytic lesions such as GCT and ABC, the biopsy should be directed towards any solid components that may be present as it is this part of the lesion that is most likely to contain diagnostic tissue [13, 14]. However, in approximately 10–15% of lytic lesions, only blood clot is aspirated and histological results from such samples have been stated to be unsatisfactory [11]. In our study, specimens containing principally blood clots were obtained in 20.8% of cases with percutaneous needle biopsy providing diagnosis allowing appropriate further management in 62 cases, for a diagnostic yield of 75%. A diagnostic accuracy of 73% was achieved, wherein surgical histological diagnoses were available to compare with the needle biopsy diagnosis. In all the cases in which blood clots were considered inadequate to make a diagnosis and subsequent surgical histology was available, none were malignant. However, the small numbers here make it difficult to derive firm conclusions from this information. Opinion is divided on the diagnostic utility of blood clots obtained at core biopsy,

with some studies reporting such aspirated blood clots to be of no diagnostic value [7, 11], and others reporting a high diagnostic value to these blood clots in making diagnoses [8, 15]. Jelinek et al. [7] stated that aspiration of fluid or blood alone is a worthless diagnostic procedure. However, the authors do not describe in their technique whether they routinely attempted aspiration of osseous blood whilst performing biopsy of lytic bone lesions. As a result of most of the effort being concentrated at obtaining bone cores whilst performing bone biopsies, aspirating blood clots may be omitted [8]. The results of our study show a sufficiently good diagnostic yield from aspirated blood clots as to necessitate routine attempts at obtaining such material. Previous studies endorse this position. Tehranzadeh et al. [15] recommended that when bone biopsy is performed not only should bone cores be obtained but clots of aspirated blood must also be sent for histological examination. Hewes et al. [8] reported that only 72% of 54 biopsies were positive for malignancy if aspirated blood clot had not been obtained, while 94% were positive for malignancy when aspirated blood clot was examined. They and others concluded that special effort should be made to aspirate blood clots and examine paraffin sections of the same for malignant cells [8, 12]. Hewes et al. [8] demonstrated the value of aspirating blood clots in a prospective study by analysing the bone cores and blood clots separately. However, their study makes no mention as to whether the histopathologist was blinded to the result of the bone cores whilst analysing the clots, when both bone cores and blood clots were obtained. The data from our series identifies that the biopsy diagnosis was from the aspirated blood clots alone and has shown the usefulness of aspirating blood clots in the routine clinical practice of a tertiary referral Bone Tumour Unit. As a subset of the study, we looked at the remaining 317 patients in whom a bone or soft tissue core was obtained with or without blood clots, and the diagnostic yield in this group was 88% (280/317 biopsies). This is in keeping with the diagnostic yield obtained in a recent study by Vicillard et al. [5], who had a diagnostic yield of 87% for biopsy of lytic bone lesions. In their study, biopsies composed only of bone had an 86% yield and those composed of both bone and soft tissue had a 64.7% yield. None of the biopsies in their series were only blood clots. However, it is not clear from their study whether lesions with predominant cystic/fluid components on imaging were excluded from having percutaneous biopsy [5].

There are certain limitations to this study that are intrinsic to any retrospective investigation. There was more than one operator performing the biopsies and small variability of biopsy technique could have influenced the type of specimen obtained and the ultimate accuracy. We did not evaluate the contribution of blood clots to diagnoses when adequate bone or soft tissue cores were also obtained with it, because of the retrospective nature of this study. However, it has been shown that in biopsies where bone cores and blood clots are available, the blood clot is better diagnostic material, especially in showing the morphology of malignant tissue [8]. The cohort of patients with lytic bone lesions in this study is not fully representative of all the intramedullary lytic lesions, but rather are those that were pre-selected for image-guided biopsy.

In conclusion, the results of our study show a sufficiently good diagnostic value in aspirating blood clots as to necessitate routine attempts at obtaining such clots while performing percutaneous biopsy of intramedullary lytic bone lesions.

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