

Embolic atrial myxoma with neoplastic aneurysm formation and haemorrhage: a diagnostic challenge

Intracranial neoplastic aneurysm formation and haemorrhage are rare neurologic manifestations of embolic/metastatic cardiac myxoma. Among the reported cases, only few were confirmed histologically. Typically, the diagnosis was defined after the primary cardiac tumour had been resected. We report a patient with a complicated neurologic history, in which resection of two intracranial haemorrhagic lesions led to the diagnosis of myxoma and subsequently to the identification of a small left atrial myxoma as a primary source of embolism.

A 41-year-old woman presented to her physicians in December of 2001 with a 12-month history of transient left-sided paraesthesias and a 5-month history of recurrent visual disturbances. Her past medical and family histories were non-contributory. Magnetic resonance imaging (MRI) of the brain at that time revealed multiple areas of decreased T2 signal within the frontal lobes bilaterally (Figure 1A) and the left parietal cortex. A subacute infarct involving the deep right parieto-occipital lobes was also identified (not shown). A transoesophageal echocardiogram was performed and reportedly normal. A right temporal lobe biopsy was obtained, which showed mild non-specific gliosis. Despite the non-diagnostic brain biopsy, clinically a vasculitic process was thought to be the likely cause of her disabilities, and she was treated with prednisone for 6 months. This was discontinued because of poor tolerance.

She was readmitted to her local hospital on March 2003 to be evaluated for seizures. Cerebral angiogram revealed intraluminal abnormalities of peripheral vessels (Figure 1C). Again, vasculitis was the suspected diagnosis and treatment with cyclophosphamide initiated. A repeat non-contrast head MRI was obtained 3 months later. The largest lesion located in the lateral aspect of the anterior right frontal lobe, 3 cm in greatest dimension, had increased in size compared with the prior exam. Repeat transoesophageal echocardiogram was performed because of the clinical suspicion of embolic myxoma, but again was interpreted as normal.

She remained stable until she suffered a right frontal haemorrhage on September 2003. Routine laboratory

tests on admission were normal except for borderline microcytic anaemia, increased erythrocyte sedimentation rate at 47 mm, and mild elevation of serum calcium and alkaline phosphatase. C-reactive protein was elevated at 56.3 mg/l. Extensive blood testing was otherwise negative including coagulation studies. Urine drug screen and 24-h urine collection for metanephrines were normal. Cerebrospinal fluid analysis was not performed. CT and MRI of the head showed recent intraparenchymal haemorrhage in the right frontal lobe, with surrounding oedema and mass effect on the right frontal ventricular horn (Figure 1B).

After admission, her left hemiparesis worsened and she was taken to the operating room. A right frontal craniotomy was performed with evacuation of right frontal and parietal haemorrhages and associated abnormal tissue (Figure 1D). Light microscopy disclosed organizing haemorrhage and tumour largely restricted to vascular spaces, causing aneurysmal dilatation of the weakened vascular walls, microscopic rupture and haemorrhage (Figure 2A–C). There was a hypocellular proliferation of bland stellate to spindle cells lacking pleomorphism, hyperchromatism and mitotic activity immersed in a myxoid background (Figure 2D). Focally, the tumour appeared to disrupt vascular walls as demonstrated by Movat pentachrome (MOVAT), trichrome and Verhoeff van Gieson (VVG) stains (Figure 2B). The stellate cells stained with calretinin and vimentin by immunohistochemistry. These findings led to the diagnosis of myxoma. A transoesophageal echocardiogram was again obtained, which revealed a small atrial septal lesion. The atrial tumour was removed 18 days later and the diagnosis of atrial myxoma confirmed histologically. In June of 2004, a positron emission tomography (PET) scan showed bone lesions involving multiple sites, including the right pelvis and femur. A biopsy of the sacral lesion showed metastatic myxoma. Consideration has been given to chemotherapy and/or radiation for the bone lesions. Limited surgical intervention was performed on one of the lesions on the ilium. Her lesions are stable on last follow-up, 23 months after surgical resection of the intracranial lesions.

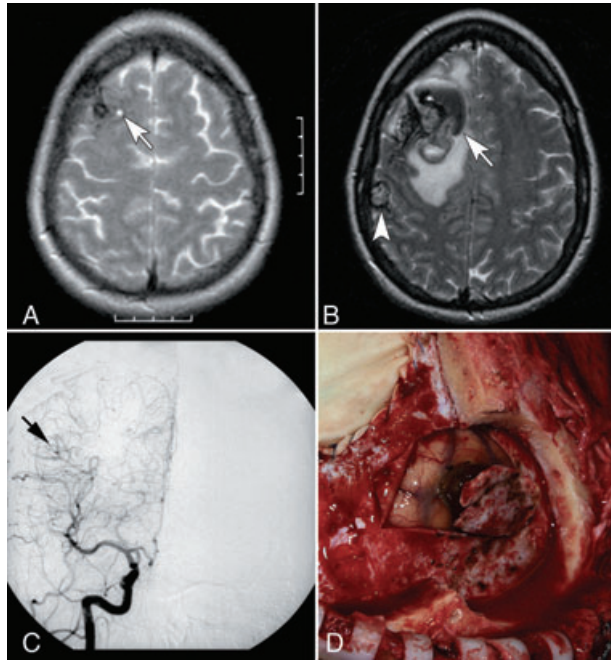


Figure 1. Imaging and intraoperative appearance of embolic myxoma. (A) Magnetic resonance imaging (MRI), T2 sequence demonstrates the right frontal lesion at the time of initial presentation (arrow). (B) There is progressive increase in size at 20 months (arrow), with the development of recent haemorrhage, vasogenic oedema and the appearance of a second right parietal lesion (arrowhead). (C) Cerebral angiogram with injection of the left internal carotid artery, demonstrating fusiform dilatation with proximal narrowing of distal right middle cerebral branches (arrow). (D) Intraoperative visualization of the right parietal lesion, resected with a portion of overlying dura.

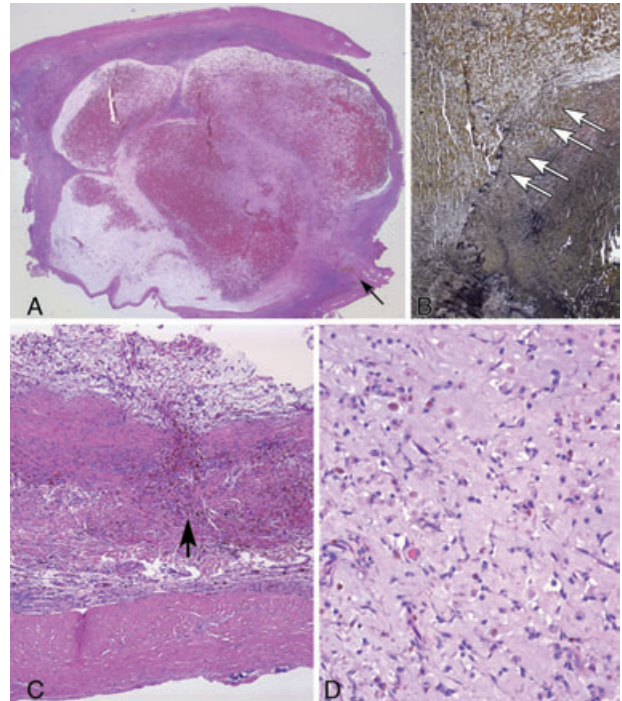


Figure 2. Histopathologic features of a neoplastic aneurysm. (A) Aneurysmatic vascular dilatation with afferent vessel (arrow). The overlying dura, centrally organizing blood clot, and scant myxomatous proliferation surrounding the clot are visible. Hematoxylin and eosin (H&E $\times 20$). (B) Loss of the internal elastic lamina at the neck of the aneurysm is visible (arrows) (VVG $\times 200$). (C) Photomicrograph revealing complete transgression of the arterial wall by invasive myxoma (arrow) (H&E $\times 200$). (D) High power photomicrograph from the centre of the parietal specimen showing a paucicellular proliferation of stellate and spindle cells in a mucoid background typical of myxoma (H&E $\times 400$).

Discussion

Because of its friable architecture and unique exposure to the bloodstream, embolism from cardiac myxoma is common. Frequently, embolism involves the central nervous system (CNS), which may be a preferential site [1]. Neurological manifestations of cardiac myxomas may be encountered in three different clinicopathological scenarios: cerebral embolism causing ischaemia [2]; neoplastic aneurysm formation with or without haemorrhage [3] as seen in our case; and intracranial mass lesion formation ('metastases') [4].

Cardiac myxoma is the neoplasm most frequently associated with cerebral aneurysm formation. A handful of cases have also been described in association with choriocarcinoma or bronchogenic carcinoma [5]. Aneurysms secondary to cardiac myxoma may present before or after

excision of the primary tumour and be responsible for delayed neurological manifestations, up to 25 years after surgery [6]. In some cases, the imaging findings may resemble those of mycotic aneurysms [7] or lead to the clinical impression of vasculitis [8]. Burton and colleagues [9] reported the first case of an intracerebral neoplastic aneurysm with autopsy pathological confirmation. Light microscopy revealed a myxomatous proliferation in the vessel wall with fragmentation of the internal elastic lamina leading to aneurysm formation. Similar findings in our patient support the view that myxoma invasion of vascular walls is the culprit. Some authors have proposed that the increase in interleukin-6 (IL-6) serum concentration and its expression in tumoral tissue may relate to vascular wall invasion, because of its induction of intercellular adhesion molecules [10]. The absolute risk for intracere-

bral haemorrhage is not known given the rarity of the condition. In a recent histopathological study of 31 patients with resected intracranial clots of unknown aetiology, a neoplasm was found to be the underlying cause in only three cases, none of which were cardiac myxomas [11].

Diagnosis of myxoma embolism in the CNS without knowledge of a primary lesion is difficult and may engender a broad and challenging differential diagnosis, both clinically and pathologically. Clinically, a complicating factor is that almost the whole primary tumour might embolize [12] preventing the diagnosis by echocardiogram even when this is suspected beforehand. This may have happened in our case explaining repeatedly negative transoesophageal echocardiograms.

In our review of the literature, of three cases in which pathological evaluation of brain lesions was performed prior to the diagnosis of an atrial myxoma [13], two were originally misdiagnosed as epithelioid haemangioendothelioma [14] and haemorrhagic granulomas [10]. The correct diagnosis was made only retrospectively following the diagnosis of a primary cardiac myxoma. In the differential diagnosis of embolic cardiac myxoma, the possibility of metastatic myxoid sarcomas and/or of a tumour of endothelial origin [14] should be entertained, while the rare presence of 'glandular' elements may raise the question of metastatic adenocarcinoma [15]. The possibility of a non-neoplastic process, such as organizing clot [16] or myxoid degeneration of an aneurysmal wall [17] should also be considered. Primary intracranial myxomas are extremely rare and generally present as extraaxial dura based masses mimicking meningiomas [18,19; personal observation].

Because of the rarity of neoplastic aneurysms due to cardiac myxoma, the limited follow-up available in reported cases and the uncertainty of their natural history, it is difficult to know how to best manage these patients after diagnosis. Removal of the cardiac myxoma, when discovered after the CNS diagnosis, is mandatory to prevent further embolization. Some patients presenting with transient ischaemic attacks benefited from antiplatelet agents [20]. Successful coil embolization has been performed on patients with giant neoplastic aneurysms from myxoma although clinical follow-up is limited [6]. Interestingly, chemotherapy has been attempted in view of the neoplastic origin of these lesions. For example, Roeltgen and colleagues [2] reported treating a 33-year-old man with a history of atrial myxoma who had subsequently

developed multiple intracerebral aneurysms with doxorubicin for 6 months. However, the main aneurysm continued to enlarge during therapy.

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