TÜBİTAK

CASE REPORT

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Sacral Chondroblastic Osteosarcoma Misdiagnosed as Chondrosarcoma and Chordoma

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Abstract: Chondroblastic osteosarcoma (COS), a subgroup of intramedullary osteosarcoma, is usually located in the knee region of the body. It is most common in adolescents and early adulthood. COS has similar clinical and radiological features to those of conventional osteosarcomas.

A 17-year-old male suffered from walking problems and lower limb pain. CT and MRI revealed a mass with soft tissue density and bone destruction at the level of L5-S1. It was described as "posttraumatic hematoma". In cytopathologic examination, initial diagnosis was chordoma in fine-needle aspiration cytology (FNAC), chondrosarcoma in incisional biopsy, and finally COS in total resection specimen.

Because sacral location of COS is very rare, this report aimed to discuss radiological and pathological diagnostic pitfalls of COS in light of the literature.

Key Words: Chondroblastic osteosarcoma, chondrosarcoma, chordoma, sacrum

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Kondrosarkom ve Kordoma ile Karıştırılan Sakral Kondroblastik Osteosarkom

Özet: Kondroblastik osteosarkoma(COS), intramedüller osteosarkom'un bir alt grubudur ve genelde diz bölgesinde yerleşir. Ergenlik çağında sıktır. COS'un klinik ve radyolojik bulguları diğer osteosarkomlara benzer.

Yürüme problemleri ve alt ekstremitede ağrı yakınması olan 17 yaşında bir hastanın tomografi ve MR incelemelerinde L5-S1 düzeyinde yumuşak doku dansitesinde ve kemikte destrüksiyona yol açan kitle saptandı. Kitle 'posttravmatik hematom' olarak rapor edildi. İnce iğne aspirasyon biyopsisi(FNAC) kordoma, insizyonel biyopsisi kondrosarkoma olarak rapor edildi ve sonuçta COS total olarak çıkarıldı.

Anahtar Sözcükler: Konroblastik Osteosarkom, Kondrosarkom, kordoma, Sakrum

Introduction

Chondroblastic osteosarcoma (COS) is a subgroup of intramedullary osteosarcoma, and primarily involves the femur and tibia. It is most common in adolescents and in early adulthood and constitutes 9-25% of osteosarcomas. COSs show similar clinical and radiological features to those of conventional osteosarcomas. Morphologically, they are characterized with chondroid and osteoid differentiation (1-3).

Chondrosarcoma (CS) is the third most frequent bone tumor (20-30%) following myelomas and osteosarcomas, respectively. They mostly occur in elderly patients with a peak incidence in the sixth decade. Shoulder, pelvis, proximal femur and costal involvement are frequently seen, but sacral involvement is very rare (2%) (4).

Chondroid chordomas (CC) are rare malignant tumors that are frequently located in the sphenooccipital region and predominantly seen in early adulthood and males. They arise from embryological notochord remnants. They are considered a subgroup of classic chordomas because of their clinical and pathological differences from classic chordomas (5-8).

These three neoplasms show chondroid differentiation. Therefore, in small biopsy specimens, differential diagnosis is difficult. Morphologically accurate diagnosis is mandatory because of different treatment and clinical features of these three malignant neoplasms. In this report, problems and solutions related to these three different entities are discussed.

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Case Report

A 17-year-old male patient with walking problems and complaints of lower limb pain was admitted to the Neurosurgery Department of Firat University, Firat Medical Center. Computed tomography (CT) showed a mass lesion with soft tissue density and bone destruction at the level of L5-S1, indicating a posttraumatic hematoma. Magnetic resonance imaging (MRI) findings included an enhancing inflammatory soft tissue mass that compressed on the nerve roots at the level of L5-S2 with bone destruction. The mass was extending into the spinal canal and involved S1 and S2 vertebral bodies (Figure 1).

In CT-guided fine-needle aspiration cytology (FNAC) of this lesion, small multinucleolar, pleomorphic, transparent malignant tumoral cells with oval-round nucleus or fusiform large nucleus in myxomatous background were observed (Figure 2). Immunohistochemical staining for S-100 (Lab Vision Corporation, CA, USA) and vimentin (Lab Vision Corporation, CA, USA) were positive. In FNAC, chordoma was diagnosed.

In microscopic examination of the biopsy specimen, lobulated chondroid areas and neoplastic cells were seen in myxoid background. In cartilaginous areas, there were

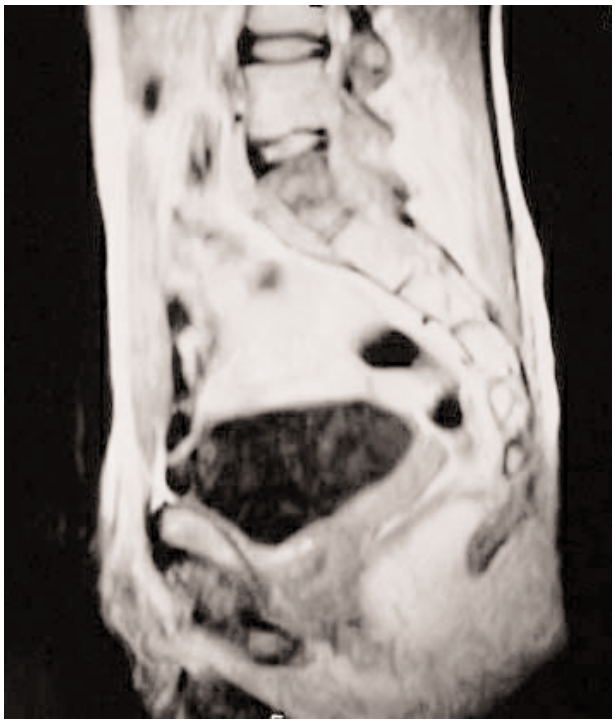

Figure 1. MRI shows soft tissue lesion inflicting vertebral destruction in the presacral region (L5-S2).

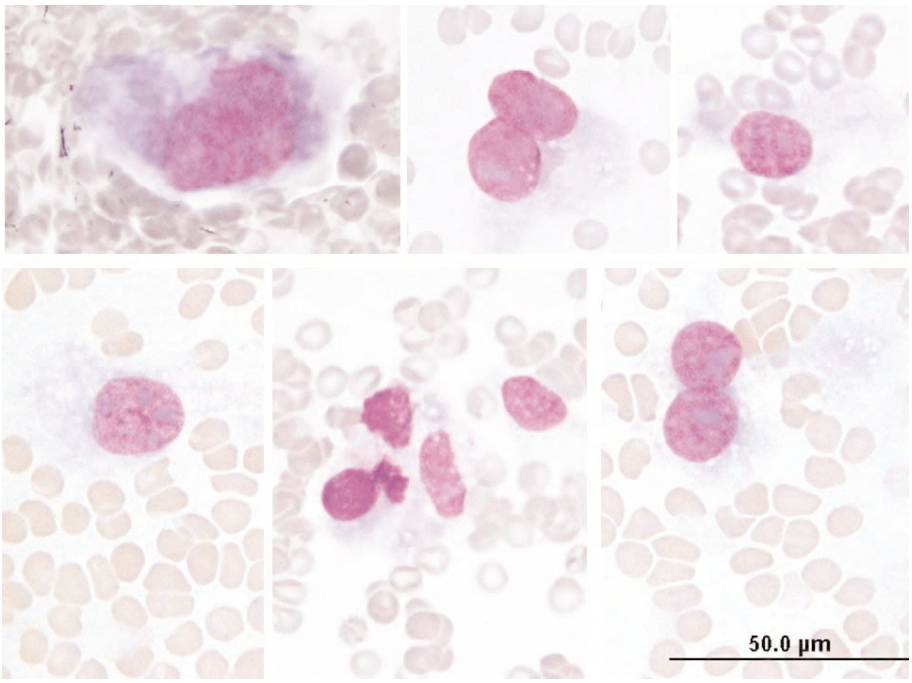

Figure 2. FNAC: Neoplastic cells show nuclear membrane irregularity, coarse chromatin, pleomorphism and hyperchromasia (MGG, x1000).

neoplastic chondrocytes, some with large nucleus and coarse chromatin and some with one or more nucleolus and irregular-edged fine chromatin within lacunae which were surrounded by hyaline matrix. Cytoplasms of the neoplastic chondrocytes were narrow with clear perinuclear halo (Figure 3). Malignant cells were present with evident pleomorphism and hyperchromatic nucleus and without a characteristic pattern within large myxoid areas around chondroid areas (Figure 4). Based on these findings, the diagnosis was CS (grade I-II).

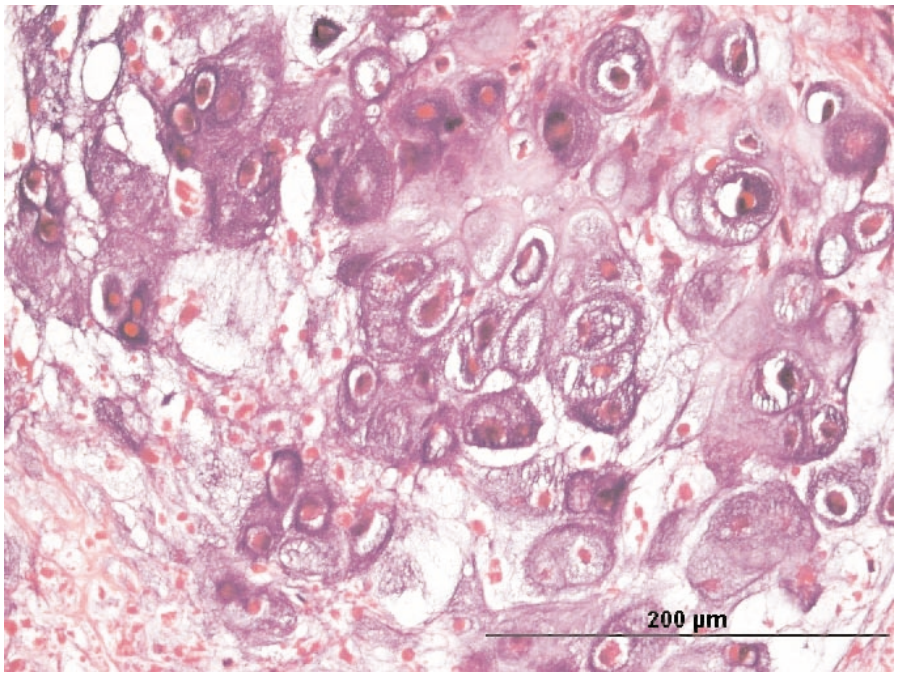

Figure 3. Malignant chondroid cells and coagulation necrosis (H&E, x400).

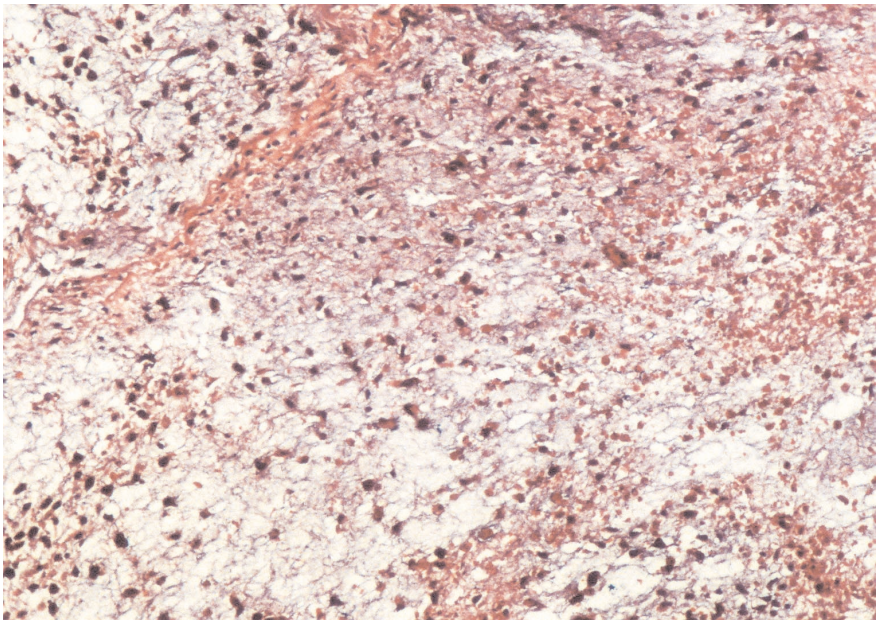

Figure 4. Malignant mesenchymal cells with hyperchromatic and pleomorphic nuclei in myxoid background (H&E, x200).

The tumor was totally resected. The specimen consisted of two pieces (8x6x3 cm and 7x5x2 cm) that contained bone and soft tissue components. In microscopic examination, there were lobulated malignant chondroid areas and oval-spindle shaped malignant cells in myxoid background. Osteoid formation was located between spindle malignant cells. Enchondral ossification was shown in chondroid areas. The tumor was diagnosed as grade III COS.

In immunohistochemical stain, neoplastic cells were positive for cytokeratin (Lab Vision Corporation, CA, USA), epithelial membrane antigen (EMA) (Lab Vision Corporation, CA, USA) and S-100 (Lab Vision Corporation, CA, USA). For this reason, initial biopsy specimens were reassessed. Serial cutting was done of the small biopsy material and the material on the slide was larger than of the first slides. There were small osteoid focuses (Figure 5) and large enchondral ossification areas. It was concluded that the first biopsy had been misdiagnosed as CS.

The patient received radiotherapy. No local recurrence or metastasis was detected in the postoperative 25th month.

Discussion

CSs are the third most frequent bone tumors with a predilection for male gender. Peak incidence is in the sixth decade. The shoulder, pelvis, proximal femur, and costae are the most frequent sites of involvement. Sacral involvement (2%) is highly rare (4).

Conventional CSs may be hyalinized, myxoid or mixed. Hyaline CSs are characterized with hypercellular hyaline cartilage with atypical chondrocytes within lacunae. Conversely, in myxoid CSs, atypical chondrocytes are not seen in the lacunae and constitute large neoplastic cell groups in myxoid matrix. Neoplastic cells are immunohistochemically positive for vimentin and S-100 and negative for epithelial markers such as keratin and EMA in CSs. Generally, typical CS diagnosis can be based on these findings, but myxoid variant can be confused with chordoma (4,6).

Chordomas have three subtypes: classical, dedifferentiated, and chondroid. Unlike conventional chordoma, CC involves the sphenooccipital region, and it is more frequent in early adulthood with a better prognosis (5,6). Conventional chordomas include large epithelioid cell cords within vesicular myxoid stroma and

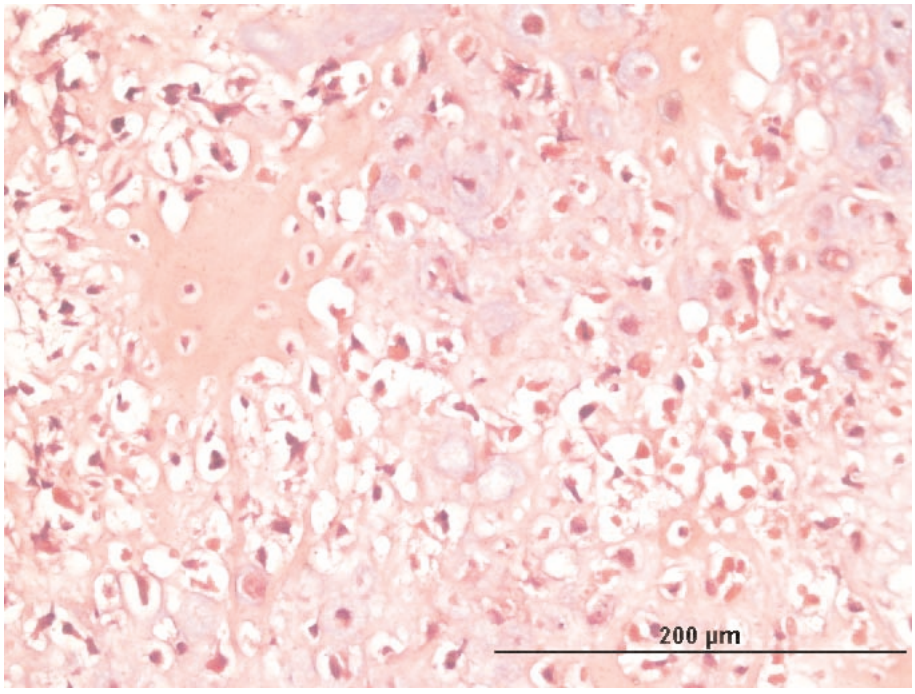

Figure 5. Osteoid production (H&E, x400).

solid nests. Chondroid variant differs from typical chordoma with its hyalinized stroma and might be confused with CS. Differential diagnosis of CS and CC is difficult (7,8). In myxoid CS, neoplastic chondrocytes are relatively small and narrow. They do not show nest formation. Conversely, chordoma cells are larger and have dense eosinophilic cytoplasms. They form groups, and desmosomes can be seen between cells. Immunohistochemical staining is very important in differential diagnosis of these two tumors. Chordomas are immunohistochemically positive for vimentin, S-100, EMA and cytokeratin (9,10).

Clinical behavior, recurrence, and metastatic characteristics of CS and CC are very different. Therefore, differential diagnosis based on pathological evaluation is necessary. Theoretically, it is possible to differentiate CC from classic CS with morphology, but in practice, it is difficult. Thus, false diagnosis is possible. In a study with 200 skull base CS, 34% of the cases were diagnosed as chordoma initially; however, further morphologic and immunohistochemical assessments showed that these were actually CS (6).

COS and conventional osteosarcoma have similar clinical, radiological, and prognostic features. COSs constitute 9-25% of conventional osteosarcomas (2). COS can be confused with CS in small biopsy specimens, and differential diagnosis can be difficult. Differential diagnosis is necessary because of clinical and treatment differences between these two neoplasms. Clinical characteristics such as age and location and radiological findings help in differentiation of these two neoplasms. Osteoid formation within the tumor is the most important morphologic diagnostic feature. It is not always possible to obtain osteoid formation in small biopsy specimens. As a consequence, cases with COS might be misdiagnosed as CS. False diagnosis rate has been reported to be as high as 44% (3).

Clinical and radiological findings must be used for differential diagnosis of COS and CS (Table 1). The most important clinical findings are patient's age and location of the lesion. As in our case, the radiological differential diagnosis of an atypically located lesion might be impossible. Unni (2) emphasized that in an adolescent patient or a patient in his/her early adulthood, if the tumor morphologically constitutes a neoplastic cartilage and osteoid formation does not accompany, unless proven to the contrary, it must be considered and treated as COS. CS is predominantly seen in the elderly (4th-6th decade) and is highly rare in adolescents and early adulthood. Prognosis in CS is better and metastatic tendency is lower (4).

Our case was initially reported as chordoma based on the cytology. Further evaluation of biopsy specimen indicated CS, while the final evaluation of the specimen showed COS. Therefore, the following points should be considered throughout the diagnostic process:

1. For accurate diagnosis of bone tumors, clinical findings such as the age of the patient and location of the lesion as well as the radiologic findings should be taken into consideration. Misdiagnosis is unavoidable if diagnosis is based on morphological findings alone (1). In our patient, we attempted to diagnose in view of the morphological findings alone, not along with clinical and radiological findings. Pathologists sometimes experience this kind of important problem, which may be called "morphology fanaticism" or "morphology captivity". Morphology captivity originates from the idea that only morphological findings are sufficient for the answers to problems without any contribution by other diagnostic findings. Although morphology is important in diagnosis in certain cases, it is necessary to base the diagnosis on other findings as well, which is also true for diagnoses of bone tumors.
2. The patient's age is a significant parameter for accurate diagnosis. Our patient was 17 years old. According to Unni (4), tumors with chondroid differentiation and without any osteoid formation in teenage patients must be diagnosed as osteosarcoma, unless proven to the contrary.
3. Another finding that cytologically supports chordoma is the location of the tumor because chordoma is the most frequent neoplasm that originates from the sacrum. In addition, the presence of neoplastic cells with vacuolized cytoplasms, which are like physaliphorous tumor cells, is supportive of a chordoma. Although physaliphorous cells are specific for chordoma, this finding is not diagnostic because these cells may also be seen in myxomatous tumors (myxoid CS) (10). However, for myxoid CS and chordoma, cytological diagnosis cannot be established

Table 1. Basic features of CC, CS and COS and comparison with our case.

	CC	CS	COS	OUR CASE
Age	Early adulthood	Adult - elderly	Adolescent - teenage	17
Location	Sphenooccipital	Pelvis and shoulder (48%) Sacral 2%	Femur and tibia (67%) Sacral <1%	Sacral
M/F	2.3/1	1.2/1	1.5/1	M
Clinical findings	Pain, compression symptoms	Swallowing, pain, pathologic fracture	Swallowing, pain, pathologic fracture	Pain, walking disorder
Radiology	Irregular bone destruction	Cortical erosion or thickening Bone expansion Calcification	Metaphyseal radiolucent mass Spurs, extension to soft tissue, Codman triangle, calcification	Hematoma? Soft tissue infection?
Macroscopy	Lobulated, myxoid mass Cartilage appearance	Lobulated chondroid Myxoid changes ±	Cortical penetration Periost reaction Extension to soft tissue Pseudocapsulated	Curetted biopsy material
Microscopy	Cartilage lobules Fibrous septa Hard groups, cordon or nest forming epithelial cells, Desmosome-like intercellular connections, Physaliphorous cells	Cell with small and narrow cytoplasm No cohesive groups, cells surrounded by matrix, mineralization ±, ossification ±	Lobulated chondrosarcomatous tumor Osteoid formation Necrosis, giant cell ±	Lobulated malignant chondroid areas, Oval-spindle shaped malignant cell in myxoid background Enchondral ossification Osteoid formation
IHC	CK, EMA, Vim, S100 and 5-nucleotidase (+)	S100, Vim (+), CK, EMA (-)	S100, Vim (+), Rarely CK, EMA (+)	S100, CK, EMA (+)
Treatment	Surgery + Radiotherapy	Surgery + Radiotherapy	Chemotherapy + Surgery	Surgery + Radiotherapy
Distant metastasis	22%	0%	Frequent	Absent
Recurrence	70%	1.5-53%	4%	Absent
10-year survey	35-45%	88-98%	75%	-

COS: Chondroblastic osteosarcoma. CS: Chondrosarcoma. CC: Chondroid chordoma. IHC: Immunohistochemistry. M: Male. F: Female. CK: Cytokeratin. Vim: Vimentin. EMA: Epithelial membrane antigen.

accurately without immunohistochemical assessment.

4. If clinical, radiological and morphologic findings are discordant, the lesion should be described and other possible diagnoses should be kept in mind to achieve an accurate diagnosis.
5. When diagnosis is made based on small biopsy specimens, whole tissue in all blocks should be cut with serial sections and no result should be declared without assessment of the entire tissue. In our case, the blocks cut with serial sections and their further reassessment showed diagnostic osteoid areas in two-fold compared to the previous evaluations of tissue sections, which supported osteosarcoma.

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