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Fine needle aspiration for the diagnosis and treatment of musculoskeletal tumours

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ABSTRACT

Objective: The aim of this study was to evaluate the diagnostic accuracy of FNA and analyse its efficacy in enabling the initiation of treatment in musculoskeletal tumours.
Methods: A total of 130 FNA were performed (94 bone and 36 soft tissue lesions) guided by CT scan (n = 64), ultrasonography (n = 36) and radioscopy (n = 30). Diagnostic yield and accuracy were evaluated. A diagnosis was considered accurate when confirmed by histology or ulterior clinical/imaging evaluation. Exclusion of malignancy or infection was considered as diagnoses.
Results: Ninety diagnoses (69.2%) were obtained: 87 (96.7%) were accurate and 3 were wrong. FNA was non-diagnostic in 40 cases (30.8%) but in 15 (11.5%) it has been possible to conclude if the lesion was malignant (n = 6) or benign (n = 9). This method was completely inconclusive in 25 cases (19.2%).
Conclusion: Despite the low diagnostic yield, accuracy was high. FNA allowed the initiation of treatment in all 87 patients with a correct diagnosis and in 9 in which malignancy was excluded. Two of the 6 biopsies with the information of malignancy were soft tissue lesions. Even here, treatment could be done, as the majority of soft tissue sarcoma protocols begin with surgery. This study validates FNA as a method with a high diagnostic accuracy.

Introduction

Fine needle aspiration (FNA) is a well-established tool for the diagnosis of palpable and non-palpable lesions such as those localised to lymph nodes, salivary glands, breast, liver and pancreas, among others. Less enthusiasm is felt for the usage of this technique in the investigation of bone and soft tissue tumours; this is primarily due to their rarity and to difficulties in studying their morphology and obtaining their diagnoses.[1]

Even in specialized centres, where pathologists integrate all the clinical and image information, FNA has not reached the value of trucut biopsy, which is considered the main alternative to incisional biopsy.[1,2] Several factors are in the basis of the existing scepticism such as the small volume of sample collected, the fact that it only characterizes the sample cytologically, the overlapping of the cytomorphology of various tumours and the large variability of results published in studies over the years.[2]

However, given that it is a less invasive procedure, performed in an outpatient basis without general anaesthesia or hospitalization, as well as having a much lower cost, FNA is an attractive technique when compared to more invasive options. FNA has also the advantage of enabling the aspiration of different parts of a same tumour, which is particularly important in large and heterogeneous neoplasms.

The purpose of this study was to evaluate the diagnostic accuracy of fine-needle biopsy, and to analyse to which extent this method enables the initiation of treatment, clarifying its role in addressing musculoskeletal tumours.

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Materials and methods

One hundred and thirty patients submitted to FNA-derived cell block over a 3-year period were retrospectively reviewed. In the majority of these cases a diagnosis of bone or soft tissue tumour was necessary to start treatment but in a few the exclusion of malignancy was also important. All procedures were performed by one single team (one orthopaedic surgeon and one radiologist) and samples were analysed by the same pathologist.

The average age of the patients was 53.2 years (12–90). There were 59 males and 71 females. Ninety-four underwent bone and 36 soft tissue biopsies. All FNA were performed under image guidance (Fig. 1). Table 1 depicts the clinical characteristics of the tumours, their anatomical location and the imagiological method used to localize them.

The most suitable route was chosen in order to avoid noble structures such as neurovascular bundles and organs. After the selection of the area, skin was anesthetized with 3–5 ml of 2% Lidocaine and cytoaspiration with a 22-gauge needle was performed. Samples were placed in CytoRich® Red Preservative Fluid and sent to laboratory. The pathologist did not do any preliminary evaluation during the procedure. All samples were centrifuged at 1500 rpm for 10 min, after which the supernatant was discarded. Haematoxylin and Histolgel® were then added and the sample was vortexed for homogenisation. Homogenised sample was then frozen. Frozen tissue was placed in biopsy cassettes and used for histology (Haematoxylin and Eosin) and immunohistochemistry (Fig. 2).

The diagnostic yield (ratio between the number of diagnosis achieved and the number of all procedures) and accuracy (ratio between the confirmed diagnosis and the number of established diagnosis) were evaluated. A diagnosis was considered to be accurate when it was confirmed by histology—trucut biopsy, incisional biopsy, surgery—or ulterior clinical and imaging evaluation as some benign tumours, metastases and hematopoietic lesions do not need histological confirmation. Diagnostic yield and accuracy of soft tissue and bone lesions were analysed and compared. Statistical analysis was performed using GraphPad Prism v. 6.0. The differences between means were compared using *t*-test. A p value < 0.05 was considered to represent a statistically significant difference.

The minimum follow up was 2 years. Exclusion of malignancy or infection, when clinically suspected, was included in the group of diagnosis.

Results

In 90 patients (69.2%) a diagnosis was obtained and in 87 (96.7%) were accurate. In 36 cases accuracy was confirmed by histology and in 54 cases by clinical and imaging valuation.

In the group of osseous lesions diagnoses were: 28 metastases, 17 primitive malignant tumours, 7 benign tumours, 10 hematologic diseases and 2 infections; in 7 cases pathology could be excluded. In this group only 2 benign lesions were misdiagnosed: a spondylodiscitis of a dorsal vertebra was diagnosed as a Giant Cell Tumour and a low-grade chondrosarcoma of the scapula was assumed as an enchondroma (Table 2).

In the group of soft tissue tumours 10 lesions were found to be benign, 6 malignant and 3 were classified as hematologic diseases.

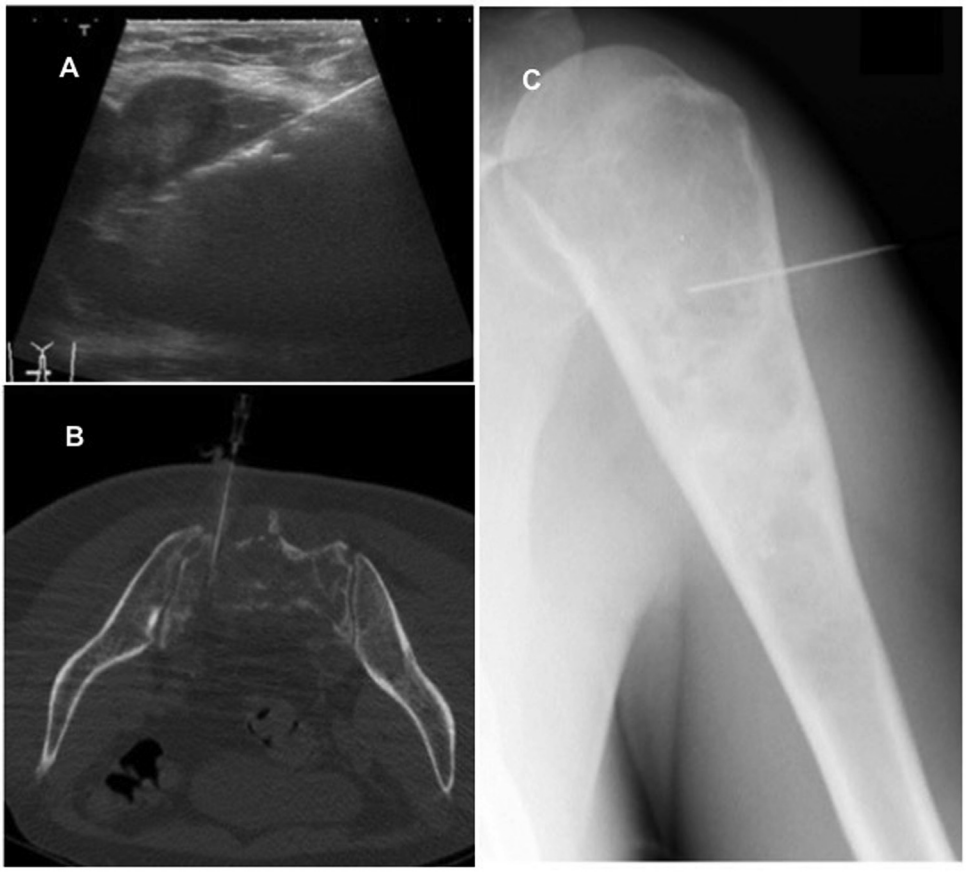

Fig. 1. Examples of the imagiological methods used for tumour localisation: A) Ultrasonographic view of a soft tissue lesion in the thigh, B) Identification of a bone lesion in the sacrum using CT, C) Identification of a bone lesion in the humerus using X-ray.

Table 1
Clinical characteristics of bone and soft tissue lesions diagnosed by FNA.

Total	Type	Gender	Mean age (range)	Anatomical location	Image guidance
130 biopsies	Bone 94 Soft tissue 36	Male 59 Female 71	53.2 (12–90)	Lower limb 45 Upper limb 22 Spine 27 Pelvis 24 Trunk 12	CT-scan 64 Ultrasonography 36 Radioscopy 30

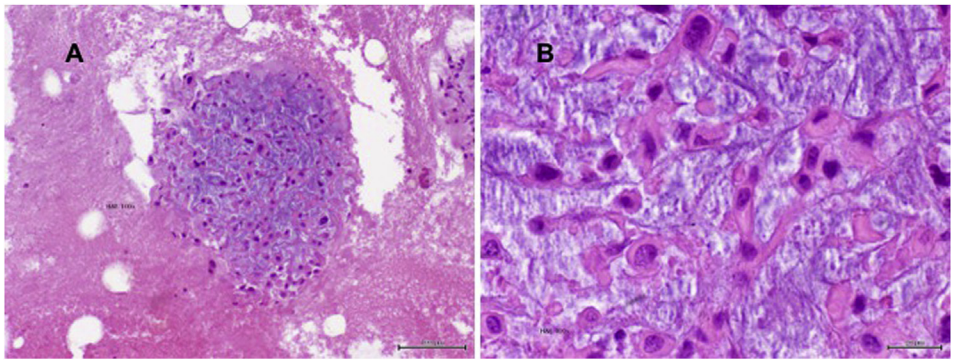

Fig. 2. Chordoma of sacrum. A (HE 100×). B (HE 400×). Although "phisaliphorous cells" are not present, epithelioid cells are characteristically arranged as cords and embedded in an extracellular myxoid matrix.

In this group an extra abdominal desmoid tumour of the dorsal paravertebral region was wrongly diagnosed as a liposarcoma (Table 2).

The overall diagnostic yield was 69.2% and the diagnostic accuracy 96.7%. The diagnostic yield for bone lesions alone was 75.5% and that for soft tissue lesions was 52.8% ($p = 0.0187$). The diagnostic accuracy for bone lesions alone was 97.2% and that for soft tissue lesions was 94.7% ($p = 0.5704$) – Table 3.

FNA was non-diagnostic in 40 cases (30.8%) but in 15 biopsies (11.5%) it was possible to conclude if the lesion was malignant ($n = 6$) or benign ($n = 9$) and this information was correct in all cases. It was then considered a completely inconclusive result in 25 cases (19.2%). There were no complications associated with these procedures and all patients were discharged on the same day of the procedure.

Discussion

All cytological results should always be interpreted integrating the clinical and imaging context, which influence the diagnosis regardless of the diagnostic modality chosen. The value of FNA also depends on the operator technique[3] and on the experience of the pathologist.[4]

The first challenge that the FNA faces is obtaining an appropriate sample - checking whether the sample is sufficient in quantity and representative enough to allow for the diagnosis. This point is measured by yield, and values can vary between 3 and 31% of inadequate samples.[2,5] There are several reasons that help to explain the wide variation of rates, including the type of lesion studied and the accomplishment of preliminary evaluation. The preliminary evaluation comes from the observation of the sample by the pathologist during the procedure, allowing its repetition if necessary, with substantially improved results when compared to studies where this evaluation is not performed.[5,6] In this study, the quantity and quality of the sample was decided by the executant alone without the presence of the pathologist. Perhaps this was the reason for the poor overall diagnostic yield (69.2%). There are two reasons for a non-diagnostic result. The first is a scant, acellular or artifactually distorted specimen. The second is when the result is incompatible with the clinical and/or image impression.[5,6] All the 25 completely inconclusive results were due to technical issues with samples. The yield, however, was significantly higher for bone tumours than for soft tissue lesions ($p = 0.0187$). Again, this difference may be explained by the same two reasons: analysis of tissue architecture and morphology are more important in identifying and distinguishing between soft tissue lesion subtypes and the fact the clinical and imaging information are more informative in the case of bone than in soft tissue lesions.[7]

The accuracy of a diagnostic technique is the most important parameter in its assessment, and obtaining an exact result is its main objective. In different studies, the diagnostic accuracy of FNA varies between 75% and 98%, where the lowest values are obtained in smaller samples.[3,8,9] If it were only considered studies with high samples ($n > 300$) this value would be greater than 95%.[2,6,10–12] Here, the accuracy was 96,7%, which is even superior to that reported in other studies[3,9,11,13] showing the reliability in the diagnosis of benign tumours, sarcomas, metastases, infections, hematologic disease lesions and in excluding pathology. No significant differences in accuracy were found between soft tissue and bone lesions ($p = 0.05704$).

In many cases of musculoskeletal tumours, the specific diagnosis has a minor role in the initiation of treatment. The histological grade, staging and anatomical location are the most important factors for therapeutic decisions and it may even be said that the existing protocols are less based on the histological subtype. Some authors go further, referring to the minor importance of histological subtype and highlighting the relevance of the distinction between sarcoma and metastasis, since the treatment of most sarcomas in adults is primarily based on its size, location and proximity to vital structures.[14] Kilpatrick et al[15] considered FNA sufficient to initiate treatment in 83% of soft tissue tumours and in 87% of bone tumours. In a study conducted in 2010, definitive treatment could be initiated based solely on FNA in 81.3% of benign, in 78% of malignant and in 43% of the indeterminate tumours.[12] Assuming the same criteria, the technique in the present study would therefore allow for the initiation of treatment in all 87 patients with a diagnosis

Table 2
Correlation between cytological and final diagnosis in bone and soft tissue tumours.

Patient	Bone/Soft tissue tumour	Cytological diagnosis	Final diagnosis
1	Bone	Osteosarcoma	Osteosarcoma
2	Bone	Benign lesion	Enchondroma
3	Bone	Malignant lesion	Ewing sarcoma
4	Soft tissue	Inconclusive	Neurofibroma
5	Soft tissue	Haemangioma	Haemangioma
6	Bone	Malignant lesion	Ewing sarcoma
7	Soft tissue	Synovial sarcoma	Synovial sarcoma
8	Bone	Metastasis	Metastasis
9	Bone	Myeloma	Myeloma
10	Bone	Benign lesion	Osteoid osteoma
11	Bone	Inconclusive	Infection
12	Soft tissue	Lymphoma	Lymphoma
13	Bone	Giant Cell Tumour	Infection
14	Bone	Giant Cell Tumour	Giant Cell Tumor
15	Soft tissue	Benign	Schwannoma
16	Bone	Chondrosarcoma	Chondrosarcoma
17	Bone	Benign lesion	Chondromyxoid fibroma
18	Soft tissue	Inconclusive	Lipoma
19	Bone	Chondrosarcoma	Chondrosarcoma
20	Bone	Myeloma	Myeloma
21	Soft tissue	Haemangioma	Haemangioma
22	Bone	Infection	Infection
23	Bone	Exclusion tumour	Exclusion tumour
24	Bone	Inconclusive	Chondrosarcoma
25	Bone	Inconclusive	Osteochondroma
26	Soft tissue	Inconclusive	Synovial sarcoma
27	Soft tissue	Myeloma	Myeloma
28	Bone	Inconclusive	Chondrosarcoma
29	Soft tissue	Lymphoma	Lynphoma
30	Soft tissue	Inconclusive	Myositis ossificans
31	Soft tissue	Benign lesion	Haemangioma
32	Soft Tissue	Inconclusive	Haemangioma
33	Bone	Chondrosarcoma	Chondrosarcoma
34	Soft tissue	Ewing sarcoma	Ewing sarcoma
35	Bone	Inconclusive	Haemangioma
36	Soft tissue	Inconclusive	Myxoma
37	Bone	Myeloma	Myeloma
38	Bone	Chondrosarcoma	Chondrosarcoma
39	Soft tissue	Ganglion cyst	Ganglion cyst
40	Bone	Inconclusive	Myeloma
41	Bone	Chordoma	Chordoma
42	Bone	Ewing Sarcoma	Ewing Sarcoma
43	Bone	Metastasis	Metastasis
44	Bone	Metastasis	Metastasis
45	Bone	Metastasis	Metastasis
46	Bone	Chordoma	Chordoma
47	Bone	Myeloma	Myeloma
48	Bone	Enchondroma	Chondrosarcoma
49	Bone	Giant Cell Tumour	Giant Cell Tumour
50	Bone	Infection	Infection
51	Bone	Metastasis	Metastasis
52	Bone	Metastasis	Metastasis
53	Bone	Metastasis	Metastasis
54	Soft tissue	Inconclusivo	Angiolipoma
55	Bone	Metastasis	Metastasis
56	Bone	Osteosarcoma	Osteosarcoma
57	Soft tissue	Benign lesion	Haemangioma
58	Bone	Benign lesion	Aneurysmal bone Cyst
59	Soft tissue	Liposarcoma	Aggressive fibromatosis
60	Bone	Benign lesion	Aneurysmal bone cyst
61	Soft tissue	Lipoma	Lipoma
62	Soft tissue	Inconclusive	Schwannoma
63	Bone	Metastasis	Metastasis
64	Bone	Brown tumour	Brown tumour
65	Bone	Exclusion tumour	Exclusion tumour
66	Bone	Osteosarcoma	Osteosarcoma
67	Bone	Exclusion tumour	Exclusion tumour
68	Bone	Angiosarcoma	Angiosarcoma
69	Bone	Exclusion tumour	Exclusion tumour
70	Bone	Benign lesion	Non ossifying fibroma
71	Bone	Metastasis	Metastasis
72	Bone	Metastasis	Metastasis
73	Bone	Inconclusive	Osteosarcoma

(*continued on next page*)

Table 2 (*continued*)

Patient	Bone/Soft tissue tumour	Cytological diagnosis	Final diagnosis
74	Bone	Chondrosarcoma	Chondrosarcoma
75	Bone	Metastasis	Metastasis
76	Soft tissue	Lipoma	Lipoma
77	Bone	Metastasis	Metastasis
78	Bone	Giant Cell Tumour	Giant Cell Tumour
79	Bone	Metastasis	Metastasis
80	Soft tissue	Lipoma	Lipoma
81	Bone	Osteosarcoma	Osteosarcoma
82	Soft tissue	Ewing sarcoma	Ewing sarcoma
83	Bone	Myeloma	Myeloma
84	Bone	Inconclusive	Infection
85	Soft tissue	Lipoma	Lipoma
86	Bone	Inconclusive	Lymphoma
87	Soft tissue	Liposarcoma	Liposarcoma
88	Bone	Metastasis	Metastasis
89	Bone	Metastasis	Metastasis
90	Bone	Metastasis	Metastasis
91	Bone	Myeloma	Myeloma
92	Bone	Chondrosarcoma	Chondrosarcoma
93	Bone	Metastasis	Metastasis
94	Bone	Metastasis	Metastasis
95	Bone	Exclusion tumour	Exclusion tumour
96	Bone	Metastasis	Metastasis
97	Bone	Myeloma	Myeloma
98	Bone	Metastasis	Metastasis
99	Bone	Metastasis	Metastasis
100	Bone	Metastasis	Metastasis
101	Soft tissue	Giant Cell Tumor tendon sheaths	Giant Cell Tumor tendon sheaths
102	Bone	Metastasis	Metastasis
103	Soft tissue	Myxofibrosarcoma	Myxofibrosarcoma
104	Bone	Inconclusive	Enchondroma
105	Bone	Lymphoma	Lymphoma
106	Bone	Metastasis	Metastasis
107	Soft tissue	Inconclusive	Liposarcoma
108	Bone	Myeloma	Myeloma
109	Soft tissue	Inconclusive	Leiomyosarcoma
110	Bone	Inconclusive	Metastasis
111	Soft tissue	Myxoma	Myxoma
112	Soft tissue	Schwannoma	Schwannoma
113	Bone	Giant Cell Tumour	Giant Cell Tumour
114	Bone	Exclusion tumour	Exclusion tumour
115	Bone	Exclusion tumour	Exclusion tumour
116	Bone	Myeloma	Myeloma
117	Bone	Ewing sarcoma	Ewing sarcoma
118	Bone	Inconclusive	Chondrosarcoma
119	Bone	Metastasis	Metastasis
120	Soft tissue	Malignant lesion	Lipossarcoma
121	Soft tissue	Malignant lesion	Leiomyosarcoma
122	Bone	Chondrosarcoma	Chondrosarcoma
123	Soft tissue	Benign lesion	Clear cell hidradenoma
124	Bone	Inconclusive	Osteosarcoma
125	Bone	Malignant lesion	Osteosarcoma
126	Bone	Metastasis	Metastasis
127	Bone	Inconclusive	Ewing sarcoma
128	Bone	Malignant lesion	Ewing sarcoma
129	Soft tissue	Malignant lesion	Lipossarcoma
130	Bone	Inconclusive	Metastasis

Table 3
Diagnostic yield and diagnostic accuracy in bone and soft tissue tumours. p Values represent the difference between bone and soft tissue tumours.

	Overall	Bone tumours	Soft tissue tumours	p (bone vs soft tissue)
Diagnostic yield	(90/130) 69.2%	(71/94) 75.5%	(19/36) 52.8%	0.0187
Diagnostic accuracy	(87/90) 96.7%	(69/71) 97.2%	(18/19) 94.7%	0.05704

proven correct and in the other 9 in which malignancy had been excluded. This would be 96 of the 130 (73.8%) – Table 4. Considering the 6 biopsies without diagnosis but with the information of being malignant, 2 were soft tissue lesions. Even in these cases, treatment could have been done, as the great majority of soft tissue sarcoma protocols begin with surgical excision. Moreover, if the treatment had been done according to the 3 wrong diagnoses, in these cases, the final result would not be considered a disaster.

Finally, caution should be taken in malignancies since the initial treatment is different according to each diagnosis. The utility of cytogenetics in the routine work-up of sarcomas collected by FNA has been reinforced.[16] It is possible, for instance, to confirm an Ewing

Table 4
Non-diagnostic results, cases in which a correct diagnosis was established and cases in which treatment was initiated in the overall cohort of patients and also in bone and soft tissue tumours. p Values represent the differences between the mean in bone and soft tissue tumours.

	Overall	Bone tumours	Soft tissue tumours	p (bone vs soft tissue)
Non-diagnostic results	40/130 30.8%	23/94 24.5%	17/36 47.2%	0.0117
Establishing correct diagnosis	(87/130) 66.9%	(69/94) 73.4%	(18/36) 50.0%	0.0109
Initiating treatment	(96/130) 73.8%	(74/94) 78.7%	(22/36) 61.1%	0.0412

sarcoma by the characteristic chromosome translocation t (11, 12) in samples of FNA. Nevertheless this was not done in this study.

In conclusion, despite the low diagnostic yield the accuracy of FNA was very high and would therefore permit the initiation of treatment in most cases, except in those in which the result suggests malignancy without a precise diagnosis.

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