

The accuracy of fine needle aspiration biopsy (FNAB) in diagnosing musculoskeletal lesion

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ABSTRACT

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Fine needle aspiration biopsy (FNAB) is a relatively non-invasive diagnosis of musculoskeletal lesions that is very challenging in some musculoskeletal cases. This study aimed to evaluate the diagnostic utility of FNAB in musculoskeletal lesions. This was a retrospective cross-sectional study involving 180 musculoskeletal patients who underwent FNAB procedure, with or without ultrasound-guided in the Department of Anatomical Pathology, Faculty of Medicine, Public Health and Nursing, Universitas Gadjah Mada/Dr. Sardjito General Hospital, Yogyakarta between 2018 and 2021. The obtained data were then statistically analyzed for sensitivity, specificity, and accuracy. Of 180 cases, 90 (50%) were confirmed with histopathology examination. Further analysis revealed that 33 cases were confirmed positive, 45 patients were true negative, 2 cases were false positive, and 10 were cases false negative. The overall diagnostic sensitivity, specificity, and accuracy of FNAB in musculoskeletal lesions were 76.8, 95.7, and 83%, respectively. FNAB can lead to misinterpretation in cases that show similar morphologic features. Therefore, clinical information and imaging results are necessary to be correlated. In conclusion, FNAB is an efficient and effective technique for early diagnosis in musculoskeletal cases. FNAB can be used to establish the diagnosis of an inoperable tumor because of its high accuracy.

ABSTRACT

Biopsi aspirasi jarum halus (AJH) merupakan metode relatif non-invasif untuk mendiagnosis lesi muskuloskeletal yang cukup sulit dilakukan pada beberapa kasus muskuloskeletal. Penelitian ini bertujuan mengevaluasi nilai diagnostik AJH pada lesi muskuloskeletal. Penelitian menggunakan rancangan potong lintang retrospektif pada 180 kasus muskuloskeletal yang menjalani prosedur AJH, dengan atau tanpa panduan USG, di Departemen Anatomi, Fakultas Kedokteran, Kesehatan Masyarakat, Keperawatan, Universitas Gadjah Mada/RSUP Dr. Sardjito, Yogyakarta antara tahun 2018 dan 2021. Data yang diperoleh dianalisis secara statistik untuk sensitivitas, spesifisitas, dan akurasi. Dari 180 kasus, terdapat 90 kasus (50%) yang terkonfirmasi melalui pemeriksaan histopatologi. Analisis lebih lanjut menunjukkan bahwa 33 kasus benar-benar positif, 45 kasus benar-benar negatif, 2 kasus positif palsu, dan 10 kasus negatif palsu. Sensitivitas, spesifisitas, dan akurasi diagnostik AJH pada lesi muskuloskeletal berturut-turut adalah 76,8, 95,7, dan 83%. Aspirasi jarum halus dapat menyebabkan misinterpretasi pada kasus yang menunjukkan ciri morfologi serupa. Oleh karena itu, perlu dilakukannya korelasi antara informasi klinis dan hasil radiologis. Dapat disimpulkan, AJH merupakan teknik yang efisien dan efektif untuk mendapatkan diagnosis dini pada kasus muskuloskeletal. Aspirasi jarum halus dapat digunakan sebagai pilihan untuk menegakkan diagnosis jika terjadi tumor yang tidak dapat dioperasi karena akurasi yang tinggi.

Keywords:

FNAB;
cytology;
musculoskeletal lesion;
accuracy

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INTRODUCTION

Open biopsy procedure has been the gold standard for diagnosing musculoskeletal cases. This procedure has high accuracy, however it has several disadvantages, such as an increased risk of infection, longer length of hospital stays, and the risk of the tumor attaching to surrounding tissue or vessel.¹ Fine needle aspiration biopsy (FNAB) has been used extensively in several organs for early diagnosis, such as breast, lung, and thyroid. Fine needle aspiration biopsy is considered a fast, easy, and affordable method to obtain a diagnosis.² Good sampling triage by experienced pathologists, ultrasound-guided technique, and sufficient clinical information of patients may contribute to higher sensitivity and specificity in FNAB.³

Studies showed that FNAB can accurately diagnose musculoskeletal lesions with an accuracy as high as 81-97%.^{4,5} However, a systematic review and meta-analysis study conducted by Chambers *et al.*⁶ reported that FNAB provides higher accuracy for benign bone lesions compared to malignant ones, but definitively diagnoses soft tissue lesions more consistently. Therefore, it is recommended to use FNAB more frequently in the diagnostic workup of bone and soft tissue lesions to minimize invasive procedures for patients.

In Indonesia, data and research on the utility of FNAB in diagnosing musculoskeletal lesions are still limited. Additionally, selecting the appropriate biopsy technique in musculoskeletal cases is complicated and often leads to diagnostic errors. This study aimed to evaluate the accuracy of FNAB in musculoskeletal cases that often can be falsely negative and positive in Dr. Sardjito General Hospital, Yogyakarta, Indonesia.

MATERIALS AND METHODS

Subjects

Fine needle aspiration biopsy cases of musculoskeletal lesions, with or without ultrasound-guided (USG), were collected retrospectively from the Department of Anatomical Pathology, Faculty of Medicine, Public Health and Nursing, Universitas Gadjah Mada/Dr. Sardjito Hospital, Yogyakarta, Indonesia, from 2018 until 2020. The study included only cases with confirmed histopathology and complete data on demographic, tumor location, and histopathological subtype. Cases with incomplete data and different histopathology locations from FNAB locations were excluded. This study was approved by the Medical and Health Research Ethics Committee (MHREC), Faculty of Medicine, Public Health and Nursing, Universitas Gadjah Mada/Dr. Sardjito General Hospital, Yogyakarta (reference number: KE/FK/0878/EC/2023).

Protocol

Fine needle aspiration biopsies were performed, both with and without USG guidance. The cytopathology finding from FNAB was considered to be the independent variable, while the histopathological result from excision and biopsy was the dependent variable. Two experienced pathologists blindly examined and documented the samples to avoid potential bias.

Statistical analysis

Data were presented in percentage, and the diagnostic analysis was performed using a 2x2 table to determine the sensitivity, specificity, and accuracy of FNAB in musculoskeletal cases.

RESULTS

Of 180 cases of FNAB in the musculoskeletal lesion, 90 (50%) met the study's criteria. Of these 90 cases, 22 cases were from 2018, 1 patient was from 2019, and 42 cases were from 2020. TABLE 1 presents general subject characteristics based on gender and age. Thirty-seven subjects were male (41.1%), and 53 were female (58.9%). The youngest subject

was 6 y.o., while the eldest was 94 y.o.

The data about the predilection of musculoskeletal lesions is shown in TABLE 2. The highest incidence was presented in the 41 to 60 y.o. group (34.5%). The most common location for musculoskeletal lesions was the femur in 20 cases (22.2%), followed by the tibia in 9 patients (10%), genu in 8 cases (8.9%), pedis in 7 cases (7.8%), meanwhile cruris and ulna in 5 cases (5.7%).

TABLE 1. Subject characteristics based on gender and age group (2018 – 2021)

Characteristic	Frequency	%
Gender		
• Male	37	41.1
• Female	53	58.9
Age		
• 0-20	28	31.1
• 21-40	21	23.3
• 41-60	31	34.5
• >60	10	11.1

TABLE 2. The predilection of the musculoskeletal lesion (2018 – 2021)

Predilection	Frequency	%
Sternoclavicular	1	1.1
Ankle	3	3.3
Antebrachia	2	2.2
Bone marrow	2	2.2
Cruris	5	5.7
Chest wall	3	3.3
Digit pedis	1	1.1
Elbow	1	1.1
Femur	20	22.2
Forearm	3	3.3
Fibula	1	1.1
Genu	8	8.9
Gluteus	3	3.3
Humerus	3	3.3
Lumbar	1	1.1
Mandibula	2	2.2
Manus	4	4.5
Maxilla	3	3.3
Pedis	7	7.8
Pelvis	2	2.2
Scapula	1	1.1
Tibia	9	10
Ulna	5	5.7

Fine needle aspiration biopsy cases confirmed with the histopathological result are presented in TABLE 3. Diagnostic analysis of 90 patients showed concordance findings of malignant results in FNAB and histopathological examination in 33 cases (36.7%). The concordance benign result of FNAB and histopathological examination was observed in 45 patients (50%). However, there was a discrepancy between malignant results in FNAB and benign results in a histopathological examination in 2 cases (2.2%). Lastly, 10 patients (11.1%) showed benign results in FNAB. Meanwhile, the histopathological findings revealed malignant results.

The diagnostic value was calculated based on data in TABLE 4. The sensitivity of FNAB in musculoskeletal cases was 76.8%. Meanwhile, the specificity was 95.7%. The positive predictive value (PPV) was 94.3%. Meanwhile, negative

predictive value (NPV) was 81.8%. In this study, the accuracy of FNAB in musculoskeletal cases was 83%.

The summary of the histopathology result of all cases is shown in TABLE 5. In this study, most cases of the malignant musculoskeletal lesion were osteosarcoma; 8 cases were conventional osteosarcoma without a specific subtype, 2 cases were conventional osteoblastic type osteosarcoma, 2 cases were conventional giant cell-rich type osteosarcoma, 1 case was epithelioid type osteosarcoma and 1 case with telangiectatic osteosarcoma. Other malignant cases were non-Hodgkin lymphoma (NHL) in 5 cases and chondrosarcoma in 5 cases. In benign musculoskeletal lesions, the most common cause was Giant Cell Tumor (GCT) in 12 cases, followed by nonspecific benign lesions in 5 cases and hemangiomas in 4 cases. FIGURE 1 shows a representative image result of FNAB.

TABLE 3. FNAB finding compared to histopathology result

	Histopathology		Total
	Malignant	Benign	
FNAB			
Malignant	33	2	35
Benign	10	45	55

Note: FNAB: fine needle aspiration biopsy

TABLE 4. Sensitivity, specificity, PPV, NPV, and the accuracy of FNAB compared to histopathology

	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	Accuracy (%)
FNAB in musculoskeletal lesion	76.8	95.7	94.3	81.8	83.0

Note: FNAB: fine needle aspiration biopsy; PPV: positive predictive value; NPV: the negative predictive value

TABLE 5. Summary of the histopathology result

Malignant	Frequency (n)	Benign	Frequency (n)
Conventional osteosarcoma, unspecific type	8	Giant cell tumor (GCT)	12
Conventional osteosarcoma, osteoblastic type	2	Benign nonspecific	5
Conventional osteosarcoma, giant cell-rich type	2	Hemangioma	4
Conventional osteosarcoma, fibroblastic type	1	Osteomyelitis	3
Osteosarcoma epithelioid type	1	Callus	2
Osteosarcoma, telangiectatic type	1	Aneurysmal bone cyst	2
Chondrosarcoma	5	Fibrous dysplasia	2
Non-Hodgkin lymphoma (NHL)	5	Benign fibrous histiocytoma	1
Metastatic breast adenocarcinoma	3	Benign odontogenic cyst	1
Metastatic papillary thyroid carcinoma	2	Neurofibroma	1
Small round blue cell tumor	2	Osteomalacia (Rickets)	1
Metastasis parathyroid carcinoma	1	Suppurative inflammation with cholesterol ester granuloma	1
Myxofibrosarcoma	1	Rheumatoid nodule	1
Myxoid spindle cell sarcoma	1	Simple bone cyst	1
Rhabdomyosarcoma	1	Chronic Synovitis	1
Classic Adamantinoma	1	Chromoblastomycosis	1
Adamantinoma with squamous differentiation	1	Ganglion cyst	1
Liposarcoma	1	Gout arthritis	1
Malignant germ cell tumor	1	Epidermoid cyst	1
Plasmacytoma	1	Lipoma	1
Rhabdomyosarcoma	1	Myofibroma	1
Undifferentiated pleomorphic sarcoma	1	Neurofibroma	1
		Pigmented villonodular synovitis.	1
		Synovial cyst	1

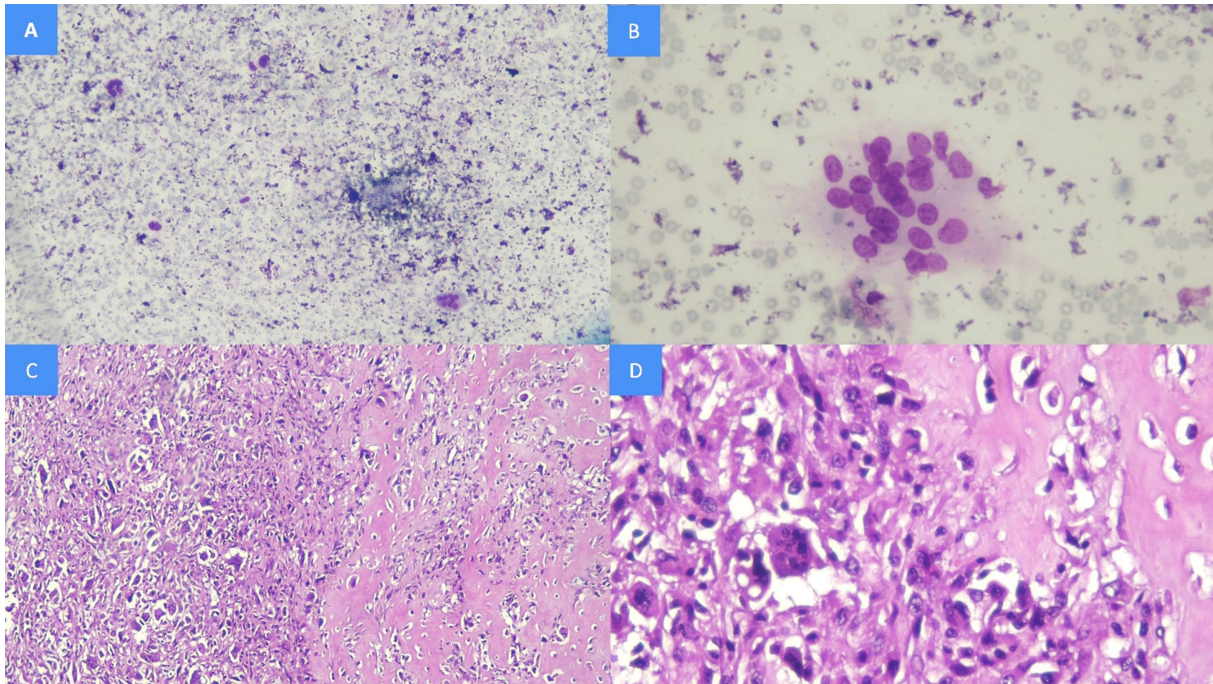


FIGURE 1. A) A representative image of FNAB showed multinucleated giant cells with necrotic debris as its background (Diff Quick,100x). B) On higher magnification, there is a multinucleated giant cell with 20-30 nuclei (Diff Quick, 400x). C) Confirmatory histopathology showed malignant tumor cells with high-grade polymorphic cells, nuclei ranging from round, oval, spindle, hyperchromatic with visible nucleoli, among them there are multinucleated giant cells (HE, 100x). D. On higher magnification, there are giant cells and surrounding tumor cells with osteoid matrix on the background (HE, 400x).

DISCUSSION

Fine needle aspiration biopsy is a minimally invasive, easy, and affordable method to diagnose musculoskeletal cases.⁷ The accuracy of FNAB in various studies ranges from 75%-98%, where the accuracy was higher in the study with a larger sample size (>300 samples).⁸⁻¹⁰ In this study, the accuracy of FNAB is 83%. This is already good, considering the sample used is below 100. Most of the false negative cases were caused by insufficient and acellular samples. This is possibly due to the problematic location of the lesion, the intact bone cortex, and the lesions that are cystic, necrotic, or hemorrhagic. In another study, it was stated that the percentage of insufficient samples reached 15%.¹¹ This, in turn, becomes the biggest challenge for FNAB

in diagnosing musculoskeletal lesions. In this study, there were 5 cases of metastatic carcinoma from other organs, where the accuracy of FNA reaches 100% in metastatic patients. This is higher compared to other similar studies.¹²⁻¹³

Giant cell tumor was this study's most benign tumor finding. There are two false positive results of GCT with FNAB, whereas confirmatory histopathological showed a giant cell riched variant of osteosarcoma (FIGURE 1). Case one was a 59 y.o. patient with a tumor located at the distal radius. There is also one false positive case of 16 a 16 y.o. female with a tumor near the tibia. Fine needle aspiration biopsy result suggested an aneurysmal bone cyst. However, the histopathological result revealed conventional osteosarcoma, a giant cell-rich variant.

Diagnosis of GCT of the bone with FNA had many challenges compared with conventional biopsy since some bone tumors presented with multinucleated giant cell (osteoclast) or giant cell-like osteoclasts, such as GCT of the bone, GCT of Paget's disease, chondroblastoma, aneurysmal bone cyst, and giant cell riched subtype of osteosarcoma.¹⁴ The ability to differentiate those entities is significant because it relates to prognosis and clinical management. The bone GCT has a preference in young adults and mainly affects the epiphysis of the long bones. At the same time, osteosarcoma mainly occurs on metaphysis-diaphysis of the long bones in adolescents and young adults, with predominance in male patients. The aneurysmal bone cyst usually occurs in the first two decades of life with a small predomination of females and mainly affects the metaphysis of the long bones.¹⁵ On the nonspecific location or clinical presentation, mutation of H3G34W and immunohistochemistry (IHC) staining of H3K36M have high specificity to diagnose GCT of the bone and chondroblastoma. The negative result of H3F3A mutation and IHC of H3G34W lead to GCT of the bone diagnosis. Detection of H3F3A mutation with or without IHC staining of H3G34W could help differentiate between malignant GCT and osteosarcoma.¹⁶ In the malignant tumor category, the most common diagnosis in this study was osteosarcoma. This finding was in line with a study by Jorda *et al.*¹⁷ The updated management of osteosarcoma is chemotherapy before surgery, which showed the importance of FNAB as an early diagnostic method.¹⁸

There are ways to make FNAB more effective in diagnosing musculoskeletal lesions. One such way is by USG guidance, which helps in providing real-time visualization of the needle tip, making the procedure more reliable and secure.^{19,20} However, there were some limitations in our study that need to be considered

before interpreting the results. Firstly, we did not take into account whether the FNAB was done with an imaging guide or not. Secondly, some lesions had only one reported case, which may not be representative enough, and could affect the diagnostic study parameters.^{17,21} Despite these limitations, this study showed that FNAB could be an effective early diagnostic tool for musculoskeletal lesions. These findings provide a basis for future research. However, to confirm the role of FNAB as a less invasive diagnostic technique in musculoskeletal cases, larger studies with adequate sample preparation, analysis of confounding variables, and a more comprehensive sample size are necessary.

CONCLUSION

Fine needle aspiration biopsy is a safe and effective early diagnostic method for detecting musculoskeletal lesions, including bone tumors, soft tissue sarcomas, and metastatic cancers. It is less invasive than other diagnostic methods, with minimal risks of complications, and provides accurate results. The obtained results help physicians to develop an appropriate treatment plan, leading to improved outcomes and quality of life for patients.

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