High-Grade Pelvic Osteosarcoma With Intravascular Extension to the Right Side of the Heart

A Case Report and Review of the Literature

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- We describe a rare case of high-grade osteosarcoma with intravascular extension to the right atrium and right ventricle in a 23-year-old woman. Osteosarcomas rarely metastasize to the heart, and only a few cases have been reported in the literature thus far. Diagnoses in some of these cases were made during investigation for severe cardiac failure and in most of these cases at autopsy. We describe a unique case of intravascular extension of the tumor embolus in a cordlike fashion from the left femoral vein to the right side of the heart that morphologically resembled a chondrosarcoma.

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The tumors that commonly invade the inferior vena cava (IVC) include Wilm tumor, testicular tumors, renal cell carcinoma, adrenal carcinoma, hepatocellular carcinoma, and uterine leiomyomatosis. Among sarcomas, chondrosarcoma and leiomyosarcoma are the most common. We report a rare case of an osteosarcoma with intravascular extension from the left femoral vein to the right side of the heart.

REPORT OF A CASE

A 23-year-old woman presented with complaints of leg weakness for 1 month. At the time of presentation, the patient was noted to have a large pelvic mass with extension into the lumbosacral region. Her legs were swollen and tender. A biopsy of the sacrum was performed via an L4 through L5 laminectomy, and the specimen was diagnosed as sarcoma.

The patient was then referred to our institution, where T2-weighted magnetic resonance imaging (MRI) was subsequently performed, which demonstrated a soft tissue mass that invaded the sacrum and bilateral iliac wings. The mass extended into the L4 epidural space. The tumor involved the lower spine and pelvis, and there were right para-aortic, iliac, and right aortic bifurcation nodes seen. Furthermore, venous thrombosis was a concern. The patient was admitted to the hospital and underwent a subsequent debulking procedure that consisted of reexposure of L4-S1 and limited tumor resection. Another biopsy was performed, and the specimen revealed osteosarcoma, chondroid variant.

Shortly after surgery, the patient underwent venography of the IVC, which demonstrated that the entire length of the IVC from the infrarenal area to the right atrium was thrombosed. A transesophageal echocardiogram demonstrated a 4.5 × 1.5-cm mass that originated in the IVC and extended into the right atrium with extension into the right ventricle. The cardiothoracic surgery department was then consulted, and the patient underwent a resection of the mass in the IVC and right atrium (Figure 1). She was subsequently referred for postoperative radiation therapy and chemotherapy. Shortly after the radiation therapy and before the start of chemotherapy, the patient died. Computed tomography of the abdomen and lung immediately before her death showed liver and lung metastases. There was no autopsy performed.

PATHOLOGIC FINDINGS

Grossly, the specimen obtained from the lumbar spine tumor consisted of multiple fragments of tan-pink soft tissue that measured 4.5 × 4.5 × 1.1 cm in aggregate. Microscopically, the tumor was highly cellular, formed by sheets of round to oval to spindle-shaped cells. The primitive-appearing cells had scant cytoplasm, mild pleomorphic nuclei and small nucleoli, and brisk mitotic activity at 15 per 10 high-power fields (Figure 2, A, inset). There were some islands of osteoid (Figure 2, A) and some filamentous form of osteoid. Some of the osteoid islands were densely mineralized and lacked osteoblastic rimming (Figure 2, B); rimming osteoblasts are most commonly observed in reactive and benign bone-forming lesions (eg, callus, myositis ossificans, osteofibrosis dysplasia, osteoma, and osteoblastoma). Immunohistochemical analysis for vimentin, S100 protein, smooth muscle antigen, pan-keratin (AE1/AE3), and CD99 showed no reactivity in the tumor cells.

A subsequent specimen from the right ventricular mass grossly consisted of fragments of tan-white firm rubbery lobulated tissue, with cartilaginous consistency that measured 5 × 4 × 2 cm. Histopathologic examination revealed lobules that contained abundant chondroid and myxoid matrix. The cells in the matrix were composed of neoplastic cartilage cells (chondrocytes) that showed severe atypia indicative of a high-grade chondrosarcoma (grade 3). The neoplastic cells in the cartilaginous matrix were...
high grade with binucleated forms, pleomorphism, nucleomegaly (Figure 3), and hyperchromasia. The periphery of the lobules was hypercellular, with hyperchromatic, pleomorphic, spindled, and stellate cells, few mitoses, and focal necrosis (Figure 3, inset). There were some areas of necrosis. The tumor cells were diffusely positive for vimentin and focally positive for S100 protein, and proliferating marker Ki-67 showed 60% staining. A diagnosis of high-grade osteosarcoma with intravascular extension to the right side of the heart was rendered.

COMMENT

Conventional osteosarcoma is a malignant tumor of unknown etiology that most frequently involves the appendicular long bones of young adults within the second decade of life, with 60% of cases occurring when they are younger than 25 years.¹ It is the most common nonhematopoietic primary malignant tumor of the bone, with an estimated incidence of 4 to 5 per million. Radiographic findings, particularly on plain x-ray films and MRIs, are an important element in the diagnostic workup.

Histopathologic features show a varied degree of cellularity, with the presence of osteoid as the key diagnostic feature.¹ ² Osteosarcoma appears to be a highly anaplastic, pleomorphic tumor in which the tumor cells are diverse and may be epithelioid, plasmacytoid, fusiform, ovoid, small round cells, clear cells, mononucleated or multinucleated giant cells, or spindle cells. Most cases are a mixture of 2 or more of these cell types. Osteosarcoma is further subdivided based on the production of varying amounts of cartilage and/or fibrous tissue into osteoblastic (50%), chondroblastic (25%), and fibroblastic (25%) var-

Figure 1. Intraoperative view of the tumor extending into the right atrium.

Figure 2. Low-power view of the pelvic mass. A, The tumor cells are round to ovoid and primitive appearing, with an island of osteoid (hematoxylin-eosin, original magnification ×200 and ×400 [inset]). B, An island of osteoid, which is calcified and lacks osteoblastic rimming (hematoxylin-eosin, original magnification ×200).

Figure 3. High-power view of the tumor cells composed of hyperchromatic, pleomorphic chondrocytes (hematoxylin-eosin, original magnification ×200). Inset, The periphery of lobules composed of stellate to spindle-shaped cells (hematoxylin-eosin, original magnification ×400).
The chondroblastic variant is predominant in the head and neck region. There is tendency for metastases to mimic the primary tumor, but exceptions (such as in the current case) are frequent; there is a higher than expected incidence of fibroblastic differentiation in metastases. Other histologic subtypes include malignant fibrous histiocytoma–like, telangiectatic, low-grade central, giant cell rich, and epithelioid.

The lack of specificity of immunoperoxidase and electron microscopy in osteosarcoma limits their use in diagnosis. Osteocalcin, osteonecetin, osteopontin, and alkaline phosphatase have been demonstrated in osteosarcoma. It has been shown that SI100 protein, osteocalcin, and proliferating cell nuclear antigen were highest in osteoblastic and stromal areas and lowest in chondroblastic areas.

Osteosarcoma of the pelvis constitutes less than 10% of all osteosarcomas. The predominance of chondroblastic osteosarcoma in the pelvis has been previously documented. Also emphasized in this study is the distribution of primary chondrosarcoma, which commonly involves the pelvis. In the absence of specific immunohistochemical markers, it is a great challenge to differentiate these 2 entities, as was the case in our patient.

Untreated osteosarcoma is universally fatal. Its course is marked by its aggressive local growth and rapid hematogenous spread. Pulmonary metastases are the most common site of clinical significance followed by bone metastases. Neoadjuvant therapy (chemotherapy and/or radiotherapy) is typically administered before resection of the primary tumor. Although local therapy (local excision and/or radiotherapy) would likely be performed in a similar fashion for both pathologic types, systemic therapy (chemotherapy) may be different between osteosarcoma and chondrosarcoma, heightening the importance of establishing an accurate diagnosis.

Tumor thromboembolism by osteosarcoma is extremely rare. To our knowledge, only 7 cases of osteosarcoma that causes pulmonary embolism have been reported in the literature thus far. The primary sites in these cases were the distal femur in 5 cases, the sacrum in 1 case, and the humerus in 1 case. The primary histologic type was osteoblastic in 2 cases, chondroblastic in 4 cases, and unknown in 1 case. Only 1 reported case involved a tumor the arose from the sacrum and extended as cord to the pulmonary vasculature. However, unless our case, the histologic type in the vasculature tree was not known. In 2 reported cases, the tumor emboli were entirely cartilaginous and no osteoid element was found, whereas the primary site was distal femur in both cases and the histologic type was chondroblastic in one case and osteoblastic in another. Another case describes a 65-year-old woman with primary chondroblastic osteosarcoma of the distal femur; the pulmonary emboli showed only cartilaginous differentiation but no osteoid. In a case of hepatocellular carcinoma with cartilaginous differentiation, there was intravascular growth. It seems therefore that chondroid or chondromyxoid patterns are associated with intravascular growth. In a previous report, 2% of patients with soft tissue or bone sarcomas showed intravascular thrombi, with associated poor prognosis; however, most of these tumors were soft tissue sarcomas.

The unique feature in our case was its primary location and the unusual intravascular and intracardiac extension. Although prior reports have documented such a presentation in the pediatric population, the constellation of features described is, to our knowledge, the first such report in an adult patient.

References