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CASE REPORT

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Epithelioid haemangioma of the heart

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Abstract The authors report a case of epithelioid haemangioma (EH) of the right atrium, the first description of this tumour originating in the heart. The lesion was found incidentally during a cardiac echocardiogram and diagnosed pre-operatively as cardiac myxoma. The tumour must be differentiated from the exceptionally rare epithelioid haemangioendothelioma (EHE) of the heart and from a cardiac myxoma. A correct pathological diagnosis is clinically important since EH is a benign tumour, whereas EHE and cardiac myxoma can recur and metastasize. The uneventful follow-up of this patient confirms the benign nature of EH.

Key words Vascular tumours · Epithelioid haemangioma · Heart

Introduction

Epithelioid haemangioma (EH), formerly called angiolymphoid hyperplasia with eosinophilia [19] or histiocytoid haemangioma [13], is a benign vascular tumour that usually arises in the skin of the head and neck or, rarely, in deep locations [1, 11]. It belongs to a family of vascular lesions characterized by epithelioid endothelial cells, which also includes epithelioid haemangioendothelioma (EHE) [18] and epithelioid angiosarcoma [18]. We report a case of EH which we believe is the first description of this tumour arising in the heart.

Clinical history

A 62-year-old Caucasian male with a history of long-lasting idiopathic arterial hypertension was hospitalized for a cardiovascular check-up. The patient had an arterial blood pressure of 180/115. The electrocardiogram showed left ventricular hypertrophy and routine laboratory tests were normal. Thoracic echocardiography revealed the presence of a right atrial mass and a transoesophageal echocardiogram revealed a homogeneous mass in the right atrium, measuring 3.5×2.5 cm, attached to the lower portion of the interatrial septum (Fig. 1). The mass was mobile and moved towards the tricuspid ring during diastole, resulting in partial obstruction of ventricular filling. Tricuspid insufficiency was not noted; there were no cardiovascular symptoms. The pre-operative diagnosis was cardiac myxoma. The patient underwent surgery and a tumour mass attached to the interatrial septum, near the entrance of the coronary sinus, was resected. He made an uneventful recovery and is healthy with no clinical evidence of recurrence 25 months after surgery.

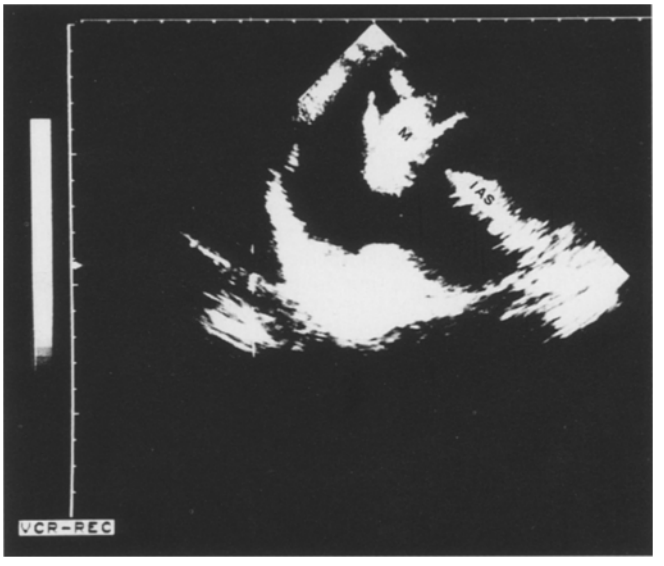

Fig. 1 Transoesophageal echocardiogram. A mass (*M*) is attached to the lower portion of the interatrial septum (*IAS*) and is bulging into the right atrium

Materials and methods

The resected specimen was fixed in 4% buffered formalin and embedded in paraffin. Sections were stained with haematoxylin-eosin

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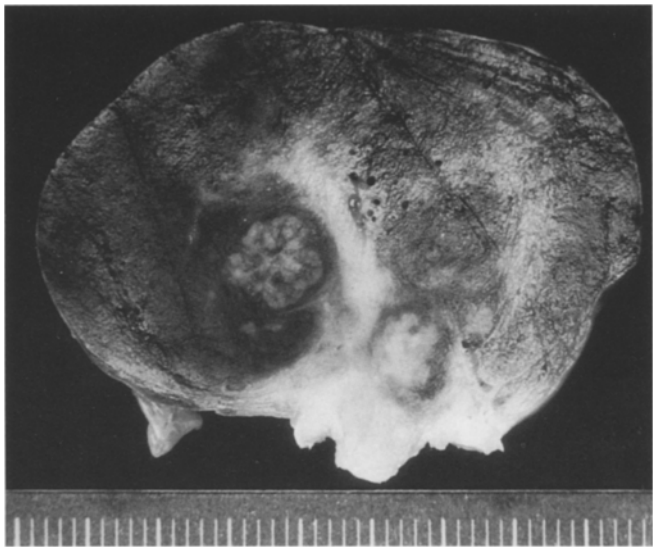

Fig. 2 Cut surface of epithelioid haemangioma of the heart. The lesion is polypoid, showing haemorrhagic areas with a vague multinodular organization

(H&E), periodic acid-Schiff (PAS), with and without diastase predigestion and alcian blue.

Immunohistochemistry was performed with the avidin-biotin-peroxidase (ABC) technique, with an ABC kit (Vector, Burlingame, Calif., USA), using antibodies to the following antigens: Factor VIII-related antigen (pre-diluted, Ortho Diagnostic System, Raritan, N.J., USA), CD34 (1:50, Becton-Dickinson, San José, Calif., USA), vimentin (1:10, Dakopatts, Santa Barbara, Calif., USA), cytokeratins (AE1-AE3, pre-diluted, Ortho Diagnostic System; Cam 5.2, prediluted, Becton-Dickinson), epithelial membrane antigen (EMA; 1:100, Dakopatts), κ and λ light chains (1:10000, Dakopatts, CD 20 (1:150, Dakopatts) and CD 3 (1:80, Dakopatts). Appropriate positive and negative controls were used in every staining run.

Pathological findings

The mass measured 3.5×2.5×1.5 cm and had a polypoid appearance with a small implantation base. On section, it was solid, grey, with large haemorrhagic areas and a multinodular pattern (Fig. 2).

Microscopically, the lesion was composed of small blood vessels, sometimes without a lumen, growing in many areas around a larger central vessel (Fig. 3). Many vessels were lined by epithelioid endothelial cells, characterized by an abundant eosinophilic cytoplasm and large hyperchromatic nuclei (Fig. 4). In a few areas, the tumour cells formed solid nests or short strands, showing occasional cytoplasmic vacuoles (Fig. 5). Mitotic figures were rarely encountered and necrosis was absent. The stroma was fibrous with focal myxoid areas and contained a prominent inflammatory infiltrate made up of lymphocytes, focally organized in nodules with germinal centres, plasma cells and a few eosinophils (Fig. 3). Extravasated red blood cells and haemosiderin deposits were present. At the implantation base, the lesion was composed of large, irregularly anastomosing vessels, dissecting the inner myocardial fibres, and lined by predominantly flat endothelial cells (Fig. 6). The endocardial surface of the tumour was lined by a normal endothelium. The lesion was completely excised. Periodic acid-Schiff, with and without diastase predigestion, and alcian blue failed to reveal glycogen or any mucin in the tumor cells, including those with cytoplasmic vacuoles.

The cells lining the vascular spaces showed a diffuse positivity for factor VIII-related antigen, a fainter positivity for CD34, and a focal positivity for vimentin; they were negative for cytokeratins and EMA. Tumour cells forming solid nests and strands, with occasional cytoplasmic vacuoles, showed the same immunoreactivity as the cells lining the vascular spaces (Fig. 7). The lymphocytes were more frequently positive for CD3 than for CD20; plasma cells showed almost equal cytoplasmic staining for κ and λ chains.

Discussion

EH is a member of a family of vascular lesions which includes EHE and epithelioid angiosarcoma [18]. These lesions are linked by the presence of epithelioid endothelial cells. However, they differ in clinical presentation, pathological features and biological behaviour, which ranges from benign to borderline to frankly malignant [18]. EH is a benign lesion that may occasionally recur [1].The diagnostic features of the tumour are summarized in the present case. Grossly, the lesion showed haemorrhagic areas and histologically it was made up of small vessels organized around a larger vessel, giving the tumour a vaguely lobulated appearance. Many vessels were lined by epithelioid endothelial cells; in some areas, the epithelioid endothelial cells formed solid nests and showed occasional cytoplasmic lumina. A lymphoplasmacytic infiltrate was prominent and contained a few eosinophils. Immunohistochemical study showed positivity of the neoplastic cells for factor VIII-related antigen and for CD34, confirming the endothelial nature of the lesion [10, 16]. The lymphoplasmacytic infiltrate was reactive, showing polyclonal plasma cells and a prominence of T lymphocytes. The presence of large vessels at the implantation base of the lesion was interpreted as an area of conventional angiomatous differentiation in an EH.

The peculiarity of this case was its location in the atrium. EH usually develops in the skin of the head and neck, but may occasionally arise in deep soft tissues, in the bone, or in blood vessels [1, 9, 11, 12]. To the best of our knowledge, it has not been described in the heart. Only one case of an epithelioid vascular tumour of the heart, belonging to the group of EHE, has been reported [5]. The differential diagnosis of this case includes EHE, a distinctive cardiovascular lesion resembling EH, metastatic adenocarcinoma and cardiac myxoma. EH differs from the EHE which has more primitive vascular differentiation, well-formed vascular channels are usually absent in EHE and the tumour is formed by short strands of epithelioid endothelial cells with frequent cytoplasmic

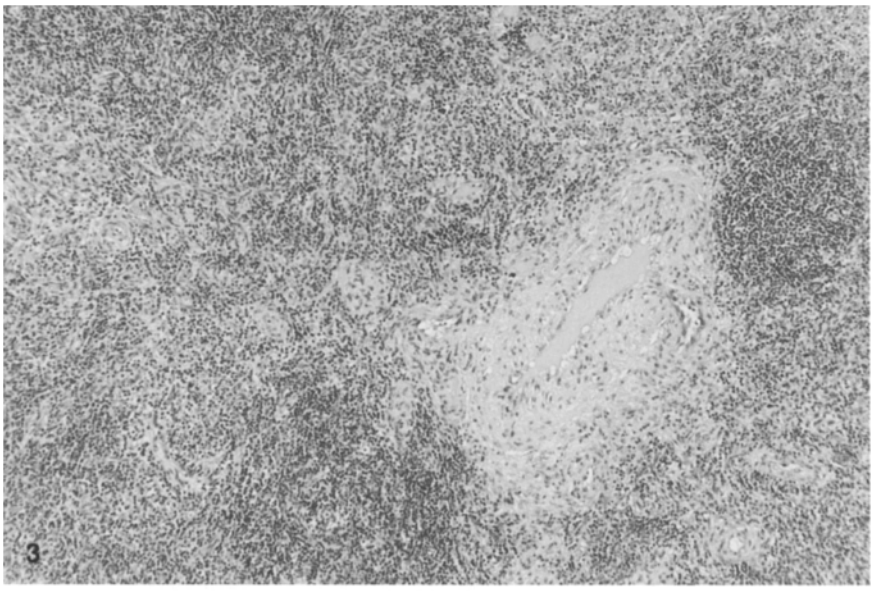

Fig. 3 Epithelioid haemangioma of the heart. Small blood vessels are organized around a larger vessel; chronic inflammatory cells are prominent (haematoxylin-eosin, ×63)

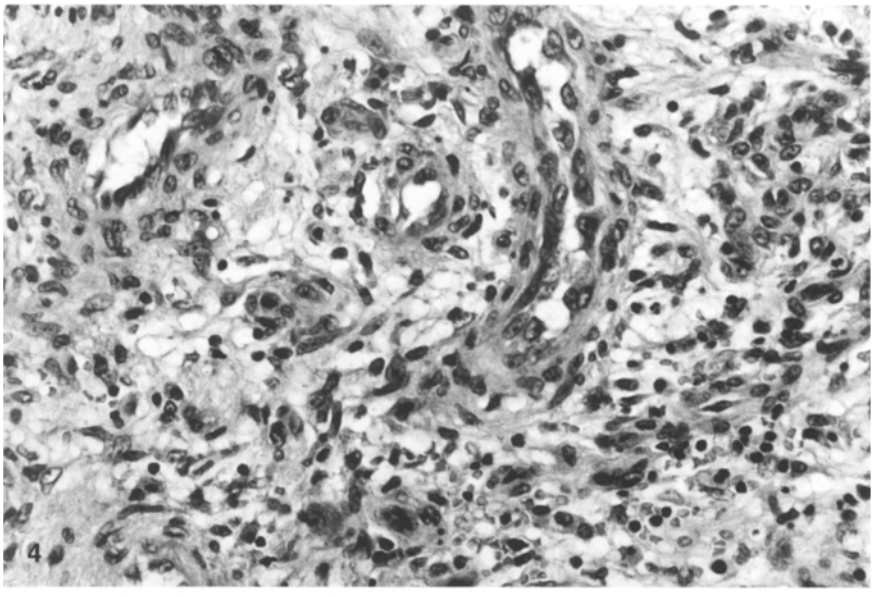

Fig. 4 Epithelioid haemangioma of the heart. Vessels are lined by epihelioid endothelial cells (haematoxylin-eosin, ×250)

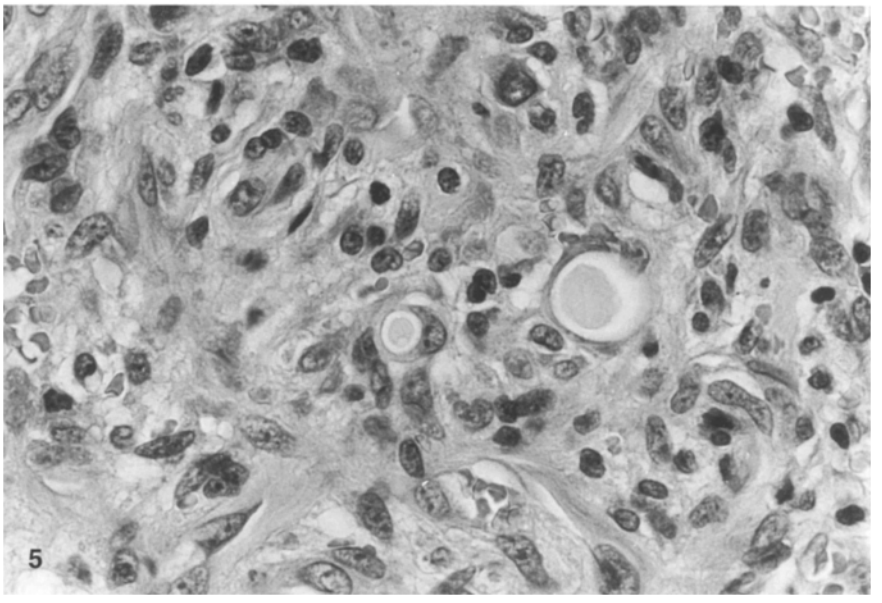

Fig. 5 Epithelioid haemangioma of the heart. Epithelioid endothelial cells showing cytoplasmic vacuolization (haematoxylin-eosin, ×400)

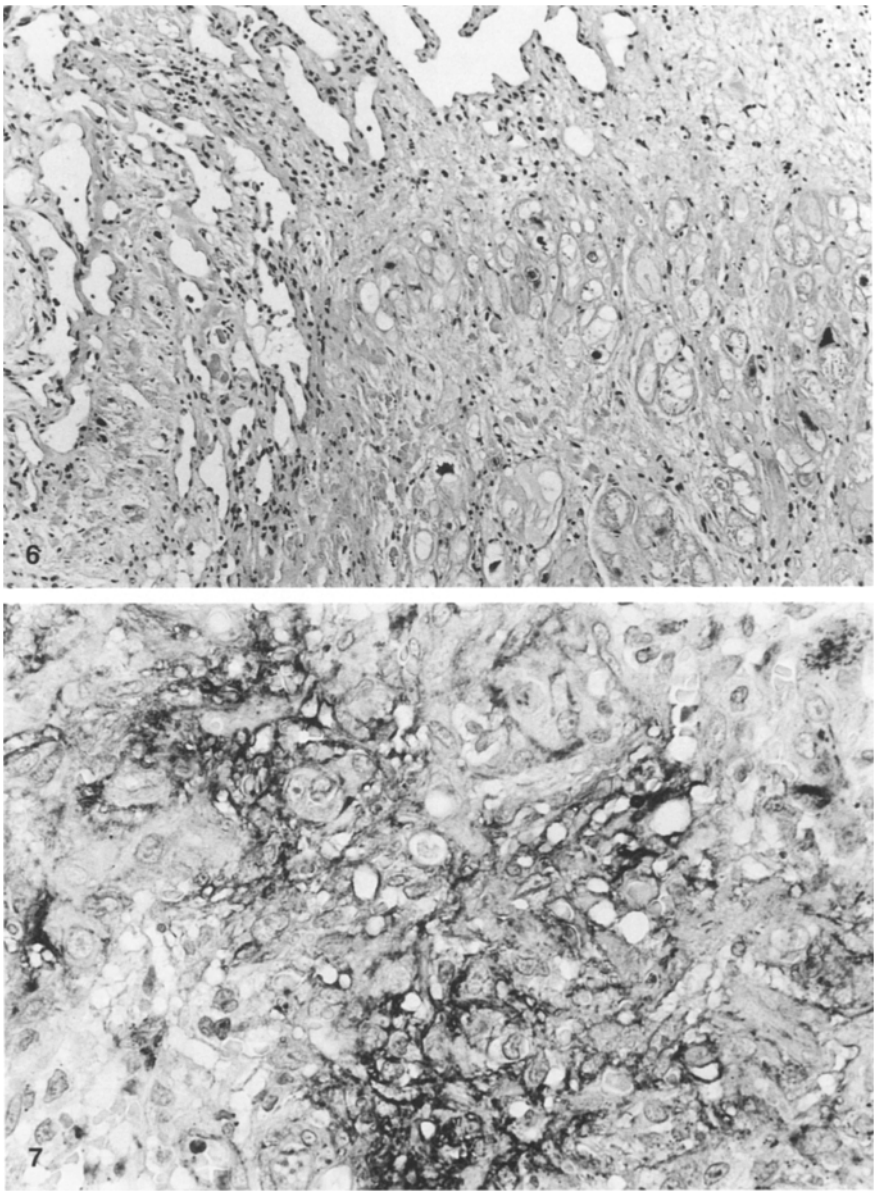

Fig. 6 Epithelioid haemangioma of the heart. Large vessels dissecting the myocardial fibres at the base of the lesion (haematoxylin-eosin, ×100)

Fig. 7 Epithelioid haemangioma of the heart. Predominantly solid tumour nests showing positive immunostaining for factor VIII related antigen (immunoperoxidase-haematoxylin ×250)

lumina [1]. Moreover, EHE, may show significant mitotic activity and tumour necrosis [1, 5]. The distinction between these two entities is important as EHE is a borderline tumour that may recur and metastasize [1]. EH of the heart must also be distinguished from the distinctive cardiovascular lesion resembling histiocytoid (epithelioid) haemangioma, which may be rarely found in the atrium, cardiac valves, aorta or pericardium [7]. This lesion is typically associated with a thrombus and is histologically made up of solid clusters of epithelioid cells, which do not form vascular channels [7]. Immunohistochemically, these cells are positive for cytokeratins, negative for factor VIII-related antigen and probably represent epicardial reactive mesothelial cells [7]. Our lesion must also be distinguished from a richly vascularized metastatic adenocarcinoma, mimicked by the epithelioid endothelial cells having cytoplasmic lumina. In our case, negativity of the vacuolated cells for mucin stains and for cytokeratins and positivity for factor VIII-related antigen and CD34 eliminated this possible confusion. It should be noted that positive staining for cytokeratins and EMA has been reported in epithelioid vascular tumours [3, 11], underlining the necessity for careful examination of vascular antigens in diagnosis. Finally, an important differential diagnosis is represented by the cardiac myxoma, the most common cardiac tumour [15], which may recur and even metastasize [14]. In this case, a correct diagnosis was only obtainable after histological examination of the mass. Cardiac myxoma is characterized by an abundant myxoid stroma containing sparse stellate or rounded tumour cells, which may be single or aggregated in strands [15]. These cells may show vasoformative features with expression of factor VIII-related antigen [8]. In our case, the atrial mass, which was entirely embedded and examined, failed to show any areas with the histopathological features of a cardiac myxoma.

Like the case previously reported as EHE of the heart [5], our patient did not have peripheral blood eosinophilia, which may sometimes be present in patients with EH and EHE. Some pathological features of EH and its occasional association with peripheral blood eosinophilia raised the possibility that EH could be similar to the pathological entity known as Kimura's disease [4]. However, more recent studies have stressed the differences between these two lesions [2, 6, 17]. The location of our case of EH in the heart adds further evidence to this distinction, as Kimura's disease arises in the dermis or subcutis and has never been described in deep sites.

Our patient has shown no evidence of tumour recurrence 25 months after surgery, confirming the benign biological behaviour of EH; moreover, it also suggests that the rare forms of deep EH behave like conventional EH [18]. EH is a benign tumour, but a few cases may represent reactive lesions [1]. This patient had no history of thoracic trauma or previous cardiac surgery and this EH can thus be considered to be a benign vascular tumour, arising in the cardiac wall.

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