Primary Carcinosarcoma of Bone: A Case Report with Review of the Literature

Tamera Paczos, MD, Brian McGrath, MD, Frank Chen, MD, PhD

Abstract
Primary carcinosarcoma of the bone is an extremely rare entity with only a few other cases reported in the literature. Here we describe such a neoplasm in a 63-year-old Caucasian male who presented with back pain and a pathologic fracture of T10 with lesions at T11, T12, and L1. A CT scan was done which showed a lytic lesion in the right posterior body of T11 measuring 2.2 cm. The patient had an open biopsy of this lesion that revealed a poorly differentiated spindle cell neoplasm. Microscopically, the lesion consists of a malignant spindle cell proliferation with marked nuclear pleomorphism, nuclear hyperchromasia, and an increased N/C ratio with some multinucleated forms present. Mitotic figures and atypical mitotic figures are also noted. Immunohistochemical analysis shows that the tumor cells are positive for Vimentin, CAM 5.2, and focally positive for low-molecular weight cytokeratin and high molecular weight cytokeratin. The tumor cells are negative for S100, HMB45, melan A, SMA, muscle specific actin, desmin, pancytokeratin, EMA, CD31, CD34, CD30, Alk-1, TTF-1, calretinin, BerEP4, and thyroglobulin. The tumor cells are also negative for mucicarmine and alician blue pH 2.5. The morphology along with the immunohistochemical profile of the tumor is diagnostic for carcinosarcoma. Further workup revealed lesions in his right hip and left rib, but no other non-osseous source for a primary lesion. The patient’s past medical history includes a resection of a scapular tumor 15 years ago that was diagnosed as low-grade chondrosarcoma. Following his open biopsy the patient underwent radiation therapy to his scapula 15 years ago. Following his open biopsy the patient underwent radiation therapy to his spine and 5 courses of chemotherapy with the MAID protocol. PET scan done following chemotherapy revealed progression of disease in his T12 and iliac region. The T11-T12 region was further treated with extracranial stereotactic body radiosurgery and the patient underwent radiation therapy to his iliac area. One year following his open biopsy the patient is still alive but deteriorating with marked weight loss and pain. No non-osseous primary lesion has been detected to this date.

Introduction

Carcinosarcoma is an unusual neoplasm defined by the presence of both epithelial and mesenchymal differentiation. These tumors are most commonly encountered in the genitourinary and gastrointestinal tracts. A primary carcinosarcoma arising in bone is extremely rare. Only five previous cases have been reported in the literature. These cases differ from ours in that they all have morphologically distinct areas of chondrosarcoma or osteosarcoma intermixed with malignant appearing epithelium. Our case consists of a malignant spindle cell proliferation with marked pleomorphism and no distinct areas of morphologic differentiation. The diagnosis of carcinosarcoma was obtained using immunohistochemistry demonstrating areas of epithelial and sarcomatous differentiation.

Case Report

A 63-year-old man complained of lumbar back pain after shoveling snow. Lumbar strain was suspected and he was treated with pain analgesics but the pain persisted. A CT scan of the abdomen was obtained that showed a lytic lesion in his T11 vertebral body measuring 2 x 2.2 cm and a second lytic lesion in his left iliac body measuring 2.2 cm. An MRI revealed findings consistent with disease involving the T10 through L1 vertebral bodies, with the most significant level of involvement at T11 with complete replacement and extension into the pedicles and spinous process (Figure 1A and B). CT guided needle biopsies were performed and were diagnostic for a poorly differentiated malignancy. To reach a more definitive diagnosis the patient elected to proceed with an open biopsy of his T11 vertebral body. The open biopsy material was diagnosed as sarcomatoid carcinoma. The patient’s past medical history is significant for a low-grade chondrosarcoma of his right scapula 15 years ago. Following his open biopsy the patient underwent radiation therapy to his spine and 5 courses of chemotherapy with the MAID protocol. PET scan done following chemotherapy revealed progression of disease in his T12 and iliac region. The T11-T12 region was further treated with extracranial stereotactic body radiosurgery and the patient underwent radiation therapy to his iliac area. One year following his open biopsy the patient is still alive but deteriorating with marked weight loss and pain. No non-osseous primary lesion has been detected to this date.

Tamera Paczos, MD, Brian McGrath, MD, Frank Chen, MD, PhD
Department of Pathology
State University of New York at Buffalo
School of Medicine and Biomedical Sciences
Buffalo General Hospital
Buffalo, NY
Materials and Methods

The open biopsy specimen was fixed with 10% formalin and embedded in paraffin. Sections were cut 4 μm thick and stained with hematoxylin and eosin. Sections were also immunostained by the avidin-biotin-peroxidase complex method with antibodies to vimentin (Clone V9, monoclonal mouse antiswine, DakoCytomation, diluted 1:400), CAM 5.2, Keratin 8/18 (Clone K8.8+ DC10; like 5D3), monoclonal mouse, Lab Vision, diluted 1:200), high molecular weight cytokeratin (AE3, monoclonal mouse, Cell Marque, diluted 1:100), low molecular weight cytokeratin (Keratin 8, clone 35B11), monoclonal mouse, DakoCytomation, diluted 1:200), S100 (polyclonal rabbit, DakoCytomation, diluted 1:1200), melanoma (HMB45, monoclonal mouse, Dako, diluted 1:50), Melan-A (A103, monoclonal mouse, DakoCytomation, diluted 1:200), smooth muscle actin (1A4, monoclonal mouse, Dako, diluted 1:400), muscle specific actin (HHF35, monoclonal mouse, BioCare, diluted 1:200), desmin (D33, monoclonal mouse, Dakocytomation, diluted 1:600), pancytokeratin (AE1/AE3, monoclonal mouse, Dako, diluted 1:300), Epithelial membrane antigen (EMA) (E29, monoclonal mouse, Dako, 1:200), CD31 (JC70A, monoclonal mouse, DakoCytomation, diluted 1:50), CD34 (QBEnd/10, monoclonal mouse, Cell Marque, diluted 1:100), CD30 (Ber-H2, monoclonal mouse, DakoCytomation, diluted 1:20), ALK-1 (ALK-1, monoclonal mouse, DakoCytomation, diluted 1:25), TTF-1 (8G7G3/1, monoclonal mouse, Cell Marque, diluted 1:40), Calretinin (DAK Calret 1, monoclonal mouse, DakoCytomation, diluted 1:100), Epithelial antigen (Ber-Ep4, monoclonal mouse, DakoCytomation, diluted 1:400), thyroglobulin (DAK-Tg6, monoclonal mouse, DakoCytomation, diluted 1:200). Sections were also stained with Mayers Mucicarmine (Sigma Diagnostics) and Alcian Blue pH 2.5 (MCB).

Pathologic Findings

The open biopsy specimen was received in two parts each labeled T11 vertebral body. The first part consisted of multiple fragments of tan-yellow soft tissue measuring 1.5 x 1.2 x 0.3 cm in aggregate dimension. The second part consisted of multiple fragments of tan-red soft tissue with small portions of bone measuring 6.5 x 6 x 0.8 cm in aggregate dimension. Both specimens were completely submitted for microscopic examination. Microscopically, the specimen consisted of a poorly differentiated malignant spindle cell neoplasm occasionally intermixed with fragments of normal appearing bone and marrow elements (Figure 2). The malignant tumor cells were composed of slender to plump elongated spindle cells with some bizarre giant cell forms intermingled throughout containing abundant eosinophilic, fibrillary cytoplasm. The cells overall were haphazardly arranged with some areas consisting of a more storiform-like and fascicular pattern. The cells exhibited moderate to marked pleomorphism with mitotic figures and atypical mitotic figures noted. There were no morphologically distinct epithelial elements identified. Immunohistochemical staining revealed that the tumor cells were strongly positive for vimentin throughout the specimen with more focal but distinctly positive staining present for low-molecular weight cytokeratin, high-molecular weight cytokeratin, and CAM 5.2. The tumor cells were negative for S-100, HMB45, melan A, smooth muscle actin, muscle specific actin, desmin, pancytokeratin, EMA, CD31, CD34, CD30, Alk-1, TTF-1, calretinin, BerEP4, and thyroglobulin. Mucicarmine and alcian blue PH 2.5 were also negative.

Discussion

Cases of multipotential neoplasms of bone have been well documented in the literature. The majority of them consist of multiple histologic elements including chondrosarcomatous, osteosarcomatous, lymphoid, vascular, adamantinomatous, squamous and adenocarcinomatous differentiation. Frydman et al. described a case of primitive multipotential primary sarcoma of bone that showed areas resembling lymphoma, areas producing osteoid matrix, and areas of epithelial differentiation. Jacobson described a large series of cases that consisted of a small round blue cell tumor that showed areas of differentiation into multiple mesenchymal cell lines, but with no areas of epithelial differentiation, which he termed ‘polyhistiomas’. Hutter et al. described a series of 25 cases in which the tumors showed a common type of undifferentiated cell and differentiation along multiple lines, including areas that appeared epithelial in nature. The most commonly cited differential diagnosis in these cases was Ewing’s sarcoma, which is unlikely in our case based on the patient’s age, the tumor location, and the histologic appearance of the tumor.

More recently, Ling et al. and Shiraishi et al. described cases with chondrosarcomatous and epithelial differentiation and Kramer et al. described a case of osteosarcoma with epithelial differentiation. Our case differs in that it shows no distinct areas of histologic differentiation, but it is similar in that immunohistochemically we show areas of mesenchymal differentiation intermixed with epithelial elements.

The pathogenesis of carcinosarcomas is still not completely understood. Two commonly cited theories are used to explain the origins of carcinosarcomas in many organs, the convergence (multiclonal hypothesis) and the divergence (monoclonal hypothesis). Molecular studies are now being used to elucidate the origins of these tumors and most recent studies support a monoclonal theory of carcinomas originating from a multipotent stem cell. This stem cell is then acted on by a combination of the microenvironment and genetic alterations to produce different histologic expressions of cell types.

There is still much to learn about the pathology and origin of carcinosarcomas. Our case is an example of the extremely rare occurrence of this type of neoplasm arising primarily in bone. Although molecular studies have not been done to date on this case, the undifferentiated nature of the cells with no obvious areas of transition supports the monoclonal theory of pathogenesis from a multipotent stem cell.
References

Figure 1. Magnetic resonance image (MRI).
(A) Axial view at the levebody with extension into the pedicles and spinous process.
(B) Sagbodies with retroperitoneal adenopathy noted at the T11 level.
Figure 2. Hematoxylin-eosin stained sections of tumor.

(A) Low power view showing poorly differentiated, pleomorphic tumor with some areas exhibiting a storiform-like and fascicular pattern.

(B) High power view showing bizarre, pleomorphic, multinucleated cells with abundant eosinophilic, fibrillary cytoplasm.

Figure 3. Diffuse and intense staining of the tumor cells with vimentin.

Figure 4. CAM 5.2 staining of the tumor cells.

Figure 5. High molecular weight cytokeratin staining of the tumor cells.

Figure 6. Low molecular weight cytokeratin staining of the tumor cells.