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Case report

Malignant endothelioma of the aorta

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Summary. An untreated case of a malignant endothelial tumour of the thoracic aorta of a 67 year-old male is reported. A tumour, $7 \times 6 \times 1.5$ cm in size occupied the lumen of the descending thoracic aorta and two daughter lesions, 0.5 cm in diameter, were located in the abdominal aorta and the left common iliac artery. Histologically, they were composed of a surface cellular lining and a underlying necrotic mass; the former was six to ten layers of bizarre epithelioid cells thick and the latter contained much nuclear debris. Innumerable tumour emboli of epithelioid tumour cells and producing ischaemic lesions were found in various organs and tissues. Ultrastructurally, tumour cells were arranged in acinar pattern with narrow lumena and immature basement membrane. There were ultrastructural appearances interpreted as Weibel-Palade bodies and immunohistochemically factor VIII related antigen and vimentin was seen in the tumour cells.

Key words: Aorta – Endothelial neoplasms – Epithelioid – Malignant

Introduction

Malignant endothelial tumours of the aorta and the large arteries are rare. Among 48 cases of primary tumours (Chen 1981; Garces and Gosink 1972; Mason et al. 1982; McAllister and Fenoglio 1977; Millili et al. 1981; Paragona et al. 1982; Weinberg and Maini 1980; etc.) 9 cases have been reported as endothelial, showing an epithelioid pattern at the primary site (Fehrenbacher et al. 1981; Kaigorodova and Berezovskaia 1963; Karhoff 1952; Lattes 1977; Leu and Sulser 1976; Schmid et al. 1984; Sladden 1964; Steffelaar et al. 1975; Winkelmann et al. 1971). A few cases were shown to be endothelial immunohistochemically and ultrastructurally (Schmid et al. 1984).

An untreated case of a malignant tumour of the aorta is reported with electron microscopic, immunohistochemical and enzyme histochemical evidence that it was of endothelial origin.

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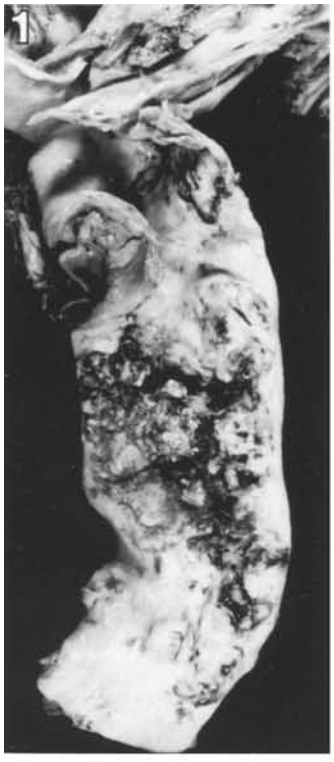
Materials and methods

Autopsy specimens were prepared as paraffin sections and routinely stained or submitted to immunohistochemical studies after trypsin treatment. Antisera to factor VIII related antigen (DAKO, Santa Barbara, CA), fibronectin (DAKO), laminin (Cappel, Worthington, PA) and vimentin (Upton et al. 1986) were applied with the avidin-biotin immunoperoxidase complex kit (Vector Lab., Burlingame, CA). Virus antigens (herpes simplex, herpes zoster, and cytomegalovirus) were detected by indirect immunofluorescence method (Honda et al. 1982). Formalin fixed tissues were submitted to Sudan III, Black B and Oil red O staining. For ultrastructural study, formalin fixed specimen were processed, and examined with a JEOL 100 CX electron microscope. Snap-frozen tissue sections were submitted to alkaline phosphatase (naphthol AS-BI phosphoric acid & fast red violet LB salt), acid phosphatase (naphthol AS-BI phosphoric acid & hexazonium pararosanilin) and non-specific esterase (alpha-naphthol acetic acid & pararosanilin) stainings.

Case report

A 67 years old Japanese male suffered from hypertension for 20 years, angina pectoris for 15 years and had a myocardial infarction 8 years ago. He smoked 60 cigarettes per day for 50 years. His father and 3 siblings of 7 died of apoplexy and 2 of heart attack.

In November 1981, he complained of intermittent claudication. Hypertension (190/90 mmHg), leukocytosis (12900/mm^3), increased erythrocyte sedimentation rate (ESR, 117 mm/h) and high C-reactive protein (CRP, +6) were found. In Aug. 1982, he was admitted to the Japanese Red Cross Medical Center, Tokyo, for palpitation, dyspnoea and weight loss. He was 162 cm in height and 39 kg in weight. Blood pressure was 190/120 mmHg. A vascular murmur was heard around the na-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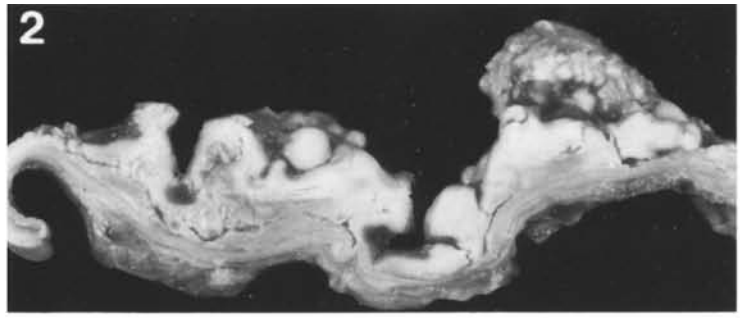
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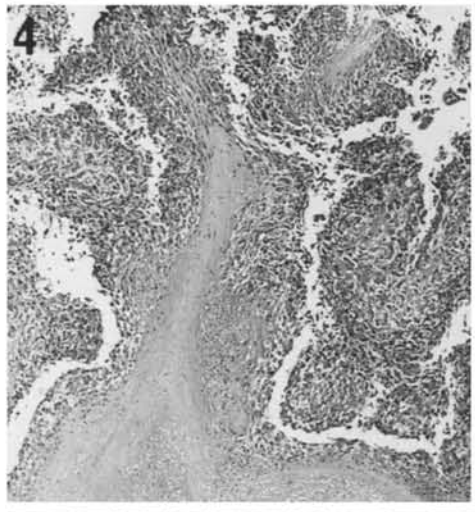
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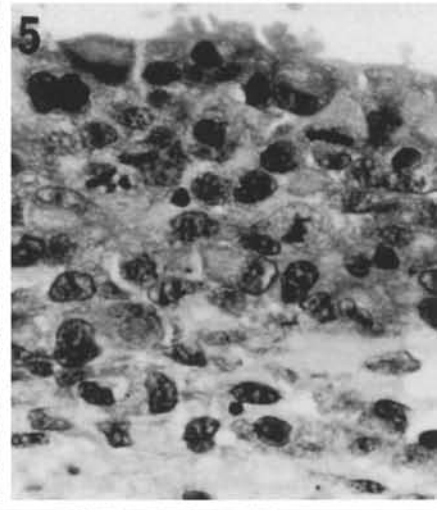
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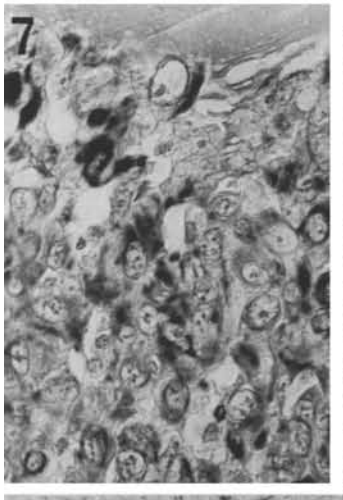
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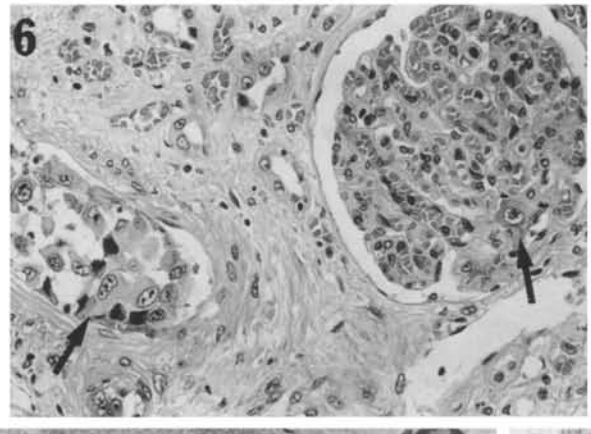
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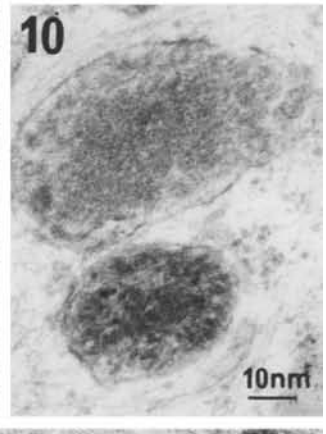
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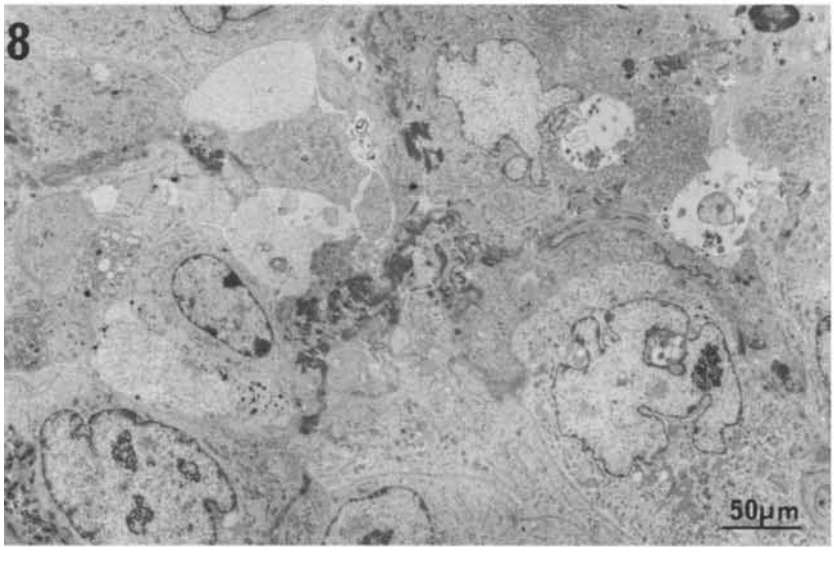
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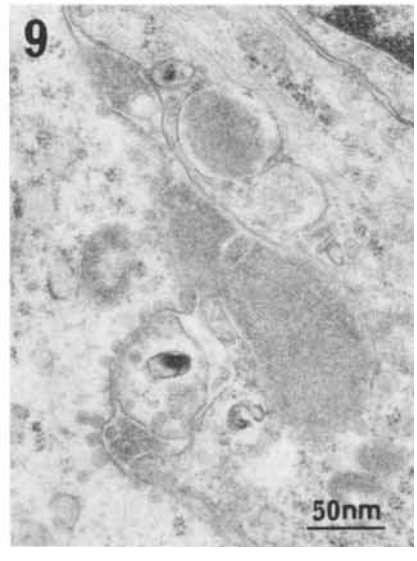
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vel and in both inguinal regions. Babinski's signs and muscle weakness were present bilaterally. There was leukocytosis (16700 mm^3), thrombocytosis (639000 mm^3) and a few atypical lymphocytes in blood smear. The fibrinogen level was high (579 mg/dl) and prothrombin time was slightly prolonged (16.2 s). Although dyspnoea and levels of GOT, GTP and LDH were improved by diuretics, high CRP, BUN, ESR and hypertension persisted. There was rapid progress of emaciation and renal failure, and he died.

An autopsy was done 2 h 50 min postmortem. A tumour, measuring $7 \times 6 \times 1.5$ cm, occupied the aortic lumen 10 cm below the orifice of the left subclavian artery (Fig. 1). It was a fragile yellow mass destroying the aortic media with gray covering (Fig. 2), which was partly villous (Fig. 3). Two daughter lesions, measuring 0.5 cm in diameter, were found in the abdominal aorta a few centimeters below the orifice of the renal arteries and in the left common iliac artery.

Histologically, a pleomorphic cell sheet covered the necrotic mass which contained numerous nuclear debris and cholesterol clefts (Figs. 4, 5). No tumour cells were found on the adventitial side of the mass or in the vasa vasora. PAS-positive thin strands of ground substance divided tumour cells into small acini, however, an angiosarcomatous pattern was not found. The daughter lesions were confined to the intima, and showed the same histopathological features.

Large tumour emboli were found in the renal arteries and the artery of Adamkiewicz. Microscopic emboli were found in all the organs examined, except for the heart, the lungs, and the head and neck including the cervical spinal cord and the brain. Usually they were confined to medium to small-sized arteries and arterioles, except for the kidneys where they were also found in glomerular capillary lumena and venules (Fig. 6). Ischaemic lesions were formed in the involved organs.

Immunohistochemically, factor VIII related antigen and vimentin were positively stained (Fig. 7). Keratin, CEA, AFP, HCG, fibronectin, laminin, lysozyme and virus antigens (herpes simplex, varicella-zoster, and cytomegalovirus) were negative. Both the cells and the necrotic part contained lipid positive for Sudan III, Black B and Oild red O. Enzyme histochemistry revealed week activities of non-specific esterase and acid phosphatase, but no alkaline phosphatase.

Ultrastructurally, the tumour cells were arranged in acinar pattern (Fig. 8) with narrow lumens and immature basement membrane. The cells had indented nuclei. Thin fibrin strands encircled each acinus but collagen fibers were not seen. The tumour cells were rich in intermediate filaments and had abundant pinocytotic vesicles and coated vesicles (Fig. 9). Though rare, structures interpreted as Weibel-Palade body were found in the cytoplasm (Fig. 10). The spindle-shaped cells in the ground substance showed no features of smooth muscle cells or of fibroblasts.

Discussion

As listed in Table 1, among the 48 reported cases of primary tumour of the aorta and large arteries (Chen 1981; Garces et al. 1972; Mason et al. 1982; McAllister and Fenoglio 1977; Millili et al. 1981; Paragona et al. 1982; Weinberg et al. 1980; etc.), only 9 have been reported to be of endothelial origin, showing epithelioid growth in the primary site (Fehrenbacher et al. 1981; Kaigorodova and Berezovskaia 1963; Lattes 1977; Leu and Sulser 1976; Schmid et al. 1984; Sladden 1964; Steffelaar et al. 1975; Winkelmann et al. 1971). A few were shown to have endothelial markers immunohistochemically, and typical structural features ultrastructurally (Schmid et al. 1984).

This case of malignant endothelioma of the aorta showed an epithelioid cell sheet covering a necrotic mass with skip lesions and intravascular dissemination. There was evidence of endothelial origin (fine lumen formation, presence of many pinocytotic vesicles, Weibel-Palade bodies, factor VIII related antigen, and vimentin, (Weibel and Palade 1964; Sehested and Hou-Jensen 1981;

Fig. 1. Macroscopic view of the tumour of the sclerotic descending thoracic aorta

Fig. 2. The transverse section of the aortic tumour

Fig. 3. Villous portion of the tumour

Fig. 4. Histology of the villous part illustrated in Fig. 3

Fig. 5. Histology of the cellular lining of the tumour. Large polygonal tumour cells in the upper layers and spindle cells buried in the underlying hyalinous ground substance. Mitotic figures are present. (H & E, $\times 400$)

Fig. 6. Tumour emboli in an arcuate artery and glomerular capillary lumens of the kidney (arrows). (H & E, $\times 40$)

Fig. 7. Immunohistochemical demonstration of vimentin in aortic tumour cells. ($\times 400$)

Fig. 8. Polygonal tumour cells with intended nucleus arranged in acinar pattern ($\times 2100$)

Fig. 9. Pinocytotic vesicles, coated vesicles and intermediate filaments in tumour cells, and moderately electron-dense material of intercellular space ($\times 20000$)

Fig. 10. Transverse section of membrane-bound Weibel-Palade bodies, measuring about 20 nm in diameter, and showing microtubular structures ($\times 62500$)

Table 1. Primary tumour of the aorta and large arteries. Histology of the reported cases

Author	Year	Age (years)	Sex	Histology	Site
Kaigorodova	1963	62	F	Malignant endothelioma**	Ascending aorta
Sladden	1964	59	M	Intimal sarcoma*[ace]	Abdominal aorta
Sladden	1964	64	M	Intimal sarcoma*	Abdominal aorta
Winkelmann	1971	56	M	Malignant endothelioma*[acdf]	Abdominal aorta and bifercation
Steffelaar	1975	70	M	Malignant endothelioma*[b]	Abdominal aorta and bifercation
Leu	1976	74	M	Malignant endothelioma*[cdf]	Femoral artery
Lattes	1977	–	–	Malignant endothelioma*[b]	Femoral artery
Fehrenbacher	1981	67	M	Angiosarcoma*[d,f]	Abdominal aorta
Schmid	1984	75	M	Malignant endothelioma*[ad]	Thoracic aorta
Present case	1987	67	M	Malignant endothelioma*[ce]	Thoracic aorta
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Breborowicz	1972	48	M	Angiosarcoma	Thoracic aorta
Otto	1977	75	M	Angiosarcoma	Femoral artery
Scannell	1979	81	M	Angiosarcoma	Popliteal artery
Mason	1982	70	M	Angiosarcoma	Abdominal aorta
Paragona	1982	67	M	Malignant haemangioendothelioma	Abdominal aorta and bifercation
–					
Grohme	1965	60	M	Myxomatous endothelioma	Abdominal aorta
Kimbrell	1973	58	M	Myxoma	Thoracic and abdominal aorta
Gough	1974	62	F	Myxoma	Ascending aorta and aortic arch
–					
Bowles	1963	53	M	Haemangiopericytoma	Thoracic aorta
Courbier	1963	64	M	Haemangiopericytosarcoma	Femoral artery
Blenkinsopp	1966	63	F	Haemangiopericytoma	Thoracic aorta
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Giaccai	1949	62	M	Fibrosarcoma	Splenic artery
Salm	1972	57	F	Fibrosarcoma	Thoracic aorta
Garces	1972	46	M	Fibrosarcoma	Iliac artery
Brodowski	1873	52	M	Fibrosarcoma	Thoracic aorta
McAllister	1977	22	F	Fibrosarcoma	Thoracic aorta
–					
Détrie	1960	22	F	Fibromyxoma	Thoracic and abdominal aorta
Kattus	1960	22	F	Fibromyxoma	Thoracic and abdominal aorta
Silverman	1972	62	F	Fibromyxoma	Thoracic aorta
–					
Karhoff	1952	55	M	Endothelioma****	Thoracic aorta
Smeloff	1956	65	F	Fibromyxosarcoma	Thoracic and abdominal aorta
Zeitlhofer	1963	3.5 months	M	Fibromyxosarcoma	Thoracic aorta
Stevenson	1968	60	M	Fibromyxosarcoma	Abdominal aorta
–					
Crum	1978	58	F	Fibroxanthosarcoma	Thoracic aorta
Weinberg	1980	48	M	Malignant fibrous histiocytoma***	Thoracic aorta
Chen	1981	66	F	Malignant fibrous histiocytoma	Thoracic aorta
Hermanek	1983	47	F	Malignant fibrous histiocytoma	Aortic bifercation
–					
Auffermann	1911	38	M	Leiomyosarcoma	Abdominal aorta
Ferrarini	1913	66	M	Leiomyosarcoma	Femoral artery
Ajello	1925	70	F	Leiomyosarcoma	Femoral artery
Sadlinski	1967	60	F	Leiomyosarcoma	Femoral artery
Hopkins	1968	55	M	Leiomyosarcoma	Iliac artery
Kevorkian	1973	71	M	Leiomyosarcoma	Femoral artery
McAllister	1977	64	M	Leiomyosarcoma	Iliac artery
Hernandez	1979	42	M	Leiomyosarcoma	Abdominal aorta
Millili	1982	64	M	Leiomyosarcoma	Abdominal aorta
–					
Miura	1891	38	M	Giant cell sarcoma	Thoracic aorta
Nencki	1949	47	M	Pleomorphic sarcoma	Abdominal aorta
Kovaleva	1959	65	M	Pleomorphic sarcoma	Abdominal aorta

* Malignant endothelioma showing epithelioid growth covering necrotic mass without vascular lumen formation in the primary site
** Possibly a case of same category as *
*** Associated with vascular prosthesis
**** Myxomatous tumour with pleomorphism, illustrated by Staemmler (1955)

[a] Surgically treated
[b] Surgically treated without recurrence
[c] Tumour emboli or intravascular dissemination of epithelioid tumour cells in distal organs
[d] Haemangiosarcomatous pattern observed in metastatic lesions
[e] Skip lesion in aorta
[f] Extravascular growth

Rungger-Braendle and Gabbiani 1983). As the tumour had no tendency to induce tumour vessels, it is likely that the cells away from the blood stream became necrotic. It may require an angiosarcomatous pattern or more time for extensive extravascular growth to develop. Whether the skip lesions were intraluminal metastases or not remains uncertain.

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