

Cholesterol Crystal in Thrombus Removed by Mechanical Thrombectomy Should be a Strong Marker for Aortogenic Embolic Stroke

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Aortogenic embolic stroke (AES) is an important stroke mechanism. However, as many stroke patients have aortic atheromatous lesions, it is unclear whether these lesions are the cause of these strokes. Cholesterol crystals are the solid, crystalline form of cholesterol that is found in atherosclerosis, but not in cardiac diseases such as atrial fibrillation, valvular diseases, and cardiomyopathy. Therefore, if a cholesterol crystal is found in a thrombus removed by mechanical thrombectomy (MT), this makes it possible to diagnose a patient as having an atheromatous lesion. Here, we report an AES case with a cholesterol crystal found in a thrombus removed by MT. A 67-year-old man was admitted due to consciousness disturbance, aphasia, and right hemiplegia. Diffusion-weighted imaging (DWI) showed a hyperintense area in the left frontal lobe, and magnetic resonance angiography demonstrated a branch occlusion of the left middle cerebral artery (MCA). MT was performed 1.5 h after stroke onset, with the thrombus removed and a left occluded MCA completely recanalized. Carotid duplex ultrasonography did not reveal any plaque in the carotid artery. Echocardiography did not show any abnormal function or findings, including thrombus. Transesophageal echocardiography showed a 4.9 mm atheromatous lesion at the aortic arch. Therefore, we suspected this patient as having an AES due to the embolic source of atheromatous lesion at the aortic arch. Pathological examination of the embolus revealed a cholesterol crystal cleft in the thrombus. Therefore, we diagnosed this patient as having AES caused by an atheromatous lesion at the aortic arch.

Keywords: Aortogenic embolic stroke—Mechanical thrombectomy—Aortic atheroma—Removed thrombus—Cholesterol crystal cleft

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Background

Aortogenic embolic stroke (AES) is an important stroke mechanism.¹ However, although most stroke patients have aortic atheromatous lesions, it is unclear whether these lesions are the cause of these strokes.

As the recent use of mechanical thrombectomy (MT) has improved outcomes in acute stroke patients with large vessel occlusion, this technique has become widely performed.^{2,3} The use of MT makes it possible to remove

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thrombus from a large vessel occlusion and pathologically investigate the thrombus.^{4,5} Cholesterol crystals are the solid, crystalline form of cholesterol found in atherosclerosis, but are not part of the thrombus found in cardiac diseases such as atrial fibrillation, valvular diseases, and cardiomyopathy.^{6,7} Therefore, if a cholesterol crystal is found in a thrombus removed by MT, this makes it possible to diagnose a patient as having atherosclerosis with an aortic atheromatous lesion. However, cholesterol crystals appear as empty, ghost clefts on the histology, because they are highly soluble in the solvents commonly used for histological preparation. Here we report an AES case diagnosed based on the pathological findings of a thrombus removed by MT.

Case presentation

A 67-year-old man was admitted due to consciousness disturbance, aphasia, and right hemiplegia. The patient had a history of dyslipidemia, taking statins, and smoking. Body temperature was 36.6°C, blood pressure was 146/98 mmHg,

while the heart rate was 60 beats/min and regular. Blood tests on admission showed a brain natriuretic peptide level of 18.5 pg/mL with a D-dimer of 1.2 $\mu\text{g/mL}$. Electrocardiography showed sinus rhythm. Diffusion-weighted imaging (DWI) showed a hyperintense lesion in the left frontal lobe (Fig1A, arrowhead). Fluid-attenuated inversion recovery (FLAIR) showed a slight hyperintense area in the left frontal lobe (Fig1C, arrowhead) and an intra-arterial sign in the left middle cerebral artery (MCA) (Fig1C, arrow). Magnetic resonance angiography demonstrated the presence of left MCA branch occlusion. MT was performed 1.5 h after onset, with complete recanalization of the left MCA achieved (Fig1D arrow, Fig1E). Ultrasonography of the carotid artery showed there were no plaques as embolic sources. Four days after the onset, transesophageal echocardiography (TEE) demonstrated that while there was an atheromatous lesion measuring 4.9 mm at the aortic arch (Fig 2A, arrowhead), there was no intracardiac thrombus or patent foramen ovale. Therefore, we suspected this patient as having AES due to the embolic source of the atheromatous lesion at the aortic arch.

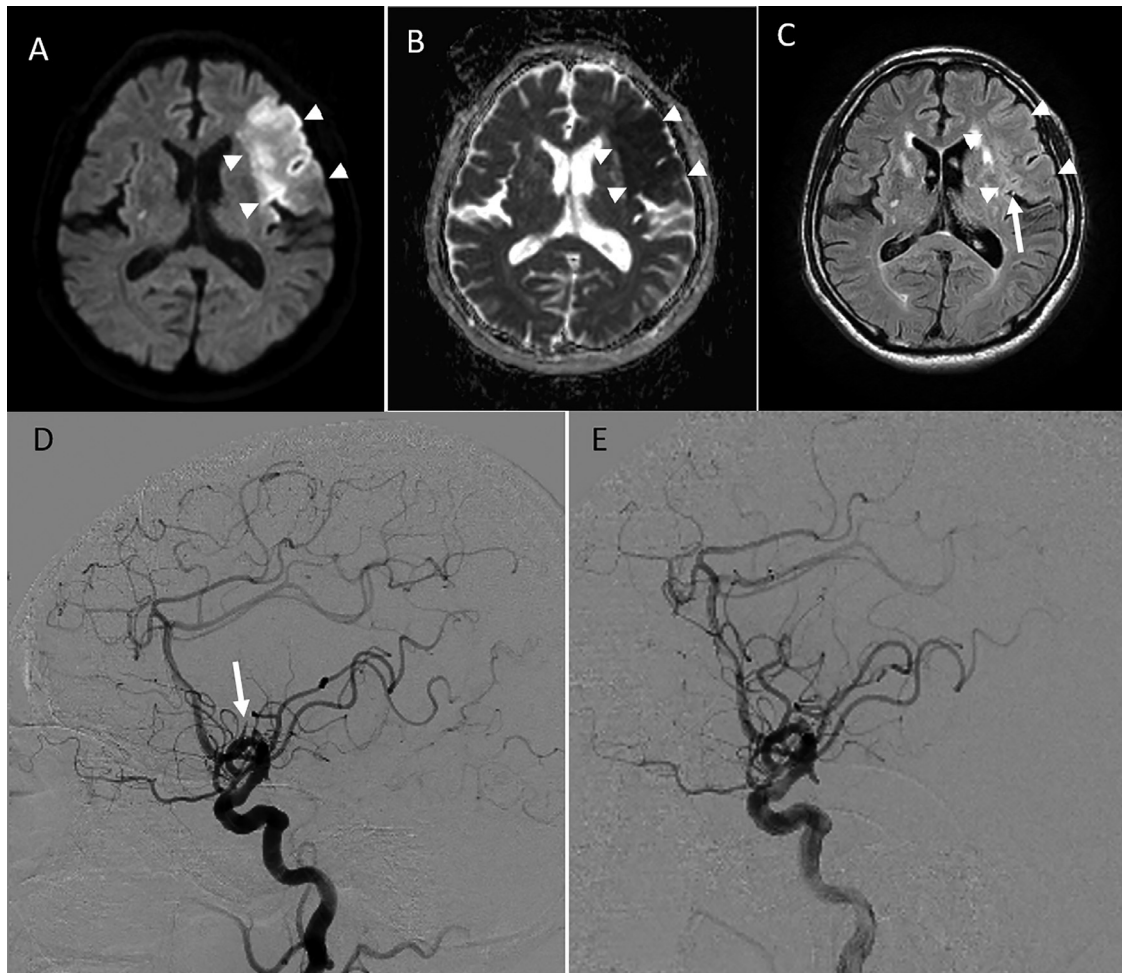


Fig. 1. A: DWI shows a hyperintense lesion in the left frontal lobe (arrowhead). B: Apparent diffusion coefficient map shows decreased apparent diffusion coefficient in the left frontal lobe (arrowhead). C: FLAIR shows a mild hyperintense area in the left frontal lobe and an intra-arterial sign in the left middle cerebral artery (arrowhead). D: Cerebral angiography shows occlusion of the M3 portion of left middle cerebral artery (arrow). E: Cerebral angiography displays the complete recanalized left middle cerebral artery after thrombectomy.

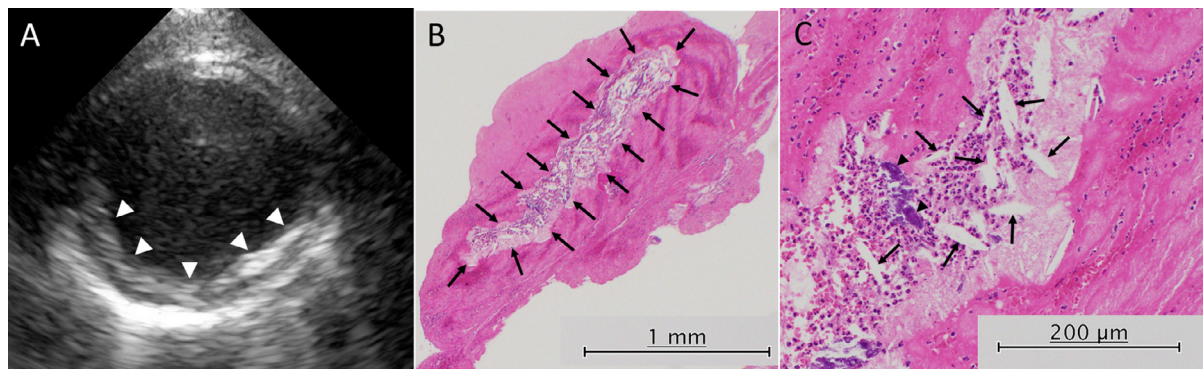


Fig. 2. A: Transesophageal echocardiography shows a 4.9 mm atheromatous lesion at the aortic arch (arrowhead) B: Pathological findings for the retrieved thrombus (Hematoxylin and Eosin staining). Cholesterol crystal cleft in the thrombus (arrow). C: Pathological findings for the retrieved thrombus (Hematoxylin and Eosin staining). Cholesterol crystal cleft (arrow) and calcification (arrowhead).

Subsequently, pathological examination of the removed embolus revealed there were red blood cells, platelets, fibrin, a small amount of calcification (Fig2C, arrowhead), and a cholesterol crystal cleft (Fig2B,2C, arrow). Based on the presence of the cholesterol crystal cleft in this patient, we diagnosed AES caused by an atheromatous lesion at the aortic arch.

The patient was treated with an oral antiplatelet drug (aspirin, 100 mg/day), rosuvastatin calcium (2.5 mg/day), and irbesartan (100 mg/day), and he stopped smoking. He was discharged to another hospital for rehabilitation with mild motor aphasia on day 14. The modified Rankin Scale score at 3 months after stroke onset was 2. He had no recurrence of cerebral infarction during the 4-year follow-up after discharge.

Discussion

To the best of our knowledge, this is the first AES case diagnosed based on the pathological findings of the thrombus removed by MT. The presence of the cholesterol crystal cleft in the thrombus removed by MT was the decisive factor for the diagnosis of AES.

Currently, AES is diagnosed when 1) brain magnetic resonance imaging findings are suggestive of embolism, 2) atheromatous lesions are found in the aortic arch by TEE, and 3) there are no other sources of embolism.⁸ However, although most stroke patients have aortic atheromatous lesions, it remains unclear as to whether these lesions are the cause of these strokes.⁹

Usui et al. reported a case of AES in which the pathological findings showed that foam cells were found in the removed thrombus.¹⁰ Foam cells are a known finding in early atherosclerosis. In contrast, the presence of a cholesterol crystal is the sign of more advanced atherosclerotic lesions as compared to foam cells. Cholesterol crystal is formed from free form cholesterol that is released from dead foam cells.⁷ Therefore, the aortic arch lesion in our case was considered to be a sign of a more advanced atheromatous lesion.

The removed thrombus may be indicative of cardiovascular lesions caused by potential embolic sources. While some previous studies have reported that cardioembolic stroke is more associated with red blood cells as compared to that for noncardioembolic stroke, other studies have indicated that platelet and fibrin levels are higher in these cases.^{4,5} Furthermore, it has also been reported that cardiac tumors, such as atrial myxoma, capillary fibroelastoma and sarcomatoid carcinoma, were found in the thrombi that were removed by MT.^{11–13} However, there are few previous reports regarding AES. Thus, if a cholesterol crystal cleft is found in a thrombus removed by MT, our current findings suggest that we should diagnose these patients as having atherosclerosis with the presence of an aortic atheromatous lesion. Therefore, overall these findings demonstrate that in order to definitively diagnose acute stroke patients, it is very important to examine the thrombus removed by MT.

Conclusion

We report an AES case diagnosed based on the pathology of the removed thrombus and the TEE findings. Current pathological findings demonstrate that a cholesterol crystal cleft in a removed thrombus is a strong marker for the diagnosis of AES in acute stroke. Therefore, the examination of a thrombus removed by MT in an acute stroke patient is useful for diagnosing the etiology of the stroke.

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