

ILLUSTRATIVE TEACHING CASE

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Cardiac Myxoma Embolization Causing Ischemic Stroke and Multiple Partially Thrombosed Cerebral Aneurysms

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A 31-year-old male of South Asian origin, with no known vascular risk factors, presented for evaluation of acute onset impaired comprehension and slurring of speech. He also reported holocranial headaches of 2 weeks duration with no telltale features of raised intracranial pressure. No other focal neurological symptoms or systemic symptoms of concern were noted. Physical examination revealed right-sided upper motor neuron facial paresis, nonfluent aphasia, and dysarthria. His baseline National Institutes of Health Stroke Scale score was 4. No signs of meningeal irritation were noted. Non-contrast computerized tomography of the head revealed a hypodensity in the left temporoparietal region suggestive of an acute infarct, along with chronic infarcts in the right cerebellum, right parietal lobe, and left thalamus. In addition, multiple hyperdense areas (largest being in the left perisylvian region) were observed in the supratentorial regions as well (Figure 1A and 1B). Computed tomography angiography of intracranial vessels followed by conventional digital subtraction cerebral angiography revealed multiple dysplastic/fusiform aneurysms, 3 involving the right pericallosal artery, 2 involving the distal right middle cerebral artery M4 branches, and 1 involving the right callosomarginal artery (Figure 1C). The inferior branch of the left middle cerebral artery was dysplastic with a partially thrombosed proximal aneurysm and a distal fusiform aneurysm (Figure 1D). Contrast-enhanced magnetic resonance imaging of the brain confirmed the presence of an acute left middle cerebral artery infarct and multiple aneurysms, with the largest being

a partially thrombosed aneurysm in the left sylvian fissure measuring 13 mm (Figure 2A through 2D). There were no parenchymal structural lesions or macro hemorrhages. Hematology investigations were unremarkable. A transthoracic echocardiogram was performed, which revealed a large mobile mass measuring 1.8×3.1 cm with calcific rim and echo lucent space in its substance, attached on the atrial side of the anterior mitral valve with limited attachment on the interatrial septum. No evidence of systolic dysfunction was observed. The differential diagnosis entertained in view of the clinical, neuroimaging, as well as cardiac imaging findings were intracardiac tumor-like myxoma versus infective or non-infective endocarditis. In view of the high-risk cardioembolic source, patient was deemed to be a candidate for early surgical resection of the cardiac lesion, which was duly performed within a week of hospitalization. Postoperative histopathologic evaluation of the resected cardiac pathology revealed features consistent with cardiac myxoma (Figure 3A and 3B). No intraoperative or postprocedural complications were noted. The cerebral aneurysms being multiple, unruptured, and secondary to underlying cardiac myxoma, were not subjected to open surgery or endovascular embolization. Plan for potential combined chemoradiotherapy and surgical intervention will be discussed based on findings of follow-up parenchymal and angiographic studies. The patient was maintained on single antiplatelet agent for secondary stroke prophylaxis, with advice for speech and language rehabilitation for his residual neurological deficits.

Key Words: dysarthria ■ headache ■ male ■ risk factors ■ speech

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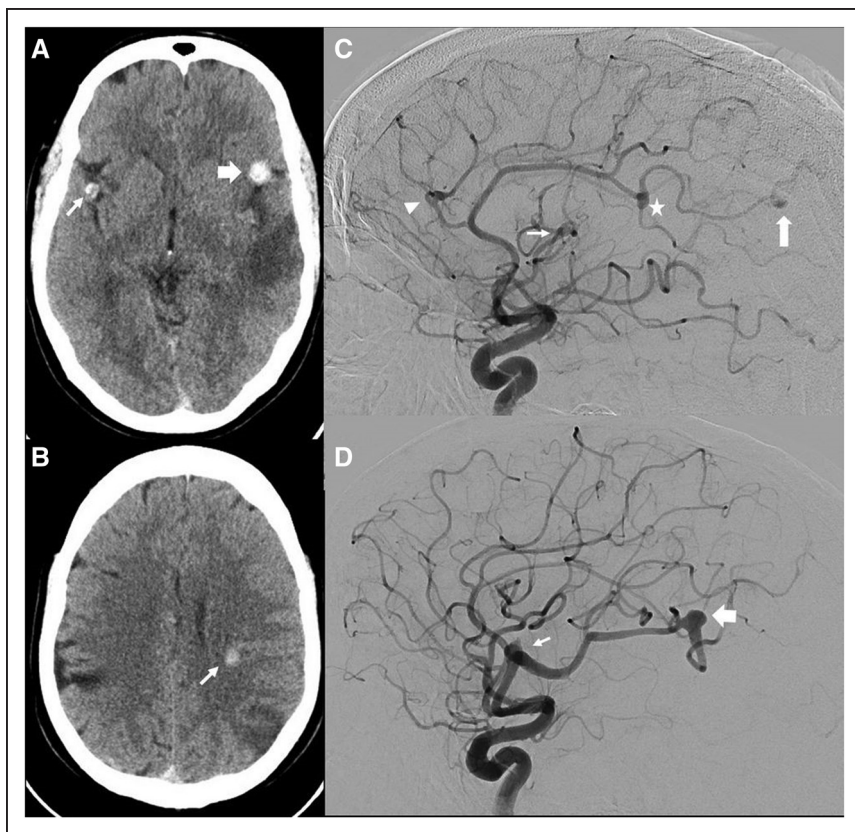


Figure 1. Noncontrast computerized tomography.

Noncontrast computerized tomography head showing multiple hyperdense lesions on axial images (**A**) in the left sylvian fissure (thick arrow); right sylvian fissure (**A**; thin arrow) as well as in the left posterior subcortical frontal region (**B**; thin arrow). **C**, Invasive cerebral angiogram of right internal cerebral artery depicting fusiform aneurysms involving the right callosomarginal artery (arrow head), pericallosal artery (star and thick arrow), as well as middle cerebral artery (MCA; thin arrow). **D**, Lateral projection views of left internal cerebral artery depict dysplastic inferior branch of MCA with a partially thrombosed aneurysm (thin arrow), as well as a distal fusiform aneurysm (thick arrow).

DISCUSSION

Cardiac myxoma is the most common primary cardiac tumor, accounting for up to 80%, with an estimated annual incidence of 0.5 per million population per year.¹⁻³ More than 80% of cardiac myxomas arise from the left atrium,² with multitude of presentations in the form of cardiac obstructive symptoms, embolization (cerebral and/or systemic) as well as constitutional symptoms.¹⁻³

Fifty percentage of cardiac myxoma patients present with symptoms related to mitral valve obstruction (dyspnea, dizziness, palpitations, and congestive heart failure) and can occur in up to 70% of them during the natural course of the illness.² Constitutional symptoms in the form of fever, weight loss, and fatigue may occur in about 58% of those with cardiac myxoma. Systemic embolization can be noted in one-third of cases at any time during the course of the illness.¹⁻³ Neurological symptoms

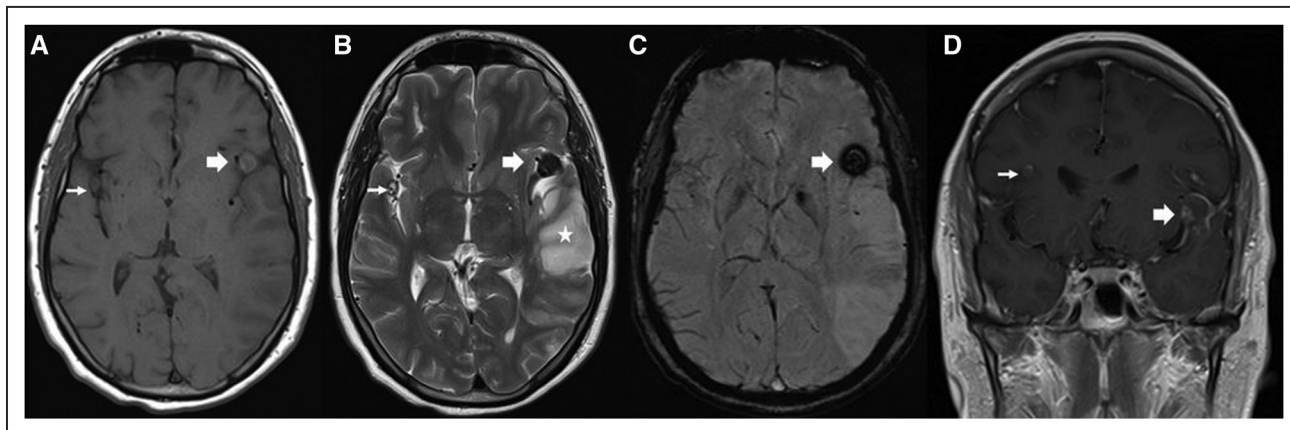


Figure 2. Contrast-enhanced magnetic resonance imaging brain.

Contrast-enhanced magnetic resonance imaging brain showing (**A**) isointense circumferential lesions on left (thick arrow) and right sylvian fissure (thin arrow) on precontrast T1 axial images. **B**, T2 axial sections reveal hypointense signal on the left sylvian fissure (thick arrow), mixed intense signal on the right sylvian fissure (thin arrow). The lesion in left sylvian fissure is hypointense on susceptibility weighted sequences (**C**; thick arrow) and exhibits circumferential enhancement of the vessel wall involving the left middle cerebral artery (MCA) in the sylvian fissure (**D**; thick arrow), with nodular enhancement on right side (**D**; thin arrow) on contrast-enhanced T1 coronal sequences. The imaging findings on the left sylvian fissure is consistent with a partially thrombosed aneurysm involving the posterior insular branch of the left MCA. In addition, there is evidence of acute infarct involving the left MCA territory (**B**; star).

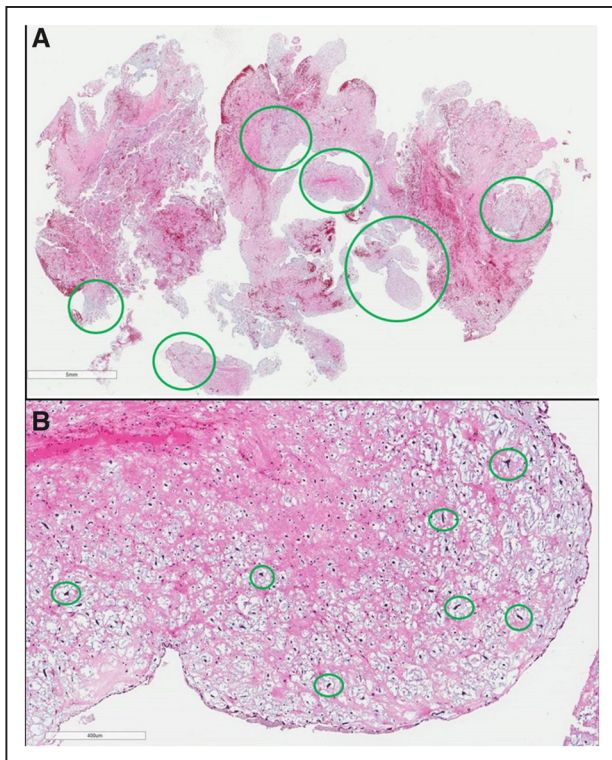


Figure 3. Hematoxylin and eosin staining.

Hematoxylin and eosin staining of the resected tissue (**A**) on low power view shows blue background of acid mucopolysaccharides with mesenchymal cells (depicted in green circles), with high power view (**B**) demonstrating round, plump, and stellate mesenchymal cells consistent with cardiac myxoma.

have been documented in about 26% to 45% of cardiac myxomas.² Cerebral embolization may present commonly as ischemic infarcts^{1,2} and rarely with myxomatous intracranial aneurysms, brain parenchymal myxomatous metastases, as well as intracerebral hemorrhage.^{3–5} Transthoracic echocardiography gives the initial clue toward the presence of a cardiac mass, with transesophageal echocardiogram) providing further details about the location as well as mobility, especially for small-sized lesions and biatrial multiple cardiac tumors.^{6,7} However, neither of the abovementioned techniques are helpful to differentiate cardiac myxomas from other cardiac tumors as well as intracardiac thrombi.⁷ Multimodality imaging in the form of contrast-enhanced cardiac magnetic resonance imaging has played a vital role in reliably diagnosing cardiac myxomas preoperatively. Cardiac myxoma exhibits T1 heterogenous hypointensity relative to the myocardium, T2 hyperintensity, as well as heterogenous contrast enhancement on magnetic resonance imaging, which are unique to myxoma compared with other primary cardiac tumors or cardiac thrombus.⁷ Surgical resection is the definitive treatment option for cardiac myxoma, as medical management even with anticoagulant therapy has been proven ineffective to prevent recurrent embolic events.^{2,6} As development of embolic phenomenon as well as sudden cardiac death occur in $\approx 10\%$ of patients

awaiting surgery, cardiac myxomas should be considered a surgical emergency, with avoidance of potential delays in those without any obvious surgical contraindications.^{6,7} Despite the lack of global consensus about the ideal surgical procedure for cardiac myxoma resection, the in-hospital mortality related to surgery seldom exceeds 3% as per available literature evidence,⁶ thereby contributing to excellent early and mid-term results if resected promptly. Antiplatelets as well as anticoagulants (Warfarin) have been traditionally used for secondary stroke prophylaxis, both pre- and postcardiac myxoma resection (for a variable duration), with no clear available evidence-based guidelines or recommendations as of now.^{1,2}

To date, there are fewer than 60 published cases of cerebral myxomatous aneurysms in literature, the first being in 1966,^{2,8} with partially thrombosed ones being rarer. Rarity of this entity has contributed to lack of knowledge about the natural course of evolution of cerebral myxomatous aneurysms, in turn leading to lack of definite management guidelines as well.^{8–10} Our patient was unique in that he had simultaneous neuroimaging evidence of both manifestations of myxomatous cerebral embolization, which include the commoner ischemic infarct as well as the less common myxomatous aneurysms.³ The latter is more often reported as a delayed complication of cardiac myxoma with mean duration between tumor resection and aneurysm detection varying between 2 and 300 months.^{3,4,8} A review of 37 published cases of myxomatous aneurysms revealed the median age of 38 years (range, 10–69 years), with female:male ratio of 2.7:1.¹⁰ These aneurysms are usually multiple, of fusiform/saccular morphology and have predilection for distal branches of middle cerebral arteries.^{2,3} Advancements in neuroimaging modalities have contributed to better delineation and identification of both myxomatous aneurysms as well as myxomatous metastases.^{4,5} On noncontrast computerized tomography brain, these myxomatous aneurysms seem hyperdense, on account of accumulation of myxoid matrix or calcification in the aneurysmal wall.¹⁰ Although the exact mechanism of development of myxomatous aneurysms is still enigmatic, the most plausible and accepted one is the metastasize and infiltrate theory, whereby the myxoma fragments embolize from the heart, seed in the cerebral vessel wall, initiate an inflammatory cascade, in-turn leading to dilatation and aneurysm formation.^{1–3,8,10} High levels of interleukin-6 in the CSF produced by the cardiac myxoma cells contribute to upregulation of MMPs (matrix metalloproteinases), which in turn promotes degradation of extracellular matrix and myxoma invasion into the walls of cerebral arteries, ultimately resulting in aneurysm formation.^{3,10} This theory is substantiated by demonstration of proliferation of myxomatous cells in the aneurysmal wall as well as the invasion of internal elastic lamina.¹⁰ An alternative less known hypothesis for myxomatous aneurysm pathogenesis is the vascular damage

TAKE-HOME POINTS

- Cardiac myxoma is the most common primary cardiac tumor and are notorious for both early as well as delayed neurological manifestations.
- Ischemic stroke is the most common neurological manifestation of cardiac myxoma, with up to 0.5% of all ischemic strokes being attributed to myxomatous embolization.
- Myxomatous aneurysms and myxomatous cerebral metastases are rarer neurological complications of cardiac myxomas, with putative pathological mechanism being metastasize and infiltrate theory.
- Mobility rather than size of the cardiac myxoma determines the embolization potential.
- Concomitant ischemic strokes and cerebral aneurysms should make one suspect the possibility of the underlying cardiac myxomas, despite being a rare entity.

theory, whereby the postembolic vascular damage and subsequent endothelial scarring contributes to hemodynamic alteration in cerebral vascular dynamics resulting in aneurysm formation.¹⁰

On account of the rarity of the cases, little is known about the natural history of myxomatous aneurysms. A meta-analysis of 37 published cases of myxomatous aneurysms highlighted that 78.4% of them were managed conservatively, with 75.9% among them demonstrating stability or regression on follow-up imaging studies.¹⁰ Hence for unruptured myxomatous aneurysms, majority of the researchers propose conservative management, with serial angiographic studies on follow-up (initially at 3 months and later on at 6–12 months interval as per stability), to look for interval change, especially any enlargement. About 20.7% cases in the study by Zheng et al¹⁰ demonstrated enlargement on follow-up angiographic studies, with all-cause mortality being 3.4%. However, there is paucity of data about the risk of rupture of cerebral myxomatous aneurysms in literature on account of rarity of cases. The risk of rupture of primary intracerebral aneurysms cannot be extrapolated to cerebral myxomatous aneurysms on account of the different respective pathological mechanisms involved.

There are isolated published reports pertaining to the role of microsurgical resection/endovascular coiling,⁸ chemotherapy, and radiotherapy⁹ in management of myxomatous aneurysms, although a definitive guideline is still lacking. In case of ruptured or enlarging aneurysm, decision to treat should be made on a case by case basis. Given that aneurysms related to cardiac myxoma are multiple, and often times involve terminal intracerebral vessels, both open microsurgical and endovascular techniques have their limitations and may not assure a complete cure. Open microsurgery may include resection or trapping of the aneurysm. Application of clips may not be feasible given the friable nature of the vessel wall. Standard endovascular coil embolization techniques are not possible given the fusiform nature of these aneurysms in majority of cases. In addition, invaded tumor cells in the vessel wall remain unattended in endovascular treatments, thereby potentially contributing to further invasion as well as recurrence.⁸ There is lack of evidence for antithrombotic

medications in management of thrombosed cerebral myxomatous aneurysms especially after resection of the cardiac myxomas. As there is histopathologic evidence of actively proliferating tumor cells in the myxomatous aneurysmal wall, chemotherapy (doxorubicin/etoposide/carboplatin) as well as radiotherapy have also been documented to be effective in individual cases.^{9,10}

On account of multiple fusiform aneurysms with no foci of active hemorrhage on imaging, our patient is being planned for follow-up vascular imaging in 3 months to assess for any interval evolution, with potential for microsurgical resection with bypass of the largest aneurysm (left perisylvian middle cerebral artery) along with chemoradiotherapy in case of any lesion enlargement or new focal neurological symptoms.

CONCLUSIONS

Cardiac myxoma may manifest de novo with neurological symptoms, with ischemic strokes being the most common presentation and myxomatous aneurysms being rarer. On account of the rarity of the latter, treatment protocols are unclear and even surgical resection of the primary cardiac tumor might not completely prevent delayed occurrence of myxomatous aneurysms or myxomatous cerebral metastases.

ARTICLE INFORMATION

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Disclosures

None.

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