Malignant Hemangioendothelioma of the Aorta

Noriharu SHIJUBO, Hisashi NAKATA, Fumiko SUGAYA, Akihiro IMADA, Akihiro SUZUKI,
Kazumi KUDOH, Masaaki SATOH*, Kohji KUROKAWA** and Shosaku ABE

We present a rare case of aortic malignant hemangioendothelioma with a mural growth pattern in which the endothelial nature was confirmed by immunohistochemical demonstration of Factor VIII-related antigen. Aortic sarcomas and malignant hemangioendotheliomas in the literature are reviewed.

(Internal Medicine 34: 1126–1129, 1995)

Key words: aortic sarcoma, factor VIII-related antigen

Introduction

Primary neoplasms of the aorta are uncommon, which have included several types of sarcomas such as fibrosarcoma, fibromyxosarcoma, leiomyosarcoma, malignant hemangioendothelioma and malignant fibrous histiocytoma (MFH) (1–10). We describe a rare case of primary aortic malignant hemangioendothelioma with a mural growth pattern, in which the endothelial nature was immunohistochemically confirmed by the presence of Factor VIII-related antigen. Here, we review aortic sarcomas and malignant hemangioendotheliomas in the literature.

Case Report

A 54-year-old Japanese man without any medical history of thoracic trauma had suffered from back pain since 1990. He had consulted an orthopedist, who found no abnormalities, and his chest X-ray was normal at that time.

In January 1992, he visited our University hospital, because of severe atypical back pain. There was tenderness over the lower part of the left back, physical examination was otherwise normal. Laboratory values were within normal limits. Chest X-ray and enhanced computed tomographic (CT) scan revealed a large mass adjacent to the descending thoracic aorta (Fig. 1). No enlarged mediastinal lymph nodes were found. Aortograph showed intact lumen of the aorta.

At operation, the tumor was located in the external wall of the descending aorta, and the capsule was connected with the outer membrane of the aorta. Macroscopically, the tumor was filled with brown-reddish grumous materials, but the lumen of

the aorta was intact. The tumor was resected, and patch plasty of the aorta was performed using a woven Dacron material. Light microscopic examination revealed coagula with calcification covered by a fibrous capsule. There were no atypical cells in the resected tumor. At that time, it was believed that the tumor was only organized hematoma.

The patient referred to us again in August 1994, complaining of severe atypical anterior chest, left back and lower abdominal pain, blood-streaked expectoration, and dyspnea on exertion of 2-month duration. Coarse crackles were present in both lungs, and persistent, severe pain was found in the right tenth rib and right ischias bone. Laboratory data showed no abnormalities except for anemia (red blood cell count, $2.86 \times 10^6/\mu\text{L}$; hematocrit, 26.5% and hemoglobin, 9.0 g/dl). Arterial oxygen tension (PaO_2) was 59.5 Torr and arterial carbon dioxide tension (PaCO_2) was 36.5 Torr. Chest X-ray and CT scan revealed a mass adjacent to the descending thoracic aorta, and reticular opacities and multiple nodules were observed in both lungs. Bone scintigraph disclosed multiple abnormal accumulation, suggesting bone metastases.

In the absence of a specific diagnosis, an open lung biopsy was done, leading to the diagnosis of malignant hemangioendothelioma. Light microscopic examination of the pulmonary nodules and samples of the aortic tumor obtained later at autopsy showed a diffuse process with highly pleomorphic malignant endothelial-appearing cells forming multiple thin-walled vascular spaces (Fig. 2). Factor VIII-related antigen and vimentin were positive by immunoperoxidase in the tumor cells (Fig. 3), but S100 protein, smooth muscle actin and myoglobin were negative. In a few tumor cells, Weibel-Palade bodies, i.e., tubular structures found in normal endothelium were revealed

From the Third Department of Internal Medicine, *the Department of Clinical Pathology, Sapporo Medical University School of Medicine, Sapporo, and **the Department of Orthopedics, Hakodate Goryokaku Hospital, Hakodate

Received for publication April 17, 1995; Accepted for publication August 7, 1995

Reprint requests should be addressed to Dr. Noriharu Shijubo, the Third Department of Internal Medicine, Sapporo Medical University School of Medicine, South-1, West-16, Chuo-ku, Sapporo 060

Figure 1. Enhanced computed tomographic scan showing a mass adjacent to the descending aorta on the first admission.

Figure 2. Microphotograph of the tumor. Highly pleomorphic tumor cells are observed, which form multiple thin wall vascular spaces (HE stain, $\times 200$).

electronmicroscopically. Interleukin-2 (160 million unit daily) was intravenously administered beginning August 31. Despite the therapy, the patient died 9 days after initiation of interleukin-2 therapy.

At autopsy, a large hemorrhage mass had destroyed the outer wall of the descending thoracic aorta and adhered to the left lung. The lumen of the aorta was intact without significant obstruction. Both lungs were heavy, and were sprinkled with countless hemorrhagic tumoral nodules. Multiple small hemorrhagic tumoral nodules were also found in the liver, bones and gastrointestinal tract.

Figure 3. Immunohistochemistry of Factor VIII-related antigen. Pleomorphic tumor cells are positive for Factor VIII-related antigen (arrows) ($\times 200$).

Discussion

In the present case, the diagnosis of malignant hemangioendothelioma was confirmed by open lung biopsy in 1994. Retrospectively, we could not diagnose the tumor resected at the first operation as malignant hemangioendothelioma.

There are two possibilities regarding the development of malignant hemangioendothelioma of the aorta described here. The first is that bleeding may sometimes have occurred in the wall of the descending thoracic aorta due to malignant hemangioendothelioma, resulting in organized hematoma and malignant hemangioendothelioma cells remained in the aortic wall at the first operation. The second possibility is that after the first operation, the aortic malignant hemangioendothelioma may have arisen due to a dysplastic effect of the artificial Dacron patch as the foreign material, since several reports on aortic sarcoma associated with the Dacron prosthetic material have been published as shown in Table 1. However, organized hematoma at the first operation cannot be elucidated by the second hypothesis.

Previous reports of primary aortic sarcomas are listed by several investigators (3, 7–9). We added several cases of aortic sarcomas that we have recently found (2, 4–6). Fifty cases of aortic sarcomas including the present case are reviewed (Table 1). [Most cases occur in male patients (male/female; 41:9), and the mean age is 57 years at diagnosis (range 3 months to 75 years). According to the growth pattern, aortic sarcomas can be divided into luminal and mural type (10). In 38 of 50 cases, aortic sarcomas showed a luminal growth pattern which presented a uniform, well-defined clinical picture; multiple embolic dissemination to the peripheral arteries caused gangrene and cutaneous inflammation. In 12 of 50 cases, aortic sarcomas showed a mural growth pattern, and they exhibited ambiguous symptoms such as pain, weight loss and general malaise.

Diagnoses of the 50 aortic sarcomas have included undiffer-

Table 1. Primary Sarcomas of the Aorta

Author	Sex, age	Growth pattern	Histology	Journal vol: page
Brodowski W (1873)	M/52	Luminal	Fibrosarcoma	Iber Leist Forschr Ges Med 8 : 243
Miura M (1891)	M/38	Luminal	Fibrosarcoma	Int Beitr Z Wissenssch Med Festchr R Virchow 2 : 249
Auffermann H (1912)	M/38	Mural	Fibrosarcoma	Z Krebsforsch 11 : 294
Nencki L (1946)	M/47	Mural	Fibrosarcoma	Cardiol 10 : 1
Karhoff B (1952)	M/55	Luminal	Hemangioendothelioma	Z Allg Pathol 89 : 46
Kovaleva AN (1959)	M/65	Luminal	Fibrosarcoma	Ark Pat 21 : 62
Kattus AA (1960)	F/22	Luminal	Fibromyxosarcoma	N Engl J Med 262 : 694
Kaigorodous RE (1963)	F/62	Luminal	Fibrosarcoma	Grudr Khir 5 : 88
Zeithofer J (1963)	M/3mo	Luminal	Fibromyxosarcoma	Krebsarzt 18 : 259
Sladden RA (1964)	M/64	Luminal	Sarcoma	J Clin Pathol 17 : 602
Sladden RA (1964)	M/59	Luminal	Sarcoma	J Clin Pathol 17 : 602
Bowles LT (1965)	M/53	Luminal	Hemangiopericytoma	Ann Thorac Surg 1 : 746
Smeloff EA (1965)	F/65	Luminal	Fibromyxosarcoma	Am J Cardiol 15 : 107
Blenkinsopp WK (1966)	F/63	Mural	Hemangiopericytoma	Thorax 21 : 193
Stevenson JE (1971)	M/60	Luminal	Fibromyxosarcoma	Am J Med 51 : 553
Winkelmann RK (1971)	M/56	Luminal	Hemangioendothelioma	Am J Med 51 : 692
Salm R (1972)	M/60	Mural	Fibrosarcoma	Cancer 29 : 73
Broborowicz D (1972)	M/48	Luminal	Hemangioendothelioma	Nowotwory 22 : 309
Steffelaar JW (1975)	M/70	Luminal	Hemangioendothelioma	Arch Pathol 99 : 139
O'Connell TX (1976)	M/59	Luminal [#]	Fibromyxosarcoma	J Thorac Cardiovasc Surg 72 : 94
Dulla Pria AF (1977)	F/51	Luminal	Fibrosarcoma	Arch De Vecchi Anat Patol 62 : 155
Crum CP (1978)	M/58	Mural	Fibroanthosarcoma	Virchows Arch A 379 : 351
Hernandez F-J (1979)	M/42	Mural	Leiomyosarcoma	Am J Surg Pathol 3 : 251
Weinberg DS (1980)	M/48	Luminal [#]	MFH	Cancer 46 : 398
Chen KTK (1981)	F/66	Luminal	MFH	Cancer 48 : 840
Fehrenbacher JW (1981)	M/67	Luminal [#]	Hemangioendothelioma	Ann Thorac Surg 32 : 297
Millili JJ (1981)	M/64	Mural	Leiomyosarcoma	Surgery 89 : 631
Mason MS (1982)	M/70	Luminal	Hemangioendothelioma	Oncology 39 : 167
Paragona O (1982)	M/67	Luminal	Hemangioendothelioma	Vasc Surg 16 : 117
Schmid E (1984)	M/75	Luminal	Hemangioendothelioma*	Cancer 54 : 1407
Wright EP (1985)	M/46	Luminal	Sarcoma**	Am J Surg Pathol 9 : 890
Hermanek P Jr (1985)	F/47	Mural	MFH	Chirurg 56 : 120
Parussis E (1985)	F/44	Mural	MFH	Pathol 6 : 282
Wenker JC (1986)	M/69	Mural	MFH	Invest Radiol 21 : 928
Moeser P (1986)	F/60	Luminal	Hemangioendothelioma	Cardiovasc Intervent Radiol 9 : 182
Guvendik L (1986)	M/47	Mural	MFH	Ann Thorac Surg 42 : 578
Kanno J (1987)	M/67	Luminal	Hemangioendothelioma*	Virchows Archiv A 412 : 1761
Guyton D (1987)	M/64	Luminal	Sarcoma	J Surg Oncol 36 : 183
Becquemin JP (1988)	M/67	Luminal	Hemangioendothelioma*	Ann Vasc Surg 2 : 225
Pruszczynski M (1988)	M/63	Luminal	Sarcoma**	Pathol 20 : 173
Herzberg AJ (1988)	M/75	Luminal	Sarcoma**	Histopathol 13 : 571
Haber LM (1988)	M/70	Luminal	Hemangioendothelioma*	Am J Surg Pathol 12 : 798
Nishikawa H (1989)	M/50	Luminal	Fibromyxosarcoma**	Heart Vessels 5 : 54
Singh AS (1989)	M/75	Luminal	Sarcoma	J Vasc Surg 9 : 493
Suzuki M (1989)	M/75	Luminal	Leiomyosarcoma	Acta Pathol Jpn 39 : 336
Fitzmaurice RJ (1990)	M/67	Luminal	Hemangioendothelioma*	Histopathol 17 : 457
Tejada E (1991)	M/69	Luminal	MFH**	Clin Cardiol 14 : 425
Weiss WM (1991)	M/56	Luminal [#]	Hemangioendothelioma*	J Vasc Surg 14 : 87
Higgins R (1991)	M/65	Luminal	Sarcoma**	Cancer 68 : 1622
present case	M/54	Mural	Hemangioendothelioma*	

[#]aortic sarcoma arising in association with Dacron prosthetic material. *,**indicate that Factor VIII-related antigen was immunohistochemically positive and negative in tumor cells, respectively. MFH: malignant fibrous histiocytoma.

entiated sarcoma (8 cases), fibromyxosarcoma (6 cases), fibrosarcoma (8 cases), fibroxanthosarcoma (1 case), MFH (7 cases), malignant hemangioendothelioma (15 cases), malignant hemangiopericytoma (2 cases), and leiomyosarcoma (3 cases). [Most cases were classified based on the histologic pattern alone, without further elucidation of histogenesis]. Recently, aortic sarcomas were electronmicroscopically and immunohistochemically subclassified into histogenetic types such as leiomyosarcoma, malignant hemangioendothelioma, and MFH (1–10). In only seven cases including the present case, the endothelial nature of sarcomas has been proven by the immunohistochemical demonstration of Factor VIII-related antigen (1–3, 5, 7, 9). All of them except the present case showed a luminal growth pattern. Recently, Burke and Virmani (10) described 11 aortic sarcomas, demonstrating only one case of aortic malignant hemangioendothelioma with a mural growth pattern. This is the second documented case of aortic malignant hemangioendothelioma with a mural growth pattern in the world literature.

The treatment of malignant hemangioendothelioma consists of surgery, irradiation, chemotherapy and interleukin-2 therapy (11–13). Surgery may provide a longer survival in patients without metastasis. The treatment of malignant hemangioendothelioma remains disappointing especially in metastatic disease. Interleukin-2 can induce, in vitro and in vivo, a heterogeneous population of non-specific cytotoxic lymphocytes. They can kill a variety of malignant tumors including malignant hemangioendothelioma (14). Interleukin-2 therapy can be clinically applied in patients with malignant hemangioendothelioma in Japan, showing approximately a 40% response rate (13). However, in patients with metastatic disease, interleukin-2 therapy also appears to result in a poor prognosis.

References

- 1) Schmid E, Port SJ, Carroll RM, Friedman NB. Primary metastasizing aortic endothelioma. *Cancer* **54**: 1407, 1984.
- 2) Haber LM, Truong L. Immunohistochemical demonstration of the endothelial nature of aortic intimal sarcoma. *Am J Surg Pathol* **12**: 798, 1988.
- 3) Becquemin JP, Lebbe C, Saada F, Avril MF. Sarcoma of the aorta: report of a case and review of the literature. *Ann Vasc Surg* **2**: 225, 1988.
- 4) Nishikawa H, Miyakoshi S, Seki A, Honda K. A case of aortic intimal sarcoma manifested with acutely occurring hypertension and aortic occlusion. *Heart Vessels* **5**: 54, 1989.
- 5) Fitzmaurice RJ, McClure J. Aortic intimal sarcoma: an unusual case with pulmonary vasculature involvement. *Histopathology* **17**: 457, 1990.
- 6) Higgins R, Posner MC, Moosa HH, Staley C, Pataki KI, Medelow H. Mesenteric infarction secondary to tumor emboli from primary aortic sarcoma: guidelines from primary aortic sarcoma. *Cancer* **68**: 1622, 1991.
- 7) Weiss WM, Riles TS, Gouge TH, Mizrahi HH. Angiosarcoma at the site of a Dacron vascular prosthesis: a case report and literature review. *J Vasc Surg* **14**: 87, 1991.
- 8) Suzuki M, Shimoda T, Ushigome S, Aizawa S. Leiomyosarcoma of the thoracic aorta associated with dissecting aneurysm. *Acta Pathol Jpn* **39**: 336, 1989.
- 9) Kanno J, Takemura T, Kasaga T. Malignant endothelioma of the aorta. *Virchows Archiv A* **412**: 183, 1987.
- 10) Burke AP, Virmani R. Sarcomas of the great vessels: a clinicopathologic study. *Cancer* **71**: 1761, 1993.
- 11) Enzinger FM, Weiss SW. Malignant vascular tumors. in: *Soft Tissue Tumors*. Statens G, Ed. C.V. Mosby Co., St Louis, 1988, p.545.
- 12) Holden CA, Spittle MF, Wilson JE. Angiosarcoma of the face and scalp: prognosis and treatment. *Cancer* **59**: 1046, 1987.
- 13) Ikeda S, Ishihara K. Phase II study of recombinant interleukin 2 (S-6820) in various malignant skin tumors. *Biotherapy* **3**: 811, 1989 (in Japanese).
- 14) Damle NK, Doyle LV, Bender JR, et al. Interleukin 2-activated human lymphocytes exhibit enhanced adhesion to normal vascular endothelial cells and cause their lysis. *J Immunol* **138**: 1779, 1987.