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CASE REPORT

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# Intimal angiosarcoma of the aorta with tumour embolisation causing mesenteric ischaemia

## Report of a case diagnosed using CD31 immunohistochemistry in an intestinal resection specimen

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**Abstract** Primary intimal angiosarcomas of the aorta (i.e. mostly intraluminal sarcomas with evidence of endothelial differentiation) are extraordinarily rare. We report a case in which the diagnosis was accurately made using immunohistochemistry in an intestinal resection specimen and confirmed during autopsy. The patient was a 64-year-old woman with mesenteric ischaemia and a "thrombus" in the abdominal aorta. Two segments of the ileum and the right colon were surgically removed. Histological examination showed multiple tumour emboli in small arteries of the submucosa, serosa and mesentery. The highly atypical cells comprising these emboli were positive immunohistochemically with antibodies to Ulex Europaeus, von Willebrand factor and CD31 and negative for CD34. During post-mortem examination, the intra-aortic mass was located around the orifices of the coeliac and the superior mesenteric arteries, and gross tumour thrombi were found in the left renal and splenic arteries. This case emphasises the need for a wide panel of immunohistochemical antibodies when tumour emboli of unknown origin are under study.

**Keywords** Aorta · Angiosarcoma · Immunohistochemistry · CD31

## Introduction

Primary malignant tumours of the aorta are distinctly uncommon and the subject of occasional single case reports (about 100 cases have been reported in the literature) [1, 10]. They have been classified as intimal or mural according to their gross features [1]. This classification is relevant in that the clinical symptoms and the survival of these neoplasms differ significantly. While intimal tumours tend to give rise to embolic phenomena, metastasise early and carry an ominous prognosis, mural lesions follow a more protracted course. Histologically, most of them are myofibroblastic sarcomas, and only a minority are angiosarcomas that express endothelial antigens. We report a case in which the diagnosis of bona fide angiosarcoma was established pre-mortem (and confirmed during autopsy) by means of immunohistochemical characterisation of multiple tumour emboli present in specimens of intestinal resection.

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## Clinical history

A 64-year-old woman (J.P.L.) presented at the emergency room of another hospital on 12 September 1999 with a 2-week history of abdominal pain and vomiting. A diagnosis of "reactive anemia and thrombocytosis and probable giant cell arteritis" had been made 9 months earlier, and corticosteroid treatment had been started. Upon examination, the patient was afebrile and appeared ill. There was widespread abdominal tenderness. The heart and lungs were normal except for a II/IV systolic aortic murmur. The patient's laboratory tests included: glucose, 149 mg/dl; creatinine, 1.5 mg/dl; amylase, 210 U/L; haemoglobin, 11.2 g/dl; haematocrit, 37.1%; platelets, $455\times10^9$/l and leucocytes, $37.6\times10^9$/l (89.6% neutrophils, 3.6% lymphocytes), without left shift. A plain film of the abdomen disclosed no significant findings. An abdominal ultrasound was followed by an emergency abdominal computed tomography (CT) scan, which showed an intraluminal, mobile aortic mass that was reported as "tumoral, thrombotic or inflammatory in origin".

The patient was immediately referred for evaluation at the Department of Vascular Surgery, Hospital Universitario de Getafe (Madrid, Spain). A thoracoabdominal CT scan and an arteriographic study were performed. These showed an intraluminal mass, together with thromboembolic occlusion of the splenic, main hepatic and left renal arteries. The spleen and the left kidney were atrophic. An exploratory laparotomy for presumed intestinal infarction was carried out on 17 September 1999. A segment of jejunum was resected, and a right ileocolectomy was performed. Due to necrosis and focal perforation in an area close to the previous surgical anastomosis, a second segment of small intestine was resected 2 days later. Later, acute renal failure ensued, and multiple infarcts were discovered on both liver lobes; the patient's condition deteriorated, and the patient died on 5 October 1999. A post-mortem examination was performed.

## Materials and methods

Tissue was fixed in formalin and processed routinely for histological study. The immunohistochemical techniques (Table 1) were performed on paraffin-embedded tissue using the streptavidin-biotin-peroxidase complex method. Antigenic retrieval was performed by means of pressure cooking or microwaving when necessary. Proteinase K was used for EA1-EA3 and CAM5.2.

**Table 1** Immunohistochemical markers employed

| Marker | Source, dilution | Result |
|---|---|---|
| Vimentin | Dako, 1:160 | + |
| CD-34 (QBEND10) | Novocastra, 1:120 | – |
| CD31 (TUK3) | Dako, 1:120 | + |
| Von Willebrand factor | Dako, prediluted | + |
| Ulex Europaeus | Dako, 1:30 | + |
| Ki-67 (MIB1) | Immuno-Tech, 1:160 | +(15%) |
| P53 protein | Dako, 1:100 | +(10%) |
| LCA | Dako, prediluted | – |
| CD20 (L-26) | Dako, 1:160 | – |
| CD3 | Atom, 1:100 | – |
| CD5 | Novocastra, 1:100 | – |
| CD43 | Dako, prediluted | – |
| CD15 (LeuM1) | Dako, 1:100 | – |
| CD30 (BerH2) | Dako, prediluted | – |
| CD68 (KP1) | Dako, 1:120 | – |
| CAM 5.2 | Menarini, 1:50 | – |
| EA1-EA3 | Dako, prediluted | – |
| Epithelial membrane antigen | Dako, prediluted | – |
| Muscle-specific actin (HHF35) | Dako, 1:120 | – |
| Smooth muscle actin | Dako, 1:140 | – |
| Desmin | Dako, 1:120 | – |
| Carcinoembryonic antigen | Menarini, 1:50 | – |

## Pathological findings

### Surgical specimens

We received two segments of small intestine (15 cm long each) and a specimen of ileocolectomy (65 cm of distal ileum and 10 cm of right colon). All showed gross and microscopic features of ischaemic necrosis with focal perforation. Within several small arteries of the submucosa, subserosa and mesenterium or mesocolon, multiple small groups of tumour cells admixed with fibrin were readily identified upon histological examination (Fig. 1). These cells showed marked cytologic atypia and featured abundant amphophilic cytoplasm and prominent nucleoli. The immunohistochemical findings and the diagnosis made on these specimens are in agreement with those of the autopsy (Fig. 2; below).

## Autopsy findings

### Gross findings

Data of septic shock were present, associated with abundant purulent material and areas of perforation in the residual small intestine. The anterior luminal surface of the abdominal aorta showed a 5.5×3.5×2.0 cm necrotic and exophytic mass that encircled the ostia of the coeliac and superior mesenteric arteries (Fig. 3, top). Upon longitudinal sectioning, no involvement of the aortic media or adventitia was noted (Fig. 3, bottom). The lumina of several arteries of large calibre, including the left renal, splenic and hepatic artery, were filled with identical tissue. Atrophy of the spleen and the left kidney and multiple geographic infarctions of the liver were additional findings. The oesophagus showed multiple shallow ulcers that histologically proved to be of herpetic origin. A patchy inflammatory infiltrate in the lung interstitium was seen along with abundant large cells with nuclear and cytoplasmic inclusions. This was diagnostic of cytomegalovirus.

### Light microscopy

Histologically, the aortic mass did not involve the media and consisted of a core of fibrin and necrotic tissue, bordered by a thick rim of viable atypical cells (Fig. 4). These were identical to those identified within vascular spaces both in the previous surgical specimens and in the tumour emboli present at the sites grossly described in the post-mortem examination.

### Immunohistochemistry

A wide panel of immunohistochemical markers, including lymphoid, epithelial and muscular antigens, was used in the surgical specimen to characterise the highly atypical cells filling some vascular lumina. On the initial panel, only vimentin could be detected in the neoplastic cells. Of a second group of antibodies, CD31, von Willebrand factor (formerly known as factor-VIII related antigen) and Ulex Europaeus were diffusely and intensely positive (Fig. 2b). Ki-67 stained approximately 15% of the

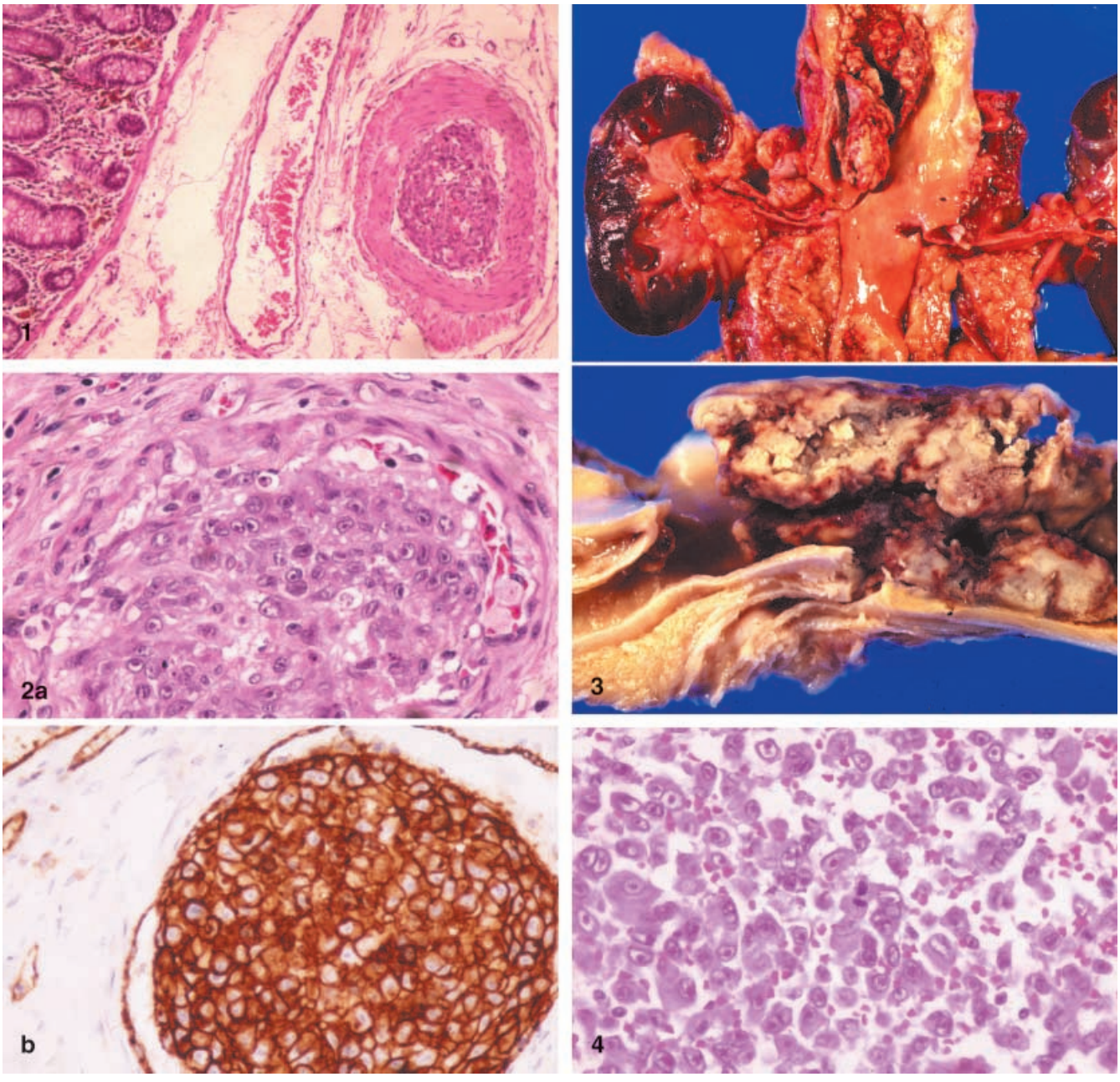


**Fig. 1** Artery of the submucosa of the ileocolectomy specimen showing occupation of the lumen by tumour cells (original magnification ×200)

**Fig. 2** **a** Higher power of the intravascular atypical cells. **b** Staining for CD31. Von Willebrand factor and Ulex Europaeus were also positive, but CD34 was negative (original magnification ×400)

**Fig. 3** During autopsy, an exophytic mass arising on the abdominal aorta (*top*) was found (fixed specimen, *bottom*) to encroach upon the origin of the coeliac and superior mesenteric artery. This was seen in the longitudinal section

**Fig. 4** Histological appearance of the viable tumour cells lining the aortic mass (high-power view). Note the marked nuclear pleomorphism and the abundance of eosinophilic cytoplasm (original magnification, ×400)

tumour cells. About 10% of the nuclei were positive for p53. All other immunohistochemical antibodies gave negative results. The same markers were employed in the autopsy specimen, with identical findings.

## Discussion

The rare sarcomas of the aorta are classified by site as intimal (those that are predominantly luminal) and mural (involving primarily the aortic wall) [1]. They are then subclassified histopathologically by morphologic and immunohistochemical means. When symptomatic, aortic intimal sarcomas (AIS) give clinical findings secondary to embolic phenomena; they can produce mesenteric ischaemia, hypertension, skin necrosis or absence of

peripheral pulses [1, 2, 6]. The diagnosis can be suspected radiologically, particularly by means of magnetic resonance imaging (MRI) [10], and it is not infrequently made on material submitted by the vascular surgeon as "thrombus". Higgins et al. proposed an algorithm for the diagnosis and management of patients who are seen with mesenteric tumour emboli [6].

Prior to the advent of immunohistochemistry (IHC), the histopathologic diagnosis of aortic sarcomas relied solely on morphologic features identified using light or electron microscopy. In a 1998 review of the literature, Seelig et al. [10] found a wide array of histological diagnoses in 87 primary malignant tumours of the aorta, of which "sarcoma" (23 cases), malignant fibrous histiocytoma (15 cases) and angiosarcoma (10 cases) were the most common. With the use of IHC, most of the recently reported cases have been found to show features of myofibroblastic differentiation, thus corresponding to myofibroblastic sarcomas. There is, however, a certain number of cases lacking morphologic evidence of angiosarcomatous differentiation that, upon immunohistochemical evaluation, show positivity for endothelial markers [5].

This case highlights the usefulness of IHC in the histopathologic work-up of an intravascular malignancy. The highly atypical cells first identified within the lumina of small arteries in the intestinal resection specimen were initially suspected of representing metastatic carcinoma, melanoma or lymphoma. Once these possibilities were reasonably excluded by means of IHC, review of the clinical findings prompted the use of additional markers. A very marked positivity for CD31, von Willebrand factor and Ulex Europaeus, together with a negative result for CD34 were found. This, in turn, underlines the need for a three-reagent immunohistochemical panel (i.e. von Willebrand factor, CD34 and CD31) when dealing with a tumour of presumed endothelial differentiation; in the review by Kuzu et al. [7], CD34 failed to stain four of six angiosarcomas and 2 of 12 hemangiomas. CD31, regarded as a highly sensitive and specific endothelial marker [4], stained only 8 of 24 soft tissue angiosarcomas. This was reported in the recent review by Meis-Kindblom and Kindblom [8]. These authors found von Willebrand factor and BNH9 (a monoclonal antibody that reacts with H and Y blood group antigens and with endothelial cells) to be the most sensitive markers in the detection of vascular differentiation of soft tissue angiosarcoma. The immunohistochemical heterogeneity of angiosarcomas is further stressed by the work of Miettinen et al. [9]. In their series, CD31 and CD34 were positive in 21 and 25 of 27 angiosarcomas, respectively.

The immunohistochemical detection of p53 protein suggests that the tumour may have had a p53 mutation. There are no previous records of p53 status in the rare cases of aortic angiosarcoma that have been studied immunohistochemically, but p53 was found in 20% of the soft tissue angiosarcomas in the series of Meis-Kindblom and Kindblom [8]. This is not an unexpected finding, since p53 mutations are frequent in aggressive neoplasms [3].

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