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【 CASE REPORT 】

Infective Endocarditis Revealed after Resolution of COVID-19 Infection

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Abstract:

A 34-year-old previously healthy Japanese woman was diagnosed with COVID-19 and treated with remdesivir and dexamethasone. She was discharge but returned the next day due to acute myocardial infarction. Conservative treatment was selected because of an embolic occlusion in the distal portion. Contrast-enhanced computed tomography and brain magnetic resonance imaging revealed a right renal infarction and multiple cerebral embolisms, respectively; she had a fever of 38.9℃ that night. Blood culture was positive for methicillin-susceptible *Staphylococcus aureus*. Transthoracic echocardiography revealed an 11-mm vegetation on the posterior mitral valve leaflet. Native mitral valve infective endocarditis causing multiple embolizations was diagnosed. She underwent surgical mitral valve replacement.

Key words: COVID-19 infection, infective endocarditis, mitral valve replacement

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Introduction

Coronavirus disease 2019 (COVID-19) has caused a global pandemic with over 500 million confirmed cases worldwide as of May 3, 2022 (1). It has been pointed out that routine medical care may become difficult in the era of the COVID-19 pandemic, leading to delays in diagnoses and missed complications and comorbidities (2).

A recent report described the relationship between COVID-19 infection and cardiovascular disease as well as associated complications (3), including infective endocarditis (IE), which is considered one of the most lethal complications of cardiovascular disease and requires early intervention. In the treatment of patients with COVID-19 infection, clinicians may tend to focus only on the specific examination and treatment of the disease itself. In addition, fear of coronavirus infection may lead to an insufficient general examination, including the physical evaluation. The treatment of patients with COVID-19 infection can lead to a risk of overlooking serious complications and comorbidities.

We herein report a patient with IE of the mitral valve that was identified after the patient developed COVID-19 infection.

Case Report

A 34-year-old previously healthy Japanese woman presented with a cough and fever that had lasted for 3 days. Her husband and son, who lived with her, had already been ill with COVID-19 and were being treated at home. Her nasopharyngeal swab for COVID-19 was positive, so she was admitted to another hospital for COVID-19 infection. Chest computed tomography (CT) revealed bilateral and peripheral ground-glass opacity (Fig. 1). Since the patient had been diagnosed with moderate COVID-19 pneumonia, intravenous remdesivir and oral dexamethasone were administered for one week. She was discharged after 10 days of hospitalization with no signs of symptoms of infection.

However, the patient returned to the hospital the day after discharge with a chief complaint of chest pain. Electrocardiography (ECG) showed ST elevation in leads II, III and aVF (Fig. 2A). She was thus diagnosed with an inferior-wall acute myocardial infarction. Emergency coronary angiography revealed an embolic occlusion in the distal part of the left circumflex branch (Fig. 2B), and conservative treatment

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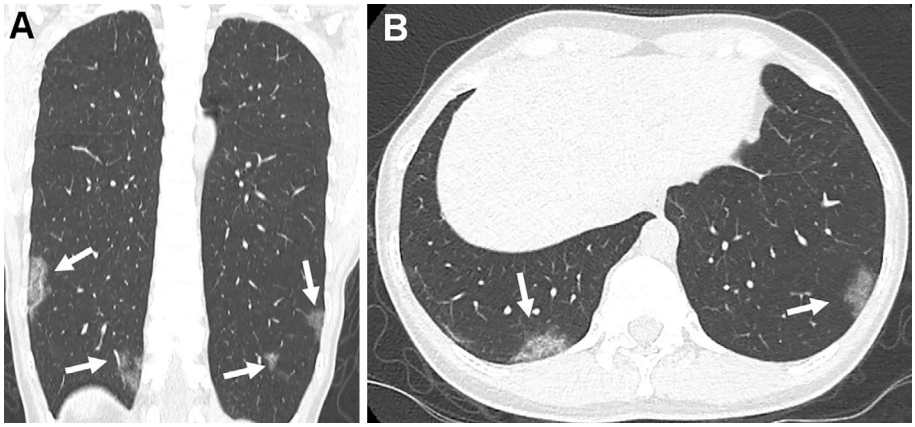

Figure 1. **Chest CT images in the coronal (A) and horizontal (B) planes obtained during the patient's admission, showing bilateral and peripheral ground-glass opacities in both inferior lobes (white arrows).**

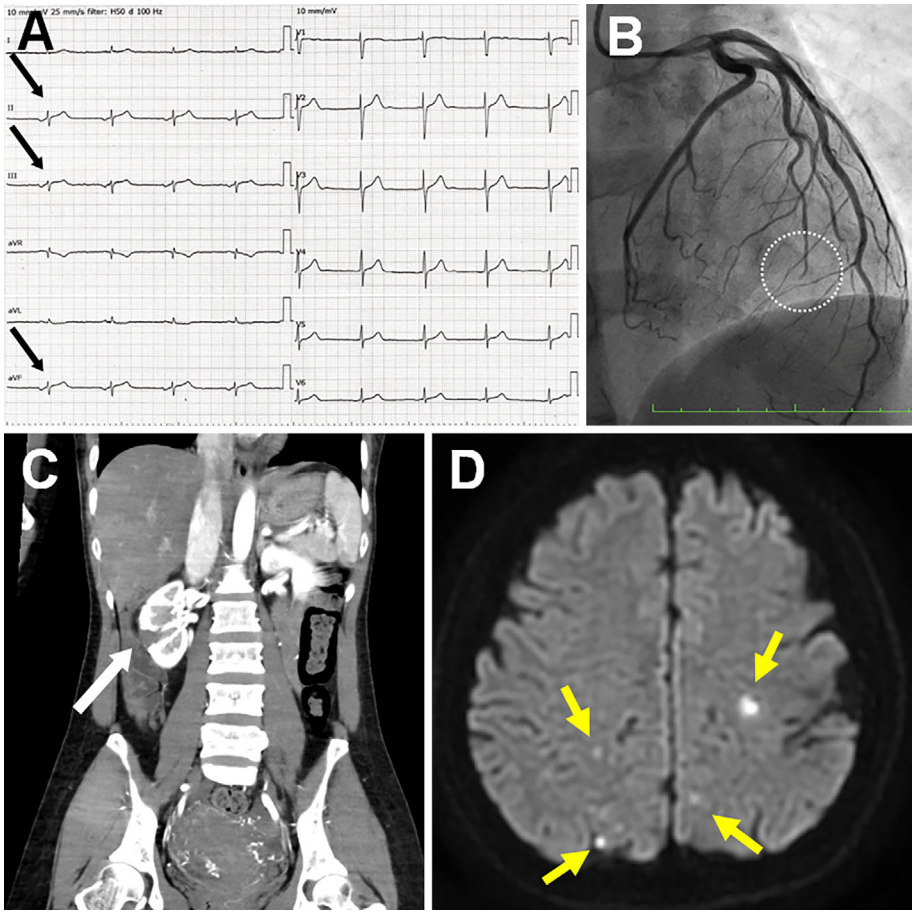

Figure 2. **(A) Electrocardiography showing ST elevation in leads II, III and aVF (black arrows). (B) Coronary angiography showing occlusion in the distal part of the left circumflex branch with thrombotic embolization (white dashed circle). (C) Contrast-enhanced CT (early phase) showing a right renal infarction (white arrow). (D) Diffusion-weighted MRI showing a multi-territory ischemic stroke, suggesting an embolic etiology (yellow arrows).**

by anticoagulation with heparin sodium was selected. Contrast-enhanced CT showed a right renal infarction (Fig. 2C). Brain diffusion-weighted magnetic resonance imaging (MRI) revealed an acute multi-territory ischemic stroke suggesting an embolic etiology (Fig. 2D), although no neurological signs or symptoms were present.

During the night of the same day as the CT and MRI examinations, the patient had a fever of 38.9℃. A blood culture was positive for Gram-positive coccus in three sets of samples (taken the day after the patient's admission for

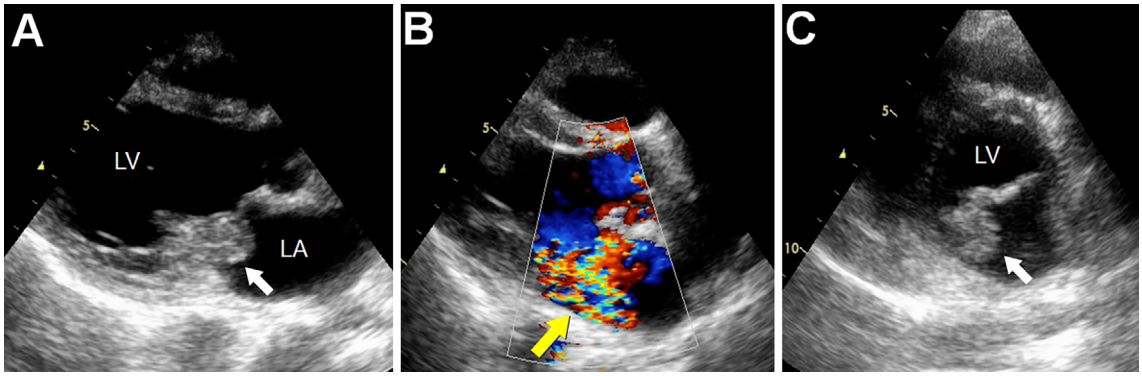

Figure 3. **Transthoracic echocardiography. Parasternal long-axis view showing a large (13.8×6.8 mm) vegetation (white arrow) on the posterior mitral valve leaflet (A) with severe regurgitation (yellow arrow) (B). Parasternal short-axis view showing large, coherent vegetation (white arrow) mainly on the medial side of the mitral valve (C). LV: left ventricle, LA: left atrium**

chest pain). Transthoracic echocardiography to assess IE revealed 11-mm vegetation on the posterior mitral valve leaflet. The left ventricular systolic function was preserved with an ejection fraction of 60%. We diagnosed her with native mitral valve IE causing multiple embolisms, including acute myocardial infarction. Treatment with intravenous vancomycin (1 g every 12 hours)+cefazolin (1 g every 8 hours) was started. She was transferred to our university hospital for more intensive care.

On admission, her consciousness level was clear, and no apparent neurological deficit was observed. Her blood pressure was 74/48 mmHg, pulse 69 beats/minute (regular). Her body temperature was 39.1℃. Her physiological examination revealed conjunctiva petechiae, hemorrhagic spots on the soft palate, and a grade II/VI pansystolic murmur audible at the apex. The results of laboratory tests were as follows: white blood cell count 20.9 K/μL with 94.8% segmented neutrophils, C-reactive protein 10.12 mg/dL, Troponin T 0.627 ng/mL, N-terminal pro-B-type natriuretic peptide (NT-proBNP) 4,041 pg/mL, and lactate 2.9 mmol/L. Chest X-ray showed no enlargement of the cardiac silhouette (cardio-thoracic ratio of 49%), pulmonary vascular congestion, or pleural effusion. ECG indicated sinus rhythm with a heart rate of 70/min and no significant changes. Transthoracic echocardiography revealed large (13.8×6.8 mm) and mobile vegetations on the mitral posterior leaflet (P3 prolapse) with severe mitral regurgitation (Fig. 3).

After admission, the causative organism was found to be methicillin-susceptible *Staphylococcus aureus* (MSSA), and optimal antimicrobial therapy was continued, although the portal of pathogen entry was not identified. Despite optimal antibacterial treatment, the patient exhibited antimicrobial refractory IE complicated by septic shock requiring circulatory agonists and a large mobile vegetation carrying a risk of embolism, although the effect of COVID-19 infection on systemic coagulation abnormalities could not be ruled out. Surgical mitral valve replacement was performed one week after her admission. The patient's postoperative course was uneventful. She was discharged without any complication on the 25th postoperative day.

Discussion

During the current COVID-19 pandemic, several cases have been reported in which the diagnosis of comorbidities was delayed because of the focus on COVID-19 treatment (4, 5). In addition to patient factors such as refraining from seeking medical care, there is also the influence of confusion in the medical process on the part of medical care providers, such as the omission of physical examinations (6). In fact, the introduction of remote medical care for COVID-19 patients has reduced opportunities for physical examinations. Even when patients are examined in person, physicians may not adequately evaluate them due to their own fear of infection (7).

Reports of COVID-19 associated with IE are rare, with one study reporting a complication rate of 0.1% for IE (8). Some of the factors that contribute to IE in an individual with a COVID-19 infection include a severe inflammatory response, endothelial damage and dysfunction, and immunosuppression caused by medications that are used to treat COVID-19 (9). One report suggests that COVID-19 itself may be responsible for valve destruction (10). COVID-19 is associated with a severe systemic inflammatory response (11), and the use of dexamethasone is recommended for patients with COVID-19 at all severity levels (12). Systemic glucocorticoids have many effects on the immune system that predispose individuals to infection, resulting in a dose-dependent increase in the risk of infection by common bacterial pathogens (13), which might also be one of the causes of IE. In patients with valvular heart disease, intracardiac prosthesis or congenital heart disease, careful precautions should also be taken to prevent infusion route infections under immunosuppressive therapy.

IE may present similarly to COVID-19 infection, both being characterized by shortness of breath and vital sign abnormalities, so IE and COVID-19 infection may thus initially be difficult to distinguish due to their similar presen-

tations. There have been case reports of misdiagnoses of IE and COVID-19 (14). Nonetheless, a rapid and accurate identification of IE is of paramount importance, as urgent surgical intervention is often indicated, and failure to intervene may have fatal consequences (15).

A meta-analysis demonstrated that mitral valve prolapse is associated with an increased risk of IE (16). Instead of providing uniform medical care to all patients, we believe that patients with a high prior probability of developing IE should be examined more carefully. In our patient's case, there was a possibility that mitral valve prolapse was present, and we believe that auscultatory findings and echocardiography during hospitalization for COVID-19 infection may have contributed to the prevention and early detection of IE. The future development of a non-invasive and contactless diagnostic medical device for the management of infectious disease is desirable. The detailed mechanisms underlying the relationship between COVID-19 and IE are unknown, so the accumulation of more clinical studies is necessary.

Conclusions

In clinical practice, physicians' fear of infection with COVID-19 often leads to an insufficient general examination, including the physical examination of the patient. In addition, it is easy to focus only on the treatment of COVID-19 infection. In the ongoing COVID-19 pandemic, it is important to treat patients while keeping in mind the potential underlying diseases and comorbidities, as the presence of a COVID-19 infection can carry a serious risk of overlooking serious complications and comorbidities.

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

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