

Original Article

Primary malignant mixed tumor of bone: a case report

Zhansan Su¹, Zhi Li¹, Baoan Liu²

¹Department of Pathology, Xiangya Third Hospital, Central South University, Changsha 410013, Hunan Province, China; ²Department of Pathology, Xiangya Hospital, Central South University, Changsha 410008, Hunan Province, China

Received March 2, 2015; Accepted April 15, 2015; Epub July 1, 2015; Published July 15, 2015

Abstract: Background: An extremely rare primary mixed tumor occurring in left proximal femurs of a 47-year old female is reported. Case report: She had left hip pain for three months in April 2004. Radiological examinations revealed that a translucent expansive lesion in the left greater trochanter. She received the curettage of lesion and bone graft surgery. Curettage specimens were diagnosed as malignant mixed tumor, considered to be metastatic. Five months later the lesion recurred. She underwent obturator neurotomy plus total hip replacement of left hip. A long-term of more than ten years follow-up showed there were no evidence of disease recurrence or metastasis and no any signs of other tumor in her body. Discussion: The tumor contained myoepithelial component with positive immunostain of S-100 protein, p63, CK-pan, and vimentin, epithelial component confirmed by CK-pan, CK-LMW and cartilage, which indicated the tumor was a mixed tumor. Cellular atypia, relative high mitosis index, cartilage consistent with grade I chondrosarcoma, focal coagulative necrosis, and infiltration between trabeculae found in the tumor indicated that the tumor had a low grade malignant nature. During long-time follow-up there were no signs of any tumor found in the patient, which strongly suggested that the tumor be a primary one.

Keywords: Primary malignant mixed tumor, bone

Introduction

Mixed tumor, also known as pleomorphic adenoma, contains two components: an epithelial cell component including myoepithelial cell and a mesenchymal component. The identification of these components is essential to the recognition of it. It is the most common tumor of major salivary gland [1] and it may, much less commonly, appear in lungs, breast, skin and soft tissue. When it occurs in the skin or soft tissue, it is also termed as "chondroid syringoma" or "myoepithelioma/parachordoma" in WHO Classification of Tumors [2, 3]. Mixed tumor occurring in bone has been described, most of which are from metastasis of malignant or benign mixed tumor in other sites [4, 5], primary ones are extremely rare, only five cases has been reported in the literature [6-10].

Case report

A 47-year-old woman was admitted to Xiangya Third Hospital because of her left hip pain for

three months in April 2004. X-ray plain and CT imaging revealed that translucent expansive bone destruction in the left greater trochanter with thinning, absorption, partial discontinuity of cortical bone (**Figure 1**). The lesion had no local soft tissue mass and the structure of the left hip joint was normal. Chest X-ray had no abnormal findings. The lesion was considered to be benign, probable a bone cyst. The patient had a history of cholecystectomy because of gallstones 15 years ago. She received the curettage of bone lesions and bone graft surgery. Curettage specimens were diagnosed as malignant mixed tumor, considered to be metastatic. No primary site was found by further physical and CT examination of the chest, abdomen-pelvis, and head and neck.

After surgery the patient gradually recovered and was able to get out of bed. However, her left hip pain recurred again in 5 months. X-ray showed that there were small dots with mixed low and high density on the outer upper edge of greater trochanter and soft tissue at outer lower

Primary malignant mixed tumor of bone

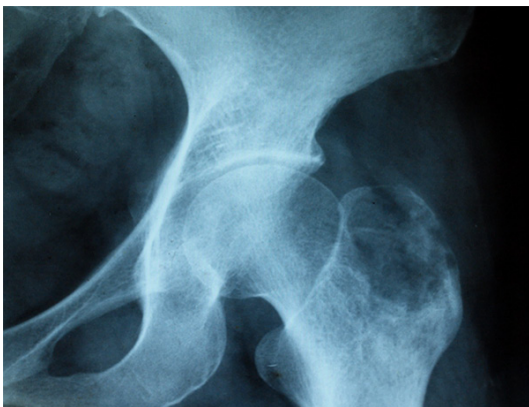


Figure 1. X-ray plain revealed a translucent expansive lesion with thinning, absorption and, partial discontinuity of cortical bone in the left greater trochanter.

edge of greater trochanter, small amount of periosteal reaction on the edge of left femoral was visible except for postoperative changes. Chest X-ray had no positive findings. The patient underwent obturator neurotomy plus total hip replacement of left hip. The microscopic findings were similar to those in previous surgical specimen and the diagnosis remained the same.

The patient recovered well after operation and refused further chemotherapy or radiotherapy. After discharge from hospital, she visited the hospital for regular examination, the last one was in Sep 2014. There were no evidence of disease recurrence or metastasis and no any signs of other tumor in other parts, except for slight claudication. So far, the disease-free survival time was more than 10 years.

Pathological findings

General inspection: The first surgical specimen was crisp small pieces, pale gray and yellow, partially colloid, total 8.0 × 7.0 × 2.0 cm. Sand-like translucent cartilage particles could be identified; The second surgical specimen was a femoral head with the greater trochanter and metaphysis damaged by gray, partially colloid tumor tissue. The tumor tissue destroyed cortical bone and slightly protruded into soft tissue. Articular cartilage was not destroyed yet.

Histopathological findings: The tumor was composed of spindle, stellate or epithelioid cells with hyperchromatic nuclei and small amount eosinophilic or clear cytoplasm. In most areas

the tumor cells were spindle, arranged in cords, nests, and strands forming a vague lobular pattern with varying cellularity, embedded in a myxoid stroma (**Figure 2A**). In hypercellular regions, there was compact cellular proliferation of epithelioid cells that had round to oval, vesicular nuclei, inconspicuous nucleoli, and eosinophilic cytoplasm, with mild nuclear pleomorphism and relatively high mitotic rates (18/10 HPF) Focal vague ductal structures with small and ill defined lumens (**Figure 2B**) and coagulative necrosis could be seen. In hypocellular areas, stellate tumor cells was scattered in a abundant myxoid matrix. In these areas it was seen that the epithelioid cells with clear cytoplasm were, frequently abrupt, transitioned into squamous epithelial cells with keratin pearl formation (**Figure 2C**). Small foci of low grade chondrosarcoma were found scattered throughout the tumor (**Figure 2D**). At the edge of the tumor, the tumor cells destroyed the host bone trabeculae or infiltrated between trabeculae (**Figure 2E**).

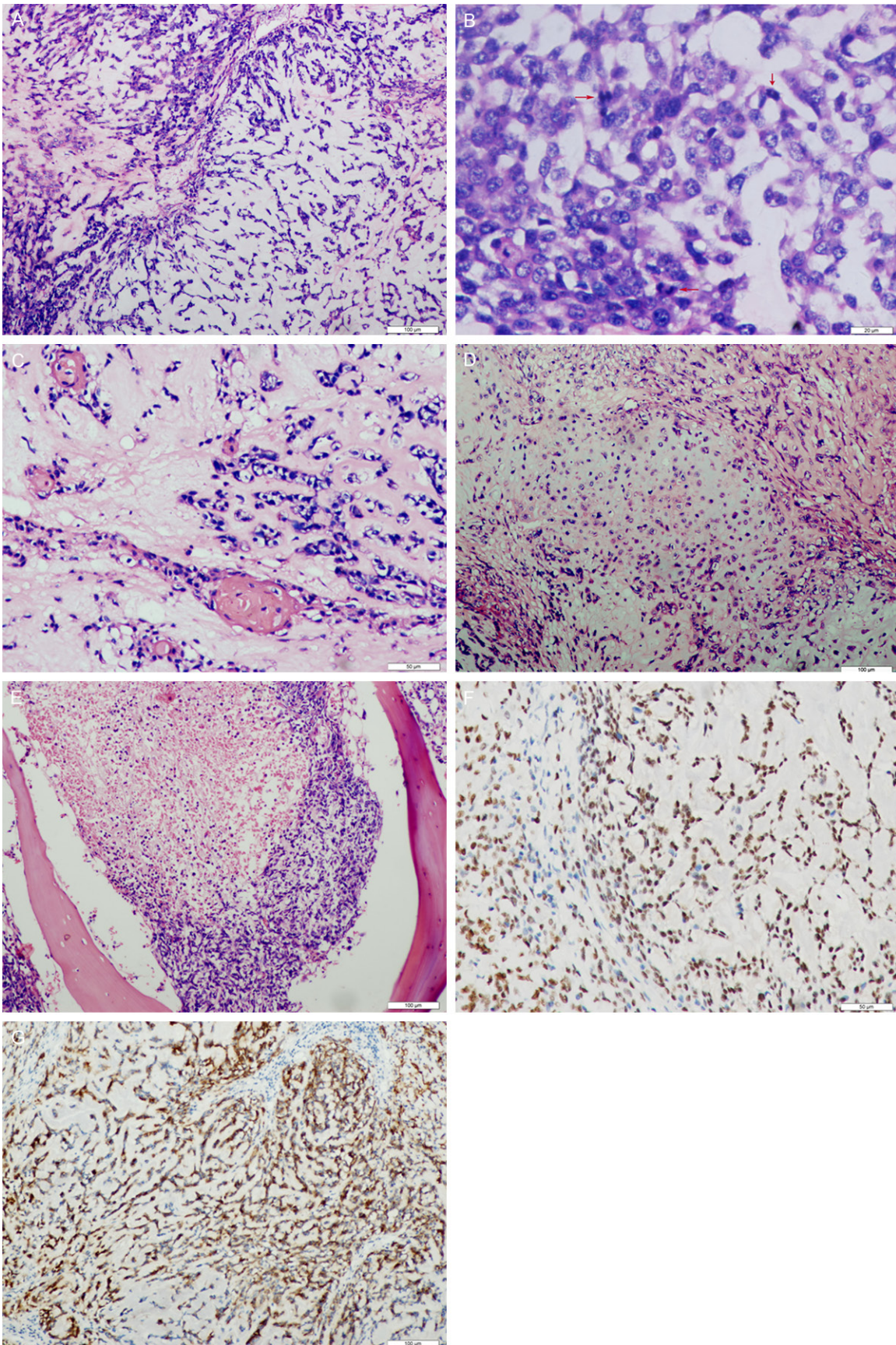
Routine immunohistochemical analyses were performed from formalin-fixed, paraffin-embedded specimens. The panel of antibodies mainly included CK-pan, CK-HMW, CK-LMW, EMA, Vimentin, S-100 protein, GFAP, Calponin, p63, SMA and Ki-67. All the antibodies were products of DAKO and staining was performed with the DAKO En Vision Kit. The sections were developed with 3,3'-diaminobenzidine tetrahydrochloride and counterstained with hematoxylin. Immunohistochemical staining showed that most of the tumor cells were strongly positive for S-100 protein, CK-pan, p63 and Vimentin (**Figure 2F, 2G**), indicating they were myoepithelial cells. The tumor cells with squamous differentiation were positive for CK-HMW and EMA, the epithelioid cells focal positive for CK-LMW and the spindle cells focal positive for calponin. GFAP and SMA were negative. The Ki-67 proliferation index was about 5%.

The pathological findings were similar in both specimens, overall features of this tumor were consistent with a mixed tumor having both epithelial and mesenchymal differentiation.

Discussion

Among primary tumors of bone, the tumors containing distinct epithelial components are rare and only adamantinoma and mixed tumor

Primary malignant mixed tumor of bone



Primary malignant mixed tumor of bone

Figure 2. A. The tumor cells were spindle, arranged in cords and strands forming a vague lobular pattern, embedded in a myxoid stroma. B. Epithelioid tumor cells that had round to oval, vesicular nuclei, inconspicuous nucleoli, and eosinophilic cytoplasm, with mild nuclear pleomorphism and an increased mitotic activity (Red arrows) (H&E stain). C. The cords of epithelioid cells with clear cytoplasm were scattered in a myxoid or myxochondroid stroma and transitioned into squamous epithelial cells with keratin pearl formation (H&E stain). D. Small foci of cellular cartilage with nuclear atypia, consistent with low grade chondrosarcoma were found scattered throughout the tumor (H&E stain). E. The dense spindle tumor cells with coagulative necrosis infiltrated between bone trabeculae (H&E stain). F. The tumor cells were positive for p63 strongly and diffusely with a pattern of nuclear staining. G. The spindle tumor cells were strongly positive for S-100 protein.

are considered as definite entities. Adamantinoma is a low-grade neoplasm with epithelial differentiation and a striking predilection to involve the tibia. Histologically, it resembles the adamantinoma of the jawbones, showing basoid pattern with peripheral palisading of cuboidal and columnar tumor cells or the pattern of fibrous dysplasia with scattering islands of epithelial cells, without myoepithelial and chondrosarcomatous components. Such histologic features were not found in the case reported here and the diagnosis of adamantinoma could be excluded.

Mixed tumors mainly occur in major and minor salivary glands and they may occasionally appear in skin, breast, lung and soft tissue. Mixed tumors also have been reported appearing in bone though most of the benign or malignant mixed tumors found in bone were metastatic from other parts of the body. However, there were four case reports in the literature showing that similar tumors could occur in bone as primary tumor though their histogenesis was still an enigma. Squamous and chondroid components as well as myoepithelial component which were confirmed by S-100 protein and p63 immunostain found in present case strongly suggested that the tumor was a mixed tumor. When the specimen of the first operation was observed, we thought that it was a metastatic mixed tumor. However, there was no primary site was found by comprehensive examination. Furthermore, during the follow-up period more than 10 years, no any tumor has been found in the patient by periodical examination at hospitals. It should be safe to assume that it was a primary mixed tumor of the bone. Though there were no obvious carcinomatous or sarcomatous components found in this case, there were cellular atypia, relative high mitosis index, cartilage consistent with low grade chondrosarcoma, focal coagulative necrosis, and infiltration between bone trabeculae. It should be reasonable to consider it a low-grade malignant mixed

tumor. The good outcome of the case might benefit from the low grade malignant nature of the tumor and the radical surgical treatment.

There were two interesting cases of chondrosarcoma with distinct epithelial differentiation reported in the literature [11, 12]. In those cases, the tumor was termed as “chondrosarcoma associated with squamous cell carcinoma” and “primary bone carcinosarcoma”. Interestingly, the histopathological findings were similar in both cases, the tumor consisted of three components: well differentiated chondrosarcoma, undifferentiated spindle cell sarcoma with varying cellularity and squamous cell carcinoma with prominent keratin pearl formation. Both patients were died of the disease at 6 months and three and a half years after diagnosis respectively. According to the description of morphology, it was not entirely impossible that the lesions were malignant mixed tumor with carcinosarcoma transformation. Further study of immunophenotyping and molecular genetics may reveal their histogenesis.

Disclosure of conflict of interest

None.

Address correspondence to: Dr. Baoan Liu, Department of Pathology, Xiangya Hospital, Central South University, 87# Xiangya Road, Changsha 410008, Hunan Province, China. E-mail: liuba118@126.com

References

- [1] Gnepp DR, Wenig BM. *Surgical Pathology of the Salivary Gland*. Philadelphia; W B Saunders; 1991. pp. 350-68.
- [2] Philip E, LeBoit PE, Burg G. (WHO) *Pathology and Genetics of Skin Tumours*. Lyon: IARC Press; 2006. pp. 147-8.
- [3] Fletcher CD, Unni KK and Mertens F. (WHO) *Pathology and Genetics of Tumours of Soft Tissue and Bone*. Lyon: IARC Press; 2002. pp. 198-9.

Primary malignant mixed tumor of bone

- [4] Manucha V, Loffe OB. Metastasizing pleomorphic adenoma of the salivary gland. *Arch Pathol Lab Med* 2008; 132: 1445-7.
- [5] Parikh HK, Parikh DM. Malignant mixed tumor of the salivary gland with bone metastasis: a case report and literature review. *Indian J Cancer* 1991; 28: 171-5.
- [6] Barreto CA, Lipton MN, Smith HB, Potter GK. Intraosseous chondroid syringoma of the hallux. *J Am Acad Dermatol* 1994; 30: 374-378.
- [7] Gadgil RK, Ranadive NU. Chondroid syringoma (mixed tumour) of radius. *Indian J Cancer* 1981; 18: 81-83.
- [8] Hirsch P, Helwig EB. Chondroid syringoma, mixed tumor of skin, salivary gland type. *Arch Dermatol* 1961; 84: 835-847.
- [9] de Pinieux G, Beabout JW, Unni KK, Sim FH. Primary mixed tumor of bone. *Skeletal Radiol* 2001; 30: 534-536.
- [10] Yu H, Liu X, Li H, Shi D, Wang C. Primary pleomorphic adenoma of bone: report of a case and literature review. *Indian J Pathol Microbiol* 2012; 55: 320-322.
- [11] Ling LL, Steiner GC. Primary multipotential malignant neoplasm of bone: chondrosarcoma associated with squamous cell carcinoma. *Hum Pathol* 1986; 17: 317-320.
- [12] Shiraishi J, Mukai M, Yabe H, Shibata R, Yamada T, Miura K, Anazawa U, Morioka H, Sakamoto M. Primary bone carcinosarcoma: Chondrosarcoma and squamous cell carcinoma with keratin pearl formation. *Pathol Int* 2005; 55: 504-509.