Brain and Heart

Late Diagnosis of Multiple Cerebral Aneurysms A Decade after Resection of Cardiac Myxoma

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Keywords

Cardiac myxoma · Cerebral aneurysms · Stroke · Embolism

Abstract

Cerebral embolism from a cardiac myxoma is a rare cause of ischaemic stroke. These emboli may later lead to the development of cerebral aneurysms. We report a case of delayed presentation of neurological manifestations in form of multiple intracranial aneurysms many years after treatment of a cardiac myxoma. Our patient, a 55-year-old right-handed female with a background history of hypertension, first presented at the age of 45 years with a sudden onset of right hemiplegia. A CT brain scan detected multiple infarcts in the territory of the left middle cerebral artery. Echocardiography revealed a cardiac myxoma for which she underwent immediate total surgical resection. Nearly 10 years after this diagnosis, she presented again with right-sided weakness and left ptosis. CT scan of the brain revealed bilateral acute superior cerebellar infarcts with interval evolution of previously known left cortical infarcts. MRI/MR angiogram showed multiple aneurysms arising from the bilateral middle, left anterior and left posterior cerebral arteries. She was managed conservatively. The management of multiple aneurysms with cardiac myxomas is highly debatable and dependent on the patient's presentation. This case highlights the importance to follow up on potential late extra-cardiac manifestations of the myxomas despite adequate resection.

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Introduction

Cardiac myxoma is one of the most frequent cardiac tumours, arising from the subendocardial multipotential mesenchymal cells. They can be either in solid or papillary intracardiac masses, usually in the atria. These tumours undergo microhaemorrhages, which result in thrombus formation over time. These thrombi may embolise resulting in myriad of neurological complications [1, 2].

Up to two-thirds of the emboli travel to the central nervous system, resulting in nearly 25–45% of the neurological symptoms seen [3, 4]. These symptoms range from ischaemic strokes, haemorrhages, headaches, to seizures. Of interest is the formation of intracranial aneurysms secondary to embolic phenomenon from these tumours. The pathophysiology responsible for the formation of these aneurysms is still not well understood. The temporal variability between the diagnosis of aneurysms and earlier treatment of cardiac myxomas remains unexplained.

We describe a patient who first presented with ischaemic stroke due to embolism from a cardiac myxoma. Nearly 10 years after excision of her myxoma, she presented with recurrent ischaemic strokes; her workup also revealed multiple intracranial aneurysms.

Case Report

A 55-year-old female, right-handed, first presented at the age of 45 year with a sudden onset of right-sided limb weakness without slurred speech or numbness. She was known to have a long-standing history of hypertension prior to this presentation with no other significant medical history of note especially of diabetes mellitus, hyperlipidaemia, heart disease, smoking, previous stroke or transient ischaemic attacks. Clinically, she was well, with no aphasia, anopia or neglect. She had a mild right-sided facial weakness and a dense right hemiplegia, with intact sensation. A CT scan of her brain revealed multiple embolic infarcts in the left middle cerebral artery (MCA) territory.

No intracranial vascular study was done at that juncture, but a transthoracic echocardiogram revealed a left atrial myxoma measuring 1.8 cm × 5.8 cm. She underwent an immediate total resection of the myxoma and recovered well post-operatively. She recovered well functionally and became independent in self-care.

Nearly 10 years after the presentation with her ischaemic stroke, she developed right-sided weakness again and left ptosis. Clinical examination revealed mild right face and limb weakness, partial left ptosis with intact pupil response to light, full eye movements, and bilateral limb ataxia. CT of the brain revealed bilateral acute superior cerebellar infarcts with interval evolution of previously known left cortical infarcts. MRI/MR angiogram showed multiple aneurysms arising from the cortical and insular branches of the MCAs bilaterally with the largest aneurysm arising from M2 of the right MCA measuring 9 × 8 mm. A 6 × 6 mm dilatation was also noted from the left anterior cerebral artery, while a tubular dilatation was seen in the left posterior cerebral artery. A digital subtraction angiogram confirmed these findings (Fig. 1, 2). The aneurysms were radiologically characterised as thick walled and likely thrombosed. Echocardiography did not reveal recurrence of the myxoma.

In view of her clinical stability and the likely cause of multiple aneurysms being embolic in nature from known cardiac myxoma, the decision was made for conservative management of her aneurysms with serial imaging. She is being treated for her hypertension as well with

well controlled blood pressure on atenolol. She continues to be monitored on a regular basis with follow-up MR angiogram to evaluate for any further increase in size of the aneurysms or development of new ischaemic infarcts secondary to vessel occlusion.

Discussion

Cardiac myxomas present at a mean age of 50 years, with the greater proportion of the patients being females. Primarily found in the left atrial fossa (nearly 75%), they can interfere with pulmonary and systemic circulation resulting in impaired valve function [1, 2, 5, 6]. They may also spread haematogenously, resulting in varied systemic manifestations. Patients may present with myriad of neurological complications including embolic infarction, intracranial cerebral aneurysm formation, subarachnoid and intra-parenchymal haemorrhage.

Stoane et al. [7] proposed that tumour cells in the emboli lead to perivascular damage, resulting in pseudoaneurysm formation following the obstruction. Another hypothesis proposed by New et al. [8] is that of endothelial damage from tumour emboli resulting in an inflammatory response at the site of injury. There is subintimal growth, destruction of arterial growth and fibroblastic proliferation leading to progressive destruction of the wall with smooth muscle proliferation; they proposed a “neoplastic variety” of aneurysm. This may explain why there is progression of aneurysms despite resection of cardiac myxoma.

A more recent postulate is that tumour emboli get lodged into the vasa vasorum of the peripheral arteries, which eventually lead to weakening of the internal elastic lamina and subsequent aneurysm formation [9]. The histopathological study of general fusiform aneurysms by other reports also attributed a similar mechanism to aneurysm formation with deposition of lipid in and beneath the intima which disrupts the internal elastic lamina and infiltrates the muscular wall [10]. The rupture of the atheroma leads to the transmural extension of the thrombus and create the characteristic fusiform shape of the aneurysm.

Further reasons to support the hypothesis of tumour emboli deposition in vessel wall leading to aneurysmal dilatation are the endocrine and secretory properties of cardiac myxoma cells. They are well known to secrete interleukins such as IL-6 and metalloproteinases which have been postulated to be the cause of the constitutional symptoms experienced by the patients. These secretory products could contribute to the degradation of the extracellular matrix and promote the proliferation of the tumour cells within the vessel wall. Yaguchi et al. [11] measured levels of IL-6 in a 23-year-old patient who presented with multiple cerebellar haemorrhages and were noted to be high in the CSF. After resection of the cardiac myxoma, these IL-6 levels in CSF returned to normal and they have thus suggested the use of CSF levels of IL-6 as a marker for neurological manifestations of cardiac myxoma. Serum levels of IL-6 may also be elevated in patients with cardiac myxoma, which may serve as a more easily obtainable biomarker [9, 12].

In our patient, the presence as well as the extent of intracranial aneurysms was unknown at the time of diagnosis of cardiac myxomas. She was diagnosed with these intracranial aneurysms nearly a decade later. Ours is one of the few case reports in which the intracranial aneurysms were diagnosed nearly a decade after the initial presentation with a cardiac myxoma. Despite the benign nature of cardiac myxomas, metastasis of these tumours due to embolic phenomenon has been recognised as early as 1970 [8] with both local recurrence as well delayed presentation of metastatic embolisms years after resection of the primary tumour. Our patient underwent complete surgical resection of cardiac myxoma and remained

asymptomatic for nearly 10 years. Namura et al. [13] reported a case of a 45-year-old gentleman who presented with recurrent embolic strokes of unknown cause until a final evaluation revealed multiple cerebral aneurysms secondary to a cardiac myxoma detected 10 and 25 years, respectively, after initial presentation. A recent study [14] reported 2 cases of delayed detection of intracranial aneurysms with previously treated cardiac myxoma 14 and 18 years before. In keeping with our case study, intracranial complications can have delayed presentation despite treatment of cardiac myxoma.

Understanding of the progression of myxomatous aneurysms remains unknown especially after the resection of the cardiac myxoma. Considering the theories that suggest the deposition of tumour emboli into the vessel walls leading to vessel wall destruction and progression into aneurysms, aneurysm progression and formation will be expected to occur despite the treatment of the original myxoma [1, 15]. However, whether these aneurysms continue to increase in size remains unknown. In our case study, the patient has been on follow-up with serial MR angiograms which have showed no change in the morphology of these aneurysms.

As can be seen from the angiogram results in the patient, the distribution of aneurysms was primarily concentrated in the MCA territory with involvement of the posterior and anterior circulation as well. This is in keeping with the current literature of the preferential distribution to the MCA territory as compared to atherosclerotic aneurysms that are limited to the vertebrobasilar circulation [16].

The management of aneurysms secondary to atrial myxoma is uncertain. While conservative management is the preferred choice, other options include microsurgery, clipping, coiling, radiotherapy and chemotherapy [17]. There are no randomised controlled trials to address this issue.

In conclusion, in a patient where the diagnosis of the cardiac myxoma is incidental, a detailed history should be elicited with regards to any presentation that is suggestive of a cerebral ischaemia. This would warrant further investigation for cerebral vessel involvement due to propensity of the emboli for intracranial deposition. On the other hand, if the patient's primary presentation is that of ischaemic stroke, initial workup is needed to look for a cardioembolic cause, including atrial myxoma. If brain imaging reveals multiple aneurysms, a cardiac evaluation is warranted to detect myxoma. Since even after surgical resection of the myxoma the possibility of having circulating emboli and aneurysmal development and growth continues, non-invasive evaluation of the cerebral arteries should be done on a regular basis to detect the presence of delayed formation of intracranial aneurysms. Further research into possible biomarkers such as IL-6 that are known to be secreted by the tumour cells could potentially help in monitoring of such patients.

Acknowledgement

The authors would like to acknowledge the patient for allowing us to use the clinical information for the publication of this case report.

Statement of Ethics

The subject for this case report has given the consent to use unidentified material for the purposes of this study. All the clinical data has been anonymized to prevent identification.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

Funding Sources

No funding sources were used for the purposes of this study.

Author Contributions

Swati Jain was responsible for gathering clinical data and writing this case report. Vincent Nga provided valuable contributions towards understanding the neurosurgical aspect of this case and reviewing the paper. Narayanaswamy Venketasubramanian provided key insights into understanding the complexity of follow-up and management of this case, guided the first author and reviewed the paper.

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Fig. 1. Right internal carotid angiogram.

Fig. 2. Left internal carotid angiogram.