INTERNAL MEDICINE

□ CASE REPORT □

An Autopsy Case of Aortic Intimal Sarcoma Initially Diagnosed as Polyarteritis Nodosa

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Abstract

A 61-year-old man had hypertension with stenosis in the left renal artery. When his fever, abdominal pain, and renal dysfunction progressed, he was admitted to our hospital. He was diagnosed with polyarthritis nodosa. His renal function rapidly deteriorated despite immunosuppressive therapy. His digestive tract perforated twice, and he subsequently died. An autopsy revealed that aortic intimal sarcoma caused stenosis in multiple arteries. Both polyarteritis nodosa and aortic intimal sarcoma are very rare diseases and the diagnoses are very difficult. It is very important to consider these entities when making a differential diagnosis of vasculitis.

Key words: polyarteritis nodosa, aortic intimal sarcoma, autopsy

Introduction

Aortic intimal sarcoma is a rare malignant tumor. Its diagnosis is often delayed because its symptoms and imaging mimic occlusive atherosclerotic disease or vasculitis (1), thus it is primarily diagnosed during surgery or an autopsy (2). Polyarteritis nodosa (PAN) is a systemic necrotizing vasculitis that typically affects medium-sized muscular arteries. Patients with PAN present various symptoms (including fatigue, weight loss, a fever, hypertension, renal insufficiency, and abdominal pain) due to vasculitis, which is also relatively rare. The differential diagnosis of aortic intimal sarcoma and PAN is challenging due to similar symptoms. We herein present a case of aortic intimal sarcoma that was considered to be PAN before definite diagnosis was made at autopsy.

Case Report

A 61-year-old man had visited his local clinic for lum-bago and fatigue 4 months previously and was diagnosed with hypertension. He began taking antihypertensive drugs (amlodipine and valsartan). Because his left kidney was atrophic on abdominal ultrasound, he was advised to undergo further assessments for hypertension. In the previous hospital, an obstruction at the origin of the left renal artery was detected by magnetic resonance angiography (MRA) and renal scintigraphy (Fig. 1). After 3 months, his body weight had decreased by 6 kg and his renal function had also deteriorated. He developed a low-grade fever and elevated inflammatory reaction. Therefore, he was referred to our hospital and hospitalization was planned. The day before his scheduled hospitalization, he suddenly developed strong abdominal pain and was emergently admitted to our hospital. A physical examination showed a blood pressure of 168/87 mmHg, body temperature of 37.6℃, and abdominal tenderness. Although he had severe abdominal pain, no abnormalities were detected by non-contrast computed tomography (CT) or abdominal ultrasound. Laboratory data on admission revealed the following: leukocytes, 12,600 cells/μL (neutrophil 93.0%); C-reactive protein level, 15.7 mg/dL;
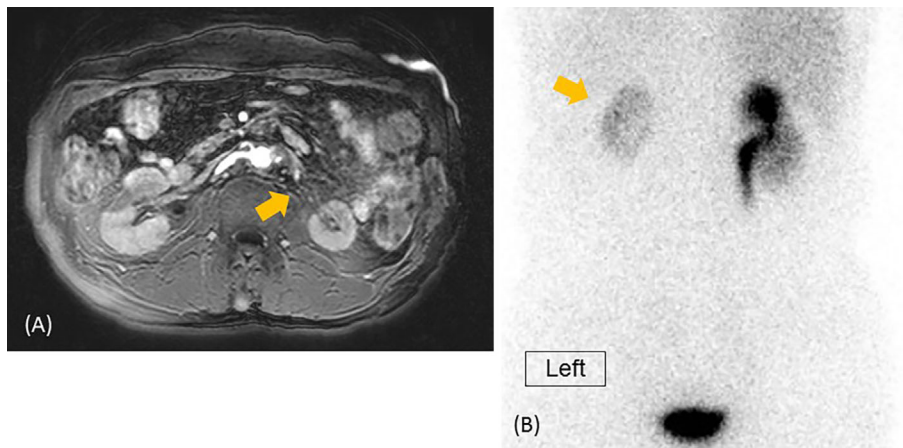
Figure 1.   Magnetic resonance angiography of the abdominal lesion and renal scintigraphy. A: Magnetic resonance angiography of the abdominal lesion showed an obstruction at the origin of the left renal artery (arrow). B: Renal scintigraphy with technetium-99m diethylene triamine pentaacetic acid (^{99m}Tc-DTPA) showed a weak accumulation, and the uptake in the left renal artery was much weaker (arrow).

Table.   Laboratory Data on Admission.

Hematology		Biochemistry			Serology		
WBC	12,600 /μL	AST	21	U/L	CRP	15.7	mg/dL
Neu	93.0 %	ALT	22	U/L	RF	17	IU/mL
Lym	3.0 %	T-Bil	0.7	mg/dL	RAPA	(-)	
Eo	0.0 %	LDH	231	U/L	ANA	(-)	
Ba	0.0 %	ALP	452	U/L	PR3-ANCA	<1.0	U/mL
Mo	4.0 %	γ-GTP	65	U/L	MPO-ANCA	<1.0	U/mL
RBC	343×10^4/μL	TP	7.1	g/dL	anti-GBM Ab	<2.0	U/mL
Hb	9.3 g/dL	Alb	3.0	g/dL	**Urinalysis**		
Ht	28.3 %	BUN	40	mg/dL	Protein	(2+)	
Plt	14.8×10^4/μL	Cr	6.92	mg/dL	Glucose	(-)	
Hematostasis		Na	136	mEq/L	Occult blood	(1+)	
PT-INR	1.17	K	4.3	mEq/L	RBC	0-1/HPF	
APTT	44.3 Secs	Cl	100	mEq/L	WBC	1-4/HPF	
					Hyaline cast	0-1/LPF	

Abbreviations: Ab: antibody, Alb: albumin, ALP: alkaline phosphatase, ALT: alanine aminotransferase, ANA: anti-nuclear antibody, ANCA: anti-neutrophil cytoplasmic antibody, APTT: activated partial thromboplastin time, AST: L-aspartate aminotransferase, BUN: blood urea nitrogen, CK: creatine kinase, Cl: chlorine, Cr: creatinine, CRP: C-reactive protein, Eo: eosinocyte, GBM: glomerular basement membrane, Hb: hemoglobin, Ht: hematocrit, K: potassium, LDH: lactate dehydrogenase, Lym: lymphocyte, Mo: monocyte, MPO: myeloperoxidase, Na: sodium, Neu: neutrophil, Plt: platelet, PR3: proteinase 3, PT-INR: prothrombin-time international normalized ratio, RAPA: rheumatoid arthritis particle agglutination, RF: rheumatoid factor, T-Bil: total bilirubin, TP: total protein, WBC: white blood cell, γ-GTP: γ-glutamyl transferase

blood urea nitrogen, 40 mg/dL; creatinine, 6.92 mg/dL; urinary protein, 2+; urinary blood, 1+; and antineutrophil cytoplasmic antibodies (ANCA), negative (Table). As he had hypertension, acute progressive renal failure, and renal artery stenosis, the patient was diagnosed with probable PAN according to the 2006 criteria of the Ministry of Health, Labour and Welfare in Japan (3). He received steroid pulse treatment, followed by 1 mg/kg/day of prednisolone, and his abdominal pain subsequently improved. However, his renal function deteriorated, and he started hemodialysis on the 7th hospital day. His abdominal pain again worsened on the 16th hospital day. A contrast-enhanced CT scan revealed a perforation in the digestive tract, which was causing his abdominal pain, and he subsequently abdominal surgery. A
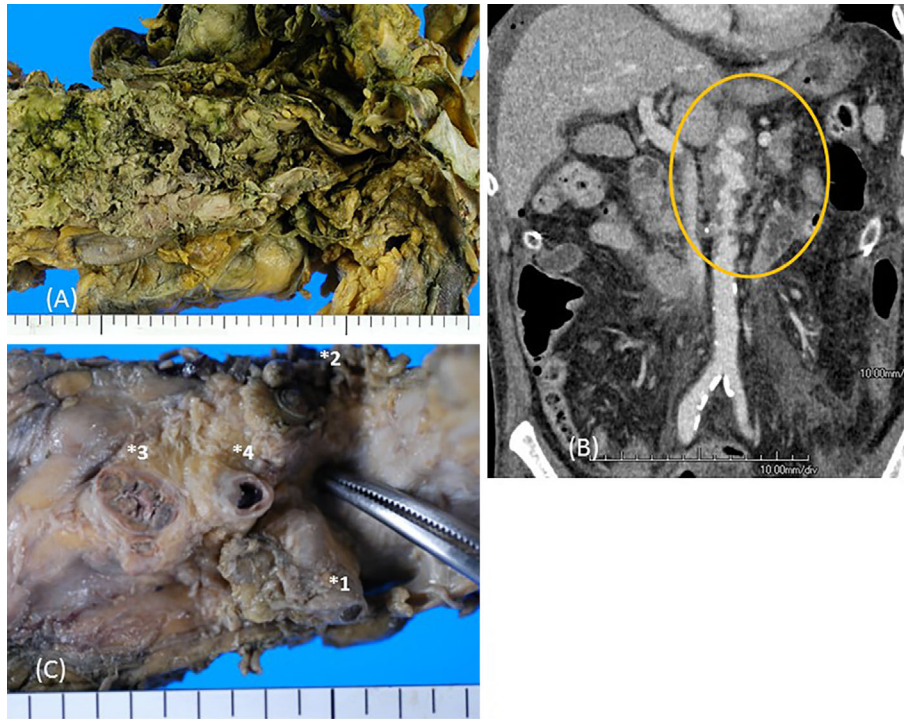
Figure 2. Macroscopic findings of the abdominal aorta. A: The wall was irregularly thick and the lumen was rough. B: Contrast-enhanced computed tomography of the abdomen on the 16th hospital day showed the irregular wall of the abdominal aorta (circle). C: Both the renal arteries (*1: right, *2: left) and celiac artery (*3) were occluded at the origin. *4: superior mesenteric artery.

perforation measuring 6 mm in diameter and located 40 cm from the ileocecum was identified and closed. Perforation of the digestive tract recurred days after surgery. Surgical findings revealed that the perforation that was at the same site, but larger, measuring 2 cm in diameter, and multiple ulcers were detected in the ileum. Partial ileal resection, including approximately 30 cm of the perforated lesion, was performed. As the resected ileum contained multiple ulcers, we considered that angiitis was not being sufficiently controlled (cytomegalovirus in the resected specimen was not examined at this time). Consequently, steroid pulse treatment and a daily administration of cyclophosphamide (50 mg/day) with antibiotic drugs were added. However, his general condition deteriorated and he died on the 35th hospital day.

An autopsy was performed with the family's consent. The wall of the abdominal aorta was irregularly thick and its lumen was rough (Fig. 2A). When we carefully reviewed the contrast-enhanced CT scan of the 1st perforation, we found that it showed an irregular lumen in the aorta (Fig. 2B) and corresponded with the anatomical findings. The superficial layer of the lumen was composed of spindle and ovoid cells with hyperchromatic nuclei (Fig. 3A and B). The origin of the celiac artery and both renal arteries was occluded (Fig. 2C) with cells of similar morphology (Fig. 3C and D). These dysplastic cells had also proliferated in the liver, splenic, and pulmonary arteries. Immunohistochemical staining of these cells showed positivity for vimentin and negativity for AE1/AE3, 34βE12, h-caldesmon, αFP, hepatocyte, α smooth muscle actin, desmin, CD31, and CD34 (data not

shown). No sign of angiitis was detected in any organ. According to these findings, the patient was diagnosed with undifferentiated aortic intimal sarcoma.

The intestine contained multiple ulcers with cytomegalovirus inclusion bodies, but no sign of angiitis. Cytomegalovirus colitis was considered to have caused the perforation of the intestine. The autopsy results identified the cause of death as purulent peritonitis.

Discussion

The causes of renal artery stenosis include atherosclerosis, fibromuscular dysplasia, and vasculitis. We initially considered vasculitis as the cause of renal artery stenosis in this case and diagnosed the patient with PAN according to the Japanese Ministry of Health, Labour and Welfare 2006 criteria (3). However, the autopsy identified tumor cells as the cause of renal artery stenosis, leading to the diagnosis of aortic intimal sarcoma. Aortic sarcoma is a rare malignant tumor and its diagnosis is often delayed in clinical settings. It is frequently misdiagnosed as vasculitis, arteritis, or occlusive or aneurysmal atherosclerosis based on an elevated inflammatory reaction, dilated aorta on imaging, or the symptoms presented (1). A previous report was also initially diagnosed with PAN (4), similar to the present case.

Aortic sarcoma is a malignant tumor that is considered to develop from intimal subendothelial mesenchymal cells or mural myofibroblastic cells. Rusthoven, et al. (2) performed a systemic review of aortic sarcoma in the English literature
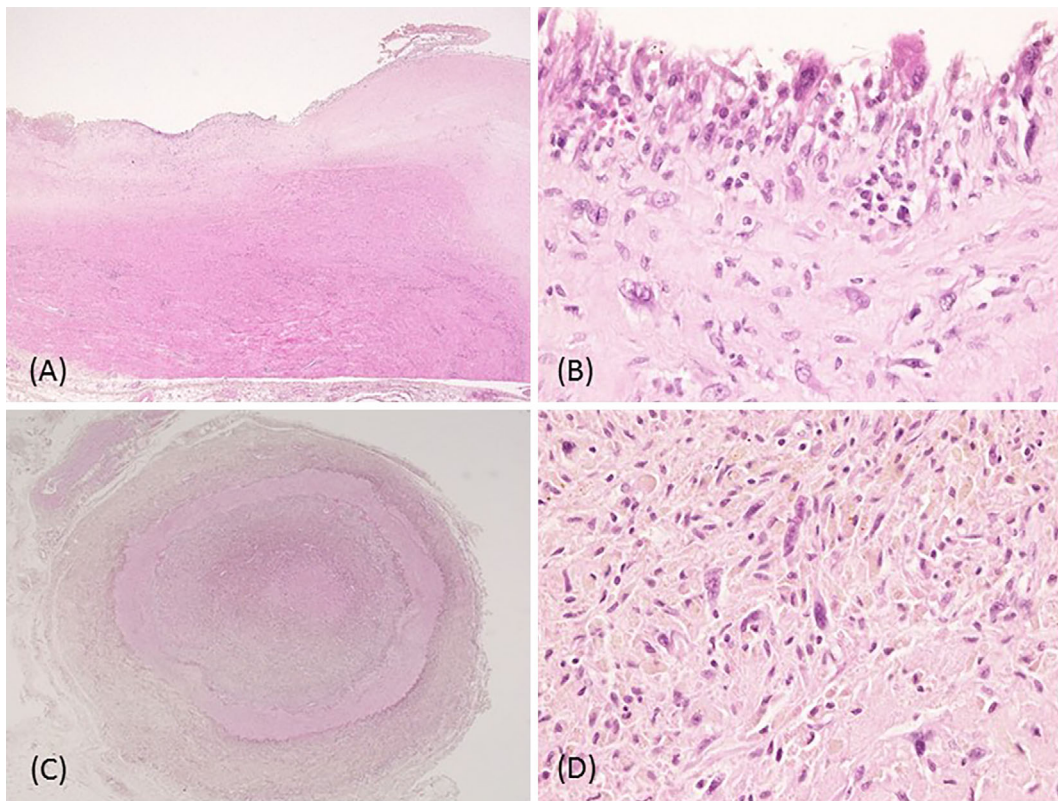
Figure 3. Histological findings. A: Spindle and ovoid cells with hyperchromatic nuclei proliferated in the superficial lumen of the abdominal aorta (Hematoxylin and Eosin (H&E) staining 20×, B: 400×). C: Spindle and ovoid cells with hyperchromatic nuclei were also observed in the left renal artery (H&E staining 20×, D: 400×).

and analyzed 165 cases reported since 1873, when it was initially described by Brodowsk. Aortic sarcoma is classified as intimal and mural according to its anatomic origin, with intimal sarcoma accounting for 66.7% of all cases. The most common histology is undifferentiated tumors (39.4%), followed by angiosarcoma (37%) and smooth muscle or leiomyosarcoma (13.3%). Forty-three cases (26.1%) were diagnosed by an autopsy, while the other 122 cases were diagnosed by surgery. Of the 122 patients diagnosed antemortem, 57 (46.7%) were managed with surgical resection, 46 (37.7%) with palliative surgery, and 19 (15.6%) underwent no tumor-directed surgery. Chemotherapy use was reported in 35 cases (28.7%). Radiation therapy directed to the primary aortic tumor was reported in 18 cases (14.7%) and to sites of metastatic disease in 17 cases (13.9%). The estimated median survival was 11 months in the 122 patients diagnosed antemortem. The factors associated with an improved survival were reported to be the absence of metastatic disease at the diagnosis and management with surgical resection according to univariate analysis. Thus, a positive diagnosis and surgery are very important.

Although imaging is used for its diagnosis, the differentiation of aortic intimal sarcoma from vasculitis or atherosclerosis on CT or magnetic resonance imaging is challenging (1). Previous studies reported that the findings of aortic sarcoma (5) and PAN (6) on CT were luminal irregularities and stenosis or occlusion of the aortic branch. However, aneurysms and segmental ectasia have been observed in 61% of PAN, and less frequently in sarcoma cases. This may assist in the differential diagnosis of aortic sarcoma and PAN. MRA with gadolinium has also been reported to be useful in the diagnosis of aortic sarcoma, because it can differentiate the tumor from the aortic wall and atheromatous thrombus and aid in the identification of periaortic extension by demonstrating tumoral enhancement (5). Additionally, it has few risks of embolization or contrast-induced renal failure associated with conventional angiography (7). ^{18}F-fluorodeoxyglucose (FDG) positron emission tomography/CT may be more useful in the differentiation between a tumor and thrombus, as aortic sarcomas exhibit a significant FDG uptake (5, 8).

In this case, we were unable to perform an accurate diagnosis based on MRA and contrast-enhanced CT. However, both aortic sarcoma and PAN are rare diseases and difficult to diagnose, thus we must consider a wide spectrum of differential diagnoses in suspected case of vasculitis.

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