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.

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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 cytotologically, 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.
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% Lido-caine 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 spondylo-discitis 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.

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**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.
In this study, the necessary, with substantially improved results when compared to the pathologist during the procedure, allowing its repetition if the preliminary evaluation comes from the observation of the sample studied and the accomplishment of preliminary evaluation. The reason for the poor overall diagnostic yield (69.2%) was 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.

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. If it were only considered studies with high samples (n > 300) this value would be greater than 95%. Here, the accuracy was 96.7%, which is even superior to that reported in other studies 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. Kilpatrick et al. 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. 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

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

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

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Fig. 2. Chordoma of sacrum. A (HE 100×). B (HE 400×). Although "philalporous cells" are not present, epithelioid cells are characteristically arranged as cords and embedded in an extracellular myxoid matrix.
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             | Haemangiomma          | Haemangiomma    |
| 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 Tumour|
| 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             | Haemangiomma          | Haemangiomma    |
| 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              | Lymphoma        |
| 30      | Soft tissue             | Inconclusive          | Myositis ossificans |
| 31      | Soft tissue             | Benign lesion         | Haemangiomma    |
| 32      | Soft tissue             | Inconclusive          | Haemangiomma    |
| 33      | Bone                    | Chondrosarcoma        | Chondrosarcoma  |
| 34      | Soft tissue             | Ewing sarcoma         | Ewing sarcoma   |
| 35      | Bone                    | Inconclusive          | Haemangiomma    |
| 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             | Inconclusive          | Angiolipoma     |
| 55      | Bone                    | Metastasis            | Metastasis      |
| 56      | Bone                    | Osteosarcoma          | Osteosarcoma    |
| 57      | Soft tissue             | Benign lesion         | Haemangiomma    |
| 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)
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...
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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