Intimal sarcoma of the superficial femoral artery with osteosarcomatous differentiation

James L. Ebaugh, MD, MPH,a,b Minsheng Yuan, MD, PhD,c Jeffery Hu,a Ahchean Chen, MD, PhD,c and Joseph D. Raffetto, MD,a,b West Roxbury and Boston, Mass

Sarcomas of the large vessels usually present centrally in the aorta, pulmonary artery, and inferior vena cava. Peripheral arterial sarcomas are exceptionally rare. They have been reported in the iliac and common or profunda femoral arteries, and are frequently undifferentiated. In this study, we describe a differentiated intimal sarcoma of the superficial femoral artery with abundant osteosarcoma within the specimen. Before knowing the diagnosis, treatment was for a presumed pseudoaneurysm using excision and bypass. Postoperatively, the patient received palliative radiation therapy. The tumor’s location and histopathology are unique. A differentiated intimal sarcoma has never been reported in the superficial femoral artery, and it represents the second peripheral arterial intimal sarcoma reported with osteosarcomatous differentiation. (J Vasc Surg 2011;53:1394-7.)

Sarcomas of the great vessels and their branches have a predilection for the pulmonary artery, inferior vena cava, and aorta, whereas peripheral arterial sarcomas are exceptionally rare. Most peripheral arterial sarcomas are leiomyosarcomas1 or angiosarcomas,2 with only one reported case of a differentiated intimal sarcoma in a peripheral artery, the common femoral artery.3 We report a case of an intimal sarcoma in the superficial femoral artery (SFA) with unusual histopathology.

CASE REPORT

An 87-year-old man presented with left lower extremity edema that he had for the past several days. Venous duplex scan showed an acute left lower extremity deep venous thrombosis (DVT), and a secondary finding of a 3.7 cm multilobular, heterogeneous, pulsatile mass consistent with either an aneurysm or pseudoaneurysm of the SFA. The patient stated that this left thigh mass had been present for several weeks and denied any trauma. His medical history included bilateral lower extremity weakness from multiple lower back operations in the 1960s for spinal stenosis, and a left total knee arthroplasty 8 years ago. He was on Coumadin for atrial fibrillation and his international normalized ratio was 2.7. Physical examination showed a 3 to 4 cm nontender, pulsatile medial midthigh mass and normal peripheral pulses. The anterior knee arthroplasty incision extended proximally to the distal extent of the pulsatile thigh mass. Knee plain films showed no bony abnormalities in the vicinity of the aneurysm.

A magnetic resonance angiogram of the lower extremities showed what seemed to be a distal SFA pseudoaneurysm (Fig 1). Differential diagnosis included direct arterial injury related to his prior knee surgery with chronic pseudoaneurysmal degeneration vs a mycotic or true aneurysm.

Endovascular treatment of the aneurysm with a stent graft was considered, but to decompress the femoral vein and relieve the patient’s significant edema we opted for open surgery. The patient underwent resection of the aneurysm with oversewing of the common femoral artery with abundant osteosarcoma within the specimen. Before knowing the diagnosis, treatment was for a presumed pseudoaneurysm using excision and bypass. Postoperatively, the patient received palliative radiation therapy. The tumor’s location and histopathology are unique. A differentiated intimal sarcoma has never been reported in the superficial femoral artery, and it represents the second peripheral arterial intimal sarcoma reported with osteosarcomatous differentiation. (J Vasc Surg 2011;53:1394-7.)

Endovascular treatment of the aneurysm with a stent graft was considered, but to decompress the femoral vein and relieve the patient’s significant edema we opted for open surgery. The patient underwent resection of the aneurysm with oversewing of the common femoral artery. A short jump graft from the distal SFA to the above-knee popliteal artery was performed using a reversed saphenous vein. Inside the mass was a significant amount of lobulation and chronic inflammation (Fig 2, a) but no purulence, and otherwise had the appearance of a typical true SFA or popliteal aneurysm. No frozen sections were sent. Due to a drop in his platelet count, he was switched from unfractionated heparin to Lepirudin pending a heparin-induced platelet antibody test, which was negative. The patient made an uneventful recovery and was discharged on postoperative day 10 with Coumadin for the associated DVT.

Pathologic features

Gross findings. The surgical specimen consisted of an irregular, firm artery varying in color from yellow to dark red-brown, measuring 5.0 × 1.5 cm with variable wall thickness.

Conventional microscopy. The tumor (Fig 3, a) seemed to arise within the lumen of the vessel and infiltrated along the arterial wall with extension into the adventitia. There were areas suggestive of in situ tumor where the malignant cells seemed to be confined within the intima and apposed beneath the endothelium. There were also areas of surface organizing thrombus that could have contributed to the clinical impression of the aneurysm. The tumor was composed of malignant spindle cells with extensive osteosarcomatous differentiation containing abundant extracellular osteoid matrix (Fig 3, b). Additionally, there were some areas indistinguishable from undifferentiated pleomorphic sarcoma or malignant fibrous histiocytoma.
The final pathologic diagnosis was high-grade intimal sarcoma with osteosarcomatous differentiation.

**Immunohistochemistry.** Tumor cells stained strongly positive for vimentin, which is found in both benign and malignant mesenchymal tumors, but they were negative for other immunohistochemical stains. Negative staining for desmin and smooth muscle actin ruled out smooth muscle origin, while negative staining for pancytokeratin, S100
protein, and CD45-leukocyte common antigen ruled out metastatic carcinoma, metastatic melanoma, and lymphoma, respectively. Absence of CD31 and CD34 staining argued against sarcoma of endothelial cell origin such as malignant endothelioma and angiosarcoma. High proliferative index (Ki-67 staining) supported the diagnosis of a high-grade malignant tumor.

Clinical course. Metastatic workup with computed tomography (CT) of the chest, abdomen, and pelvis was negative, but magnetic resonance imaging (MRI) of the thigh 1 month later showed a residual 7 × 5 × 3 cm tumor within the vastus medialis (Fig 2, b). Due to chronic disability and advanced age, an above-knee amputation was recommended for curative resection. This was delayed several weeks due to the patient’s slow convalescence from the first surgery.

Several days before the amputation, 2 months after his pathologic diagnosis was made, the patient developed pneumonia, pleural effusions, urosepsis, and a non-ST segment myocardial infarction, postponing the surgery. A chest CT showed multiple new bilateral pulmonary nodules, consistent with metastatic disease, and the thigh mass enlarged and became tender, with a CT showing it had now grown to 11 × 10 × 7 cm, with extrinsic bypass graft compression. Palliative radiation therapy (6600 CGy over 6 weeks) was initiated to prevent bypass graft thrombosis and for pain relief, with only modest effect. The patient passed away 7 months after his initial presentation with no autopsy performed.

DISCUSSION

This is the first known case of a peripheral arterial differentiated intimal sarcoma arising from the SFA. The tumor also displayed osteosarcomatous differentiation, an extremely rare histology for this type of tumor.

Primary neoplasms of the major blood vessels are divided into three categories based on their site of origin: from the large veins, the pulmonary artery (PA), or the aorta and its branches. Over 60% of reported sarcomas of the aorta and its branches are intimal sarcomas, arising from the tunica intima of large blood vessels, rather than from endothelial, medial, or adventitial cells. Other common sites for intimal sarcoma include the PA and inferior vena cava, although the majority of sarcomas of the major veins are derived from medial smooth muscle. Hemangioendotheliomas (angiosarcomas) of endothelial origin and mural tumors derived from the media and adventitia represent the majority of the remaining classes of peripheral arterial tumors. To differentiate intimal sarcomas from these other two, histology and immunohistochemistry patterns are used. Angiosarcomas show endothelial cells on microscopy and stain positively for vimentin, factor VIII, and CD 34. Leiomyosarcomas, on the other hand, have characteristic spindle-shaped cells and stain positively for desmin and actin. Intimal sarcomas, which have an unknown cell of origin, usually show undifferentiated cells with variable immunophenotyping.

Large vessel intimal sarcomas tend to occur in the elderly with a history of peripheral vascular disease, and usually present with advanced disease with an aggressive course. Many are centrally located, and can present as a symptomatic thoracic aneurysm, or with dyspnea, sudden death, or distal embolization. Aortic intimal sarcomas have also been reported at the site of prior vascular anastomoses. Peripheral arterial tumors frequently present with edema, local pain, claudication, motor or sensory loss, signs of peripheral embolization, or an inguinal mass. This patient presented with a nontender, pulsatile mass in his medial thigh, and painful edema from an associated DVT.

Imaging of peripheral arterial tumors, if the diagnosis is suspected before surgery, includes a preoperative MRI to determine resectability. A CT of the chest, abdomen, and pelvis is mandatory in these patients in light of the reported 50% to 70% incidence of metastatic disease at the time of initial diagnosis. These studies are also useful in detecting an unknown primary, because arterial tumors that present peripherally could be metastases.

Treatment of peripheral arterial intimal sarcoma is similar to that of primary aortic sarcomas. If the diagnosis of a malignancy is known preoperatively, surgery consists of local node sampling and en bloc resection with arterial reconstruction with an interposition graft or bypass. Adjuvant therapy using doxorubicin and ifosfamide is recommended after resection regardless of margin status, and also in the presence of embolic or metastatic disease. External beam radiation therapy can be used to treat residual or unresectable tumors, although due to the low numbers of reported cases, any benefit from chemotherapy, radiation therapy, or a combination of the two is difficult to demonstrate. Despite advances in surgery, chemotherapy, and radiation therapy, the 1-year survival rate with large vessel sarcoma has remained 13%, with a mean survival of 14 months.

In a review of 180 primary sarcomas of large arteries, 109 (61%) were classified as intimal sarcomas, and of these, 28 (26%) were differentiated. Differentiated intimal sarcomas show a spectrum of histopathological morphologies with variable immunophenotyping. Commonly reported types include angiosarcoma, leiomyosarcoma, myxofibrosarcoma, epithelioid hemangioendothelioma, myxoid chondrosarcoma, and undifferentiated pleomorphic sarcoma (or malignant fibrous histiocytoma). Rarer differentiation such as osteosarcoma and rhabdomyosarcoma have been reported in PA and aortic origin. Intimal sarcoma. Osteosarcomatous differentiation in a peripheral arterial intimal sarcoma has been described in a patient with radiation-induced intimal sarcoma of the common femoral artery, but never as a spontaneous tumor, and never in the SFA, as in our case.

Intermediate and high-grade intimal sarcoma subtypes behave aggressively and have a high incidence of metastases at the time of diagnosis. There was extensive osteosarcoma within this neoplasm, which usually suggests a more benign course. Despite this, the rapid postoperative
tumor growth and short survival of our patient implies that this differentiation does not alter the poor prognosis.

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REFERENCES

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