SM Journal of Orthopedics ISSN: 2473-067X

Case Report

Osteoblastoma-Like Osteosarcoma of the Proximal Humerus. Case Report of Uncommon Tumor and Brief Review of the Literature

Jessica Jahoda[1,3], Carolyn Coles[2], Chinenyenwa Okoye[2], Keoni Campbell[2], Izunna Ezekwesili[2], Ashley Gonsalves[2], Helen Diaz[2], Mohamed Aziz[3]*

[1]Department of Pathology, American University of the Caribbean School of Medicine, Cupecoy, St. Maarten

[2]St. George University School of Medicine, West Indies, Grenada

[3]Research Writing & Publication (RWP) LLC, NY, USA

Abstract

Osteoblastoma-like osteosarcoma (OBLOS), is a rare malignant lesion with risks of both local recurrence and distant metastasis. It is considered a rare variant of osteosarcoma. The distinction between (OBLOS), and aggressive osteoblastoma is still debatable and challenging. Based on the initial clinical, radiological, and histological findings, a definitive diagnosis might only sometimes be achievable. On the other hand, the significance of a proper diagnosis must be accomplished because the approach to treatment varies greatly depending on the type of lesion. Sufficient tissue sampling is essential to provide the proper diagnosis. In clinicopathological and radiological discordance cases, a high index of suspicion and significant experience are requirements for an appropriate diagnosis. The OBLOS is categorized as a conventional (high-grade) osteosarcoma in the World Health Organization (WHO) classification system. However, several cases that have been published have been identified as low-grade malignant tumors. There are no precise morphological criteria to discriminate between low- and high-grade lesions. We describe a case of osteoblastoma-like osteosarcoma in an 11-year-old boy involving the right proximal humerus. We provide a brief review of the pertinent literature including diagnosis, differential diagnosis, debatable grading of this type of tumors, management, and prognosis.

Keywords: Osteosarcoma, Osteoblastoma, Histomorphology, Low-grade, High-grade

ABBREVIATION

Osteoblastoma-Like Osteosarcoma (OBLOS), conventional osteosarcoma (COS)

INTRODUCTION

Osteosarcomas are a relatively rare cancer, accounting for about 3% of all childhood cancers, less than 1% of all adult cancers, and the most common type of primary bone cancer, accounting for about 20% of all cases. It predominantly affects children, adolescents, and young adults, with a peak incidence during the teenage growth spurt and early adulthood.

Most cases occur in the lower extremities, especially the distal femur or proximal tibia. It can also occur in other bones, such as the pelvis, shoulder, and jaw. Before modern medicine and imaging techniques, Osteosarcoma was often misdiagnosed or mistaken for other bone conditions [1]

Compared to Osteosarcoma, osteoblastoma is benign bone-forming tumors that favor the axial spinal, specifically the spinal vertebra, unlike most primary bone neoplasms that prefer the extremities. The second most common location for osteoblastoma formations is the meta-diaphysis of long bones within the lower extremities. They are relatively rare, accounting for up to 5% of all benign tumors and only 1% of bone tumor cases **[2].** Adolescents between the ages of 10-15 are most affected by osteoblastoma, with a peak incidence rate occurring in the second and third decades of life. These benign osteolytic neoplasms tend to behave aggressively and cause damage to the surrounding bone and soft tissue. **[3]**. Osteosarcoma and osteoblastoma are bone tumors but differ in various aspects. Histologically osteoblastoma is identified by interconnecting trabecula arranged in sheets surrounded by a single layer of osteoid-producing osteoblast and a fibrotic stoma that is richly vascularized **[4].** Osteosarcoma is characterized by malignant osteoblasts that produce immature bone tissue**: [5].**

Osteoblastoma and Osteoblastoma-Like Osteosarcoma (OBLOS) have similar histological features. However, because OBLOS is a malignant lesion, there is a substantial risk of death if it is not properly treated**.** It is still challenging to identify and treat cases of aggressive osteoblastoma, borderline osteoblastoma, and OBLOS. Theoretical understanding indicates these three tumor kinds are distinct entities [6]. Despite the misleading nature of histology, there is no tolerance for misdiagnosis because the treatment plan for OBLOS is very different, and a mistake in

Submitted: 03 September 2023 | **Accepted:** 26 September 2023 | **Published:** 30 September 2023

***Corresponding author:** Badarou ChaibouMohamed Aziz*, Division of Research, Research Writing & Publication (RWP) LLC, 2475 Lefferts Place Bellmore NY, USA

Citation: Jahoda J, Coles C, Okoye C, Campbell K, Ezekwesili I, et al. (2023) Osteoblastoma-Like Osteosarcoma of the Proximal Humerus. Case Report of Uncommon Tumor and Brief Review of the Literature. SM J Orthop 6: 5.

judgment would undermine local and systemic tumor control or cause excessive morbidity. Determining the best treatment option and prognosis for osteoblastoma requires a precise diagnosis. [7,**8**]. We present a case of OBLOS and highlight the significance of adequate sampling of the tumor, differential diagnosis, pathogenesis, and relationship to Osteosarcoma.

CASE PRESENTATION

An 11-year-old boy presented to the emergency room with right shoulder pain after a fall during a school soccer game. The pain was constant, tender to palpation, and associated with soft tissue swelling. The pain and swelling were limiting his range of motion. The family reported that the boy had been complaining of discomfort in his right shoulder for five months, and they decided to seek medical attention when he fell during the soccer game and was complaining of severe pain. The patient did not have any other associated symptoms and had no other comorbidities or medication use. Previous medical history and physical examination were unremarkable.

An X-ray of the right shoulder showed a permeative lytic lesion over the right proximal metaphyseal region of the right humerus with extension into the epiphyseal region. The loss of the cortex laterally suggested an aggressive bony lesion (Figure 1A). A coronal CT bone window showed a destructive lytic lesion in the proximal right humerus. There was destruction of the lateral cortex of the upper humerus with a soft tissue component that expanded moderately out of the lateral side of the lesion. The findings were suspicious for a malignant bone lesion (Figure 1B). MRI post-contrast T1 images demonstrated enhancement, which corresponds almost exactly with the area of the high T2 signal. MRI studies showed considerable bony destruction involving the lateral and posterolateral cortex through the metaphyseal region, extending to the epiphysis, with an elevation of the periosteum and moderate extension beyond the periosteum. The extensive periosteal reaction and cortical changes at the lateral and posterolateral aspects of the proximal metaphyseal region were predominantly lamellated rather than sunburst in type (Figure 1C). The lesion measured 6x5x4 cm with approximately one and a half cm of extension into the soft tissue. This favored malignancy over infection, given that there is no extension of edema beyond the areas of enhancement. A tissue diagnosis was recommended.

A true-cut needle biopsy was performed, and the pathology diagnosis was most consistent with osteoblastoma, likely of the aggressive type. However, the pathology report indicated that the sample was limited, and although the identified histomorphological atypia was minimal, a more advanced lesion could not be ruled out. A true-cut needle biopsy was performed, and the pathology diagnosis was most consistent with osteoblastoma, likely of the aggressive type. Due to suspicious radiological features and undermined definitive pathology diagnosis, an open incisional biopsy was performed. Microscopic examination of the biopsy showed major components suggestive of aggressive osteoblastoma, including high-level cellularity, nuclear atypia, immature bone lace-like osteoid, and epithelioid osteoblasts. In addition, the biopsy revealed trabecular bone formation, osteoclastic giant cells, and prominent epithelioid osteoblasts associated with a prominent vascular network that are characteristic of aggressive osteoblastoma (Figure 2A). However, the pathologic diagnosis of Osteoblastoma-like Osteosarcoma (OBLOS) was established with the prominent nuclear pleomorphism, high mitotic figures (>12 mitosis/10HPV) permeation of surrounding bone, entrapment of bone trabeculae, and a lack of maturation toward the edges (Figure 2B-C).

A tumor board multidisciplinary meeting recommended the same treatment as conventional osteosarcoma. The patient received neoadjuvant chemotherapy with high-dose methotrexate, anthracycline, and cisplatin (CDDP), followed by en-block tumor resection with wide margins and total right shoulder joint reconstruction. The excised tumor showed 85% tumor treatment necrosis. Post-operative treatment with three cycles of adjuvant chemotherapy with anthracycline and

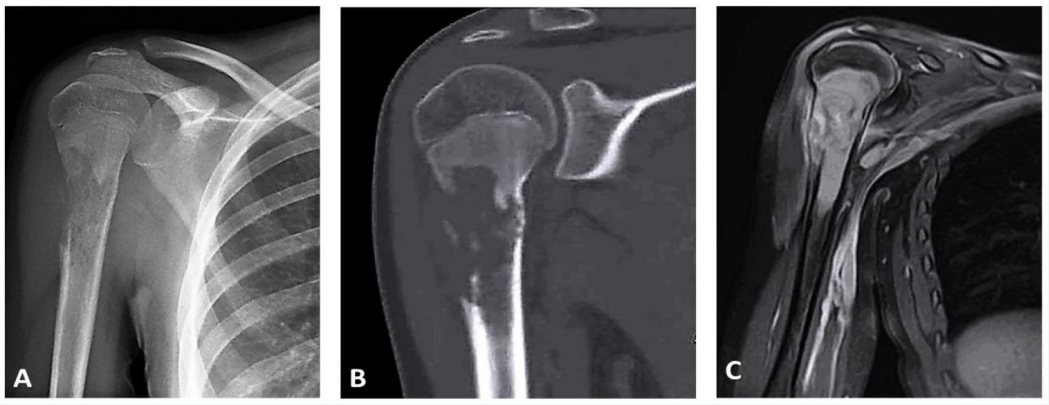

Figure 1 Radiographic findings of the tumor
1A: X-ray of the right shoulder showed a permeative lytic lesion over the right proximal metaphyseal region of the right humerus with extension into the epiphyseal region. The loss of the cortex laterally suggested an aggressive bony lesion
1B: A coronal CT bone window showed a destructive lytic lesion in the proximal right humerus
1C: MRI post-contrast T1 images demonstrated enhancement, which corresponds almost exactly with the area of the high T2 signal

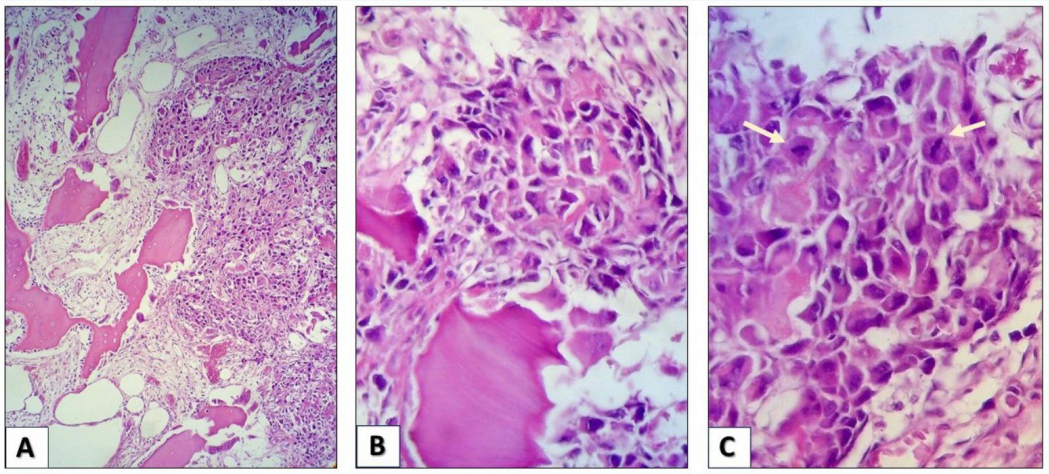

Figure 2 Microscopic examination of the tumor
2A: Low power view of the biopsy showed major components suggestive of aggressive osteoblastoma, including high-level cellularity, and epithelioid osteoblasts (H&E X20).
2B: High power view showed permeation of surrounding bone, entrapment of bone trabeculae, and a lack of maturation toward the edges (H&E X40).
2C: High power view showed prominent nuclear pleomorphism, and high mitotic figures (arrows) (H&E X60).

ifosfamide was administered. At 37 months postoperatively, the patient was alive with no local recurrence or metastasis.

DISCUSSION

Osteosarcoma is a common primary bone cancer that accounts for 20% of all primary bone cancers. It is often found in males less than 20 years of age. The age of onset of osteosarcoma has two peaks, with the first peak being male adolescents accounting for 60% of all cases and the second peak being adults more significant than 40 years of age. The adult population only accounts for 13% of all osteosarcomas. Osteosarcoma is rarely found in the elderly, but if found, it is due to secondary predisposing factors, including prior history of Paget disease of bone, bone infarcts, radiation, familial retinoblastoma, or Li-Fraumeni syndrome **[9].** Osteoblastoma, on the other hand, is a benign tumor typically >2cm that customarily involves the vertebrae. Other common locations include the mandible and long tubular bones, especially the lower extremities, compared to the upper extremities. When it arises in the lower extremities, it is observed in the meta diaphysis **[10]**. In contrast to osteosarcoma, osteoblastoma is more often an asymptomatic incidental finding. If symptomatic, the patient usually presents with a dull, localized pain unresponsive to NSAIDs. On X-ray, osteoblastoma only demonstrates overlying periostitis in the setting of a pathologic fracture. The patient will likely present with a recent injury history when this is the circumstance. In contrast, osteosarcomas will present with aggressive forms of periostitis, which give it its characteristic "sunburst" appearance **[11].** Histologically, osteoblastoma shows the formation of disorganized osteoid and immature bone trabecula with vascularization. Unlike osteosarcoma, osteoblastoma does not infiltrate or permeate preexisting lamellar bone structures. Instead, the lamellar bone in osteoblastoma is separated by a distinct, narrow layer of bone-free fibrous tissue. This layer differentiates osteoblastoma from osteosarcoma **[12].**

Osteoblastoma-like Osteosarcoma (OBLOS) is a rare variant of osteosarcoma that histologically resembles an osteoblastoma and is considered a rare low-grade variation of osteosarcoma [13]. OBLOS accounts for 1.1% of all osteosarcomas and presents with a tender, persistent ache that can sometimes minimize the range of motion on physical examination [14]. The two histologic features most important in differentiating osteosarcoma from osteoblastoma are tissue maturation and peripheral location. Osteosarcoma permeates surrounding tissues with a lack of maturation at the periphery, while osteoblastoma shows peripheral maturation and is entirely circumscribed. Tumor permeation of the surrounding tissue helps differentiate OBLOS from osteoblastoma [**12**].

The etiology of osteoblastoma and its risk factors are yet unknown. In a series of 15 patients presented by **Gambarotti et al.**, Patients' ages ranged from 11 to 47 years (median = 25); eight male and seven female patients. All tumors were single and involved: the tibia (five cases), vertebrae (four cases), femur (two cases), hip (two cases), foot (two cases). All patients in the series had local pain. Two patients presented with swelling, and one had a limited range of motion. The initial symptoms may not be suspicious of such an uncommon tumor and are frequently not distinguishable from osteoblastoma and osteosarcoma. However, after an initial diagnosis of osteoblastoma, worsening symptoms and fresh clinical findings must concern the orthopedic oncologist in favor of malignancy [13]. OBLOS shares radiological features with osteoblastoma and osteosarcoma. The lesions often appear as lytic and expansile in radiographs. Irregular ossification or a sclerotic nidus may be observed inside a translucent lesion [**14**].

Pathological differentiation of OBLOS from osteoblastoma

is nearly impossible to make with limited tissue, such as needle biopsy and may be impossible even with adequate tissue. Insufficient tumor sampling may cause diagnostic errors, and a true cur biopsy is recommended to identify the areas of COS as the case in our patient. Microscopic examination usually shows areas like conventional osteoblastoma with infiltration of the host bony trabeculae, the presence of lace-like osteoid, no formation of trabeculae, and the absence or presence of areas of conventional osteosarcoma (COS). Areas of COS usually display osteoblastic-type featuring thin, lace-like trabeculae and very abundant osteoid associated with disorderly architecture [**13**]. Differential diagnoses may include osteoblastoma, aneurysmal bone cyst changes, low-grade osteosarcoma, high-grade osteosarcomas, and giant cell tumor, among other tumors. The so-called aggressive osteoblastoma is characterized by "epithelioid" osteoblasts twice the size of osteoblasts with rounded cells, larger nuclei, and abundant cytoplasm. Furthermore, the bone trabeculae of these aggressive cells are wider and more irregular than conventional osteoblastoma while tending to have no cement lines. The histological grade must be determined individually for each OBLOS case and treated accordingly [15].

At present, almost all low-grade osteosarcomas are either central or surface tumors histologically characterized by a relatively bland fibrous stroma containing somewhat parallel streamers of immature bone with a molecular signature of MDM2 amplification that all other osteosarcomas do not possess. Virtually all different osteosarcoma types are considered high-grade tumors, except for periosteal osteosarcoma, which is the only osteosarcoma termed intermediate-grade by the WHO classification [16]. In most cases described in the literature, grading was not specified. Some authors [6,17]**.** have reported the tumor as a low-grade malignancy, while Kumar et al. described a high-grade malignant lesion [18].

In 2016 Gorgun et al. reported a case suggesting osteoblastoma may undergo malignant transformation [19]. However, in 2019, Geller D et al. y. Performed an in-depth genetic characterization of two distinct tumors that historically have been believed to be along the same spectrum of disease, Osteoblastoma and Osteosarcoma. They reported near-zero overlap in the somatic small variants, somatic copy number variation pattern, and predicted structural variants in the osteoblastoma compared with the osteosarcoma. They reported that findings from their study argue against malignant transformation as an evolving or stepwise process and conversely support two distinct neoplasms with dissimilar genetic makeups [20].

Osteoblastoma-like osteosarcoma needs to be recognized by the pathologist to achieve the right treatment which is wide surgical procedure [6]. Neoadjuvant and adjuvant chemotherapy can be also utilized based on individualized evaluation as the case in our report. In 15 cases of OBLOS reviewed by Gambarotti et al, five patients developed metastasis and five patients developed local recurrences (all after incomplete surgery). Eleven patients were alive without disease, while four patients died of their disease. They concluded that with the important limitation of a small cohort of patients, the presence of areas of conventional (high-grade) osteosarcoma is the only parameter to predict the aggressiveness of OBLOS [13].

CONCLUSION

Osteoblastoma-like osteosarcoma is a rare type of osteosarcoma. No precise morphological criteria exist to discriminate between low- and high-grade lesions. It may be helpful to clinically categorize osteoblastoma-like osteosarcoma based on the presence of areas of traditional osteosarcoma. The most important factors to distinguish these tumors and to foretell an aggressive outcome seem to be the existence of areas of typical osteosarcoma. It is advisable to do an open biopsy whenever a lesion's radiographic appearance suggests malignancy, regardless of where the tumor is located. Even if the clinical characteristics in this situation are those of osteoblastoma, the surgeon must be on the lookout for tumor growth, recurrence, and metastasis. To help the pathologist, clues in clinical behavior and radiological exams must be carefully evaluated. Close collaboration between the orthopedic oncologist, musculoskeletal radiologist, and musculoskeletal pathologist can lead to an appropriate pathological diagnosis.

Even though the malignant transformation of osteoblastoma to osteosarcoma has historically been acknowledged, a literature survey has revealed a dearth of solid data, and disagreement has persisted. Malignant transformation appears to be an evolutionary or progressive process and, on the other hand, supports the existence of two distinct neoplasms with different genetic compositions. By adding cases of this tumor to the limited body of knowledge, we aim to increase the awareness of clinicians and pathologists to include it differential diagnosis of aggressive bone lesions.

Human subjects

Ethical review and approval were not required for the study on human participants in accordance with the local legislation and institutional requirements. The paper has been sufficiently anonymized to keep patient's confidentiality

Conflicts of interest

In compliance with the ICMJE uniform disclosure form, all authors declare the following:

Payment/services info: All authors have declared that no financial support was received from any organization for the submitted work.

Financial relationships: All authors have declared that they have no financial relationships at present or within the previous three years with any organizations that might have an interest in the submitted work.

Other relationships: All authors have declared that there are no other relationships or activities that could appear to have influenced the submitted work.

Patient's consent

Patients was lost to follow up, all attempts to reach the patient

or family member are unsuccessful. Therefore, the paper has been sufficiently anonymized to keep patient's confidentiality.

Author contributions

Study concept and design: Jessica Jahoda and Carolyn Coles. Writing the manuscript: Chinenyenwa Okoye, Keoni Campbell, Izunna Ezekwesili, Ashley Gonsalves, Helen Diaz, and Carolyn Coles. Data collection: Chinenyenwa Okoye and Keoni Campbell. Analysis and interpretation: Chinenyenwa Okoye and Keoni Campbell. Reviewing and editing the manuscript: Jessica Jahoda and Mohamed Aziz, Editing, critical review, and final approval: Mohamed Aziz

ACKNOWLEDGMENT

Special thanks to Viviana Crespo, Brian, Phuoc Brian Duong and Alan Bencosme MD candidates at the American University of the Caribbean for their assistance in reviewing the final manuscript.

REFERENCES

1. Mirabello L, Troisi RJ, Savage SA. International osteosarcoma incidence patterns in children and adolescents, middle ages and elderly persons. Int J Cancer. 2009 Jul 1;125[1]:229-34. doi: 10.1002/ijc.24320. PMID: 19330840; PMCID: PMC3048853.

2. Wu, Minhao, et al. "Diagnostic and Management Options of Osteoblastoma in the Spine." Medical Science Monitor, vol. 25, 2019, pp. 1362–1372, https://doi.org/10.12659/msm.913666.

3. Atesok, Kivanc I., et al. "Osteoid Osteoma and Osteoblastoma." American Academy of Orthopaedic Surgeon, vol. 19, no. 11, 2011, pp. 678–689, https://doi.org/10.5435/00124635-201111000-00004.

4. P. Bhat, Shubha, et al. "Osteoblastoma of the Temporal Bone – a Familiar Tumour at an Uncommon Site." *Biomedicine*, vol. 43, no. 02, 2023, pp. 794–796, https://doi.org/10.51248/.v43i02.1479.

5. Wadhwa, Neelam. "Osteosarcoma: Diagnostic Dilemmas in Histopathology and Prognostic Factors." Indian Journal of Orthopaedics, vol. 48, no. 3, 2014, pp. 247–254, https://doi.org/10.4103/0019-5413.132497.

6. Bertoni F, Bacchini P, Donati D, Martini A, Picci P, Campanacci M. Osteoblastoma-like osteosarcoma. The Rizzoli Institute experience. Mod. Pathol. 1993; 6; 707–716.

7. Xarchas KC, Leviet D. Osteoblastoma of the carpal scaphoid frequency and treatment. Acta Orthop Belg. 2002;68(5):532–536

8. Limaiem F, Byerly DW, Mabrouk A, et al. Osteoblastoma. [Updated 2023 May 14]. In: StatPearls [Internet]. Treasure Island [FL]: StatPearls Publishing; 2023 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK536954/

9. Xu Q, Gao T, Zhang B, Zeng J, Dai M. Primary osteosarcoma in elderly patients: A report of three cases. Oncol Lett. 2019 Aug;18(2):990-996. doi: 10.3892/ol.2019.10446. Epub 2019 Jun 7. PMID: 31423158; PMCID: PMC6607338.

10. Limaiem F, Byerly DW, Mabrouk A, et al. Osteoblastoma. [Updated 2023 May 14]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2023 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK536954/

11. Kroon HM, Schurmans J. Osteoblastoma: clinical and radiologic findings in 98 new cases. Radiology. 1990 Jun;175(3):783-90.

12. Bertoni F, Unni KK, McLeod RA, Dahlin DC. Osteosarcoma resembling osteoblastoma. Cancer. 1985 Jan 15;55(2):416-26. doi: 10.1002/1097-0142(19850115)55:2<416::aid-cncr2820550221>3.0.co;2-5. PMID: 3855268.

13. Gambarotti M, Dei Tos AP, Vanel D, Picci P, Gibertoni D, Klein MJ, Righi A. Osteoblastoma-like osteosarcoma: high-grade or low-grade osteosarcoma?. Histopathology. 2019 Feb;74(3):494-503.

14. Ozger H, Alpan B, Söylemez MS, Ozkan K, Salduz A, Bilgic B, Sirin B. Clinical management of a challenging malignancy, osteoblastoma-like osteosarcoma: a report of four cases and a review of the literature. Ther Clin Risk Manag. 2016;12:1261-1270 https://doi.org/10.2147/TCRM.S102966.

15. Dorfman HD, 1984 Weiss SW (1984) Borderline osteoblastic tumors: problems in the differential diagnosis of aggressive osteoblastoma and low-grade osteosarcoma. Semin Diagn Pathol 1215-1234

16. Rosenberg AE, Cleton-Jansen A-M, de Pineux G, Deyrup AT,Hauben E, Squire J. Conventional osteosarcoma. In FletcherCDM, Bridge JA, Hogendoorn CWH, Mertens F eds.WHO classi-fication of tumours of soft tissue and bone. 4th ed. Lyon: IARCPress, 2013; 282–288

17. Abramovici L, Kenan S, Hytiroglou P, Rafii M, Steiner GC. Osteoblastoma-like osteosarcoma of the distal tibia. Skeletal Radiol. 2002; 31; 179–182.

18. Kumar NL, Rosenberg AE, Raskin KA. Osteoblastoma-like osteosarcoma of the cuboid: a case report. J. Orthop. Surg. Res. 2010; 5; 52.

19. Gorgun O, Salduz A, Kebudi R, Ozger H, Bilgic B. Malignant transformation of aggressive osteoblastoma to ostesarcoma. Eklem HastaLilari Cerrahisi-Joint Disease and Related Surgery. 2016 Jan 1;27(2):108-12.

20. Geller DS, Levine NL, Hoang BH, Yang R, Weiser D, Morris J, Gorlick R, Gill JB, Roth ME, Tingling J, Brohl AS. Genomic analysis does not support malignant transformation of osteoblastoma to osteosarcoma. JCO Precision Oncology. 2019;3.