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Mechanical Thrombectomy for Acute Ischemic Stroke Caused by Prosthetic Aortic Valve Endocarditis Due to Exophiala dermatitidis Infection: A Case Report

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Abstract

Prosthetic valve endocarditis (PVE) can cause large cerebral vessel occlusion. Many reports suggested that mechanical thrombectomy (MT) is effective and useful for early diagnosis from the histopathological findings of thrombus. We present the case of a 62-year-old man, with a history of prosthetic aortic valve replacement and pulmonary vein isolation for his atrial fibrillation, who developed a high fever and an acute neurological deficit, with left hemiplegia and speech disorder. He was diagnosed as having an acute right middle cerebral artery embolism and underwent an MT. The embolic source was found to be a PVE vegetation. However, histopathological analysis of the thrombus could not detect the actual diagnosis. Although he was treated for bacterial endocarditis, his blood culture revealed a rare fungal infection with *Exophiala dermatitidis* not until >3 weeks after admission. Subsequently, a ß-D-glucan assay also indicated elevated levels. Although he underwent an aortic valve replacement on day 36, MRI showed multiple minor embolic strokes till that day. Early diagnosis of fungal endocarditis and detection of the causative pathogen are still challenging, and the disease has a high risk of occurrence of early and repeated embolic stroke. In addition to clinical findings and pathological studies, ß-D-glucan assay might be a good tool for the diagnosis and evaluation of fungal endocarditis.

Keywords: thrombectomy, embolic stroke, endocarditis, fungi, exophiala

Introduction

Although acute ischemic stroke (AIS) is a well-known neurological complication of infective endocarditis (IE), many reports suggested the usefulness of mechanical thrombectomy (MT) for large vessel occlusion[1,2] and the significant contribution to histopathological analysis of the thrombus.[3]

We herein describe a rare case of MT for an acute middle cerebral artery (MCA) embolism in which the cause was later identified as a prosthetic valve endocarditis (PVE) due to *Exophiala dermatitidis*, a black yeast fungus. The lesson we learned from this case is that despite the removal of the thrombus and sending it to the laboratory for further analysis, the correct diagnosis was still difficult to confirm. This pathological process is usually misdiagnosed and not included in the differential diagnosis list because of the rarity of fungal IE-related stroke.

Case Report

A 62-year-old man had undergone aortic valve replacement with a prosthetic valve, mitral annuloplasty, and tricuspid annuloplasty for multiple valvular heart disease 6 months before admission.

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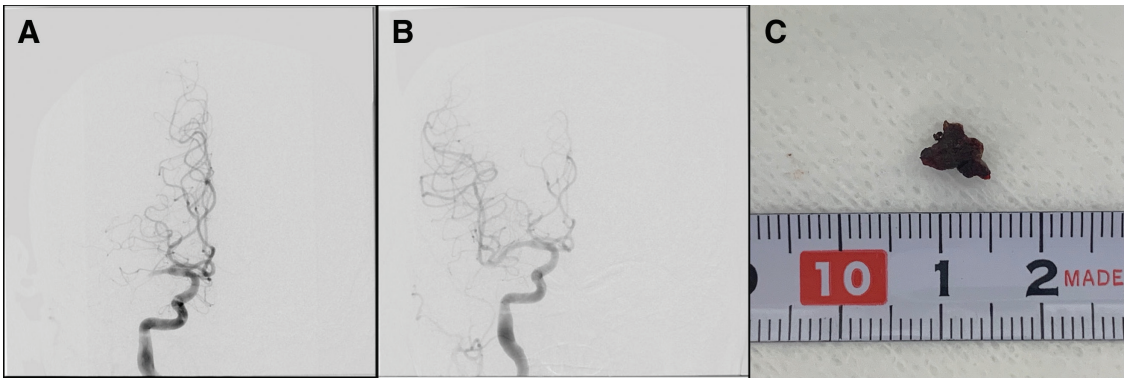

Fig. 1 Cerebral angiogram showing a right middle cerebral artery occlusion (A) and complete recanalization by mechanical thrombectomy (B). The retrieved thrombi were grayish and hard in consistency (C).

He had an uneventful course except for new-onset atrial fibrillation 1 week after the surgery, for which he received aspirin and warfarin. Because his atrial fibrillation became permanent, he underwent pulmonary vein isolation ablation 4 months later at the same institution; thereafter, his sinus heart rhythm recovered. However, 2 weeks later, he began experiencing occasional fatigue, chills, headache, joint pain, and left-sided abdominal pain. On several visits to a local clinic during the next month, only symptomatic therapy was offered.

After that, he was brought to our emergency department because his family found him in a stupor. This was preceded by difficulty in speaking and aggravating headache for 4.5 hours. On examination, his Glasgow coma scale score was 10 (E3V2M5), and left hemiplegia with hypoesthesia, aphasic, and dysarthric with an initial National Institutes of Health Stroke Scale (NIHSS) score of 20 were observed. He was febrile (39.1°C), his blood pressure was 120/61 mmHg, and his pulse was regular (75 bpm). Laboratory workup revealed an increasing white blood cell count (10.1×10^9/L) and increased prothrombin time/international normalized ratio (PT/INR, 2.96) and D-dimer level (4.1 μg/mL). Plain brain CT revealed a right-sided hyperdense MCA sign and hypodense areas in the right insular cortex, putamen, and anterior temporal lobe, corresponding to an Alberta Stroke Program Early CT score of 7 of 10. CTA revealed a distal M1 segment occlusion in the right MCA. Furthermore, a CT perfusion image showed a moderate decrease in cerebral blood volume within a large area of decreased cerebral blood flow and increased mean transit time (Supplementary Figure, available Online).

Intravenous thrombolysis was contraindicated because of suspected endocarditis and prolonged PT/INR and because this occlusion was found after the therapeutic time window. Thus, we decided to conduct MT. The procedure was conducted through the right femoral approach, with the patient under local anesthesia, and complete recanalization was achieved with two passes. The modified thrombolysis in cerebral infarction (mTICI) scale score was 3 (Fig. 1A and 1B). Eventually, the onset-to-door time was 310 minutes; the door-to-puncture time, 37 minutes; puncture-to-reperfusion time, 49 minutes; and the onset-to-reperfusion time, 396 minutes. Two pieces of embolic specimens were obtained. They were grayish and hard in consistency, unlikely to be from a cardiogenic embolism originating from atrial fibrillation (Fig. 1C). The first pathological examination revealed a fibrin clot containing numerous round ghost cells suggestive of atypical lymphocytes with necrotic and degenerative changes. Accordingly, a pathologist suggested that it might be a tumor embolization due to malignant lymphoma.

We introduced the patient to broad-spectrum antibiotics after blood cultures were performed considering the possibility of PVE, which was suggested by the patient's febrile state, past history of heart surgery, and vegetation-like embolus. A day later, his NIHSS score became 15, and CT the next day revealed a hemorrhagic transformation with an intraparenchymal hematoma in the insular cortex and diffuse subarachnoid hemorrhage (SAH) (Fig. 2A). MRI revealed complete recanalization (Fig. 2B) but also detected a large core of MCA territory infarction (Fig. 2C and 2D). Transthoracic echocardiography revealed the possibility of an existing vegetation on the prosthetic atrial valve (Fig. 3A). Nine days later, only one of four blood samples was positive for methicillin-resistant coagulase-negative *Staphylococcus epidermidis* (MRCNS). Because the patient remained in a mild febrile state (37–38°C), we repeated blood cultures considering that the previous result was due to skin contamination.

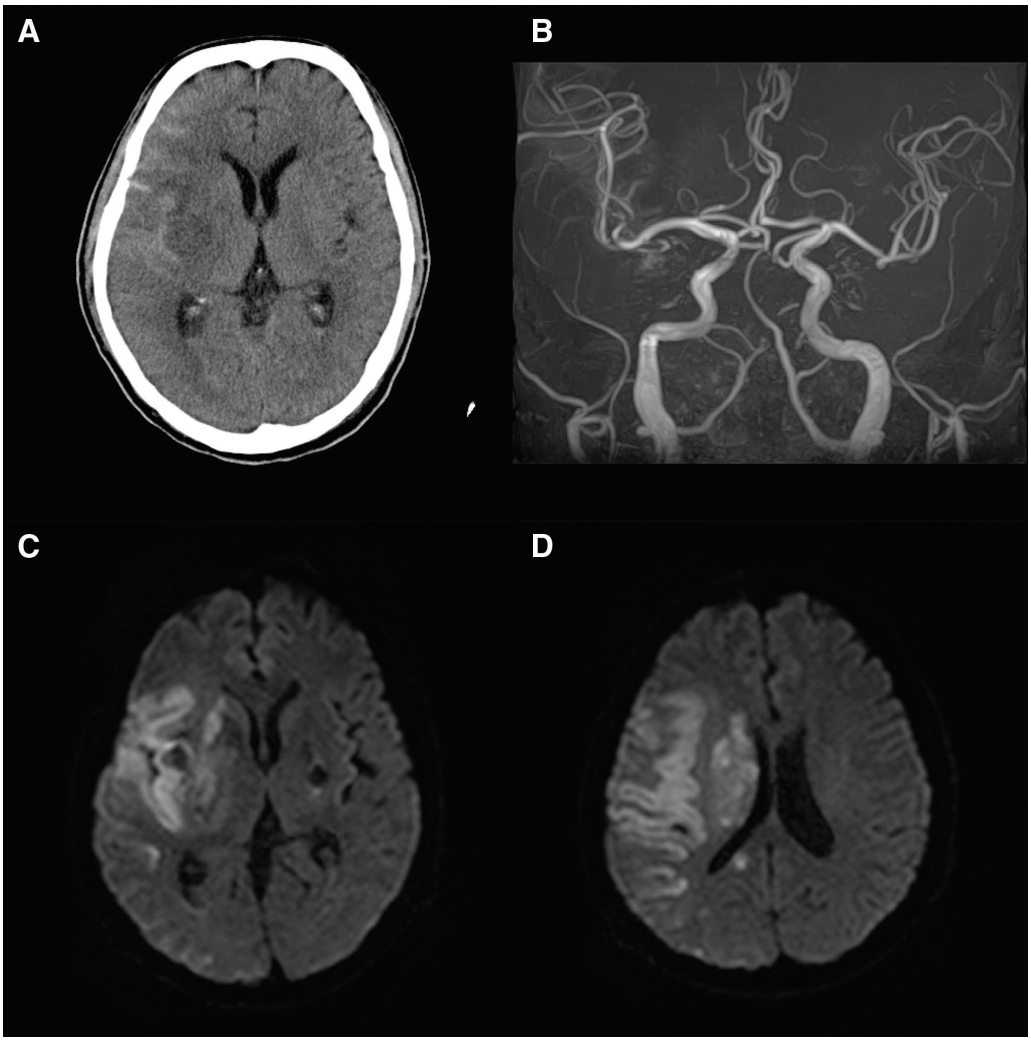

Fig. 2 CT image of the brain 1 day after the mechanical thrombectomy, showing a hemorrhagic transformation in the insular cortex and diffuse subarachnoid hemorrhage (A). The MRA confirms the complete recanalization (B) with infarction of a large core of middle cerebral artery (MCA) territory (C, D).

Fourteen days later, he was transferred to his previous hospital, where he had a heart valve surgery, and continued the intensive antibacterial treatment; however, he remained in a mild febrile state. Transesophageal echocardiography revealed mobile prosthetic aortic valve vegetations. However, 16 days later, an aerobic blood culture sample collected on the ninth day after hospital admission was found positive for *Exophiala* species, and the other aerobic blood cultures collected again in the other hospital also grew *E. dermatitidis*, confirming the diagnosis. We therefore performed a ß-D-glucan assay, which yielded a high value: 12420 pg/mL (normal, <20 pg/mL). Accordingly, intravenous amphotericin B was started on day 26. In addition, enhanced CT of the abdomen confirmed a lesion in the spleen, which suggested an infarct or abscess (Fig. 3B); thus, a splenectomy was performed on day 29. Furthermore, he underwent an aortic valve replacement on day 36, which revealed the formation of huge blackish fungal vegetation and abscess around the prosthetic valve (Fig. 3C). A mass of yeast-like spores, including pseudohyphae, was confirmed pathologically by Grocott methenamine silver staining. Although no neurological deterioration was observed during that time, brain MRI on day 20 and day 33 revealed new cerebral infarctions (Fig. 3D).

The patient received amphotericin B for 6 weeks without any adverse effects. Three months after the onset of the ischemic stroke, he regained his normal cognitive function but still required a feeding tube because of pseudobulbar palsy. His left hemiplegia showed improvement of upper manual muscle testing (MMT) grade 2 and lower MMT grade 3; accordingly, gait training with a long leg brace was attempted.

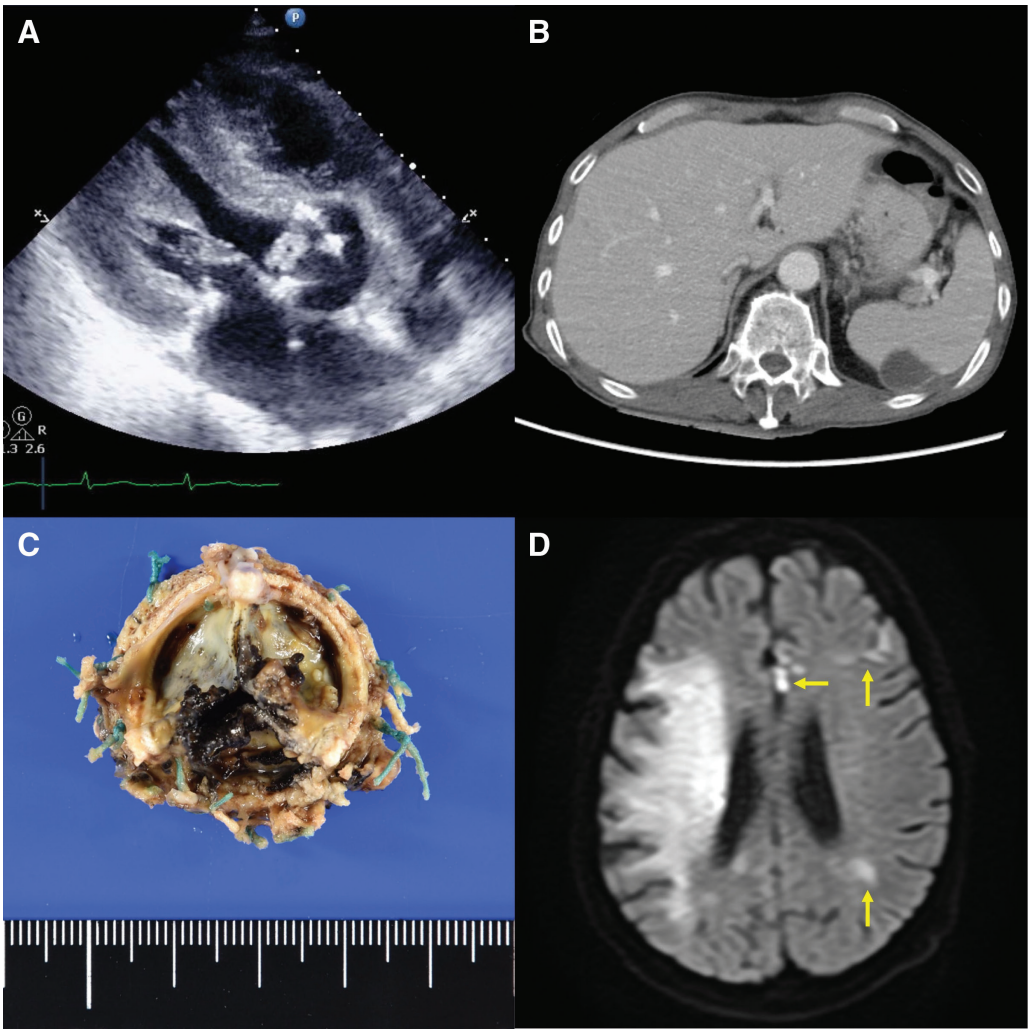

Fig. 3 Transthoracic echocardiography image suggesting the presence of vegetation on the prosthetic atrial valve (A). The enhanced CT scan of the abdomen shows a splenic lesion that suggests either an infarct or an abscess (B). The surgically removed prosthetic aortic valve shows the formation of a huge blackish fungal vegetation (C). MRI on day 33 (D) revealed the recurrence of new cerebral infarctions (arrows).

After obtaining these results, we ordered a reexamination of the embolic specimens. All the cells considered as atypical lymphocytes initially were Grocott staining-positive, yeast-like fungi, and contained chain-like mycelial cells. This microscopic finding was consistent with *E. dermatitidis* infection (Fig. 4). Until this point, neither the patient's medical history nor the laboratory results had suggested an immune disorder. Thus, we considered that he developed this rare fungal infection, despite being immunocompetent, as a result of his previous heart valve surgery or an endovascular catheter ablation.

Discussion

Among patients with a prosthetic heart valve, the incidence of PVE is 6.0/1000 per year.[4] Although *Staphylococcus aureus* (>40%) and coagulase-negative staphylococci (17–28%) are the common causes of PVE, fungal infections also occur though infrequently (3–4%).[5,6] A high proportion of fungal IE cases are caused by *Candida* and *Aspergillus* species,[7] but *E. dermatitidis* infections have rarely been reported. This fungus is black and yeast-like and can be found in man-made synthetic indoor habitats around water sources.[8] To our knowledge, only one report has described PVE caused by *E. dermatitidis* infection in an immunocompetent patient.[9] We believe that our patient represents the first reported case of PVE due to *E. dermatitidis* infection with a large cerebral vessel occlusion treated successfully with MT. AIS secondary to IE is a common neurological complication, but in the case of fungal IE, the diagnosis is usually difficult,

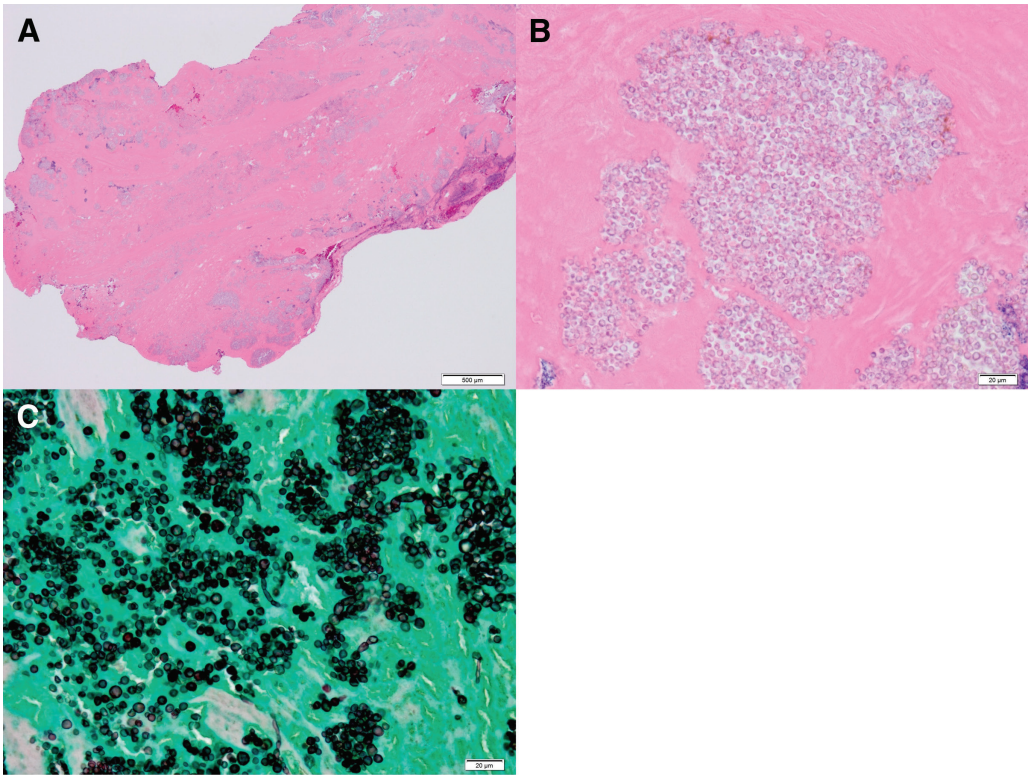

Fig. 4 First pathological examination result indicating fibrin clots containing masses of round cells showing a morphology similar to that of atypical lymphocytes in hematoxylin–eosin staining, which suggests a tumor embolization due to malignant lymphoma (A, B). The additional investigation revealed that almost all the cells considered initially as atypical lymphocytes were in fact yeast-like fungi consisting of chain-like mycelial cells in Grocott staining (C).

and previous cardiac surgery alone is usually not considered a risk factor for fungal infection. However, in the present case, we did not consider fungal infection until blood culture result confirmed the presence of *E. dermatitidis*.

Fungal blood cultures are the standard for diagnosis in such cases, but it takes time to obtain results, and the sensitivity is <50%.[7,10] Moreover, in our case, the first blood culture was negative for fungal infections. Few reports suggested that histopathological examination of thrombus obtained by MT contributes to early diagnosis,[3] and our current report suggests the same. However, our case had a rare fungal infection caused by *E. dermatitidis* that had morphology similar to atypical lymphocytes in hematoxylin–eosin staining, which led us to misdiagnose the disease. Thus, the PVE with *E. dermatitidis* infection was not diagnosed until >3 weeks after admission.

It was necessary to include fungal infection in the differential diagnosis because of the patient's continuous fever, despite him receiving broad-spectrum antibiotics, and because of risk factors associated with prosthetic valve replacement and endovascular treatment. The fungal biomarker ß-D-glucan contributes to early diagnosis of invasive fungal infections, with high sensitivity and specificity.[11] This biomarker could advance the initiation of antifungal treatment before fungal blood culture results.[12] Early introduction of ß-D-glucan to the laboratory workup for PVE- or IE-related stroke cases might be useful, but further study with a larger sample is needed to confirm this.

Because patients with fungal endocarditis are at high risk for cerebral embolism, early surgical treatment of the heart valve is strongly recommended.[10] Our patient was fortunate in that no new neurological symptoms developed until after valve replacement surgery, but the follow-up MRI showed recurrence of cerebral infarctions.

In our patient, a head CT the day after surgery revealed SAH, which might have resulted from the use of a stent retriever. Some reports suggested that pathogens and inflammatory cells contained in fragments of septic emboli may cause pyogenic arteritis, microabscesses, or immune complex-mediated arteritis and can exacerbate intracranial

hemorrhage without aneurysmal formation.[13,14] In patients with AIS secondary to IE, blood vessels might be more fragile than in patients with typical AIS. Hence, in similar cases wherein septic emboli is suspected, direct aspiration alone may be a better choice because it exerts direct mechanical pressure on the wall of the proximal part of the target blood vessel.

In conclusion, early diagnosis of fungal PVE and detection of the causative pathogen remain challenging even after embolic specimens are obtained in MT. In addition to routine clinical investigations, ß-D-glucan assay may be an effective tool for the diagnosis.

Informed Consent

Consent was acquired from the patient's guardian (his wife).

Acknowledgment

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Conflicts of Interest Disclosure

The authors declare that there is no conflict of interest.

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