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Intimal-type primary sarcoma of the aorta

Report of a case with evidence of rhabdomyosarcomatous differentiation

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Abstract We report an intimal sarcoma presenting as an aortic aneurysm. A 68-year-old man suffered from chest pain and speech disturbance. Computed tomography showed a sacciform aneurysm of the aorta, which was resected, revealing a polypoid tumour measuring 1.5×2×2.5 cm projecting into the lumen. This proved to be a poorly differentiated high-grade sarcoma having morphological, immunophenotypic and ultrastructural features consistent with rhabdomyosarcomatous differentiation. Primary sarcomas of the aorta are extremely rare. Many cases have been diagnosed as ”intimal” on the basis of their site of origin, and they are not easy to classify from their histological pattern. Electron microscopy and the use of a more comprehensive panel of immunohistochemical markers should be applied in the histological classification of ”intimal” sarcoma.

Key words Rhabdomyosarcoma · Aorta · Immunohistochemistry · Electron microscopy

Introduction

Primary sarcomas very rarely occur in the great vessels [4, 21], being seen most commonly in the pulmonary artery, followed by the inferior vena cava [4]. Since the first report by Brodowski [3], only around 45 cases have been reported as arising in the aorta, most of these in its abdominal part [1, 4, 9, 14, 16, 19–21, 25]. In the aorta, the most common histological type has been reported as poorly differentiated (so-called intimal); other less common subtypes include leiomyosarcoma, malignant fibrous histiocytoma, and angiosarcoma [4, 19]. A diagnosis of fibrosarcoma has been made in some cases [23]. Occasional fibrosarcomas, rhabdomyosarcomas or sarcomas with focal rhabdomyosarcomatous differentiation, chondrosarcomas, osteosarcomas, malignant fibrous histiocytomas, and malignant mesenchymoma have been reported in the pulmonary artery, but leiomyosarcomas predominate in the inferior vena cava [4, 7, 11, 18, 24]. Rhabdomyosarcomas have not been reported in the aorta. In general the diagnosis has not been supported by such techniques, as electron microscopy and immunohistochemistry; in most cases the diagnosis has been made on the basis of light microscopy alone.

We report a case of primary pleomorphic sarcoma occurring in the thoracic aorta, which showed histological, immunohistochemical, and ultrastructural evidence of rhabdomyosarcomatous differentiation.

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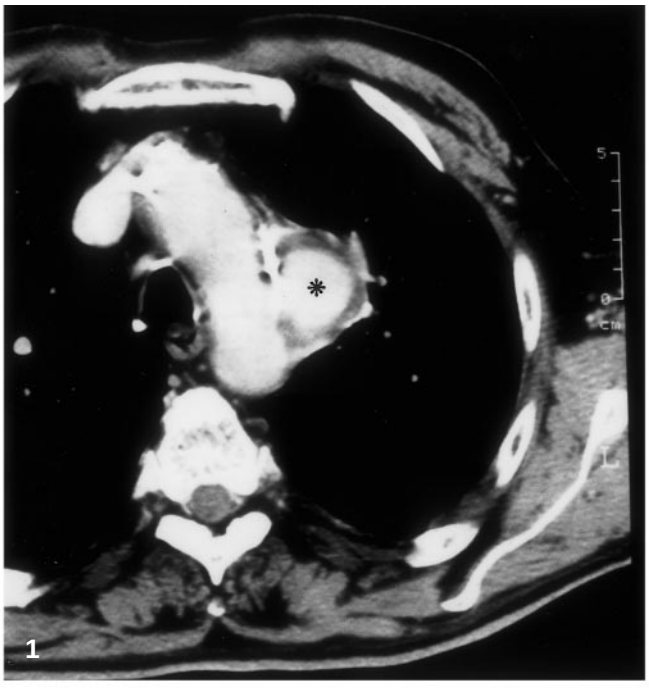
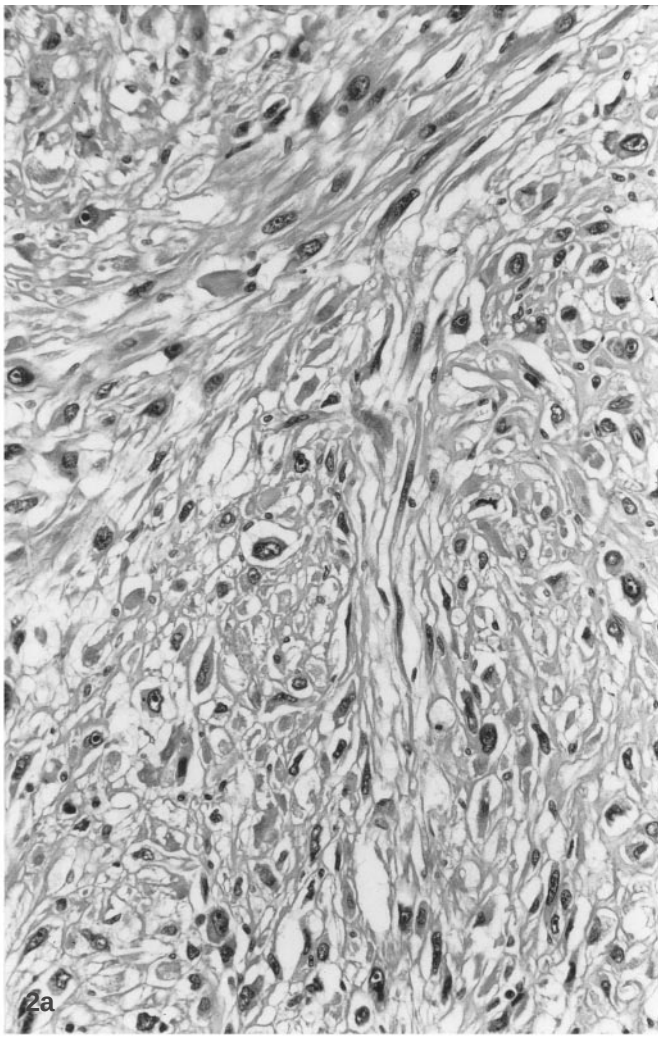
Clinical history

A 68-year-old man was admitted with chest pain and speech disturbance. His past medical history was not significant; there was some evidence of ischaemic heart disease. Computed tomography showed mild atherosclerotic calcification in the thoracic and abdominal aorta, and a sacciform aneurysm extending from the inferolateral aortic wall between the arc and the descending tract. This did not show adherence to other structures (Fig. 1). The affected part of the aorta tract was removed and the hole was closed with synthetic material (Fig. 1). The specimen was examined histologically, and sarcoma with a rhabdomyosarcomatous differentiation was diagnosed. Staging of the tumour while the patient was hospitalized revealed no metastases and no mediastinal diffusion. The patient refused to undergo further surgery or additional therapies. After 4 months, a worsening of his clinical condition led to the patient’s readmission to the hospital. Dynamic computed axial tomography revealed a pleural effusion on the left side of the chest and some highly vascularized, solid masses in the anterior mediastinum and in the space between the aorta and the pulmonary artery. Skeletal scintigraphy and an abdominal computed tomogra-





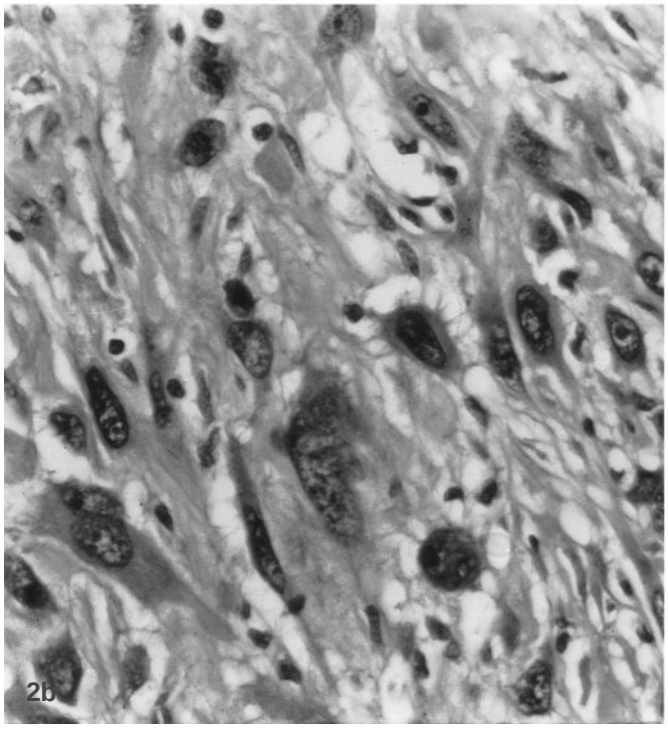


Fig. 1 Computed tomographic scan demonstrating aortic saccular aneurysm (*asterisk*)

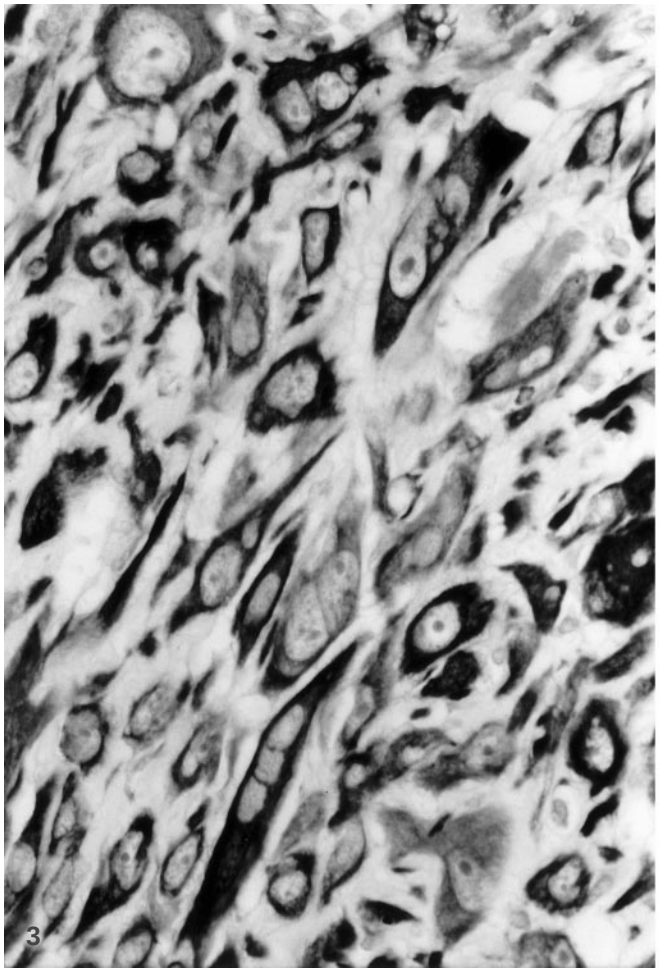
Fig. 2 **a** Typical pleomorphic tumour pattern with ribbon-shaped and polygonal cells. **b** Vacuolated cytoplasm confers a spider-web shape to some neoplastic cells. Haematoxylin-eosin, original magnification ×100, ×200

phy revealed bone and hepatic metastases, respectively. The patient underwent radio- and chemotherapy and a clinical improvement was observed. Eight months after surgery the patient is still alive, albeit with disease.

Pathological findings

The resected specimen measured about 4 cm in its greatest diameter; an intraluminal, 1.5×2×2.5-cm solid polypoid mass partly covered with thrombotic substance was contained in it; the remaining aortic wall was slightly thicker than normal, with a few uncomplicated atherosclerotic plaques.

The entire polypoid mass was composed of a proliferation of cells extending from the lumen through the wall, infiltrating the adventitia and the margins at some sites. In very small peripheral areas, a few layers of fibrin were seen on the luminal side of the tumour. The neoplasm showed a pleomorphic pattern (Fig. 2a), consisting of sheaths of intersected spindle cells and polygonal, tad-



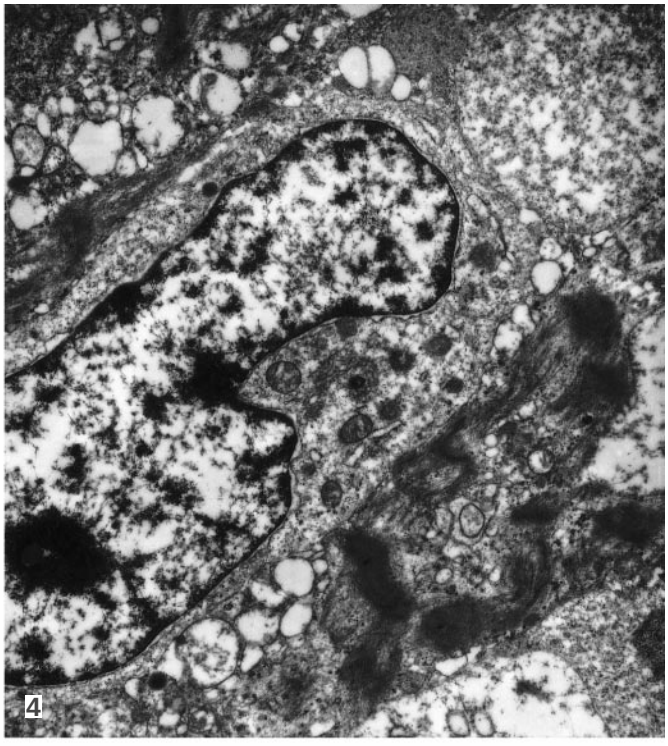


Fig. 3 Cytoplasmic positivity for sarcomeric actin. APAAP, ×400

Fig. 4 Tumour cell showing ultrastructural features of rhabdomyosarcoma. Note a rudimentary sarcomeric structure. Uranyl acetate-lead citrate, original magnification ×7000

pole- or racquet-shaped, sometimes multi- or binucleated cells, which were loosely textured and intermingled with erythrocyte-filled pseudovascular spaces. Nuclei were large and clear, and usually had a prominent central nucleolus. Cytoplasm was abundant and strongly eosinophilic; spider-web shaped cells were also seen (Fig. 2b). In a few ribbon-shaped cells, cross-striations were just recognizable.

Cytoplasmic positivity was detected for vimentin (Dako, Milan, Italy; 1:400), desmin (Dako; 1:200), myoglobin (Novocastra, Newcastle, UK; 1:20), MyoD1 (Ylem, Milan, Italy; oven pretreatment, 1:50), Myf 3 (Novocastra, Newcastle, UK; oven pretreatment, 1:40), sarcomeric actin (Dako; 1:100) (Fig. 3), and muscle-specific actin HHF35 (Biogenex, Florence, Italy; prediluted, 1:10). Tumour cells were completely negative for alpha smooth-muscle actin (Sigma, Milan, Italy 1:50), AE1–AE3 cytokeratins (Biogenex; 1:2000), CD31 (Dako; 1:40), CD34 (Biogenex; 1:10), and S-100 (Biogenex; 1:500).

Electron microscopic examination showed prominent rough endoplasmic reticulum, bundles of thin and thick filaments, and glycogen particles in many tumour cells. In some cells, filaments with fusiform densities were also evident. In a few cells, striations and Z-band material were discernible (Fig. 4). Subplasmalemmal attachment plaques were not observed.

Discussion

The aorta is a very rare site for sarcomas, which mainly involve its abdominal part when they do occur [4]. The mean age of the patients so far reported at the time of presentation is about 60. The initial clinical presentation may be nonspecific, with constitutional symptoms of fever, weight loss, and anorexia [4, 21]. The most common mode of presentation is related to embolic phenomena; chest pain and rupture of an aneurysm have also been reported [4, 13]. According to their site of origin, aortic sarcomas have been divided into intimal and mural types [4]. The intimal type, which is the more frequent, may form plaques along the aortic intima, or grow as polypoid intraluminal vegetations; the mural type may arise in the media or in the adventitia [13, 23]. The two types bear different prognoses, the luminal type being characterized by a more aggressive behaviour leading to death within months [4]. Since they are not easily classifiable, many sarcomas primarily involving the intima have been classified as ”intimal” and are pleomorphic spindle-cell

undifferentiated sarcomas, often found to be positive to vimentin and sometimes to smooth muscle actin, suggesting a myofibroblastic origin [4, 13]. Some cases have been diagnosed as "undifferentiated" sarcoma, (myo)fibrosarcoma, fibro(myxo)sarcoma, angiosarcoma, malignant fibrous histiocytoma, and leiomyosarcoma [1, 9, 10, 14–16, 20, 25]. Mural sarcomas are less frequent and are more often described as leiomyosarcoma and angiosarcoma [4]. Rhabdomyosarcomatous differentiation has occasionally been demonstrated in great vessel sarcomas, mainly located in the pulmonary artery [7]. In our case, the histological pattern in large areas resembled that of some previously reported "intimal" sarcomas, with prominent pleomorphic spindle-cell growth, although the morphology of many cells suggested rhabdomyosarcomatous differentiation, which was confirmed by ultrastructural and immunohistochemical data. Tumour cells expressed immunoreactivity for desmin, myoglobin, MyoD1, Myf 3, sarcomeric actin, and HHF35. The *MyoD* gene family encodes nuclear phosphoproteins, which are expressed only in skeletal muscle cells at an early stage of differentiation [6, 27–30]. Although weak and scattered positivity with MyoD1 antibody has seldom been observed in other sarcomas, particularly pleomorphic leiomyosarcoma [29], *MyoD* gene family products are considered the most sensitive and reliable markers of rhabdomyoblastic differentiation, as they have been found even in cases with no expression of any other marker of skeletal muscle [6, 8].

Sarcomas with unequivocal rhabdomyosarcomatous differentiation have not previously been reported in the aorta. In many of the previously reported cases, no extensive histochemical or electron microscopic evaluation was performed, and in some cases the diagnosis was based on the histological pattern alone. It is accepted that in tumours with a pleomorphic pattern a diagnosis of rhabdomyosarcoma must always be excluded and that rhabdomyosarcomas in other sites may be characterized by the predominant presence of spindle cells [5]. Some spindle-cell rhabdomyosarcomas may also express smooth muscle actin [22]; furthermore, a rhabdomyosarcomatous, biphenotypic differentiation has been found in some otherwise unequivocal leyomyosarcomas [29]. In some cases the use of a larger panel of antibodies could allow reclassification of aortic sarcomas diagnosed as undifferentiated or as another histological type. It has been suggested that sarcomas of great vessels derive from a pluripotent precursor cell, which can differentiate into a variety of histological subtypes [17]. It has been suggested that rhabdomyosarcomas in the pulmonary artery originate from pluripotent cells of the bulbus cordis [2]; a similar origin might be suggested for such tumours occurring in the aorta. As they are so rare, aortic sarcomas are not always suspected preoperatively. However, even if they have a poor prognosis, surgery has resulted in a longer disease-free period in a few cases [4, 17, 21].

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