

OSTEOGENIC SARCOMA WITH EPITHELIAL DIFFERENTIATION (CARCINOSARCOMA): REPORT OF TWO CASES

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ABSTRACT

Epitheloid osteosarcoma (carcinosarcoma) of the bone is a rare malignant tumor and only a few cases have been reported in the literature. In this study, we report two cases of osseous carcinosarcoma (epitheloid osteosarcoma) with immunohistochemical studies. The morphological and immunohistochemical data in these two cases support the theory of divergent differentiation of primitive, uncommitted multipotential stem cell to produce biphenotypic tumors.

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Key Words • Carcinosarcoma • osteosarcoma • epithelial differentiation • immunohistochemistry

Introduction

Osteosarcoma is a mesenchymally derived malignant tumor that produces osteoid and/or bone.^{1,2} Osteosarcoma usually shows various histologic patterns in different areas of the same tumor, which is considered to be an expression of the heterogeneous cell types in the tumor tissue.²⁻⁴

However, the combination of primary osteosarcoma of bone with carcinoma has been rarely documented.^{2,5} Mirra et al. designated this entity as epitheloid osteosarcoma.² These carcinosarcomas are rare malignant neoplasms and occur also in many other organs such as genitourinary tract, gastrointestinal tract, skin, breast and lung.^{6,8}

Microscopically, in these tumors, there is

an intermingling of carcinomatous (squamous, transitional or adenocarcinoma) and sarcoma-like elements (rhabdomyosarcoma, leiomyosarcoma, chondrosarcoma or osteosarcoma).⁵

Case Report

Case 1:

The patient was a 12-year-old girl, who noticed dull pain around the right knee and distal part of the right thigh without any gait disturbance in September 1997. The pain increased along with swelling of the distal part of the right knee and thigh over the following two months. She was admitted to the Orthopedic Department of Chamran Hospital for investigation in November 1997. Roentgenograms showed a destructive bone lesion in the metaphyseal part of the right femur with erosion and interruption of cortical bone and soft tissue invasion. A bone scan showed involvement of the lower third of the

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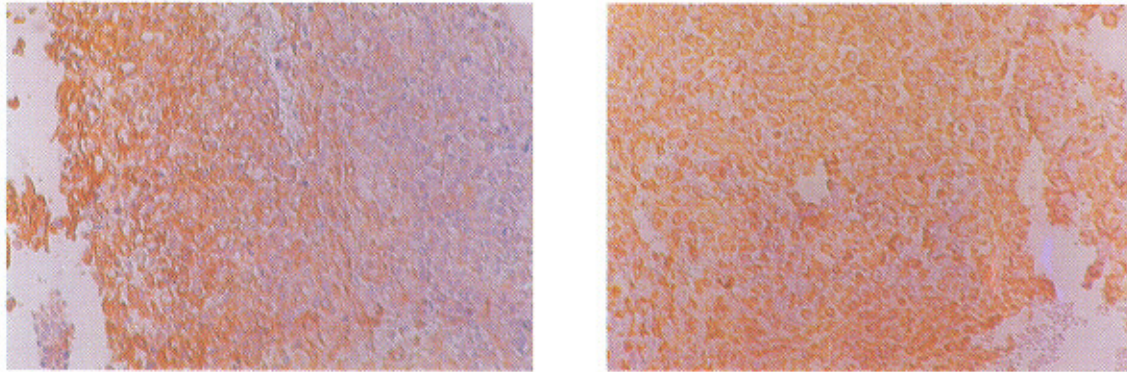


Figure 1: Left) Malignant osteoid surrounded by malignant cells (H&Ex200), Right) Epithelial-like cells with eosinophilic cytoplasm and round nuclei. Malignant spindle mesenchymal cells with hyperchromatic nuclei are seen. (H&Ex200)

femur without extension to the rest of the skeleton.

The alkaline phosphatase (ALPase) level in the serum was elevated significantly at 400 U/l. An open biopsy specimen revealed osteosarcoma with prominent epithelial-like cell differentiation. Chemotherapy was started. Due to extensive soft tissue involvement and rapidly growing mass, disarticulation of the right hip was planned and later performed. Post-operative chemotherapy was continued using a combination of cisplatin, adriamycin, vincristine and high dose methotrexate.

However, she died of respiratory failure in August 1998 due to multiple lung metastasis.

Case 2:

The patient was a 17-year-old male referred to Chamran Hospital in January 1998 with a three months history of non-traumatic right shoulder pain and swelling. He was otherwise well with no systemic complaints.

Physical examination was remarkable for diffuse swelling of the right shoulder with tenderness on palpation. Radiography showed a destructive and osteolytic lesion in the right scapula with wide transitional zone and

suspected invasion of the glenoid fossa. CT scan revealed a destructive lesion invading both anterior and posterior parts of scapula with soft tissue swelling and invasion.

An incisional biopsy of the lesion was interpreted as osteogenic sarcoma, epithelial type. The patient was initially treated with chemotherapy consisting of methotrexate, vincristine, cisplatin and adriamycin. Two months later, chest X-ray showed multiple bilateral well-defined small masses. The patient, refused additional treatment and three months later died of respiratory distress.

Pathologic Findings

The first case showed a dark yellowish tumor measuring 8×5×5 cm which totally occupied the femoral medullary cavity of metaphysis with cortical erosion and soft tissue involvement.

The second case showed grossly an oval, solid, partially encapsulated grayish brown tumor measuring 11×8×7 cm arising from and destroying the upper portion of the scapula with soft tissue extension.

Histologically, both tumors were composed of necrotic and viable tumor tissue. The viable

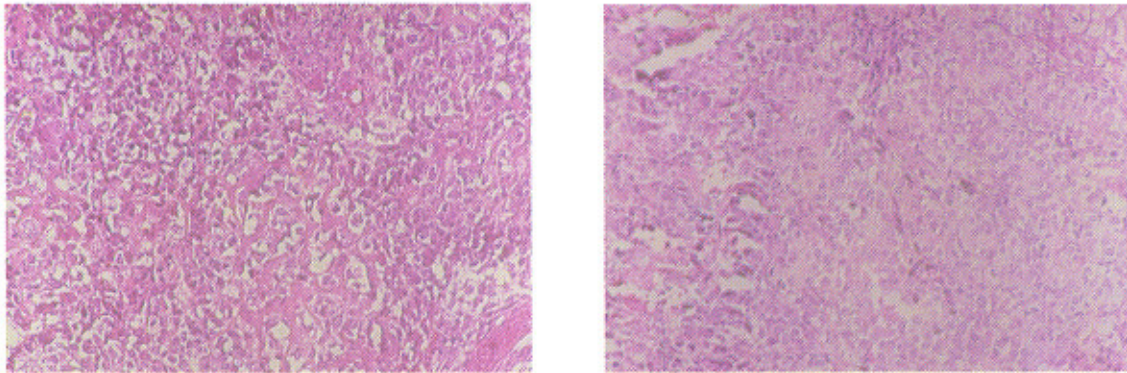


Figure 2, Left) Immunocytochemical stain for vimentin demonstrating immunoreactivity in cells adjacent to epithelial like area(x200), **Right)** Immunohistochemical stain for cytokeratin demonstrating strong immunoreactivity in the epithelial like cells (x200)

part of the tumor consisted of both carcinomatous and sarcomatous components. The carcinomatous component consists of sheets of uniform round epithelial cells, displaying a fairly abundant eosinophilic cytoplasm, round nuclei with prominent nucleolus and some cells with pale clear cytoplasm. The sarcomatous component showed pleomorphic malignant spindle cells containing frequent mitoses. Presence of lacy malignant osteoid in many regions helped in diagnosing the tumor as osteogenic sarcoma (Fig. 1 left, right).

Immunohistochemical studies were performed on the formaldehyde-fixed, paraffin-embedded section of both cases using the biotin-strep avidin-peroxidase conjugate technique.⁹ Expression of keratin (Dako), epithelial membrane antigen (Dako) and vimentin (Dako) were investigated.

In both cases, the foci which morphologically resembled epithelial differentiation demonstrated a strong staining reaction, positive for cytokeratin and epithelial membrane antigen and negative for vimentin.

Conversely, the areas of the tumors with malignant osteoid and spindle cells stained strongly positive for vimentin and were

negative for cytokeratin and epithelial membrane antigen (Fig. 2, left, right).

Discussion

Osteosarcoma is the second most common primary malignant neoplasm of bone after myeloma and accounts for approximately 20% of primary malignant bone tumors.^{1,10} It is well documented that osteosarcoma manifests a variety of histologic patterns among different cases and/or in separate areas of the same tumor.^{11,12} Among these histologic patterns, there are only a few observations of osteosarcoma with areas in which the malignant cells were arranged in sheets or gland-like patterns suggesting epithelial malignancy admixed with malignant sarcoma and accompanied by osteoid formation.^{2,3,5,13-15}

These cases are usually seen in young patients and this entity has been designated epitheloid osteosarcoma (carcinosarcoma).^{2,5} Histologically these tumors can be mistaken for adamantinomas and metastatic carcinomas. Presence of malignant osteoid differentiates the osteosarcoma from the above tumors.

Many theories¹⁶⁻¹⁸ have been proposed in regard to the histogenesis of this tumor;

however, the most widely accepted hypothesis suggests that the pathogenesis of biphenotypic tumors are that of the uncommitted, multipotential stem cell. This theory suggests that biphenotypic tumors arise from a primitive mesenchymal cell whose differentiation is in a non-random fashion, resulting in specific biphenotypic tumor types and postulates that differentiating mesenchymal-cells can acquire an epithelial cell morphology with expression of epithelial antigen markers.⁵ The divergent differentiation may be caused by the influence of microenvironment, cytogenetic abnormalities, retroviral genome integration or variation in protooncogen amplification.^{5,19}

The five-year survival rate of patients with osteosarcoma has approached 70 % with recent improvements in chemotherapy and surgery.^{7,20,21}

References

- 1 Bullough GP: *Bullough and Vigorita's Orthopaedic Pathology*. 3rd ed. Mosby-Wolf Co 1997:34q.353.
- 2 Mirra JM, Picci P, Gold RH: *Bone tumors: Clinical, Radiologic and Pathologic Correlation*. Philadelphia: Lea & Febiger, 1989:248-389.
- 3 Yoshida H, Yumoto T, Adachi H, et al: Osteosarcoma with prominent epithelioid features. *Acta Pathol Jpn* 1989;39: 439-45.
- 4 Okada K, Hasegawa T, Yokoyama R: Rosette-forming epithelioid osteosarcoma: a histologic subtype with highly aggressive clinical behavior. *Hum Pathol* 2001;32:726-33.
- 5 Kramer K, Hicks DG, Palis J, et al: Epithelioid osteosarcoma of bone. Immunocytochemical evidence suggesting divergent epithelial and mesenchymal differentiation in a primary osseous neoplasm. *Cancer* 1993;71:2977-82.
- 6 Bodner-Adler B, Boder K, Obermair A, et al: Prognostic parameters in carcinosarcomas of the uterus: a clinico-pathologic study. *Anticancer Res* 2001;21:3069-74.
- 7 Gu M, Antonescu CR, Guiter G, et al: Cytokeratin immunoreactivity in Ewing's sarcoma: prevalence in 50 cases confirmed by molecular diagnostic studies. *Am J Surg Pathol* 2000;24:410-6.
- 8 Rosai J: *Ackerman's Surgical Pathology*. 8th ed. 1996:1936-46.
- 9 Sternberg LA, Sternberg NH: The unlabeled antibody method comparison of peroxidase-antiperoxidase with avidin-biotin complex by a new method quantification. *Histochem Cytochem* 1988;34:599-605.
- 10 Klein MJ, Kenan S, Lewis YM: Osteosarcoma: Clinical and pathological consideration. *Orthop Clin North Am* 1989;20:327-45.
- 11 Ayala AG, Raymond AK, Jaffe N: The pathologist's role in the diagnosis and treatment of osteosarcoma in children. *Human Pathol* 1984; 15:258-66.
- 12 Dahlin DC, Coventry MB: Osteogeni sarcoma: A study of 600 cases. *J Bone Joint Surg* 1967;49A:101-10.
- 13 Hasegawa T, Shibata T, Hirose T, et al: Osteosarcoma with epithelioid features. An immunohistochemical study. *Arch Pathol Lab Med* 1993;117:295-8.
- 14 Derrick I, Schatz JE, Colgan TJ: Osteogenic sarcoma with epithelial differentiation. *Ultrastruct Pathol* 1992;16:463-74.
- 15 Spjut HJ, Dorfman Hd, Fechner RE, et al: Tumors of bone and cartilage. In: Armed Forces Institute of Pathology. Fascicle 5. Washington DC: 1971:166-74.
- 16 Hutter RVP, Foote FV, Francis KC, et al: Primitive multi-potential primary sarcomas of bone. *Cancer* 1966; 19:1-25.
- 17 Fromowitz FB, Rond RM, Leopold GK: The epithelial origin of nine malignant mesodermal mixed tumors of the bladder: Report of cases with long term survival. *J Urol* 1984; 132:978-81.
- 18 Silverberg SG: Malignant mixed mesodermal tumors of the uterus: An ultra-structural study. *Am J Obstet Gynecol* 1971;111:698-702.
- 19 Gould VE: Histogenesis and differentiation: A re-evaluation of these concepts as criteria for the classification of tumors. *Human Pathol* 1986;17:212-5
- 20 Glasser DB, Lanc JM, Huvos AG, et al: Survival, prognosis and therapeutic response in osteogenic sarcoma. The Memorial Hospital experience. *Cancer* 1992;69:698-708.
- 21 Harvey S, Solheim Q: The prognosis in osteosarcoma: Norwegian National data. *Cancer* 1981;48:719-23.