INTERNAL MEDICINE

□ CASE REPORT □

Thoracic Aortic Graft Infection due to *Candida Albicans* with Multiple Embolism in the Left-side Vessels of the Body

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Abstract

A 79-year-old Japanese man who had undergone thoracic aortic replacement 10 years prior presented with a 3-day history of sore throat. He was initially diagnosed with pharyngitis; however, multiple emboli in the vessels of the left side of the body were recognized. He was diagnosed with thoracic aortic graft infection caused by *Candida albicans*, with multiple embolisms. Anti-fungal therapy was initiated, but surgical removal of the graft was not performed because of the high risk associated with the operation, and he eventually died. Inappropriate use of antibiotics might have led to a severe fungal infection. As such, the inappropriate use of antimicrobial agents should be avoided.

Key words: prosthetic vascular graft infection, *Candida albicans*, multiple embolism

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Introduction

Prosthetic vascular graft replacement can be complicated by infection in 0.5-2% of cases (1) and is associated with considerable morbidity and mortality. It is sometimes difficult to timely diagnose and treat a thoracic aortic graft infection, which is a challenge for the management of infection (2).

Staphylococcus species are the most commonly implicated causative organisms in this type of infection (3), whereas fungal infection of thoracic aortic grafts is rare. According to Doscher, *Candida albicans*, *C. tropicalis*, *C. parapsilosis*, *Aspergillus fumigatus*, *A. terreus*, *Histoplasma capsulatum*, *Mucor* species, *Penicillium* species such as *Mycelia sterilia*, and a variety of fungi have been reported to cause graft infection (4).

Uncertainty remains regarding the clinical features of thoracic aortic graft infection. There have been few reports of cases with late-onset thoracic aortic graft infection complicated with multiple emboli that developed more than four months after surgery (5).

Case Report

A 79-year-old Japanese man was admitted because of a 3-day history of a low-grade fever and sore throat. His medical history included thoracic aortic aneurysm, which had been treated with artificial vascular graft replacement 10 years prior, and sternal osteomyelitis treated with surgical debridement and antibiotics 9 years prior.

He was admitted to the otolaryngology department of our hospital under the diagnosis of acute pharyngitis and was set to receive treatment with flomoxef (2 g/day for 2 weeks). His sore throat ameliorated; however, the low-grade fever persisted. On Day 23, he suddenly experienced pain on the left side of his neck and developed redness, swelling, and tenderness on the left arm. Computed tomography (CT) of the head and upper extremities revealed thrombus formation in the arteries and veins of the left upper limb and common carotid artery. Anticoagulation therapy was initiated for the thrombus. In addition, a team from the general internal

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Table. **Laboratory Data at the Time of Consultation.**

CBC	
WBC	8,800 /μL
seg	82.9 (%)
lym	9.5 (%)
mono	6.7 (%)
eosi	0.5 (%)
baso	0.4 (%)
Hb	11.4 g/dL
plt	288,000 /μL
Coagulation	
PT-INR	1.48
APTT	37.4sec
fbg	411 mg/dL
D-dimmer	3.7 μg/mL
Protein C	63 (%)
Protein S	51 (%)
AT III	82 (%)

Biochemical examination	
TP	6.9 g/dL
Alb	3.2 g/dL
T-Bil	0.4 mg/dL
AST	39 IU/L
ALT	66 IU/L
LDH	206 IU/L
ALP	353 IU/L
γ-GTP	111IU/L
CK	16 U/L
Cr	0.55mg/dL
BUN	10.3mg/dL
Na	133mEq/L
K	4.4mEq/L
Cl	98mEq/L
Glu	101mg/dL

Immunological test	
CRP	7.05mg/dL
MPO-ANCA	negative
PR3-ANCA	negative
Anti-cardiolipin antibody	negative
Lupus anticoagulant	negative

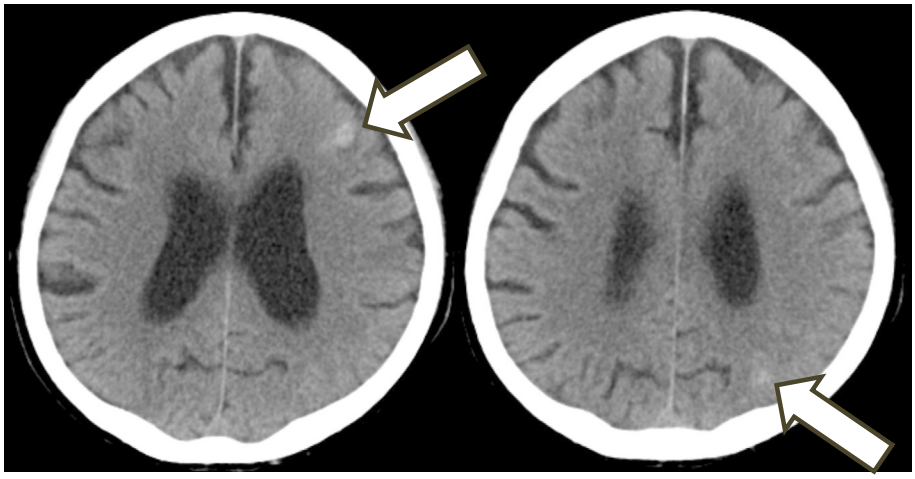

Figure 1. **Head CT scan images without contrast enhancement. Non-enhanced CT of the brain showed subarachnoid hemorrhage in the left frontotemporal portion.**

medicine department was consulted regarding the unknown cause of embolism and persistent inflammatory reaction revealed by laboratory tests.

On a physical examination, he was alert and oriented. His vital signs were normal, and he had left subconjunctival hemorrhaging. Redness, swelling, and tenderness on the left upper limb were noted. He had no cardiac murmur, and no Janeway lesion or Osler node were observed. The findings from a neurological examination were normal.

Laboratory data showed mild anemia (Hb 11.4 g/dL), elevated liver enzymes (aspartate aminotransferase (AST), 39 IU/L; alanine aminotransferase (ALT), 66 IU/L; alkaline phosphatase (ALP), 353 IU/L; and γ-glutamyl transpeptidase (GTP), 111 IU/L), and elevated serum inflammatory markers (C-reactive protein (CRP), 7.05 mg/dL). There were no signs of vasculitis or thrombotic disease from the laboratory findings (Table).

While performing workup on the embolism, blood cultures for the possible bacteremia were repeatedly obtained in addition to the first culture on admission. The antibiotic therapy was discontinued because the causative pathogen was unidentified at that time and it was considered to mask the bacteriologic workup in detecting pathogen. On Day 31, sudden onset of hoarseness and right hemiplegia occurred. Head CT showed subarachnoid hemorrhaging (Fig. 1), and brain MRI showed multiple cerebral emboli in the left hemisphere (Fig. 2). Based on the suspicion of possible endocarditis, transthoracic echocardiography was performed, but there were no abnormal findings, including vegetation formation on the heart valves. Chest CT revealed increased soft-tissue density around the artificial graft, with thrombus formation in the proximal area of the left common carotid artery (Fig. 3).

Ampicillin-sulbactum (12 g/day) was initiated under the diagnosis of a thoracic aortic graft infection with multiple emboli. We repeatedly drew a total of 15 blood culture bottles to identify the organism. Consequently, *C. albicans* (minimum inhibitory concentration (MIC): amphotericin (AMPH)-B; 0.5 μg/mL Fluconazole (FLCZ); 0.25 μg/mL) was grown from a blood culture taken on Days 28 and 35, and the treatment was switched from ampicillin-sulbactum to anti-fungal agents. On Day 35, the patient developed left

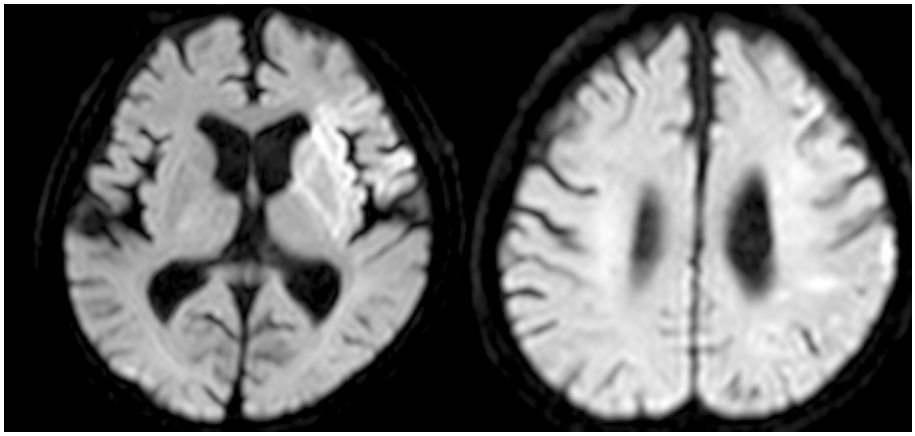

Figure 2. **Brain MRI (diffusion-weighted image). Magnetic resonance imaging of the brain showing acute ischemic infarct in the left MCA territory.**

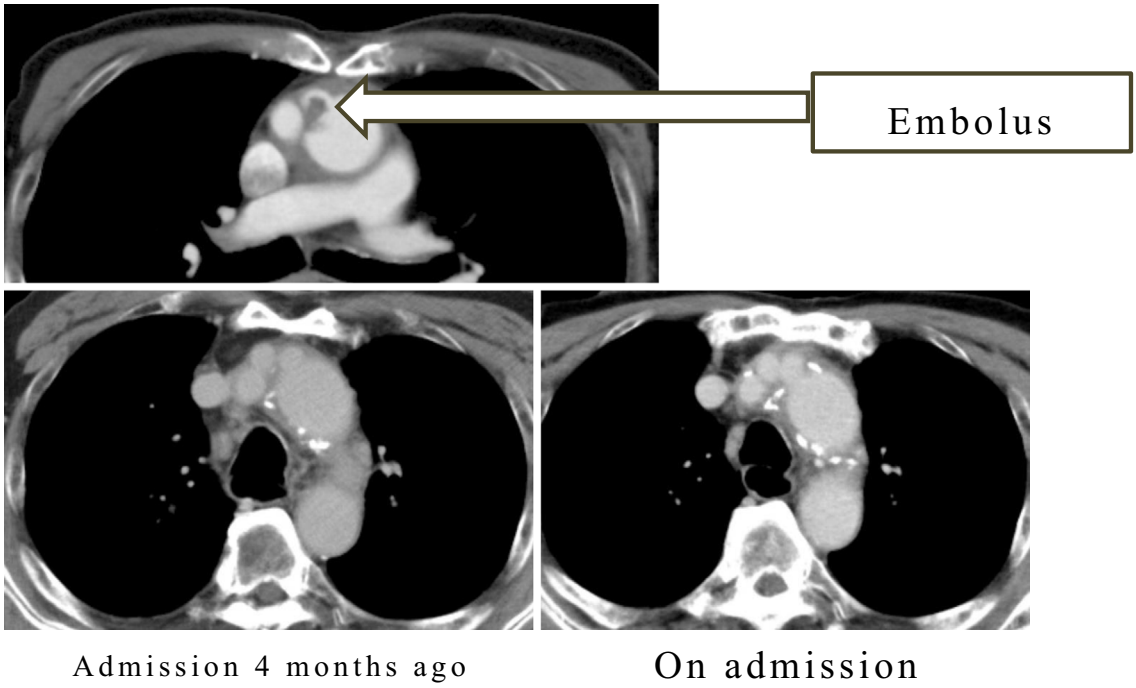

Figure 3. **Chest CT scan image with contrast enhancement. Contrast-enhanced CT scan performed on admission showed embolus in proximal area of the left common carotid artery. First contrast-enhanced computed tomography (CT) scan performed on admission 4 months ago did not have increased soft tissue densities around the artificial graft and second contrast-enhanced CT scan performed on admission revealed ectopic increased soft tissue densities around the artificial graft suggesting a prosthetic graft infection.**

visual disturbance and ciliary injection. Deep cells in the anterior chamber, retinal hemorrhaging, and white patches were observed on the fundus of the left eye, and the patient was diagnosed with Candida endophthalmitis. Fluconazole (200 mg/day) was initiated but was later switched to liposomal-amphotericin B (250 mg/day) due to a lack of clinical effectiveness along with the emergence of endopthalmitis and newly emergent liver dysfunction. The drug change improved the liver dysfunction. Surgery was considered but was ultimately not performed after considering the high risk of operation based on the patient's medical background and multiple morbidities. Despite the treatment effort, the patient's condition gradually deteriorated, resulting in his death (Fig. 4).

The patient had no apparent risk factors for fungal infection at the time of admission. After admission, a careful examination of his medical history revealed that he had intermittently received multiple 2-week courses of levofloxacin for unknown cause of inflammation, as detected by laboratory tests during the 1-year period prior to admission.

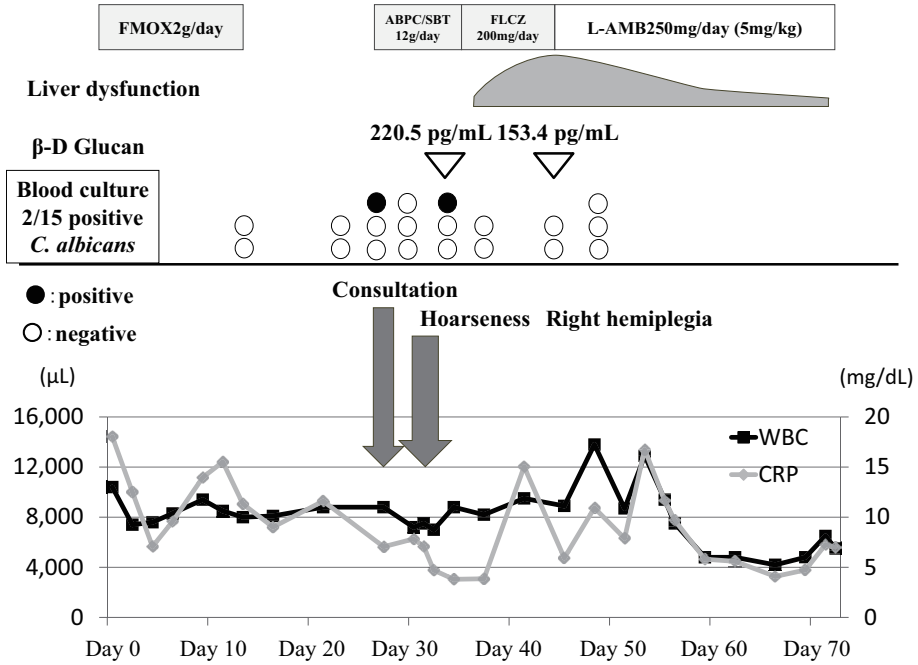

Figure 4. **Clinical course of the patient. *Candida albicans* was detected in 2 blood culture bottles from the repetition collected total 15 blood culture bottles. Although we had switched from ABPC/SBT to FLCZ on day 35, inflammatory reaction was not improved. Moreover, we had switched to L-Amph on day 42 because of lack of clinical effectiveness and newly emergent liver dysfunction. Consequently, inflammatory reaction improved.**

Discussion

Prosthetic aortic graft infection can be classified as early-onset infection (usually defined as occurring within 4 months after surgery) or late-onset infection (2). Clinical manifestations of aortic graft infection may vary according to the length of time after the operation. The presentation of late-onset infection tends to be more subtle than early-onset and usually manifests non-specific signs and symptoms. These patients are more likely to present with signs of complications of aortic graft infection, such as pseudo-aneurysm and abscess formation (6). According to the report by Varino Sousa (7), the mean time interval from primary intervention to occurrence of infection is 8.1 (standard deviation, 11.7) months. *Staphylococcus* species are the most commonly implicated causative organisms (3), and fungi causing prosthetic aortic graft infections have been reported to be rare. Therefore, patients at risk for fungal infection (e.g., those administrated broad-spectrum antimicrobial drugs) should be considered also at risk of fungal prosthetic aortic graft infection. To our knowledge, this case is extremely rare for the following reasons: the infection occurred 10 years after surgery; the pathogen was *C. albicans*; the condition was complicated by multiple emboli, and the emboli were identified only in the vessels of the left side of the body.

In our case, the reason for a fungus (*Candida*) being the causative microorganism remains to be evaluated. Broad-spectrum antimicrobial agents can disturb the normal flora of the gastrointestinal tract. Consequently, antibiotic-resistant microorganisms, such as fungi and *Clostridium difficile*, can proliferate in the gastrointestinal tract. Fungemia might have developed in the present patient via translocation from the gastrointestinal tract to the blood stream. A previous study on transplant patients suggested that fluoroquinolone use can be a risk factor for candidemia (8). In the present case, the patient had no other risk factors for developing fungal infections, and it is possible that repeated administration of levofloxacin induced fungemia. Broad-spectrum antimicrobial agents occasionally induce serious complications, and inappropriate use of antimicrobial agents should be avoided, as in our case.

The patient did not respond well to treatment, possibly because fluconazole was insufficient for prosthetic vascular graft infection and antimicrobial agents did not effectively reach the lesion. In addition, opsonization by antibodies does not work well because of bacterial biofilms (9). Bordi (4) reported an approximately 80% mortality in fungal graft infection patients if the patients had no surgical excision or *in situ* replacement of aorta. Furthermore, it was reported that the gold standard for the treatment of infected prosthetic aortic grafts is the explantation of the graft and reperfusion of the area by placing a new graft via an uninfected extra-anatomic route (10). In our case, surgical treatment was not performed because the patient had poor general and background medical conditions and was as too high a risk to receive surgery. For the management of prosthetic vascular graft infections, treatment options are occasionally limited to various medical treatments, although this can lead to a high mortality rate.

From our case, we would like to emphasize that aortic graft infections can appear with multiple emboli, and the inappropriate use of antimicrobial agents should be avoided.

The authors state that they have no Conflict of Interest (COI).

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