【 CASE REPORT 】

The First Report of Purulent Pericarditis Associated with Aortic Stent-graft Infection Caused by Methicillin-susceptible *Staphylococcus aureus*

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Abstract:
We herein report the first case of purulent pericarditis associated with aortic stent-graft infection in an 80-year-old Japanese man that was caused by methicillin-susceptible *Staphylococcus aureus*, which appropriate antibiotics failed to treat. The detailed clinical course and autopsy images revealed that purulent pericarditis associated with aortic stent-graft infection caused cardiac tamponade and eventually led to mortality. We therefore suggest that surgical procedures, including drainage, should be introduced for such cases.

Key words: purulent pericarditis, autopsy, stent-graft infection

Introduction

Purulent pericarditis is a rare condition that is associated with high morbidity and mortality (1). It can cause severe complications, such as cardiac tamponade, which can be fatal without acute pericardial drainage because it can cause sudden cardiac decompensation (2, 3). *Staphylococcus aureus* is the most common pathogen causing purulent pericarditis (31%), followed by *Streptococcus pneumoniae* (22%) (3, 4). Hematogenous spread, direct spread from adjacent organs, extension from subdiaphragmatic infections, and complication of trauma or surgery are the known causes (1, 5). Treatment options include appropriate antibiotics and emergent pericardial drainage.

Although the incidence of endograft infection ranges from 0.2% to 5%, its mortality rate is high (6). *S. aureus* is the most common causative pathogen, with a prevalence of 30-70% (7, 8). Treatment options include the surgical removal of the endograft with adequate antibiotics. As mentioned above, purulent pericarditis and endograft infection share common pathogens and characteristics of requiring surgical intervention with an elevated mortality rate.

We herein report, to our knowledge, the first case of purulent pericarditis associated with aortic stent-graft infection caused by methicillin-susceptible *S. aureus* (MSSA), which appropriate antibiotics failed to treat.

Case Report

An 80-year-old man with a history of aortic arch aneurysm treated with thoracic endovascular aortic repair (TEVAR) and end-stage renal cell carcinoma (RCC) was referred to our hospital due to gradually worsening dyspnea and a fever.

Two years prior to admission, he had been diagnosed with MSSA bacteremia after TEVAR and treated with meropenem and vancomycin for one month. Five days prior to admission, he experienced general malaise and shortness of breath on exertion. One day prior to admission, his body temperature increased to 38.0℃, and he was transferred to our hospital. He was alert and had nonacute distress on admission. He denied any upper respiratory, abdominal, or urinary symptoms. His vital signs included a body temperature of 38.6℃, blood pressure of 166/92 mmHg, heart rate of 100 beats/min, respiratory rate of 20/min, and O₂ saturation
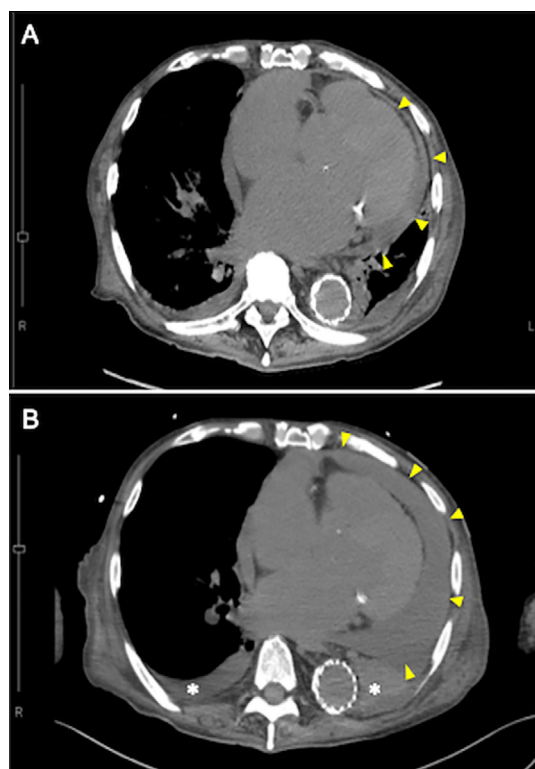
Figure 1.   Pericardial effusion detected by computed tomography. A: Slight pericardial effusion was detected by nonenhanced computed tomography (CT) on day 3 (arrowheads). B: Follow-up CT was performed on day 9 because of deterioration of the patient's general condition. The amount of pericardial effusion dramatically increased over six days (arrowheads). Bilateral pleural effusion became evident (asterisk).

of 96% in room air. On a physical examination, his oral hygiene was unremarkable. He had jugular vein distention, and his wheezes were audible bilaterally on auscultation. Neither cardiac murmur nor pericardial friction rub was audible. The results of abdominal examinations were benign. His lower extremities were cold with slight edema. On the surface of the skin, no decubitus, tinea unguium, or scratches were detected.

Chest X-ray revealed cardiomegaly and pulmonary congestion. Small pleural effusion was shown bilaterally. 12-lead electrocardiography (ECG) revealed sinus tachycardia and T-wave inversion in precordial leads from V2 to V5. Blood test results revealed a slight elevation in the white blood cell count (9,810 cells/μL) that was associated with an increase in C-reactive protein levels (up to 9.6 mg/dL). His serum creatinine level showed an increase compared with a previous test (from 1.86 to 2.09 mg/dL). Brain natriuretic peptide levels increased to 1,562 pg/dL. There was no evidence of pericardial effusion according to echocardiography performed at admission.

His body temperature decreased and pulmonary congestion disappeared soon after diuretics and broad-spectrum antibiotics (piperacillin-tazobactam 4.5 g/day) were administered as an initial treatment after two sets of blood cultures had been obtained. On day 3, his blood culture turned positive for MSSA; subsequently, antibiotics were de-escalated from piperacillin-tazobactam 4.5 g/day to cefazolin 4 g/day. Sputum and urinary cultures were negative, and echocardiography showed no valvular vegetation or deterioration of any valvular regurgitation other than the slight accumulation of fluid in the pericardial space, which was also observed on computed tomography (CT) (Fig. 1A, arrowheads). His vital signs were stable with no signs of cardiac tamponade. Therefore, pericardial fluid was considered nonspecific, and we decided to conduct follow-up using echocardiography.

At this time, an endograft infection was considered the most likely differential diagnosis despite the cause of the infection being unclear. On day 5, his dyspnea did not improve, and peripheral malperfusion was still observed, although the blood culture was negative. Echocardiography revealed the massive accumulation of pericardial effusion within two days after the last follow-up. It was challenging to perform therapeutic pericardiocentesis due to the small amount of pericardial effusion on the anterior surface (<10 mm) and his poor physical status. Surgical pericardiocentesis was thus considered as the treatment choice. However, taking his physical status and prognosis of end-stage RCC into consideration, we decided to avoid invasive therapy after a discussion with his family.

His blood urea nitrogen level increased considerably with a concomitant decrease in urine output, although his body temperature did not increase after the initiation of antibiotic therapy, and his blood culture remained negative. Acute exacerbation of renal failure due to a low cardiac output was considered as a cause of his low urine output. Subsequently, the administration of diuretics was ceased, and renal replacement therapy using hemodialysis was performed. However, his renal function did not improve after treatment. His consciousness suddenly deteriorated on day 9 without any overt findings from blood gas testing or 12-lead ECG, and he died. Written informed consent was obtained from his family for an autopsy and postmortem CT (PMCT).

PMCT revealed the massive accumulation of fluid in the pericardial space (Fig. 1B, arrowheads), bilateral pulmonary congestion, and consolidation surrounding the descending aorta. No intratracheal foreign body or sputum was detected. Cardiac tamponade was clinically considered as a possible cause of death based on the PMCT findings. The autopsy was performed 4 hours after his death. Notable autopsy findings included a massive amount of pus (roughly 500 mL) in the pericardial space (Fig. 2A and B) and around the outer layer of the aortic endograft (Fig. 3A and B), significant mediastinal lymphadenopathy, and systemic metastasis of malignancy (pancreas, liver, lungs, abdominal aortic lymph nodes, and peritoneum). RCC was considered the origin of the metastases. MSSA was identified from cultures of both the pericardium and periaortic tissues. However, continuity of the pus from the ascending aorta to the pericardial space was not clearly identified. Severe neutrophil infiltration was observed in the pericardium and no microscopic bacterial infiltration was observed in aortic stent
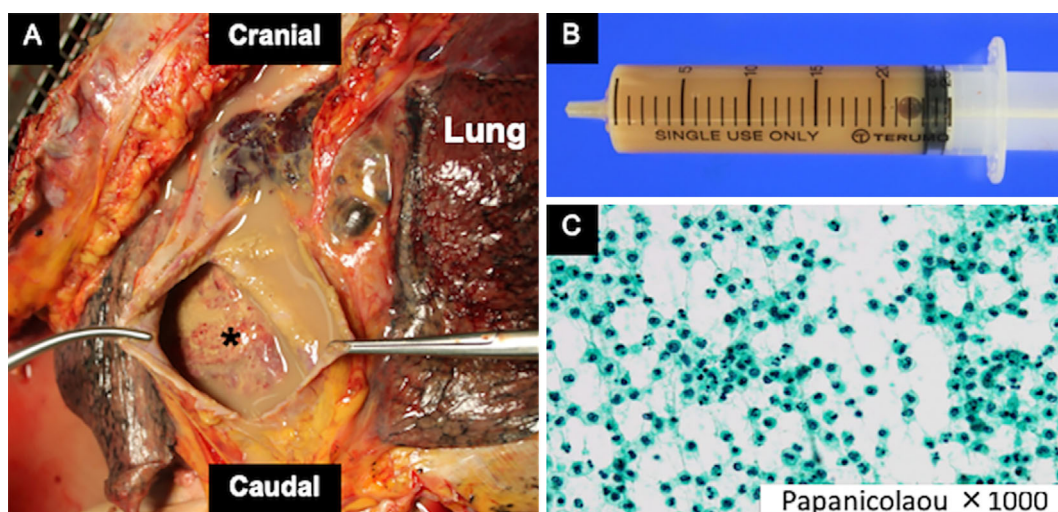
Figure 2. Autopsy findings of the mediastinum. A: The mediastinum was observed from a ventral view. The asterisk indicates the heart. A massive amount of pus was observed in the pericardial space. B: Collection of the pus from the pericardial space. In total, approximately 500 mL of creamy pus was collected. C: Cytological findings of the pus. Papanicolaou staining was performed. Infiltration of numerous neutrophils was observed. These findings were compatible with purulent pericarditis.
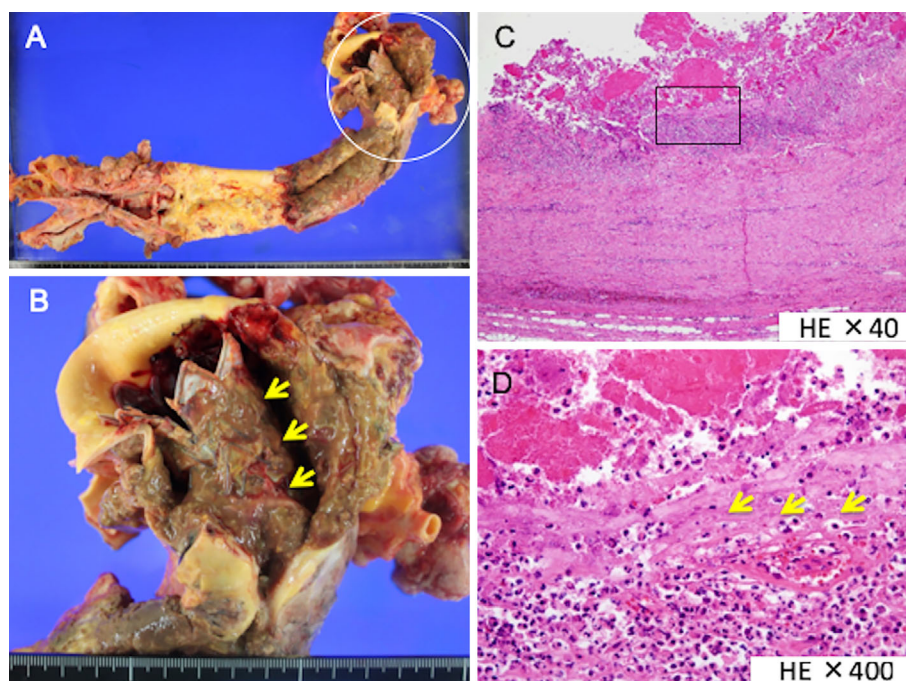

Figure 3. Autopsy and pathological findings of the aorta. A: Pus was observed around the outer layer of the aortic stent-graft from the ascending aorta to the descending aorta. B: Magnified view of the ascending aorta. Pus was observed around the outer layer of the aortic stent-graft (arrow). No penetration or tearing of the intima was observed. C: Histopathological findings of pus. Hematoxylin and Eosin staining was performed. Numerous neutrophils infiltrated the pericardial tissues. D: Magnified view of pus of the aorta. Neutrophil (not bacterial) infiltration was observed.

(Fig. 2C and D). The autopsy did not reveal apparent coronary thrombosis, valvular vegetation, pulmonary embolism, aortic dissection, intratracheal foreign body or sputum, or massive hemorrhaging in the pleural, pericardial, or abdominal spaces. These findings suggested that the cause of death was cardiac tamponade due to purulent pericarditis associated with aortic stent-graft infection by MSSA.

Discussion

Purulent pericarditis is rare but can be fatal even if adequate treatment is provided, and its early detection and treatment are necessary in order to reduce the morbidity and mortality. However, the diagnosis of purulent pericarditis is

challenging and difficult to establish until an autopsy is performed (5).

In the present case, the patient never complained of chest pain during the hospital course. Furthermore, ECG revealed no signs of pericarditis, except for T-wave inversion in precordial leads on admission, which was generally not compatible with pericarditis but was compatible with coronary artery disease. In addition, blood cultures were negative after antibiotic therapy, and echocardiography revealed no vegetation and only slight pericardial effusion. Finally, the decrease in body temperature after the initiation of antibiotics incorrectly suggested that the patient was under appropriate treatment and that the infection was responding to the treatment. Together, these conditions were considered to have delayed the purulent pericarditis diagnosis. This view is supported by two previous studies that reported that patients with purulent pericarditis were less likely to complain of chest pain than those with acute pericarditis associated with other causes (3, 5).

Although our patient appeared physically active before admission, he had chronic kidney disease and end-stage RCC, both of which were considered critical risk factors for purulent pericarditis in the present case (9). The recurrence of aortic stent-graft infection due to MSSA was a possible cause of this clinical course in this patient, as he had a history of MSSA bacteremia after TEVAR two years prior to admission that was treated via long-term antibiotic therapy. The recurrence rate of MSSA bacteremia after appropriate antibiotics therapy was 2.1% in a previous study, but the recurrence rate of aortic stent-graft infection by MSSA was not reported (10).

In the present case, the autopsy revealed a massive amount of pus around the outer layer of the aortic stent-graft at the TEVAR site in addition to the pericardial space. This finding raised a chicken-and-egg issue regarding the primary focus of infection. There were no findings suggesting a direct invasion of infection from the aorta to the pericardium. In addition, pericardial effusion was not observed on admission. Considering these findings, it is reasonable to conclude that the aortic stent-graft site is a primary focus of infection and that subsequent hematogenous spread to the pericardial space can occur. However, several case reports have demonstrated purulent pericarditis complicated with infected aneurysm, where the direct spread of infection from the aorta to the pericardial space was suspected (11, 12). In the present case, the possibility of direct pathogen invasion from the ascending endograft to the pericardial space could not be completely ruled out because the proximal part of the endograft was located across the pericardial reflection on CT.

Although enhanced CT may be useful for identifying the focus of infection, we refrained from using it due to the pa-

tient's worsening renal function. Another diagnostic option is positron emission tomography (PET)-CT. The diagnostic utility of PET-CT was reported in a case of graft infection of the aorta (13). If the patient had been in a good condition, first-line therapy would have been emergent surgical drainage followed by aortic replacement therapy with long-term antibiotics administration. However, the patient's general condition gradually deteriorated after admission, and no surgical treatment could have been performed, even if a precise diagnosis had been made in the present case.

In conclusion, we herein report, to our knowledge, the first case of purulent pericarditis associated with aortic stent-graft infection caused by MSSA, which appropriate antibiotics failed to treat successfully. We suggest that surgical procedures, including drainage, should be introduced in such cases.

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

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