RESEARCH ARTICLE

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Histopathological Comparison of Biopsy and Resection Materials in Bone and Soft Tissue Tumors: The Experience of a Tertiary Oncology Referral Center "Istanbul Medeniyet University Prof.Dr. Süleyman Yalçın City Hospital"

ABSTRACT

Objective: To evaluate the consistency of pathology results in biopsy and resection materials of bone and soft tissue tumors referred to a tertiarry referral center.

Methods: 270 patients who were admitted to the Department of Orthopedics and Traumatology of Istanbul Prof. Dr. Suleyman Yalcin City Hospital between January 2015 and March 2021, were retrospectively reviewed. Collected data included demographic data, type of biopsy technique, the pathology report of biopsy and resection.

Results: Bone tumors had been detected in 125 patients (mean age: 38.3 years, 58 female, 67 male). Tumor localizations were most common in the lower extremity (53.6%) and upper extremity (28%), followed by clavicle, rib, hip, and vertebra. Core needle (n=109) or incisional biopsy (n=16) was performed. The rate of biopsy material that deemed adequate in core needle and incisional biopsies was 89.91% and 93.75%, respectively. Biopsy was done in 145 patients due to soft tissue tumors. (mean age: 38.8 years, 75 female, 70 male). Tumor localizations were most common in the lower extremity (64.1 %) and upper extremity (22%), followed by neck, hip, retroperitoneal, and scapula. For diagnosis, core needle (n=136), incisional biopsy (n=7) or fine needle aspiration (n=2) was performed. In 94.78% of soft tissue tumors with adequate first biopsy material, the biopsy and resected material pathology was found to be consistent.

Conclusions: A multidisciplinary approach plays an important role in increasing the diagnostic accuracy after biopsy in bone and soft tissue tumors. In patients with inconsistent clinical and radiological findings, repeat biopsy is mandatory in order to plan the correct treatment approach..

Keywords: Biopsy, Bone Tissue Neoplasms, Soft Tissue Neoplasms.

Kemik Ve Yumuşak Doku Tümörlerinde Biyopsi Ve Rezeksiyon Materyallerinin Histopatolojik Karşılaştırılması: Üçüncü Basamak Onkoloji Referans Merkezi Deneyimi "İstanbul Medeniyet Üniversitesi Prof.Dr. Süleyman Yalçın Şehir Hastanesi"

ÖZET

Amaç: Üçüncü basamak bir sevk merkezine sevk edilen kemik ve yumuşak doku tümörlerinin biyopsi ve rezeksiyon materyallerinde patoloji sonuçlarının tutarlılığını değerlendirmek.

Gereç ve Yöntem: Ocak 2015-Mart 2021 tarihleri arasında İstanbul Prof.Dr. Süleyman Yalçın Şehir Hastanesi Ortopedi ve Travmatoloji Anabilim Dalı'na başvuran 270 hasta retrospektif olarak incelendi. Toplanan veriler, demografik verileri, biyopsi tipini, biyopsi ve rezeksiyonun patoloji raporunu içeriyordu.

Bulgular: 125 hastada kemik tümörü saptandı (ortalama yaş: 38.3 yıl, 58 kadın, 67 erkek). Tümör lokalizasyonları en sık alt ekstremitede (%53,6) ve üst ekstremitede (%28), ardından klavikula, kaburga, kalça ve omurgadaydı. Hastalara core needle (n=109) veya insizyonel biyopsi (n=16) yapıldı. Çalışmamızda, core needle ve insizyonel biyopsilerde yeterli biyopsi materyali oranı sırasıyla %89.91 ve %93.75 idi. 145 hastamıza yumuşak doku tümörü nedeniyle biyopsi uygulandı (ortalama yaş: 38.8 yıl, 75 kadın, 70 erkek). Tümör lokalizasyonları en sık alt (%64.1) ve üst ekstremitede (%22) görülmekle birlikte daha az sıklıkta sırasıyla boyun, kalça, retroperitoneal ve skapula bölgelerinde yerleşim göstermekteydi. Tanı amacıyla tru-cut biyopsi (n=136), insizyonel biyopsi (n=7), veya ince iğne aspirasyonu (n=2) yapıldı. İlk biyopsi materyali yeterli olan yumuşak doku tümörlerinin %94,78'inde biyopsi ve rezeksiyon patolojisinin uyumlu olduğu saptandı.

Sonuç: Biyopsi sonrası tanısal doğruluğu arttırmak amacıyla çok disiplinli yaklaşım önemli rol oynamaktadır. Uyumsuz klinik ve radyolojik bulgular görülen hastalarda tedavi yaklaşımının doğru planlanabilmesi için biyopsinin tekrar edilmesi gereklidir.

Anahtar Kelimeler: Biyopsi, Tümörler, Kemik Doku, Yumuşak Doku Neoplazileri.

INTRODUCTION

Bone and soft tissue tumors are rare neoplasms and pose a diagnostic challenge due to the high differentiation capacity of mesenchymal tissue. Reactive and tumor-like lesions may morphologically overlap with benign or malignant tumors (1). In addition to specialized knowledge and experience, a multidisciplinary perspective is important (2).

As clinical, laboratory, radiological, and pathological data are evaluated with a multidisciplinary approach, it is possible to diagnose and plan the appropriate treatment in most of the bone and soft tissue lesions. As a result of the clinical and radiological evaluation, a biopsy should be performed to reach a definitive diagnosis in aggressive looking and behaving lesions. In majority of bone and soft tissue tumors, histopathological evaluation forms the basis of diagnosis and treatment.

Due to the heterogeneity of bone and soft tissue tumors, different areas of the tumor may show different tissue characteristics, and the histological grade of the cells may not reflect the whole lesion. Considering this situation, clinicians should take tissue from the area that can reflect the aggressive nature of the lesion as much as possible in cooperation with radiologic findings. An accurate biopsy result would avoid unplanned resections in malign bone and soft tissue tumors.

Based on these, this study aims to compare the adequacy rates of the preoperative biopsies of the patients and the compatibility of biopsy results with final resection materials..

MATERIAL AND METHODS

270 patients who were admitted to the Department of Orthopedics and Traumatology of Istanbul Prof. Dr. Suleyman Yalcin City Hospital between January 2015 and March 2021, were retrospectively reviewed. Collected data included type of biopsy technique, the pathology report of biopsy and resection. The age and sex of the patients, the localization of the tumor, the biopsy method, histopathological diagnosis of biopsy, and resection materials were retrieved from the pathology archives of our hospital.

Exclusion criteria included absence of preoperative biopsy report, local recurrence of primary sarcoma or metastatic lesion of a previously diagnosed malignancy, having a biopsy report outside our institution. They were evaluated in two groups as bone and soft tissue tumors. Our study cohort consisted of 270 patients, 125 of them were diagnosed with bone tumors, and the remaining 145 patients had soft tissue tumors.

Biopsy materials with findings compatible with the neoplastic process were evaluated as adequate, and those without benign or malignant neoplastic processes were evaluated as inadequate. Biopsy materials that were evaluated as adequate were divided into three subgroups as "benign," "malignant," and "benign or malignant differentiation could not be made." Those in the group benign or malign differentiation could not be made were further subdivided into three groups as "descriptive benign," "descriptive malignant," and "unspecified."

RESULTS

Bone Tumors: Bone tumors had been detected in 125 patients (mean age: 38.3 years, 58 female, 67 male). Tumor localizations were most common in the lower extremity (53.6%) and upper extremity (28%), followed by clavicle, rib, hip, and vertebra. Core needle (n=109) or incisional biopsy (n=16) was performed.

Biopsy results were first divided into "adequate" or "inadequate" biopsy material. In adequate biopsies, samples were further subdivided into three groups as described above (Table 1-2).

Table 1. The adequacy of bone biopsy material according to biopsy technique

Biopsy technique	Adequate (no of patients)	Inadequate (no of patients)	Total (no of patients)
Incisional	15	1	16
Core needle	98	11	109
Total	**113**	**12**	**125**

Table 2. Biopsy results of all bone biopsies

Biopsy result	Number of patients
Adequate	113
benign or malignant differentiation could not be made	5
Descriptive- benign	3
Descriptive-malign	2
Benign	38
Malign	70
Inadequate	12
Total (number of patients)	**125**

The rate of biopsy material that deemed adequate in core needle and incisional biopsies was 89.91% and 93.75%, respectively. In all malignant bone tumors with a single biopsy, biopsy and resection results were found to be consistent.

The second biopsy was indicated in ten patients that were clinically and radiologically thought to be malignant; however, the first biopsy was reported as benign or inadequate with non-diagnostic features. The results were compared with the pathology results of the initial biopsies and resection materials. Cases that had been underwent second biopsy with adequate material for diagnosis, the result of biopsies and resection materials were consistent (Table 3).

Table 3. Details regarding patients with second bone biopsy

Cases	First biopsy result	Second biopsy result	Diagnosis of resection material
Case 1	Benign	Benign	Benign
Case 2	Benign	Benign	Benign
Case 3	Benign	Benign	Benign
Case 4	Benign	Benign	Benign
Case 5	Benign	Malign	Malign
Case 6	Benign	Malign	Malign
Case 7	Inadequate	Descriptive benign	Benign
Case 8	Inadequate	Benign	Benign
Case 9	Inadequate	Descriptive benign	Benign
Case 10	Inadequate	Malign	Malign

In patients with malignant tumours who underwent a single biopsy, the diagnostic accuracy of the biopsy was found to be 100% compared to histopathological findings of the resected specimen. Two cases of cartilage tumors, which were reported to be benign in their initial biopsies, were found to be malignant in the curettage material. In these two cases, the final pathology was reported as atypical cartilaginous tumor/Grade I chondrosarcoma (Table 4). Final pathology of bone tumors was shown in Table 5.

Table 4. Comparison of first biopsy results with the final resection diagnosis

	Diagnosis of resection material		
First biopsy diagnosis	**Benign**	**Malign**	**Total**
Benign or malign differentiation could not be made	**3**	**2**	**5**
Descriptive-benign	3		3
Descriptive-malign		2	2
Benign	**30**	**2**	**32**
Malign		**70**	**70**
Unspecified + inadequate	**7**	**1**	**8**
Total	**40**	**75**	**115**

Table 5. Final pathology of bone tumors according to WHO 2020 Classification

Undifferantiated round cell sarcoma	10
Chondrogenic tumors	22
Osteogenic tumors	18
Fibrogenic tumors	3
Vascular tumors of bone	2
Osteoclastic giant cell rich tumors	14
Notochordal tumors	5
Other mesencymal tumors of bone	16
Hematopoetic neoplasms of bone	9
Metastatic carcinoma	26
Overall	125

Soft Tissue Tumors: Among 145 patients with soft tissue tumors, the mean age was 38.8 years. (75 female, 70 male). Tumor localizations were most common in the lower extremity (64.1 %) and upper extremity (22%), followed by neck, hip, retroperitoneum, and scapula. A core needle biopsy was performed in 136 cases. Incisional biopsy was performed in 7 cases. Fine needle aspiration was done in 2 patients.

Biopsy materials with findings compatible with the neoplastic process were evaluated as adequate, and those without benign or malignant neoplastic processes were evaluated as inadequate. Biopsy materials that were evaluated as adequate were divided into three groups as "benign," "malignant," and "benign or malignant differentiation could not be made". Those in the group that could not be differentiated as benign or malignant differentiation could not be made were further divided into three subgroups "descriptive benign, "descriptive malignant," and "unspecified." (Table 6).

Table 6. Biopsy results of soft tissue tumors according to WHO 2020 Classification

Biopsy result	Number of patients
Adequate	139
Benign or malign could not be made (descriptive benign/ descriptive malign/unspecified)	23
Benign	68
Malign	48
Inadequate	6
Total	145

The biopsy material was sufficient in 100% of the patients who underwent incisional biopsy . In tru-cut biopsy, this rate declines to 95.59% of all patients. The diagnostic accuracy rate of the first biopsy in soft tissue tumors was 94.78%. Diagnostic error in soft tissue tumors was 5.22%.

The second biopsy was performed in 6 cases that were clinically and radiologically considered to be malignant, however, that came of to be inadequate or not diagnostic in the first biopsy. These were compared with the pathology results of the initial biopsies and resection materials. Diagnostic accuracy was determined in 4 (66.8%) patients. The biopsy technique in these cases was tru-cut biopsy. In patients with a second biopsy, insufficient biopsy material was obtained in one patient (16.6%). The accuracy of the diagnosis could not be determined in one patient (16.6%).

Three cases, whose diagnosis was descriptively interpreted as benign in the first biopsy, were reported as malignant in the resection material. In these cases, no findings in favor of malignancy were observed in the first biopsy materials. The pathological diagnoses in the resection materials were reported as cribriform carcinoma, atypical lipomatous tumor, and myxoid liposarcoma. The malignant potential could not be determined in the tru-cut biopsy material of the patient diagnosed with cribriform carcinoma. It was interpreted in favor of benign lesions since it did not contain significant atypia and necrosis. Lipoblast was not observed in the tru-cut biopsy material of the patient who was diagnosed with atypical lipomatous tumor, and since no staining with MDM2 and CDK4 was detected immunohistochemically, it was evaluated in favor of lipoma. Myxoid lipomatous tumor was considered in the tru-cut biopsy material of the patient who was diagnosed with myxoid liposarcoma, but it was evaluated in favor of lipoblastoma due to age of 15 years.

Of the 6 cases whose diagnosis was classified as unspecified in the first biopsy, 4 cases were evaluated as benign, and resection diagnoses were reported as benign peripheral nerve sheath tumor, inflammatory myofibroblastic tumor, solitary fibrous tumor and nodular fasciitis. Two cases were reported as atypical lipomatous tumor/well-differentiated liposarcoma in the final resection specimen.

Initial biopsies of 3 cases regarded as benign were hibernoma, papillary endothelial hyperplasia, and benign endothelial vascular proliferation/hemangioendothelioma. However, resection diagnoses were myxoid liposarcoma, myxoid liposarcoma, and angiosarcoma, respectively. In the case, which was initially reported as benign in the biopsy material but evaluated as angiosarcoma in the resection material, the tumor had a heterogeneous structure with well-differentiated angiosarcoma, papillary endothelial hyperplasia, and kaposiform hemangioendothelioma-like areas in the resection material. The diagnosis of the resection material was evaluated in favor of angiosarcoma since metastases were detected in the early postoperative period. The initial biopsy material consisted of papillary endothelial hyperplasia-like areas, resulting in inconsistent findings between the first biopsy result and the histopathological examination of the resection material. In another case whose initial biopsy result was reported as dermatofibrosarcoma protuberans, the final result in the resection material was nodular fasciitis. Final pathology of soft tissue tumors was shown in Table 7.

Table 7. Final pathology of soft tissue tumors

Fibroblastic and myofibroblastic tumors	38
Vascular tumors	6
Adipocytic tumors	39
Smooth muscle tumors	3
Skeletal muscle tumors	4
Peripheral nerve sheath tumors	13
Tumors of uncertain differentiation	32
Undifferantiated small round cell sarcomas	2
Nontumoral lesions	7
Chondroosseous tumors	1
Overall	145

DISCUSSION

Biopsy is essential to determine the diagnosis, the need for neoadjuvant chemo or radiotherapy, and determine the surgical treatment strategy in aggressive lesions that cannot be definitively diagnosed with clinical and radiological evaluation. In our series with bone and soft tissue tumors, the diagnostic yield was comparable to literature (3). The concordance between the preoperative malignant bone biopsy results and final resection material was 100%.

Morphological features of Grade 1 chondrosacomas in cartilage tumors were usually similar to enchondromas. Entrapment, permeative spread, cellularity and pleomorphism, which are signs of malignancy, may not be seen or detected in biopsy materials. In our study, 2 cases were diagnosed as cartilage tumors in the biopsy material, and no signs of malignancy were found. However, the final pathology was reported as Grade 1 chondrosarcoma/atypical cartilaginous tumor. Laitinen et al. found that the rate of consistency between the biopsy and final pathology in cartilaginous tumors was 43%. This finding confirms our two cases which were initially mistaken for benign cartilaginous tumor (4).

Since biopsy materials in atypical lipomatous tumors may represent lipoma-like areas, it is critical to interpret biopsy materials carefully. If malignancy is suspected in the clinical preliminary diagnosis, it should be considered that tru-cut biopsy material may not be sufficient for definitive diagnosis. Thavikulwat et al, reported lower accuracy of diagnosis in atypical lipomatous tumors/ well-differentiated lyposarcomas (5). Sung et al. (6) found that there is a low accuracy of biopsy results in heterogeneous soft tissue tumors which included angiosarcoma, liposarcoma, synovial sarcomas, and hemangiomas. In our series,

we encountered such heterogeneous tumors. Our discordant cases was performed non image-guided biopsies in early experience in our clinic.

It is known that papillary endothelial hyperplasia and angiosarcoma may have similar histomorphological features. It is not uncommon when a final diagnosis results in angiosarcoma after a biopsy report with papillary endothelial hyperplasia (7).

Nodular fasciitis (NF) which may also be referred as an infiltrative or pseudosarcomatous fasciitis, is a benign, self-limited fibroblastic and myofibroblastic proliferative process (8). Nodular fasciitis is usually misdiagnosed as a soft tissue sarcoma as reported by Plaza et al. (9). The histolopathological findings are usually similar to those found in sarcoma but most often differentiated by plump, immature looking fibroblasts, in short irregular bundles and fascicles with positive staining with alpha smooth muscle actin (SMA) (10). Hence, tumor heterogeneity is again an important point. Due to the heterogeneity of bone and soft tissue tumors, different areas of the tumor may show different characteristics. In this context, the histological grade in the biopsy sample may not represent the whole tumor. Although, the immunohistochemical Ki 67 proliferation index is often helpful in distinguishing benign or malignant bone tumors it may rarely be useless due to low grade thus proliferating capacity of the tumoral tissue (11,12). A high Ki-67 proliferation index in soft tissue tumors is also diagnostically significant for malignancy (13).

With the tumor growth, nutritive blood vessels may become insufficient. This will lead to necrotic areas within the lesion. Sampling from necrotic areas may result in non-diagnostic sampling. The optimal site for biopsy is the periphery of the tumor tissue. It is necessary to avoid core needle from central areas with dense necrotic tissue (14).

One important issue to consider is that there is a shift towards taking biopsy samples from bone and surrounding soft tissue in recent years. Moreover, open biopsy is replaced by imaging-guided biopsy, which is performed even by orthopedic surgeons in the outpatient setting. Also, image-guided bone biopsy is commonly performed in the operating room. All these facilities provide higher accuracy in a biopsy procedure (15).

Although literature is not enough to determine the best biopsy technique, we tend to prefer core needle biopsy instead of open biopsy due to low risk of contamination and no need of anesthesia (16). Intraoperative frozen biopsy is used in our center, but we didn't include those cases due to small number of patients which warrants further investigation (17).

CONCLUSION

A multidisciplinary team approach by an orthopedic oncologist, radiologist and pathologist is essential in the evaluation of patients whose clinical and radiological findings do not overlap with histopathological findings. If necessary, a repeat biopsy should be performed, and the treatment planning should be carried out according to the biopsy result.

It should be kept in mind that the biopsy material of cartilage tumors may not always reflect malignancy criteria. However, this does not rule out malignancy, especially radiological imaging findings should be taken into consideration.

REFERENCES

1. Stiller CA, Trama A, Serraino D, Rossi S, Navarro C, Chirlaque MD, et al. Descriptive epidemiology of sarcomas in Europe: Report from the RARECARE project. Eur J Cancer. 2013;49(3):684-95.
2. Siegel GW, Biermann JS, Chugh R, Jacobson JA, Lucas D, Feng M, et al. The multidisciplinary management of bone and soft tissue sarcoma: An essential organizational framework. J Multidiscip Healthc. 2015;8:109-15.
3. Banks JS, Garner HW, Chow AZ, Peterson JJ, Bestic JM, Wessell DE. Radiology-pathology correlation for bone and soft tissue tumors or tumor-like masses: single institutional experience after implementation of a weekly conference. Skeletal Radiol. 2021;50(4):731-8.
4. Laitinen MK, Stevenson JD, Parry MC, Sumathi V, Grimer RJ, Jeys LM. The role of grade in local recurrence and the disease-specific survival in chondrosarcomas. Bone Joint J. 2018;100(5):662-6.
5. Thavikulwat AC, Wu JS, Chen X, Anderson ME, Ward A, Kung J. Image-Guided Core Needle Biopsy of Adipocytic Tumors: Diagnostic Accuracy and Concordance With Final Surgical Pathology. AJR Am J Roentgenol. 2021;216(4):997-1002.
6. Sung K-S, Seo S-W, Shon M-S. The diagnostic value of needle biopsy for musculoskeletal lesions. Int Orthop. 2009;33(6):1701-6.
7. Guilbert MC, Frost EP, Brock JE, Lester SC. Distinguishing papillary endothelial hyperplasia and angiosarcoma on core needle biopsy of the breast: The importance of clinical and radiologic correlation. Breast J. 2018;24(4):487-92.
8. Anderson WJ, Doyle LA. Updates from the 2020 World Health Organization Classification of Soft Tissue and Bone Tumours. Histopathology. 2021;78(5):644-57.
9. Plaza JA, Mayerson J, Wakely Jr PE. Nodular fasciitis of the hand: a potential diagnostic pitfall in fine-needle aspiration cytopathology. Am J Clin Pathol. 2005;123(3):388-93.

10. Khanna V, Rajan M, Reddy T, Alexander N, Surendran P. Nodular fasciitis mimicking a soft tissue sarcoma–a case report. Int J Surg Case Rep. 2018;44:29-32.
11. Helfenstein A, Frahm SO, Krams M, Drescher W, Parwaresch R, Hassenpflug J. Minichromosome maintenance protein (MCM6) in low-grade chondrosarcoma: distinction from enchondroma and identification of progressive tumors. Am J Clin Pathol. 2004;122(6):912-8.
12. Jong R, Davis AM, Mendes MG, Wunder JS, Bell RS, Kandel R. Proliferative activity (Ki-67 expression) and outcome in high grade osteosarcoma: a study of 27 cases. Sarcoma. 2000;4(1-2):47-55.
13. Campos M, Pegorin De Campos SG, Ribeiro GG, Eguchi FC, Morini Da Silva SR, De Oliveira CZ, et al. Ki-67 and CD100 immunohistochemical expression is associated with local recurrence and poor prognosis in soft tissue sarcomas, respectively. Oncol Lett. 2013;5(5):1527-35.
14. Peer S, Freuis T, Loizides A, Gruber H. Ultrasound guided core needle biopsy of soft tissue tumors; a fool proof technique? Med Ultrason. 2011;13(3):187-94.
15. Pouedras M, Briand S, Crenn V, Cassagnau E, Gouin F. Non image-guided core needle biopsies can be used safely to improve diagnostic efficiency for soft tissue tumors. Surg Oncol. 2021;37:101518.
16. Traina F, Errani C, Toscano A, Pungetti C, Fabbri D, Mazzotti A, et al. Current concepts in the biopsy of musculoskeletal tumors: AAOS exhibit selection. JBJS. 2015;97(2):e7.
17. Miwa S, Yamamoto N, Hayashi K, Takeuchi A, Igarashi K, Tada K, et al. Accuracy of histological grades from intraoperative frozen-section diagnoses of soft-tissue tumors. Int J Clin Oncol. 2020;25(12):2158-2165.