

CASE REPORT

Intimal sarcoma arising from the common iliac artery presenting with artery occlusion : a case report and literature review

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Abstract : We present a rare case of intimal sarcoma arising from the common iliac artery in an 82-year-old man who presented with intermittent claudication. He had undergone endovascular therapy with self-expanding stents to both iliac arteries that had occluded soon after placement. After salvage bypass grafting, a diagnosis of intimal sarcoma with angiosarcoma phenotype from the iliac artery was made. Further bypass graft surgery relieved symptoms temporarily. However, the tumor progressed and the left limb became ischemic. The chemotherapy of eribulin did not prevent tumor progression. The patient died of the disease 20 months after the first surgery. *J. Med. Invest.* 66 : 205-208, February, 2019

Keywords : intimal sarcoma, great vessels, salvage bypass grafting, eribulin

INTRODUCTION

Intimal sarcoma is a rare malignant tumor that arising in large blood vessels of the systemic and pulmonary circulation (1). Soft tissue sarcoma has an annual incidence of approximately 50 per million population, accounting for 1% of all malignant tumors (1). Primary sarcoma of the great vessels is particularly rare (2, 3) and mimics obstructive aorta disease, therefore the diagnosis may be delayed (3-5). However, even when an early diagnosis is made, the prognosis of primary sarcoma of the great vessels is poor.

Here we report the case of a patient with an intimal sarcoma arising from an occluded lower limb artery in whom palliative prosthetic bypass grafting slowed progression of limb necrosis on the other hand chemotherapy of eribulin is not effective to prevent tumor progression.

We have got permission by oral agreement from his family and this study was approved by the Ethics Committee of Tokushima University.

CASE PRESENTATION

An 82-year-old man presented to a local doctor with intermittent claudication and imaging revealed stenosis from aorta to bilateral common iliac artery (Figure 1). He had hypertension and hypercholesterolemia and had also past history of skin cancer and was operated 2 years ago of this first visit. He underwent endovascular therapy with self-expanding stents for right and left iliac arteries on different dates. He took warfarin and clopidogrel bisulfate after the

self-expanding stents surgery. Restenosis occurred 7 months after the first surgery (Figure 2). He underwent prosthetic bypass grafting at another hospital during which the abdominal aorta was connected to the right external iliac artery and left common iliac artery. The surgery successfully improved the blood flow in his legs. The surgical specimen, which was thought to be an arterial embolus was found to be a high-grade sarcoma. Tumor cells were at the superficial layer next to necrotic tissue. The tumor had atypical spindle cells with nuclear polymorphism, enlarged nucleoli, and mitotic ability. Immunohistochemistry revealed the tumor was

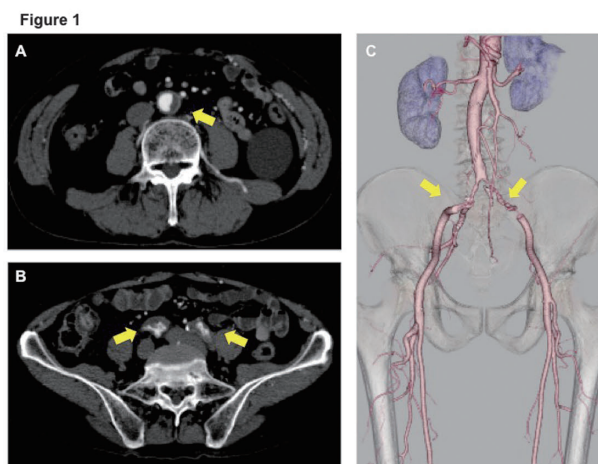


Figure 1. Contrast enhanced computed tomography (CT) scans before the initial treatment shows artery stenosis at aorta and common iliac artery. Yellow arrows show stenosis of the vessels. Axial view (A) (B) present the stenosis is severe at bifurcation, and 3-dimensional CT scan (C) shows discontinuity at the both common iliac artery.

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strongly positive for CD31, ERG, and factor VIII, cytokeratin and alpha-smooth muscle actin, and negative for desmin. Ki67 rate was 50%. Based on these findings, the final diagnosis was intimal sarcoma with angiosarcoma phenotype of the bilateral common iliac artery.

An immediate referral was made to our musculoskeletal tumor clinic; however, the patient did not attend this clinic until 4 months after the second surgery. At presentation to us, the left fifth toe was noted to be necrotic and the patient reported left-sided pelvic pain. CT and 18F-fluorodeoxyglucose-positron emission tomography (FDG-PET) revealed osteolytic lesions and FDG accumulation in the left side of the pelvis, left L3 pedicle, left femur, and left tibia (Figure 3). The SUV-max was 20.46 in the left ilium. On a core needle biopsy taken from the left ala of the ilium, the histology showed atypical spindle cells (Figure 4, A) and the cells were strongly positive for CD31 (x100) (Figure 4, B), and factor VIII (x100) (Figure 4, C). The pelvic lesion was confirmed to be a metastatic intimal sarcoma to bone. The patient declined chemotherapy with paclitaxel but accepted treatment with denosumab for the multiple bone metastases and radiation to the pelvis and left femur 2

months after visiting our hospital.

Two months later (4 months after first visiting us), circulation deteriorated in both lower limbs, particularly the left limb. A third revascularization procedure was performed in which a prosthetic bypass graft was used to connect the axillary and femoral arteries, which improved blood flow again. The patient received two cycles of eribulin as palliative chemotherapy. He had a few mild side effects of dysgeusia, numbness in his both legs, and mild pancytopenia but there is no dysfunction of kidney and liver and also no nausea and no vomiting. Despite of the chemotherapy, there was tumor progression. The femoral artery tumor had enlarged in the proximal direction and reached the bifurcation of the celiac artery (Figure 5). Necrosis in the left leg had worsened. The patient was transferred to hospice care at this time. Finally, the skin necrosis progressed to the level of umbilicus. At one week before he died, he could not eat any food. Without limb amputation, he died of the disease 9 months after the first visit to our hospital (20 months after the first surgery).

Figure 2

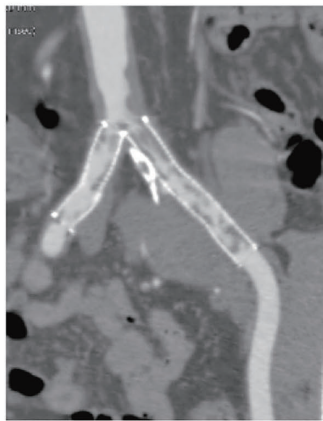


Figure 2. Contrast enhanced CT scan of 7 month after the first surgery with stents shows restenosis and non-enhanced area in the vessels indicates tumor progression.

Figure 3

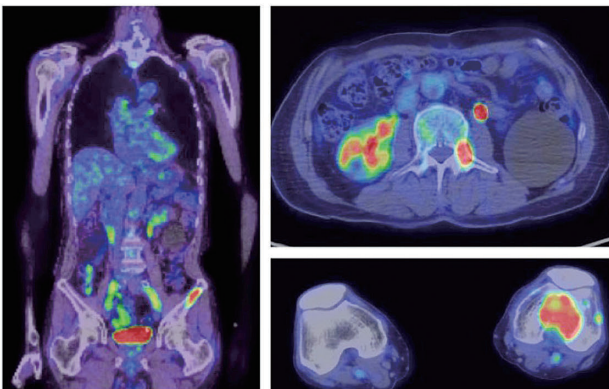


Figure 3. CT scan and PET-CT after second surgery shows osteolytic lesions and FDG accumulation (SUV-max : 20.46) in the left side of the pelvis, left L3 pedicle, left femur, and left tibia. There are no abnormal accumulation except with bone and great vessels.

Figure 4

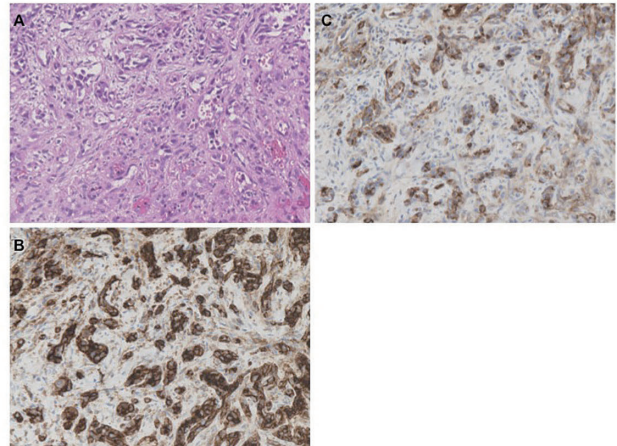


Figure 4. Biopsy findings. There are atypical spindle cells with large nucleus forming irregular blood vessels in Hematoxylin-eosin staining (x100) (A). The tumor was strongly positive for CD31 (x100) (B), and factor VIII (x100) (C).

Figure 5

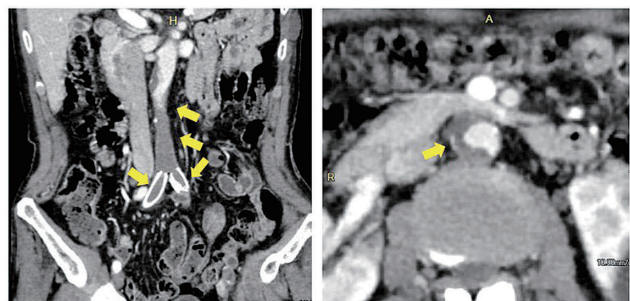


Figure 5. Enhanced CT 2 months after third surgery shows tumor reaching the bifurcation of the celiac artery. Yellow arrows show tumor progression reaching to the proximal site of aorta.

DISCUSSION

Blood vessels are composed of three layers, tunica externa, tunica media, and tunica intima. Intimal sarcomas are considered to be from tunica intima and grow in the blood vessels and often occlude great vessels (1, 6). Thalheimer *et al* described sarcomas from tunica externa and media are defined as mural sarcoma (6). While WHO classification defined intimal sarcoma as independent category, nomenclature for intimal sarcoma is controversial because there is no clear discussion of whether they should be subclassified based on tumor type or location (3).

According to the report from 2 years in 3 European regions, intimal sarcoma is less than 5 cases in 1558 all sarcomas and the crude rates are estimated to be less than 0.015 per 100,000 people (7). Staats *et al* reported the subtype of intimal sarcoma from the aorta and iliofemoral arteries (3). Among the 26 cases, histologically and immunohistochemically, 13 were categorized as poorly differentiated angiosarcomas, 7 as undifferentiated sarcomas, 3 as osteosarcomas, 2 as myxofibrosarcomas, and 1 as myxoid sarcoma, not otherwise specified. According to these reports, we considered this is intimal sarcoma with angiosarcoma phenotype.

Our patient presented with intermittent claudication at his first visit. In a previous report on 26 patients with intimal sarcoma of the aorta or iliofemoral artery, symptoms were pain, claudication, weight loss, pulsatile masses, and constitutional symptoms (3). Another report on patients with sarcoma of the thoracic aorta described escalating systolic hypertension, dyspnea, and chest discomfort (8). These symptoms are very similar to those of more common diseases of the aorta and great vessels. Malignant potential was suspected before tissue sampling in a very small number of cases (0/26 and 3/21) (3, 6). Magnetic resonance imaging was demonstrated to be useful for distinguishing between malignant and benign aortic disease (4, 8). FDG-PET/CT may be useful for differentiating between a malignant tumor and thrombosis; mean maximum standardized uptake values were significantly higher for pulmonary artery sarcoma (7.63 ± 2.21 , $n = 3$) than for pulmonary embolism (2.31 ± 0.41 , $n = 10$) (9).

Tissue sampling is one of the major problems encountered with sarcoma of the great vessels. Essentially, the biopsy tract should be cleared by wide resection to avoid contamination. However, performing such a biopsy is difficult when a major vessel is involved unless the tumor is extravascular. In previous reports, pathological diagnosis was made from either a thrombus taken by endarterectomy, resection of the aorta, or from a metastatic site (4, 8, 6). In a further report, 4 of 26 cases were diagnosed at autopsy (3). Thrombus with an atypical appearance should be checked histologically.

On histopathology, intimal sarcomas are usually poorly differentiated mesenchymal malignant tumors, consisting of mildly to severely atypical spindle cells with varying degrees of mitotic activity, necrosis and nuclear polymorphism (1). On immunohistochemistry, intimal sarcoma is positive for MDM2 in up to 70% (1). Angiosarcoma is often positive for CD31, CD34, ERG, and FLI1 (1). The presence of factor VIII and pancytokeratin is reported to be useful for excluding other types of sarcoma (3).

In general, complete resection with an R0 margin is necessary to control soft tissue sarcoma. In one series, 4 of 28 patients were alive at final follow-up (8, 6). One of these patients was followed up for 2 years and another for 17 years; both underwent wide resection (complete resection with a negative margin and graft replacement) and received chemotherapy. In both cases, the histological diagnosis was obtained from a thrombus prior to surgery and chemotherapy. There is another report on a patient who underwent abdominal aortic endarterectomy alone but no follow-up duration was noted (10). Another patient underwent graft interposition without adjuvant therapy but was followed up for 6 months

only (11). Chemotherapy that have been used were reported as follows: MAID (Mesna, doxorubicin at 60 mg/m², ifosfamide at 1.5 g/m²/day⁴ days continuous infusion, and dacarbazine 800 mg/m², for a total of six cycles), doxorubicin, and cisplatin (8, 12). According to the European chemotherapy guidelines, the first-line treatment for soft tissue sarcoma is anthracycline-based, and combination chemotherapy using an adequate dose of an anthracycline plus ifosfamide can be considered depending on histology and performance status (13). A taxane such as docetaxel with or without gemcitabine is also an option in patients with angiosarcoma (13, 14). Therefore, the ideal treatment may be biopsy of thrombus following complete resection and chemotherapy in the case of non-metastatic disease.

Unfortunately, treatment of intimal sarcoma is unlikely to be curative. Metastatic disease was reported to be present at the time of presentation in 6 of 8 cases in sarcoma arising from great vessels (8). In another report, distant metastasis occurred in 76.2% of cases, with a mean survival time of 12.8 months (6). The 5-year survival rate of soft tissue sarcoma with metastatic disease at the initial visit is less than 20% (15, 16). Survival time in our patient was 20 months from the first visit, which is consistent with previous reports, given that the mass in a great vessel had already metastasized when we first saw him.

Maintaining quality of life is an important issue in patients with advanced sarcoma of the great vessels. In patients with advanced sarcoma affecting a major blood vessel, prevention of arterial occlusion and subsequent necrosis is crucial. Surgical resection with graft replacement is the best method for achieving local control. However, thromboendarterectomy or bypass should be considered, depending on the patient's condition (6, 8). In our patient, the first operation was performed only to insert self-expanding stents without removal of thrombus, which resulted in early occlusion. The subsequent bypass surgery relieved the limb necrosis, albeit only temporarily.

Radiotherapy may have been an option in our patient. No formal radiotherapy trials for intimal sarcoma have been conducted. The effects of radiotherapy were unclear in two studies involving 2/7 patients (8) and 2/21 patients (6) with intimal sarcoma arising from a great vessel who received radiotherapy. In basic research, the radiosensitivity of vascular endothelial cells was increased when they were exposed to low-concentration paclitaxel (17).

There are some reports of chemotherapy, including taxane-based chemotherapy, being useful in patients with advanced angiosarcoma (18-21). Few cases of advanced intimal sarcoma have been reported. Our patient declined taxane-based chemotherapy because of his advanced age. Therefore, we used eribulin for palliative care, but this did not prevent disease progression. Because the skin necrosis progressed to the level of umbilicus and he could not eat any food 1 week before he died, we think the tumor obstruction would reach celiac artery and necrosis of intestines occurred, which caused the direct death.

CONCLUSIONS

We described a case of primary intimal sarcoma arising from the iliac artery that was discovered as a result of circulatory disorder of the lower limbs. MRI and FDG-PET may be useful for avoiding a delayed diagnosis in such cases, but diagnosis and curative treatment would still prove difficult. Bypass surgery is one of treatment options for palliative strategy that can prevent limb necrosis or slow its progression, but the effect is temporary.

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