Dynamic Angiographic Nature of Cerebral Mycotic Aneurysms in Patients With Infective Endocarditis

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Case 1
A 41-year-old male with nonischemic cardiomyopathy and left ventricular assist device on coumadin presented with constitutional symptoms for 1 week. Blood cultures were drawn. The next day, he developed severe headache (Hunt–Hess grade II), and noncontrast head computed tomography (CT) showed Fisher grade II subarachnoid hemorrhage over bilateral frontal convexities. International Normalized Ratio was 9. The blood cultures grew methicillin-resistant *Staphylococcus aureus* within a day. He was diagnosed with an infected left ventricular assist device and started on intravenous vancomycin. Brain CT angiography was negative for any vessel abnormality. Cerebral angiography on post bleed day 1 showed areas of subocclusive emboli in the left M3 segment of the middle cerebral artery (MCA) and left pericallosal artery, but did not reveal any identifiable source for subarachnoid hemorrhage. On post bleed day 2, the patient developed left frontal seizures that eventually progressed to status epilepticus. Repeat CT head showed a new intraparenchymal hemorrhage within the left frontal operculum, measuring 1.8 cm in diameter. Repeat cerebral angiography on post bleed day 2 revealed a new left M3 fusiform mycotic aneurysm (MA) in the exact location of the previously seen left M3 segment embolus. The pericallosal branch embolus had progressed to near vessel occlusion rather than aneurysm formation. The patient’s family withdrew care because of his poor cardiac and neurological status (Figure 1).

Case 2
A 31-year-old female with history of Tetrology of Fallot that had been repaired when she was a child, and previous infective endocarditis secondary to intravenous drug abuse requiring aortic valve replacement, presented with constitutional symptoms after relapsing with intravenous drug abuse. Blood cultures grew *Streptococcus viridans* and peptostreptococcus, and she was diagnosed with prosthetic aortic valve infective endocarditis along with paravalvular abscess. She was started on intravenous ceftriaxone. Magnetic resonance imaging of the brain was performed for a recent episode of transient aphasia and showed multiple punctate foci of susceptibility in bilateral cerebral and cerebellar hemispheres compatible with microhemorrhages, and 1 foci of old left posterior parieto-occipital subarachnoid hemorrhage. Brain magnetic resonance angiography was negative for any vessel abnormality. Cerebral angiography demonstrated 1 fusiform MA (2 mm) of the right M4 parieto-occipital MCA branch, and 1 saccular MA (2 mm) of the left superior M2 MCA branch. Medical management with antibiotics was recommended given the risk of surgical/endovascular treatment and because cardiac surgery was not imminent. Repeat cerebral angiography 2 weeks later was stable, however, repeat cerebral angiography 4 weeks from the first angiogram revealed significant enlargement of the right MCA MA, whereas the left MCA MA had completely resolved. The right MCA aneurysm was treated with coiling and Onyx embolization. She underwent aortic valve replacement the next day (Figure 2). Follow-up angiography a month after treatment showed no residual or new aneurysms.

Discussion
Intracranial MA are rare, accounting for 0.7% to 5.4% of all cerebral aneurysms.1 They are localized arterial dilatations caused by septic emboli, commonly in patients with infective endocarditis (IE) or similar sources of central bacterial embolus. Infection of the arterial wall causes inflammation and neutrophil infiltration followed by degradation of the media and adventitia, fragmentation of the internal elastic lamina and proliferation of the intima. Pulsatile pressure on the weakened vessel wall leads to aneurysm development and growth. Histological sections in animal models of cerebral MA have shown an acute inflammatory response to bacterial invasion of the muscularis layer with early aneurysmal dilatation as early as 24 hours after septic embolism development.2 Rupture of MA can be devastating and accounts for 5% of the neurological complications in patients with IE. A recent meta-analysis reported a 13% mortality in patients with MA1 and ≤80% mortality if rupture occurs.3 The overall prevalence of cerebral MA in IE remains unknown. Extracranial MA are uncommon, but can involve the aorta, peripheral, and visceral arteries. The prevalence of infected aortic aneurysms is 0.7% to 1% of all surgically treated aortic aneurysms. The femoral and superior mesenteric arteries are the most frequently involved peripheral and visceral artery, respectively.4
Cerebral angiography is the “gold standard” for detection of MA. Some findings on angiography that point toward MA are the fusiform shape, multiplicity, distal location, and change in size on follow-up angiography. The diagnostic yield of cerebral angiography in IE was evaluated in 2 recent studies. Hui et al\(^5\) found MA in 8.9% (15/168) of patients who underwent cerebral angiography, of which 93.3% presented with intracranial hemorrhage. CT and magnetic resonance angiography was performed in 7 and 6 of these patients, respectively, and identified MA in 3 (42.9%) and 2 (33.3%) cases, respectively. In patients

**Figure 1.** Initial cerebral angiogram (A) showing subocclusive filling defects in the left pericallosal (black arrows) and M3 middle cerebral artery branch (white arrow) arteries. Follow-up angiography shows near occlusion of the left pericallosal branch (B), and fusiform mycotic aneurysmal dilatation of the previous left M3 lesion (C and D).

**Figure 2.** Initial cerebral angiogram showing fusiform mycotic aneurysm (MA) of right M4 parieto-occipital middle cerebral artery (MCA) branch (A), and saccular MA of the left superior M2 MCA branch (C). Follow-up angiography 4 weeks later shows significant enlargement of the right MCA MA (B), and complete resolution of the left (D).
who presented with hemorrhage, 14 of 63 (22.2%) harbored an MA. In a similar study, Monteleone et al identified MA in 7 of 151 (4.6%) patients who underwent cerebral angiography. Only one MA >3 mm was identified by noninvasive imaging (sensitivity, 0.17). This is in keeping with the diagnostic sensitivity of noninvasive imaging, which decreases dramatically for the detection of intracranial aneurysms <3 mm. These rates of MA detection represent the prevalence in patients with IE deemed at high enough risk to warrant cerebral angiography, and not the prevalence in all patients with IE. Monteleone calculated a negative predictive value of 0.977 (95% confidence interval, 0.879–0.996) of the absence of intracranial hemorrhage on magnetic resonance imaging for diagnosis of MA. The negative predictive value of clinical examination features such as the absence of focal neurological deficits and altered mental status was 0.990 and 0.944, respectively. However, caution should be exercised with the latter because occult magnetic resonance imaging cerebral lesions, in particular, cerebral microbleeds, and acute ischemic lesions, are frequent in IE (≤72%). There are currently no standards to guide clinical decision making for treatment of MA. MA are typically thin-walled and friable, often with a wide or absent neck, making them difficult to treat. Treatment modalities include antimicrobial agents, surgery, endovascular treatment, or a combination of therapies. Ruptured aneurysms should be immediately secured via open surgical or endovascular means, with the choice individualized based on aneurysm morphology, patient comorbidities, and the presence of associated intracerebral hemorrhage. For unruptured MA, the decision is not as clear. Although antibiotic treatment guided by blood cultures is the mainstay of therapy, invasive management is advised based on surgical risk. Antibiotic therapy alone is reasonable in high-risk surgical cases. Close angiographic follow-up is critical for MA managed conservatively. As demonstrated in our cases, focal occlusions from septic emboli and MA are dynamic lesions, with potential for rapid change even within the same patient. The evolution of MA with antibiotic therapy can be unpredictable: they may disappear, regress, persist, enlarge, or rupture. Antimicrobial therapy can be continued without intervention for aneurysms that resolve or regress. However, endovascular or surgical methods should be considered for aneurysms that increase in size despite antimicrobial therapy. For unruptured MA with low surgical risk, invasive treatment is advised.

Summary

MA are rare, and difficult to treat cerebrovascular lesions most commonly seen secondary to hematogenous spread of septic emboli from a proximal source, such as bacterial endocarditis. Cerebral angiography is the gold standard imaging modality for detecting MA. Although the sensitivity of noninvasive CT and magnetic resonance imaging to detect small MA is low, the absence of intracranial hemorrhage on noninvasive imaging conveys a high negative predictive value. Thus, patients with IE presenting with intracranial hemorrhage should undergo vascular imaging, preferably with cerebral angiography. There have been no randomized clinical trials or prospective cohort studies evaluating various treatment approaches. Invasive treatment is based on rupture status and surgical risk. However, when MA are managed conservatively, close angiographic follow-up is warranted given its unpredictable nature and potential for rapid changes even on appropriate antibiotics. In addition, focal occlusions from septic emboli should be considered high risk for MA formation.

TAKE-HOME POINTS

- Patients with infective endocarditis presenting with intracranial hemorrhage should undergo vascular imaging, preferably with cerebral angiography that remains the gold standard for diagnosis of mycotic aneurysms (MAs)
- The sensitivity of noninvasive computed tomography and magnetic resonance imaging to detect small MA is low, but the absence of intracranial hemorrhage on noninvasive imaging conveys a high negative predictive value for MA detection.
- MAs are dynamic lesions with potential for rapid change. If conservative antimicrobial management is pursued, close angiographic follow-up is warranted.
- Septic emboli in the cerebral vasculature can progress to vessel occlusion or bloom into MAs. Focal occlusions from septic emboli should be considered high risk for MA formation.

Disclosures

None.

References


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