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A 61-YEAR-OLD WOMAN WITH OSTEOMALACIA AND A THORACIC SPINE LESION

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CLINICAL HISTORY AND IMAGING STUDIES

A 55-year-old woman presented with bilateral hip and rib pain. A chest radiograph revealed multiple bilateral rib fractures with callus formation. Insufficiency fractures of the right superior and inferior pubic rami and ischium and possibly of the sacrum were noted on hip and pelvic radiographs, and a subsequent MRI showed avascular necrosis of the left femoral head. Laboratory studies demonstrating hypophosphatemia, in combination with the patient's clinical presentation of osteomalacia, prompted further investigation for the underlying cause.

A parathyroid scan, an octreotide body scan, and a whole body sestamibi scan all revealed normal results with no evidence of neoplasm. The patient's diagnosis of avascular necrosis in combination with pain refractory to non-operative measures resulted in a left total hip arthroplasty.

The patient was lost to follow up until six years later when she presented with bilateral weakness and shooting pains in her legs after a recent fall. She denied back pain and bowel or bladder dysfunction. The work-up included a full body positron emission tomography/computed tomography (PET/CT), which revealed a 4.3 cm greatest dimension fluoro-deoxyglucose (FDG^{18})-avid expansile lytic lesion involving the left posterior T12 neural arch. At that time the patient's serum fibroblast growth factor-23 (FGF-23) level was found to be elevated. Subsequently, an MRI of the spine was performed. Sagittal (Figure 1) and axial (Figure 2) T2-weighted, unenhanced and axial T1-weighted, contrast-enhanced, fat-suppressed (Figure 3) images revealed a multi-lobulated, vividly enhancing, heterogeneous mass centered in the left pedicle and laminae of T12, with extension into the epidural space (thick arrows) and posterior paraspinal musculature (thin arrows). The patient underwent T11 to L1 laminectomies and tumor resection.

GROSS AND MICROSCOPIC PATHOLOGY

The gross specimen consisted of multiple fragments of soft tissue and attached bone. The cut surfaces were crunchy and showed areas of focal hemorrhage and cystic degeneration. Histologic examination revealed a fairly well circumscribed, partially encapsulated (Figure 4), moderately cellular tumor with heterogeneous composition (Figure 5). The tumor contained variably sized cystic spaces including large dilated ones filled with blood (Figure 6). The tumor cells appeared spindled with normochromatic, small nuclei and indistinct nucleoli (Figure 7). There was no significant nuclear atypia and mitoses were difficult to find. The tumor cells were focally embedded in a myxochondroid and osteoid-like matrix (Figures 8 and 9) with scattered areas of dystrophic calcification (Figure 8). Peripheral foci of ossification were also noted (Figure 10). The tumor was penetrated by capillary-sized vessels and intermixed with scattered osteoclast-like giant cells (Figure 11). Bone invasion was focally present.

What is your diagnosis?

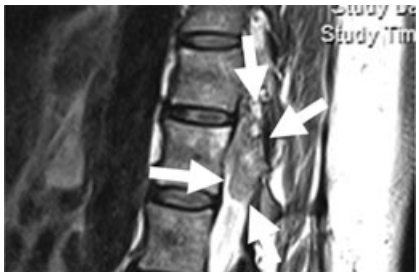

Figure 1.

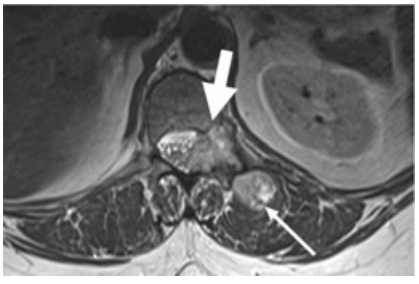

Figure 2.

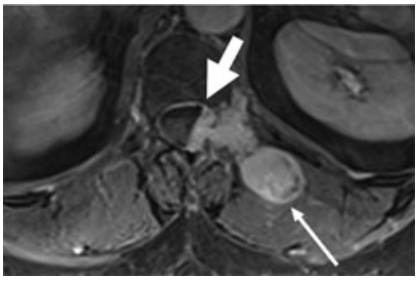

Figure 3.

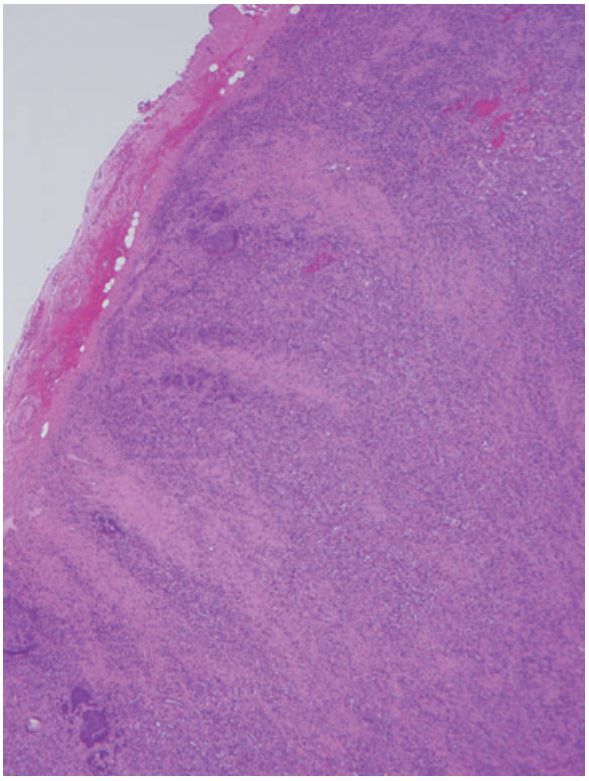

Figure 4.

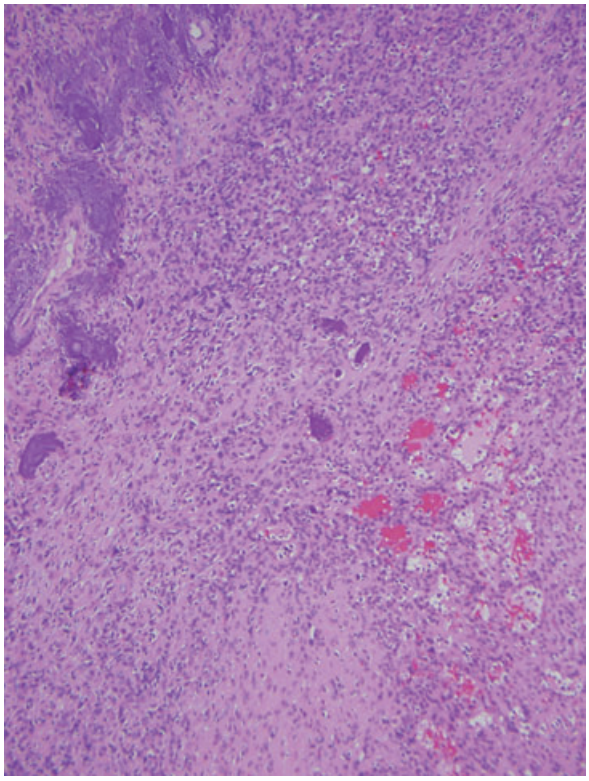

Figure 5.

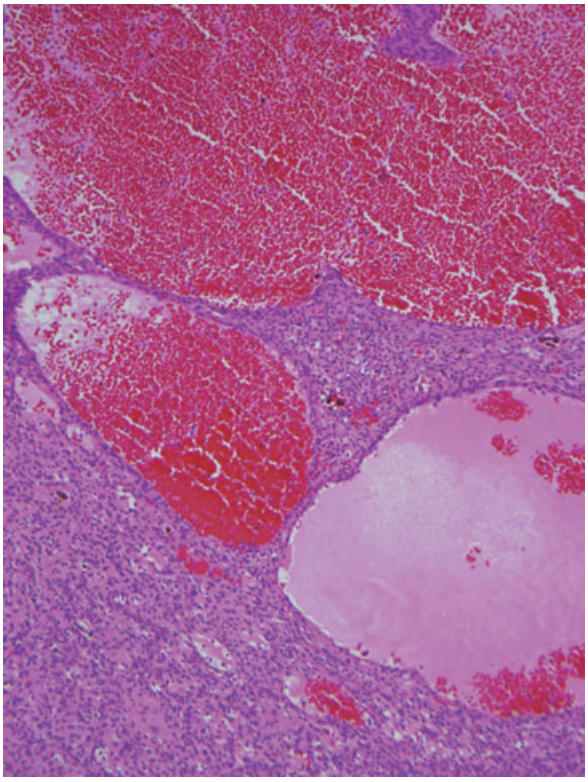

Figure 6.

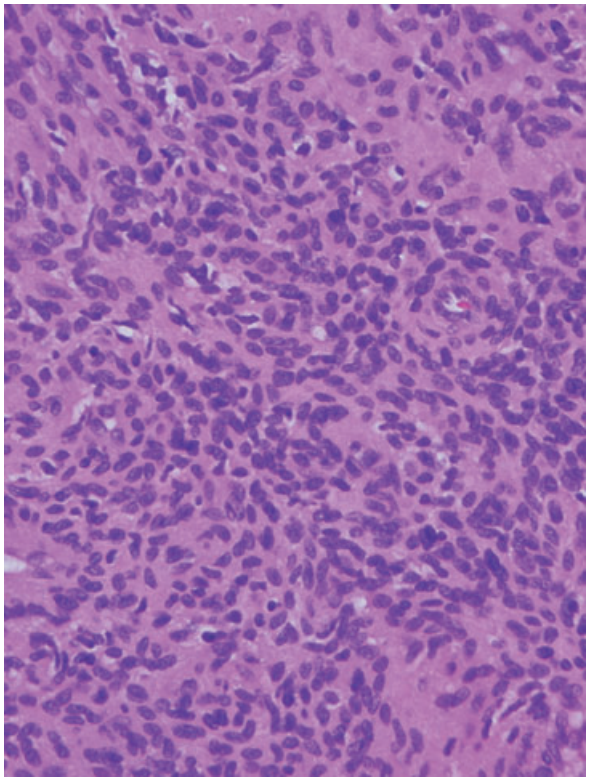

Figure 7.

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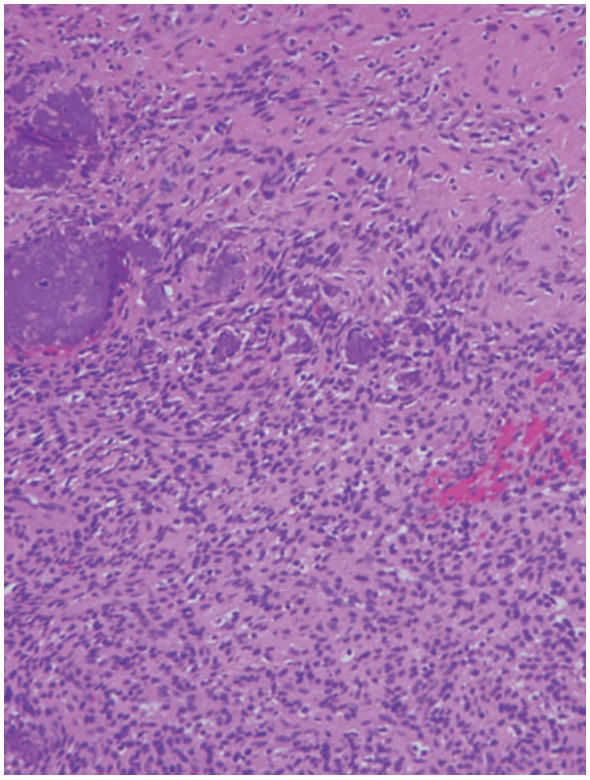

Figure 8.

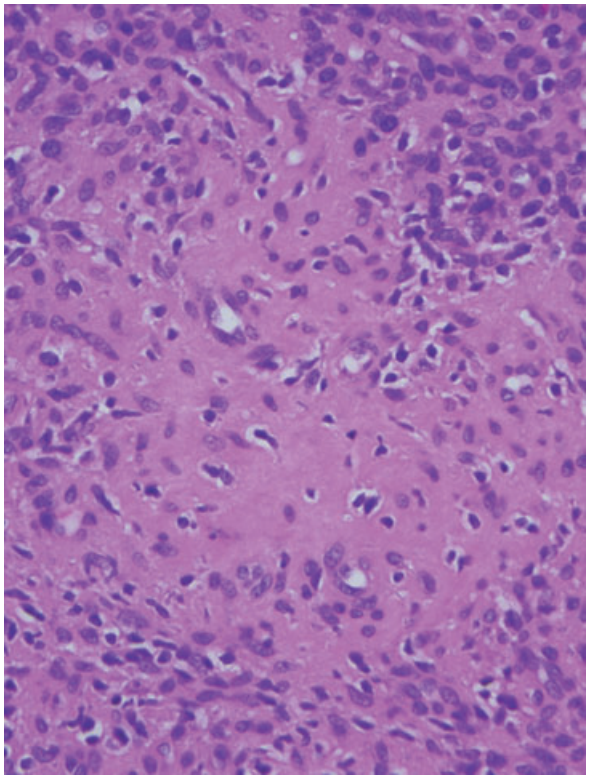

Figure 9.

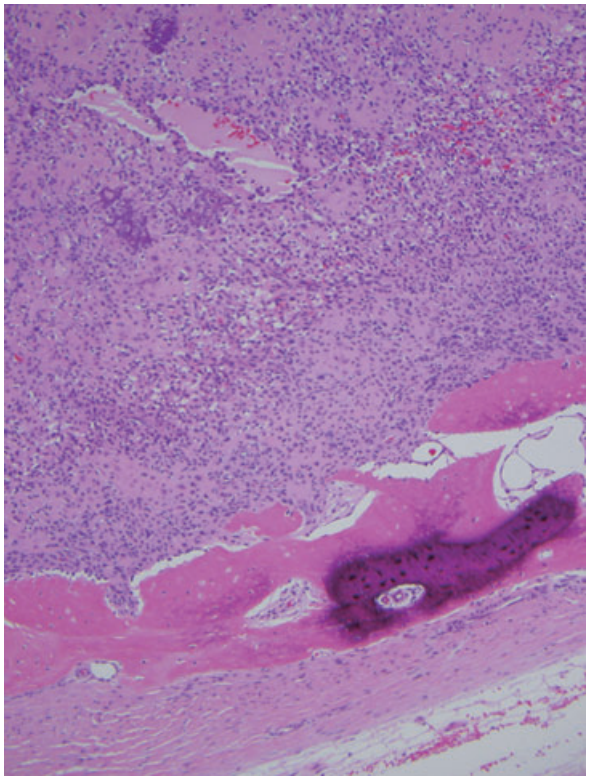

Figure 10.

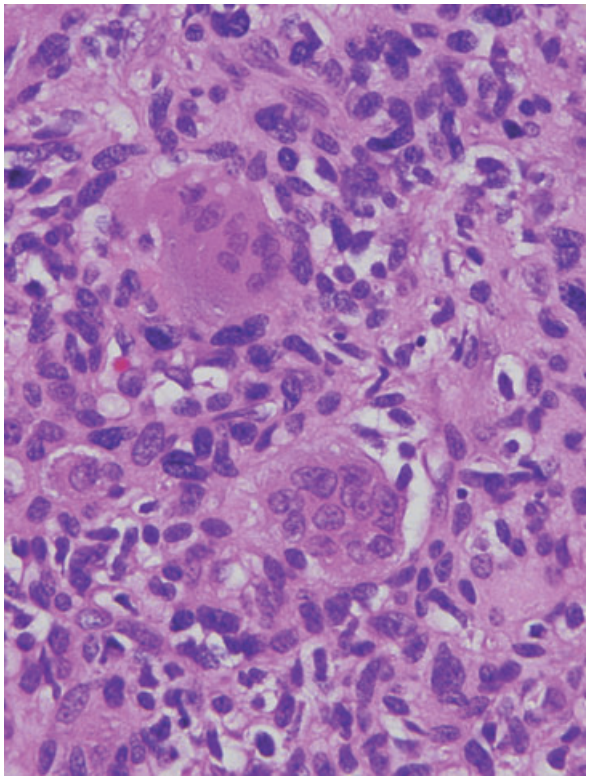

Figure 11.

DIAGNOSIS

Phosphaturic Mesenchymal Tumor, Mixed Connective Tissue Variant (PMT-MCT)

DISCUSSION

PMT-MCT is the most common cause of oncogenic osteomalacia (1, 6, 10, 11). PMT-MCT may not be easily recognized because of its rarity and polymorphic histologic features. Classic histopathologic characteristics include bland spindle cells with small nuclei surrounded by a myxochondroid and osteoid-like "smudgy" matrix. Other characteristic features include areas of flocculent calcification, osteoclast-like giant cells, and a well-developed capillary network (1). Examples that do not show the entire morphologic spectrum of PMT-MCT are more difficult to recognize. The index case showed classic PMT-MCT features. In conjunction with an appropriate clinical presentation and laboratory findings, the diagnosis of PMT can often be made on H&E sections; ancillary immunostains with antibodies against FGF-23 and dentin matrix protein 1 (DMP1) are also helpful in confirming the diagnosis (1, 9).

Patients with PMT-MCT commonly have a protracted history of bone pain and multiple fractures as well as hypophosphatemia, hyperphosphaturia, elevated alkaline phosphatase activity, and low or inappropriately normal serum 1,25-dihydroxyvitamin D_3 levels. Patients also fail to respond to vitamin D therapy (1, 4, 8). Rarely, osteomalacia may be absent (1). Lesions are often inapparent due to their small size and slow growth. The patient in this case exhibited hypophosphatemic osteomalacia for six years before the tumor was identified despite a thorough work-up and numerous radiological studies(1, 2, 5, 6). Complete surgical resection of the tumor is curative, resulting in resolution of symptoms associated with osteomalacia (1, 2, 4, 8).

PMT-MCT can originate in the bone or soft tissue of any location, although the extremities or appendicular skeleton account for most cases (1, 6). Reis-Filho *et al* reported a case of PMT-MCT occurring in the cavernous sinus (5). Similar to our case, this patient presented with a protracted history of osteomalacia and hypophosphatemia, and surgical resection was curative. In addition to the morphologic features described in that case, the case described herein displayed a wider morphologic spectrum of PMT-MCT including the characteristic osteoid-like matrix, dystrophic calcification, and ossification (5).

Even though PMT-MCT is a rare tumor and occurs infrequently in the axial skeleton (1, 7, 12), the surgical neuropathologist may occasionally encounter a case like the one described herein. Awareness of the existence of PMT-MCT as a distinct clinicopathologic entity is crucial for optimal patient outcome since complete surgical resection without additional treatment is curative. Therefore, PMT-MCT should be added to the differential diagnosis of spinal and paraspinal lesions.

For a more complete discussion please go to: http://path.upmc.edu/divisions/neuropath/bpath/cases/case196/dx.html

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ABSTRACT

Phosphaturic mesenchymal tumor, mixed connective tissue variant (PMT-MCT) is a rare, largely benign, mesenchymal neoplasm almost invariably associated with oncogenic osteomalacia. It is generally found in the soft tissue and bone of the extremities. We report a case of a 61-year-old female with long-standing osteomalacia who was found to have PMT-MCT of the thoracic spine. There have been very few previously reported cases of PMT involving the spinal vertebrae and neuropathologists should be aware of this lesion. Recognition of PMT-MCT is critical for optimal patient care since complete surgical resection without additional therapy is curative.