*Case Report*

Short-term aneurysm formation and rupture due to septic embolism diagnosed with a thrombus retrieved from another occluded artery

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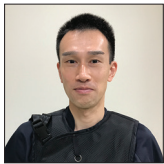
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ABSTRACT

Background: In rare cases, septic embolism is diagnosed on the basis of pathological findings of retrieved thrombi. Infected aneurysms can rapidly form and rupture after septic embolism, leading to a poor prognosis. We report a case of subcortical hemorrhage due to an infected aneurysm forming shortly after septic embolism in the left anterior cerebral artery.

Case Description: In this case, the diagnosis of septic embolism was made on the basis of pathological findings of a thrombus retrieved from the simultaneously occluded left middle cerebral artery, and endovascular embolization of the infected aneurysm was performed.

Conclusion: The pathological findings of a retrieved thrombus were useful for making a diagnosis of septic embolism. The possibility of short-term formation and rupture of an infected aneurysm after septic embolism should be noted. Endovascular embolization of occluded vessels due to septic embolism may prevent aneurysm formation and subsequent bleeding.

Keywords: Aneurysm, Pathology, Rupture, Septic embolism, Thrombus

INTRODUCTION

Recently, the usefulness of mechanical thrombectomy for large vessel occlusion due to infectious endocarditis has been reported.[9,10] Early diagnosis of stroke due to septic embolism is challenging, especially in patients with few signs of infection. In rare cases, septic embolism is diagnosed on the basis of pathological findings of retrieved thrombi.[2,4] Infected aneurysms can rapidly form and rupture after septic embolism, leading to a poor prognosis. We report a case of subcortical hemorrhage due to an infected aneurysm forming shortly after septic embolism in the left anterior cerebral artery (ACA), which was diagnosed on the basis of pathological findings of a thrombus retrieved from the simultaneously occluded left middle cerebral artery (MCA) and was treated by endovascular embolization.

CASE REPORT

History and examination

A 58-year-old man collapsed on the street and was raced to our emergency room. He had a prior history of hypertension, dyslipidemia, and dysuria. Time last known well was 90 min before arrival. His blood pressure was 155/81 mmHg and his pulse rate was 90 bpm. His body temperature was 36.9°C. On neurologic examination, his Glasgow Coma Scale score was E3V1M5 (total score 9). He had total aphasia, right-sided hemiparesis, and left conjugate deviation of the eyes. His initial National Institutes of Health Stroke Scale (NIHSS) score was 20. Hematology test results were as follows: white blood cell count 9500/μL; C-reactive protein 3.46 mg/dL; brain natriuretic peptide <5.8 pg/mL; and D-dimer 1.1 μg/mL. Computed tomography (CT) of the head showed no intracranial hemorrhage and early ischemic change was absent (CT – Alberta Stroke Program Early CT Score 10). Diffusion-weighted images from magnetic resonance imaging of the head showed a high signal intensity area in the left MCA territory (diffusion-weighted image – Alberta Stroke Program Early CT Score 4), with a small high signal intensity area in the peripheral region of the left ACA [Figure 1a], which was barely delineated in fluid-attenuated inversion recovery sequence. Magnetic resonance angiography showed occlusion of the M1 segment of the left MCA. Although the onset of symptoms was unknown on arrival, magnetic resonance imaging results indicated it to be within 6 h. Mechanical thrombectomy was performed with a door-to-puncture time of 75 min. Recombinant tissue plasminogen activator was not administered.

Thrombectomy

The right femoral access was obtained. A 9-French balloon guiding catheter was placed in the left internal carotid artery. The left internal carotid artery angiography showed occlusion of the distal part of the M1 segment of the left MCA and the peripheral region of the pericallosal artery of the left ACA [Figures 1b-d]. The stent retriever (Embotrap II 5.0 × 33 mm; Cerenovus, Irvine, CA, USA) was deployed from the M2 segment to the M1 segment and retracted into the aspiration catheter (REACT 71; Medtronic, Minneapolis, MN, USA) in the M1 segment that was proximal to the thrombus. On the second attempt, the clot was retrieved, and reperfusion of the left MCA was achieved with a puncture-to-reperfusion time of 51 min [Figure 1e]. Because the occlusion site of the left pericallosal artery was peripheral and collateral blood flow was observed distal to the occlusion site, thrombectomy was not performed [Figures 1f and g].

Course after thrombectomy

After thrombectomy, aphasia and right-side hemiparesis improved quickly. His NIHSS score improved to 4.

Electrocardiographic monitoring showed no atrial fibrillation. Head magnetic resonance imaging obtained 4 h after thrombectomy showed a reduced diffusion-weighted imaging high signal intensity area in the left MCA territory with a small high signal intensity area in the peripheral region of the left ACA [Figure 2a]. Head CT obtained 24 h after thrombectomy showed a small high-density area in the left ACA territory [Figure 2b]. He was diagnosed with hemorrhagic infarction and antihypertensive therapy was started. Thirty-eight hours after thrombectomy, aphasia and right-sided hemiparesis appeared again. Head CT showed subcortical hemorrhage in the left ACA territory and intraventricular hemorrhage [Figure 2c]. Head CT obtained 48 h after thrombectomy showed enlargement of subcortical hematoma and intraventricular distension [Figure 2d]. After endoscopic intraventricular hematoma removal, septostomy, and third ventriculostomy, a ventricular drain was placed. In addition, endoscopic subcortical hematoma removal was performed from the parietal lobe side. After the intracranial pressure was reduced, the operation was terminated, leaving the hematoma in the deep area around the hemorrhage source. Postoperative CT showed residual hematoma around the infarct area in the left ACA territory [Figure 2e]. On the 4th day of hospitalization, fever in the 38°C range appeared, and blood testing showed elevated such inflammatory markers as white blood cell 8400/μL and C-reactive protein 7.07 mg/dL, which were considered postoperative changes.

The retrieved thrombus

On the 6th day of hospitalization, the diagnosis was made on the basis of pathological findings of the thrombus retrieved from the left MCA. The thrombus was a single mass of 8 × 5 mm, with a visually recognizable red component mixed with a localized white component. It was firm and maintained the shape of the vessel at the distal part of the M1 segment and the bifurcation [Figure 3A]. Hematoxylin-eosin staining showed that the thrombus consisted mainly of fibrin and platelets, with bacterial colonies and focally abundant neutrophils at the margins of the thrombus. Gram staining showed that the bacteria were Gram-positive cocci [Figures 3B-G]. Consistent with the visually recognizable white component of the thrombus, Gram-positive cocci were observed [Figures 3A-C].

Embolization

After the pathological diagnosis of the thrombus was made, an infected aneurysm was suspected of the source of the left frontal subcortical hemorrhage. CT angiography was performed, which revealed an aneurysm in the peripheral region of the left ACA [Figure 4a]. On the 7th day of hospitalization, endovascular embolization was performed. The left femoral access was obtained. A 6-French guiding

catheter was placed in the left internal carotid artery. The left internal carotid artery angiography and three-dimensional rotational angiography showed a 5.8 mm saccular aneurysm in the peripheral region of the pericallosal artery of the left ACA [Figures 4b-d]. The location of the aneurysm coincided with the occlusion area identified during thrombectomy [Figures 1d and g]. No aneurysm was formed in the recanalized distal part of the left M1 segment. A microcatheter (Marathon; Medtronic) was navigated into the aneurysm using a microguidewire. Coils and *n*-butyl cyanoacrylate were used to embolize the aneurysm and the parent artery of the left pericallosal artery. Posttreatment angiography showed complete occlusion of the aneurysm [Figures 4e and f].

Postoperative course

A diagnosis of septic embolism was made, and ceftriaxone and vancomycin were administered. *Streptococcus gallolyticus* developed from the blood culture taken on the 6th day of hospitalization. The antibiotics were switched to aminobenzylpenicillin, and the patient was treated for 5 weeks after the blood culture became negative.
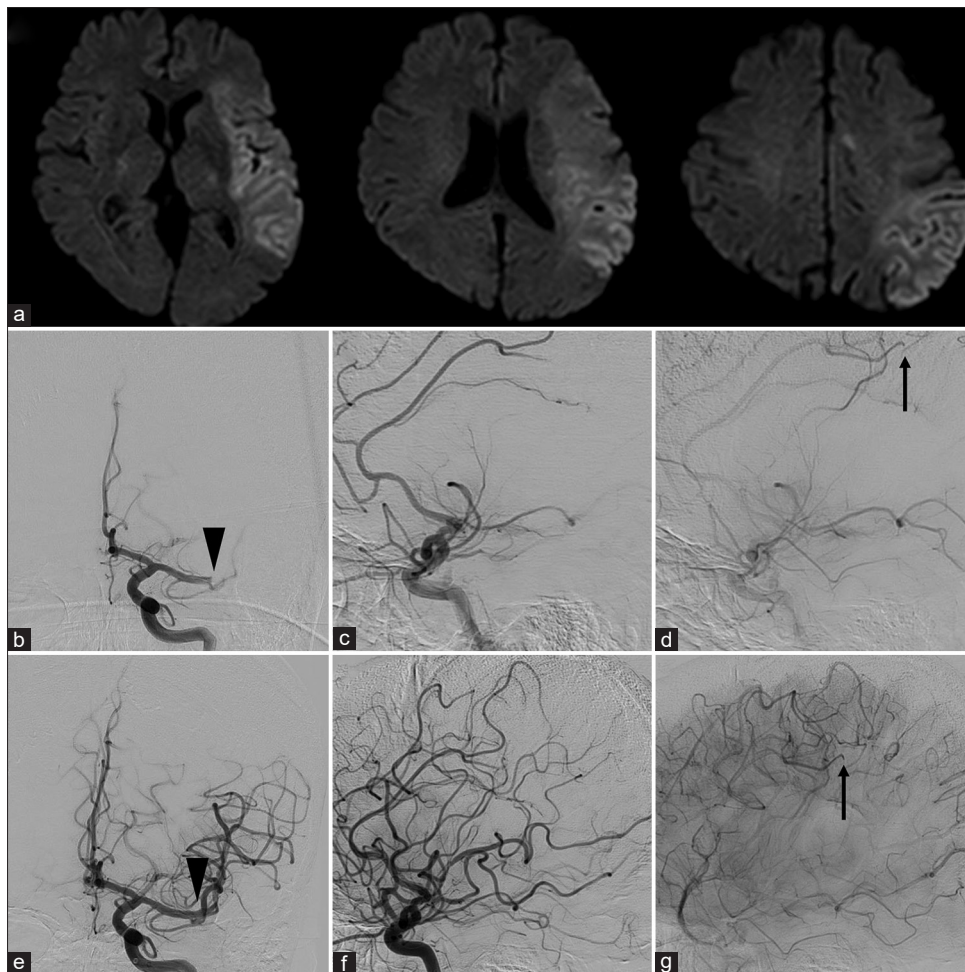

Figure 1: Imaging findings before and during thrombus retrieval. (a) Magnetic resonance imaging diffusion-weighted imaging showing a high signal intensity area in the left middle cerebral artery territory (diffusion-weighted imaging – Alberta Stroke Program Early Computed Tomography Score 4), with a small high signal intensity area in the peripheral region of the left anterior cerebral artery. (b and c) Early-phase left internal carotid artery angiography before thrombectomy (b: anteroposterior view and c: lateral view) showing occlusion of the distal left middle cerebral artery (arrowhead). (d) Late-phase left internal carotid artery angiography before thrombectomy (lateral view) showing occlusion of the left peripheral pericallosal artery (arrow). (e and f) Early-phase left internal carotid artery angiography (e: anteroposterior view and f: lateral view) after thrombectomy showing recanalization of the M1 segment (arrowhead). (g) Late-phase left internal carotid artery angiography after thrombectomy showing occlusion of the left peripheral pericallosal artery (arrow).
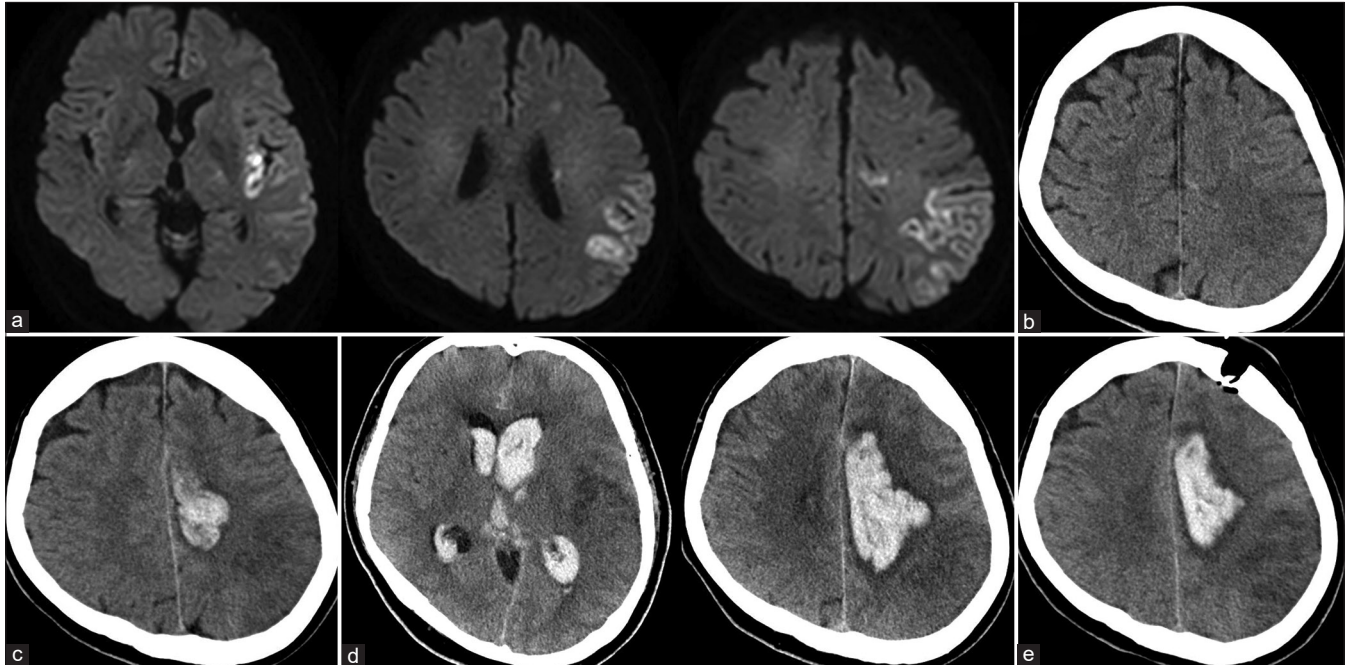
Figure 2: Imaging findings after thrombus retrieval. (a) Head magnetic resonance imaging obtained 4 h after thrombectomy showing a reduced diffusion-weighted imaging high signal intensity area in the left middle cerebral artery territory with a small high signal intensity area in the peripheral region of the left anterior cerebral artery. (b) Head computed tomography obtained 24 h after thrombectomy showing a small high-density area around the infarct area in the anterior cerebral artery territory. (c) Head computed tomography obtained 38 h after thrombectomy showing subcortical hemorrhage in the left anterior cerebral artery territory and intraventricular hemorrhage. (d) Head computed tomography obtained 48 h after thrombectomy showing enlargement of subcortical hematoma and intraventricular distension. (e) Postoperative computed tomography showing residual hematoma around the infarct area in the left anterior cerebral artery.

Because of his poor general condition, transesophageal echocardiography was not performed. Postoperative magnetic resonance angiography and CT angiography of the head showed no new intracranial aneurysms. On the 49th day of hospitalization, he was transferred to a rehabilitation hospital. At the time of transfer, he was still suffering from aphasia and right hemiparesis (NIHSS score of 21), with a modified Rankin scale score of 5.

DISCUSSION

The patient had a left MCA occlusion and a peripheral left ACA occlusion due to septic embolism. After thrombectomy, successful reperfusion of the left MCA was achieved, and his neurological symptoms resolved markedly [Figure 5a]. Early after thrombectomy, neurological symptoms worsened again due to rupture of the infected aneurysm in the peripheral left ACA [Figure 5b]. After the exacerbation of neurological symptoms, pathological findings of the retrieved thrombus confirmed the diagnosis of septic embolism. Although endovascular embolization of the infected aneurysm was successfully performed and antibiotic therapy was initiated, the prognosis was poor due to intracranial hemorrhage that had already occurred [Figure 5c].

White clots have been reported to be associated with atypical etiologies, in particular infective endocarditis.[13] In this case, the thrombus had a mixture of red and white components, and the white component and the Gram staining-positive area were consistent. The thrombus was firm and maintained the shape of the vessel at the distal part of the M1 segment and the bifurcation. Unlike other clots, septic emboli contain bacterial colonies, inflammatory cells, and hyaline.[11,14] Emboli of infectious endocarditis may be tighter due to higher inflammatory contents and compacted fibrotic nature.[12]

Infected aneurysm is caused by infection and destruction of the arterial wall. Infected emboli occlude the vessel and lead to cerebral infarction and subsequent focal infection. Infection can spread from the inside to the outside of the vessel wall, leading to aneurysm formation.[3] As shown in this case, if recanalization occurs when the intima has already become fragile, the vessel may dilate and form an aneurysm. In this case, since bacteria were distributed around the clot, infiltration may have been more likely to occur. Infected aneurysms carry higher risk of rupture and fatal bleeding when compared to other aneurysms.[1,3] Size is not a reliable predictor of potential rupture of infected aneurysms.[3] Not enough is known about the speed of formation of infected aneurysms. Only a few reports are available about infected
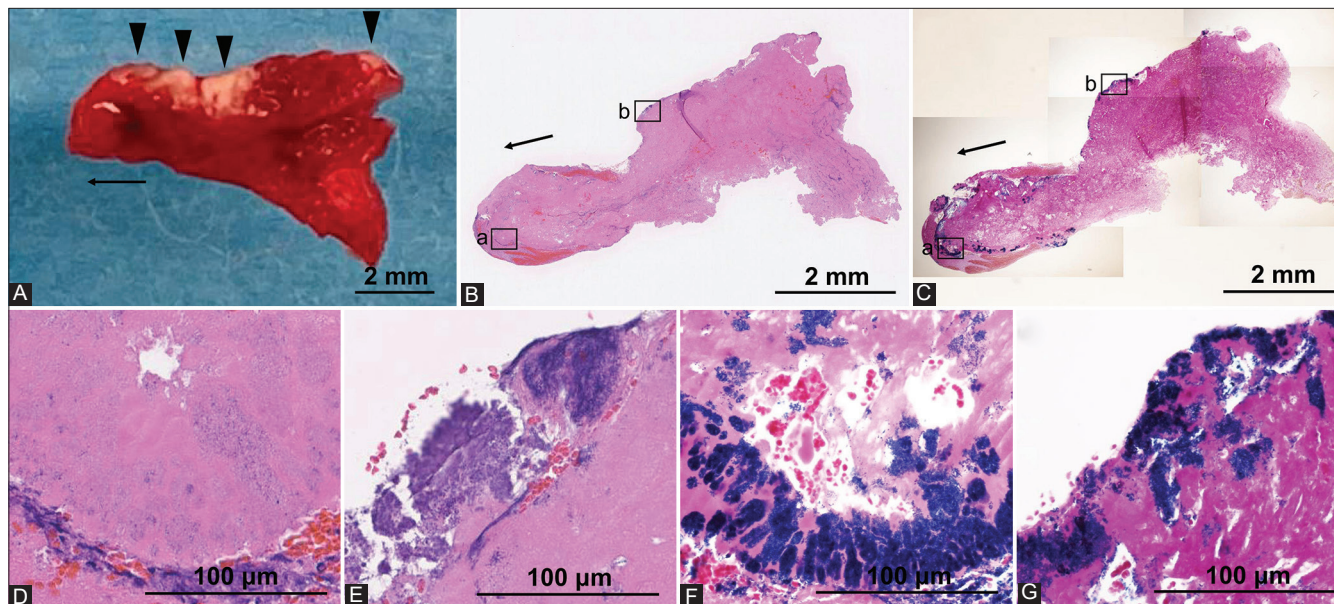
Figure 3: Imaging findings of the thrombus. (A-C) Overall thrombus findings. The arrows show the proximal side of the M1 segment of the middle cerebral artery. (a) The thrombus was a single mass of 8 × 5 mm, with a visually recognizable red component mixed with a localized white component (arrowheads). It was firm and maintained the shape of the vessel at the distal part of the M1 segment and the bifurcation. (b) Hematoxylin-eosin staining showing that the thrombus consisted mainly of fibrin and platelets. (c) Consistent with the visually recognizable white component of the thrombus, Gram-positive cocci were observed. (D and E) D and E correspond to the squares "a" and square "b" in B, respectively. Hematoxylin-eosin staining showing the formation of spherical bacterial colonies at the margins of the thrombus and focally abundant neutrophils. (F and G) F and G correspond to the squares "a" and square "b" in C. The spherical bacteria at the margins of the thrombus were Gram staining positive.

aneurysms forming shortly after septic embolism.[6,15] In this case, no aneurysm was found during thrombectomy, but small hemorrhage appeared around the infarct area of the ACA territory on head CT obtained 24 h after thrombectomy [Figure 2b], indicating that the process of aneurysm formation and rupture can occur shortly after septic embolism. When an infected aneurysm results in intracerebral hemorrhage instead of subarachnoid hemorrhage, there is a risk of misdiagnosing it as hemorrhagic infarction. Given that there was no aneurysm formation in the distal M1 segment of the left MCA where thrombectomy was performed, direct removal of the septic embolus at early onset may have been helpful. Recently, depending on the size of the ischemic core and penumbra, thrombectomy is performed up to 24 h after onset.[7] The arterial wall may have already become fragile at the time of late thrombectomy, leading to the increased risk of hemorrhagic complications.

This case met one major clinical criterion (positive blood culture) and two minor clinical criteria (fever and vascular lesions) of the revised Duke criteria, and the diagnosis of infected endocarditis was not definite.[5] Since microorganisms were observed in the histology of the embolus and other infection sites were not evident, we considered that the patient had a high probability of infective endocarditis. *S. gallolyticus* (formerly called *Streptococcus bovis* type I) is one of the most important causative organisms of infective endocarditis. *S. gallolyticus* bacteremia has been associated with colon polyps and colon cancer.[8] In this case, the route of infection was unknown, and there was a possibility of a latent colorectal tumor, but colonoscopy was not performed due to the patient's poor general condition.

In this case, septic embolism was not recognized early because he had no fever on admission and blood tests showed only mildly elevated inflammatory markers. If pathological findings of the retrieved thrombus can be used to make a diagnosis of septic embolism, antimicrobial therapy and aneurysm evaluation can be initiated promptly. The problem is that it takes several days to make a pathological diagnosis, during which fatal outcomes due to hemorrhagic complications may occur. When recognizing an atypical thrombus on visual examination, it is important to keep in mind atypical etiologies such as septic embolism. If septic embolization results in residual peripheral occlusive lesions, close imaging follow-up should be performed with the possibility of rapid aneurysm formation and rupture in the future. In this case, if the occluded peripheral region of the left ACA had been found to be septic embolism early or before thrombectomy, embolization of this region might have prevented aneurysm formation and rupture [Figure 5d].
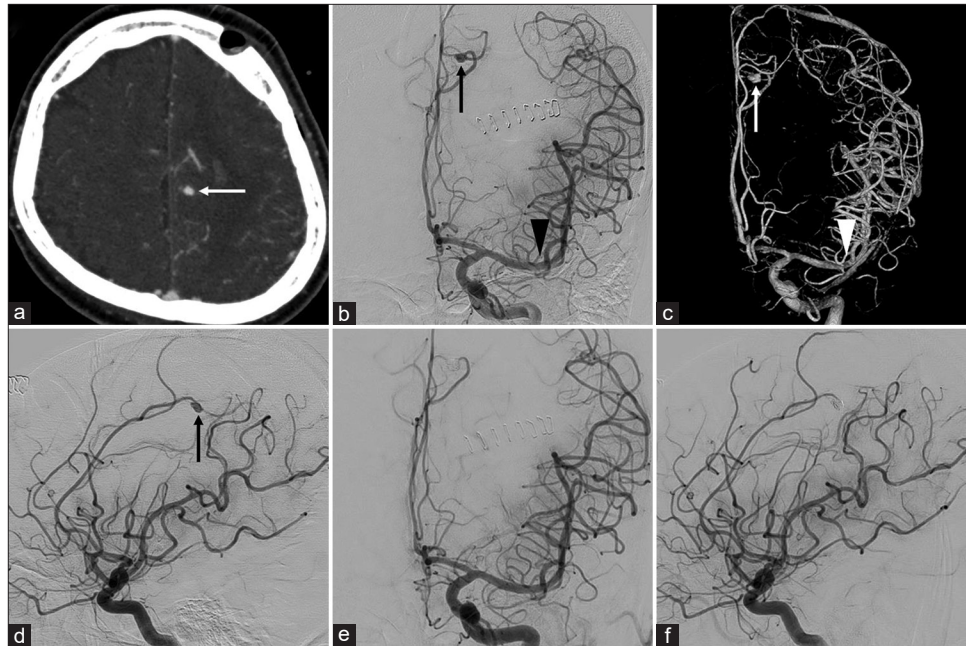
Figure 4: Imaging findings of the aneurysm before and during embolization. (a) An axial view of computed tomography angiography of the head showing an aneurysm in the peripheral left anterior cerebral artery (arrow). (b-d) The left internal carotid artery angiography (b: anteroposterior view, c: three-dimensional anteroposterior view, and d: lateral view) showing a 5.8 mm saccular aneurysm in the peripheral region of the pericallosal artery of the anterior cerebral artery (arrows) and no aneurysm formation in the recanalized distal part of the left M1 segment (arrowheads). (e and f) The left internal carotid artery angiography after embolization (e: anteroposterior view and f: lateral view) showing occlusion of the aneurysm.
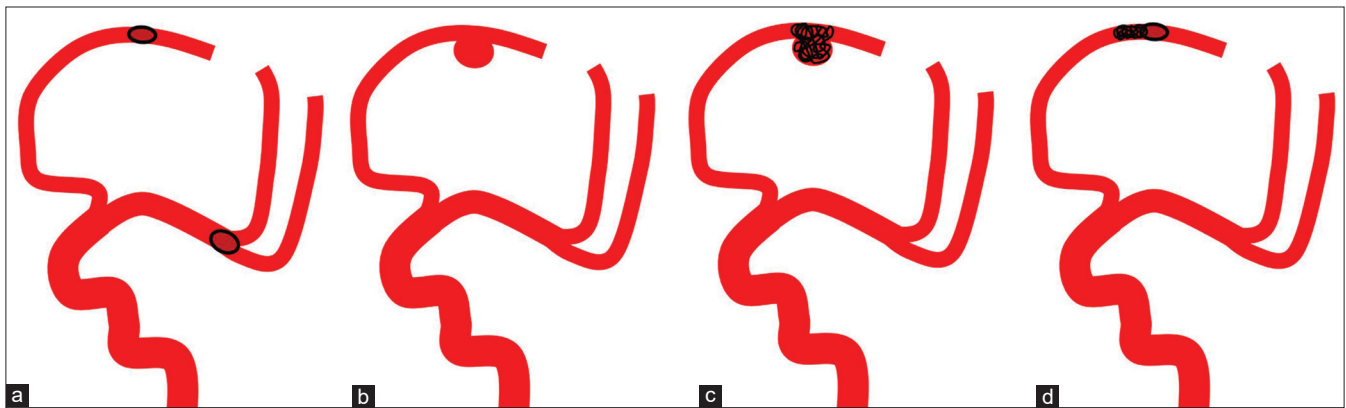

Figure 5: Schema of this case. (a) Septic embolism was seen in the left middle cerebral artery and anterior cerebral artery. (b) An aneurysm was formed in the anterior cerebral artery with residual occlusion, but no aneurysm in the middle cerebral artery that was reperfused after thrombectomy. (c) The aneurysm in the peripheral anterior cerebral artery and the parent vessel was occluded. (d) Endovascular embolization of occluded vessels due to septic embolism may prevent aneurysm formation and subsequent bleeding.

CONCLUSION

The pathological findings of a retrieved thrombus were useful for making a diagnosis of septic embolism. The possibility of short-term formation and rupture of an infected aneurysm after septic embolism should be noted. Endovascular embolization of occluded vessels due to septic embolism may prevent aneurysm formation and subsequent bleeding.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent.

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Nil.

Conflicts of interest

There are no conflicts of interest.

REFERENCES

1. Alawieh A, Chaudry MI, Turner RD, Turk AS, Spiotta AM. Infectious intracranial aneurysms: A systematic review of epidemiology, management, and outcomes. J Neurointerv Surg 2018;10:708-16.
2. Hernández-Fernández F, Rojas-Bartolomé L, García-García J, Ayo-Martín Ó, Molina-Nuevo JD, Barbella-Aponte RA, *et al.* Histopathological and bacteriological analysis of thrombus material extracted during mechanical thrombectomy in acute stroke patients. Cardiovasc Intervent Radiol 2017;40:1851-60.
3. Kannoth S, Thomas SV. Intracranial microbial aneurysm (infectious aneurysm): Current options for diagnosis and management. Neurocrit Care 2009;11:120-9.
4. Kim JM, Jeon JS, Kim YW, Kang DH, Hwang YH, Kim YS. Forced arterial suction thrombectomy of septic embolic middle cerebral artery occlusion due to infective endocarditis: An illustrative case and review of the literature. Neurointervention 2014;9:101-5.
5. Li JS, Sexton DJ, Mick N, Nettles R, Fowler VG Jr., Ryan T, *et al.* Proposed modifications to the Duke criteria for the diagnosis of infective endocarditis. Clin Infect Dis 2000;30:633-8.
6. Matsuzono K, Ishiyama Y, Higaki A, Namba K, Aoyama Y, Igarashi T, *et al.* Successful endovascular coiling of infectious cerebral aneurysm following *Staphylococcus haemolyticus* endocarditis. J Int Med Res 2021;49:3000605211058857.
7. Nogueira RG, Jadhav AP, Haussen DC, Bonafe A, Budzik RF, Bhuva P, *et al.* Thrombectomy 6 to 24 hours after stroke with a mismatch between deficit and infarct. N Engl J Med 2018;378:11-21.
8. Pasquereau-Kotula E, Martins M, Aymeric L, Dramsi S. Significance of *Streptococcus gallolyticus* subsp. *Gallolyticus* association with colorectal cancer. Front Microbiol 2018;9:614.
9. Ramos C, Mayo P, Trillo S, Gómez-Escalonilla C, Caniego JL, Moreu M, *et al.* Management of large vessel occlusion stroke related to infective endocarditis: Is mechanical thrombectomy a safe option? J Stroke Cerebrovasc Dis 2020;29:105248.
10. Sader E, Abdalkader M, Thom N, Nguyen TN, McDonald S, Greer D, *et al.* Endovascular treatment of infective endocarditis-related acute large vessel occlusion stroke. J Stroke Cerebrovasc Dis 2021;30:105775.
11. Scharf EL, Chakraborty T, Rabinstein A, Miranpuri AS. Endovascular management of cerebral septic embolism: Three recent cases and review of the literature. J Neurointerv Surg 2017;9:463-5.
12. Settarzade E, Peker A, Topcuoglu MA, Arsava EM, Demircin M, Arat A. Clinical challenges associated with the endovascular treatment of acute stroke in a patient with infective endocarditis. J Cerebrovasc Endovasc Neurosurg 2020;22:176-81.
13. Sgreccia A, Duchmann Z, Desilles JP, Lapergue B, Labreuche J, Kyheng M, *et al.* Association between acute ischemic stroke etiology and macroscopic aspect of retrieved clots: Is a clot's color a warning light for underlying pathologies? J Neurointerv Surg 2019;11:1197-200.
14. Thiene G, Basso C. Pathology and pathogenesis of infective endocarditis in native heart valves. Cardiovasc Pathol 2006;15:256-63.
15. Wang JL, Hinduja AP, Powers CJ. Successful coil embolization of a ruptured mycotic aneurysm that developed three days after septic embolic infarction: Case report and review of the literature. J Clin Neurosci 2017;39:95-8.

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