

Primary Intimal Sarcoma of Thoracic Aorta Presenting as Hypertensive Crisis

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We report a 45-year-old woman who presented to our facility in a hypertensive crisis. Computed tomography (CT) revealed a thoracic aortic tumor, and tissues obtained via endovascular biopsy revealed undifferentiated sarcoma. A final diagnosis of intimal sarcoma was made by intra-operative pathological examination. Despite undergoing surgical resection followed by adjuvant chemotherapy, the patient died from progressive multiple metastasis and severe sepsis. Although aortic sarcoma is rarely diagnosed, it should be considered a possible etiology of hypertensive crisis.

Key Words: Aortic tumor • Endovascular biopsy • Hypertension crisis • Intimal sarcoma

INTRODUCTION

Primary aortic malignant tumors are rare, and diagnosis of aortic tumor can be challenging because of the diverse clinical manifestations. Herein, we report a rare case of intimal sarcoma that presented as a hypertensive crisis and coarctation-like syndrome. We also review the literature and discuss the diagnostic strategy, treatment and prognosis.

CASE REPORT

A 45-year-old woman presented to our emergency room with epigastric pain, radiating to the back, as well as nausea of 3 days duration. Her previous medical history was unremarkable. Upon admission, her blood pressure was 219/115 mmHg, and she had a pulse rate,

body temperature, and respiratory rate of 89 beats per minute, 37.1 C, and 19 breaths/minute, respectively. Clinical examination revealed epigastric bruit and normoactive bowel sounds. Abnormal pulsations, masses, rebound tenderness, or muscle guarding was not observed. An examination of the patient's 4 limbs revealed weaker and delayed bilateral femoral pulses relative to the brachial arteries. The pulses in the bilateral dorsal pedis were considerably weaker, and both feet were cold. Blood pressure measurements in the patient's lower limbs were 87/48 mmHg in the left ankle and 69/44 mmHg in the right ankle. Laboratory evaluation revealed normal liver and renal function. Additionally, mild anemia was reported (hemoglobin level = 9.6 g/dL). Subsequent to review of the patient's medical information and diagnostic testing, a diagnosis of hypertensive emergency with abdominal aortic dissection was considered. Subsequent computed tomography (CT) revealed a hypodense lesion occupying the aortic lumen in the distal thoracic aorta, causing significant narrowing of the aortic lumen (Figure 1A). Hypodense areas were also present in the spleen (Figure 1B). The patient was treated with parenteral nitroglycerin, labetalol and nicardipine. Her systolic blood pressure subsequently decreased to approximately 130~140 mmHg. An additional laboratory evaluation reported insignificantly elevated

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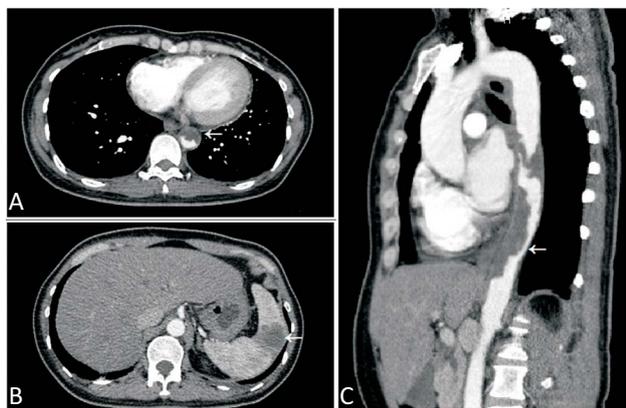


Figure 1. (A, C) Computed tomography revealed hypodense lesion that occupied aortic lumen in distal thoracic aorta (white arrow). (B) There were hypodense areas of spleen (white arrow).

erythrocyte sedimentation rate of 16 mm/h (normal < 12 mm/h), negative test results for lupus anticoagulant and antinuclear factor, and normal anti-DS DNA and rheumatoid factor levels. However, acute kidney injury accompanied by oliguria developed 3 days later. Due to concern regarding disease progression and a different treatment strategy for differential diagnosis of aortic thrombus and aortic tumor, we performed an endovascular biopsy in the cardiac catheterization lab via the transfemoral artery approach (Figure 2A). Histological evaluation revealed an undifferentiated sarcoma, and the patient was then referred for surgery.

The entire descending thoracic aorta was excised (Figure 2B) and reconstructed with a 24 mm single-branch hemi-shield graft. Histopathological evaluation of the resected specimen indicated a grade III intimal sarcoma that had formed a polypoid, mucoid, annular tumor (Figure 2C). The size of the sarcoma was 12 × 4.5 × 1 cm with tumor necrosis. The tumor involved the intimal and partial medium layers of the aorta, and was found to extend to the adjacent vessel and lymph node. Immunohistochemical staining was performed, and the tumor was positive for vimentin (Figure 2D), Wilms tumor protein-1, and CD99 expression, whereas staining for S-100, Melan-A, D2-40, CD31, factor VIII, desmin, smooth muscle actin, CD10, alpha-fetoprotein, hepatocyte paraffin 1, leukocyte common antigen, CD2, and paired box protein 5 were negative. Because the spleen hypodense lesion was strongly suspected to be a metastasis, we determined the stage of this tumor to be high-grade T2N1M1.

The patient recovered gradually with improved blood pressure control, and she was discharged on the 14th postoperative day. Two weeks after the operation, adjuvant chemotherapy was initiated with 2 cycles of epirubicin. A later CT test conducted 3 months postoperatively revealed no recurrent or residual tumor at the connection site between the graft and the native aorta. However, there were multiple hypodense masses involving the hiatal region, posterior mediastinum, splenic hilum and splenic parenchyma, and multiple metastases were strongly suspected. The patient's chemotherapy regimen was changed to bevacizumab and cyclophosphamide. One week later, a palpable painful mass was noted on the left thigh. Magnetic resonance imaging (MRI) revealed a metastasis in the femoral bone and adjacent muscle. Radiotherapy for the site of the left thigh metastasis was initiated. Approximately 6 months later, the patient died from progressive multiple metastases and severe sepsis.

DISCUSSION

Primary vascular neoplasms are rare entities. Of these, aortic sarcoma is the most common type of primary malignant aortic tumor.¹ The descending thoracic

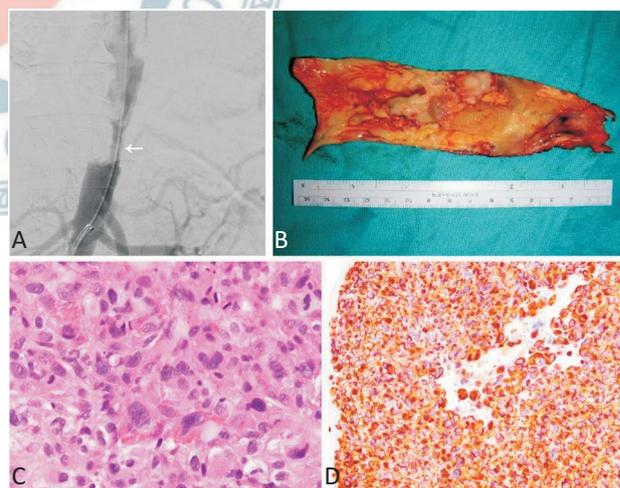


Figure 2. (A) Aorta angiography revealed filling defect at lower thoracic aorta (white arrow). (B) resected aorta contained a polypoid, mucoid, necrotic intimal mass. (C) Histologically, the tumor is composed of malignant spindle cells that display nuclear pleomorphism and atypia (hematoxylin and eosin stain, original magnification × 200). (D) Immunohistochemistry results indicate that the tumor cells stain positively for Vimentin (original magnification × 200).

aorta is the most frequent location for aortic sarcoma (35%), followed by the abdominal aorta (27%), thoraco-abdominal aorta (27%), and ascending aorta or arch (11%).²

Aortic sarcomas are categorized according to their predominant location, specifically whether they arise primarily from the intima or mural (including adventitial). Approximately 80% of primary aortic sarcomas are intimal sarcomas. These neoplasms can be further subclassified according to the immunohistochemical patterns of the tumors. The most common reported subtypes are intimal sarcomas (referring to an undifferentiated type), angiosarcomas (of endothelial origin) and leiomyosarcomas.³ The intimal type often forms intraluminal polyps that cause aortic obstruction or peripheral emboli, and the mural type usually extends extramurally to para-aortic tissues.⁴

Intimal aortic sarcomas are poorly differentiated neoplasms, which are usually composed of myofibroblastic spindle cells showing features of atypia, pleomorphism, and necrosis.⁵ In immunohistochemical studies, endothelial-type sarcomas tend to be reactive to factor VIII or other endothelial-specific antigens such as CD31 or CD34. Those tumors of undifferentiated stromal cell origin tend to be reactive to vimentin or other mesenchymal-specific antigens such as desmin or actin.¹

The clinical presentation is related to the location of the tumor and the occurrence of obstruction. Typically, these obstruction symptoms include claudication, ischemic bowel disease, pulse deficits, and renal hypoperfusion caused by proximal obstruction. In addition to intraluminal obstruction, tumor embolization can cause extremity or specific organ ischemia.⁶ Other clinical symptoms include abdominal pain, back pain, fatigue, and metastatic complications. Aortic rupture as an initial presentation has also been reported.⁷ Among the previously reported cases, the most common chief complaints were acute arterial embolization (20.6%), claudication (18%), abdominal complaints (e.g., nausea, vomiting, abdominal pain, 21%), back pain (9%) and constitutional symptoms (8.5%).⁸ Overall, approximately 18% of aortic sarcoma patients present with signs of hypertension. In most of the previous cases, malignant hypertension was secondary to renal artery stenosis caused by tumor involvement. However, in this case, we examined the renal arteries during the endovascular

biopsy and found that both maintained patency without any filling defects. The possible mechanism of elevated blood pressure was the narrowing of the involved thoracic aorta, which cause higher pressure proximal to the coarctation. In addition, activation of the renin-angiotensin system secondary to reduction of renal blood flow distal to the coarctation may also be responsible for elevated blood pressure in this patient. In the previous literature, only a few cases presented with severe hypertension and a coarctation-like clinical scenario.⁹ Our case could have been misdiagnosed as ordinary uncontrolled hypertension if we had not detected abdominal bruit, a weak pulse and reduced blood pressure in the lower limbs.

The preoperative diagnosis of aortic sarcoma is difficult because this condition presents with diverse symptoms. CT, MRI, and transesophageal echocardiography have been used to diagnose these neoplasms. However, the differential diagnoses resulting from imaging studies are broad and may include vasculitis, arteritis, atheroma, mural thrombus, aneurysm and tumor.^{10,11} In our case, inflammatory aortitis (e.g., Takayasu disease), aortic thrombus, and aortic tumor were initially considered. In most of the previous cases, the patients were diagnosed via intra-operative pathological examinations. Tissues were obtained via preoperative intravascular biopsy in only a few previous cases. Our patient underwent percutaneous endovascular biopsy without complications. When the clinical presentation and results of imaging studies did not facilitate a diagnosis, the preoperative biopsy provided valuable information for the further treatment strategy and surgical planning, thereby avoiding unnecessary major invasive surgery.

The prognoses of both intimal and mural aortic sarcomas depends on the tumor histological grade, resectability, and location. Treatment via surgical resection with synthetic or venous grafting is a typical measure frequently undertaken in these circumstances. However, despite undergoing surgical resection, patient prognosis has generally been poor. The reported mean overall survival of patients with primary aortic tumors is less than 16 months, with a 5-year survival rate of 8%.² Additionally, recurrences and metastases frequently occur. In such cases, the most frequent metastasis sites are the bones, lungs and lymph nodes, although other reported metastatic sites include the liver, skin, adrenal

gland, kidney, spleen, peritoneum, and brain.¹² Adjuvant chemotherapy has been considered in embolic, metastatic or nonresectable situations.¹³ However, the effectiveness of adjuvant chemotherapy remains controversial. Doxorubicin has remained the most active drug for the treatment of soft tissue sarcoma, with response rates of 10-25%.¹⁴ Other active drugs or combinations include ifosfamide and gemcitabine with or without docetaxel. Despite a favorable trend, the overall survival advantage of postoperative chemotherapy was not found to be significant. External beam radiation can be used to treat bony metastases.

CONCLUSIONS

Herein we reported a rare case of aortic sarcoma that resulted in a hypertension crisis and coarctation-like syndrome. In cases of unexplained hypertensive crisis, a detailed examination should be performed to detect secondary diseases, and aortic sarcoma should be considered as a possible etiology. In this case, percutaneous endovascular biopsy of uncertain aortic lesion provided important information for further treatment strategy.

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