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Case report

A curious Takotsubo cardiomyopathy after COVID-19☆

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ABSTRACT

We present the case of a 66-year-old woman undergoing chronic dialysis who developed pneumonia and enteritis after being infected with COVID-19 and had severe wall motion reduction similar to a left ventricular aneurysm. There was concern that the condition might worsen due to left ventricular wall thinning and curious wall motion abnormalities, but echocardiography one month later showed normalization. After four months, simultaneous binuclear myocardial scintigraphy of thallium and BMIPP showed that the mismatch had disappeared. We considered that there may be other factors specific to COVID-19 infection in addition to the stress associated with infection and reviewed the literature.

Introduction

Severe acute respiratory syndrome coronavirus type 2 (SARS-CoV-2) infection was first reported in China in late 2019 and spread across the world in just a few months, raising concerns about health complications, including the risk of cardiovascular disease [1,2]. The exact mechanism by which novel coronavirus infection (COVID-19) increases the risk of cardiovascular disease is still under investigation, with several hypotheses focusing on immunomodulatory abnormalities (e.g., cytokine storm) and myocardial viral tropism [1,3]. Inflammation-induced cytokine storms and procoagulant states in novel coronavirus infection have been reported to increase the risk of cardiac injury, fainting, coronary artery spasm, and acute myocardial infarction [4]. We report a case of Takotsubo cardiomyopathy that occurred as a COVID-19 cardiovascular symptom.

Case report

The patient was a 66-year-old woman on chronic hemodialysis who developed a fever on December 17, 2022, and was diagnosed as COVID-19 positive on December 19. She was treated with Molnupiravir at her dialysis hospital and had home care afterwards. Subsequently, vomiting continued, and she visited her previous doctor, who observed an increased cTnI value and an electrocardiogram abnormality. Transthoracic echocardiography revealed abnormal wall motion, and ACS was suspected and the patient was referred to our hospital. She had been feeling nauseous and vomited repeatedly since December 26, but did not complain of chest pain or dyspnea.

The patient had been diagnosed with high blood pressure and diabetic nephropathy in 2019 and had been on dialysis since January 2022, and had a history of left humerus fracture, cataract, and lumbar compression fracture.

Body temperature 37.5 degrees, HR 87 bpm, blood pressure 175/81 mmHg, respiratory rate 23 /min. Her bloodwork was a WBC 4.5×10^9/L (Nuet 82.8%, Lym 10.8%, Mono 6.4%, Eos 0.0%, Bas 0.0%), Hemoglobin 129 g/L, PLT 149×10^9/L, Blood creatinine 392μmol/L, Creatine kinase 156 IU/L, Creatine kinase-MB 12 IU/L, C-reactive protein 43,600 μmol/L, D-dimer was 1.5×10^3 μg/L, cTnI 3265.7 ng/L, and NT-pro BNP 92,951 pmol/L. A COVID-19 nasal PCR test was positive, with a CT value of 22.8.

The electrocardiogram showed ST elevation of I, V, and 1-V4 and ST depression of II, III, and aVf (Fig. 1A) An echocardiographic apical 3-chamber image showed thinned ventricular aneurysm-like abnormal wall motion from the middle of the left ventricle to the apex (Video 1A). Plain CT of the chest and abdomen revealed mild pneumonia and enteritis (Fig. 2A). Although no chest pain was observed, STEMI was strongly suspected based on elevated myocardial enzymes, electrocardiogram changes, and abnormal left ventricular wall motion on echocardiography. Accordingly, emergency coronary angiography was performed. As no significant stenosis was observed in the coronary

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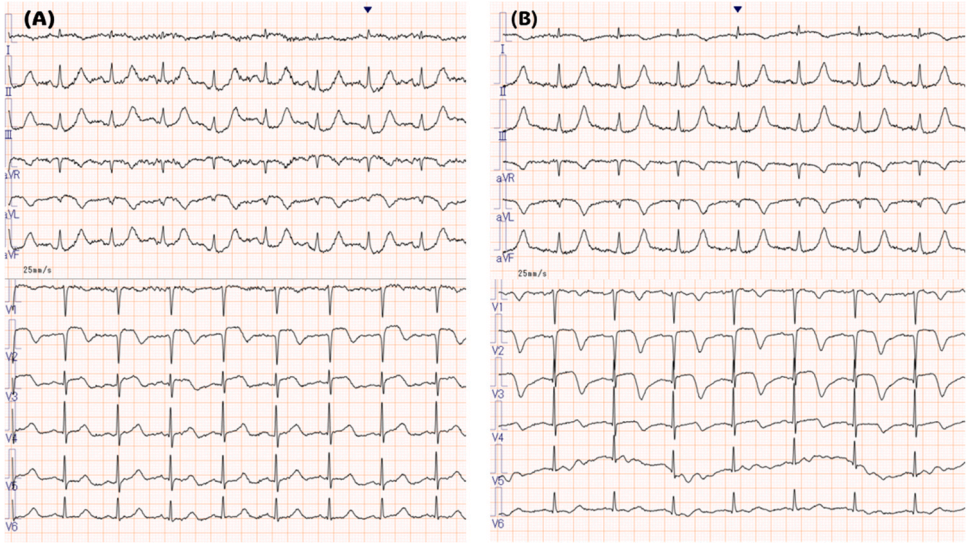

Fig. 1. 12-lead electrocardiograms taken on the first and second days. ST elevation of I, V1-V3 and ST depression of II, III, and aVf (A) and giant negative T waves observed in IaVL V1-V5 (B).

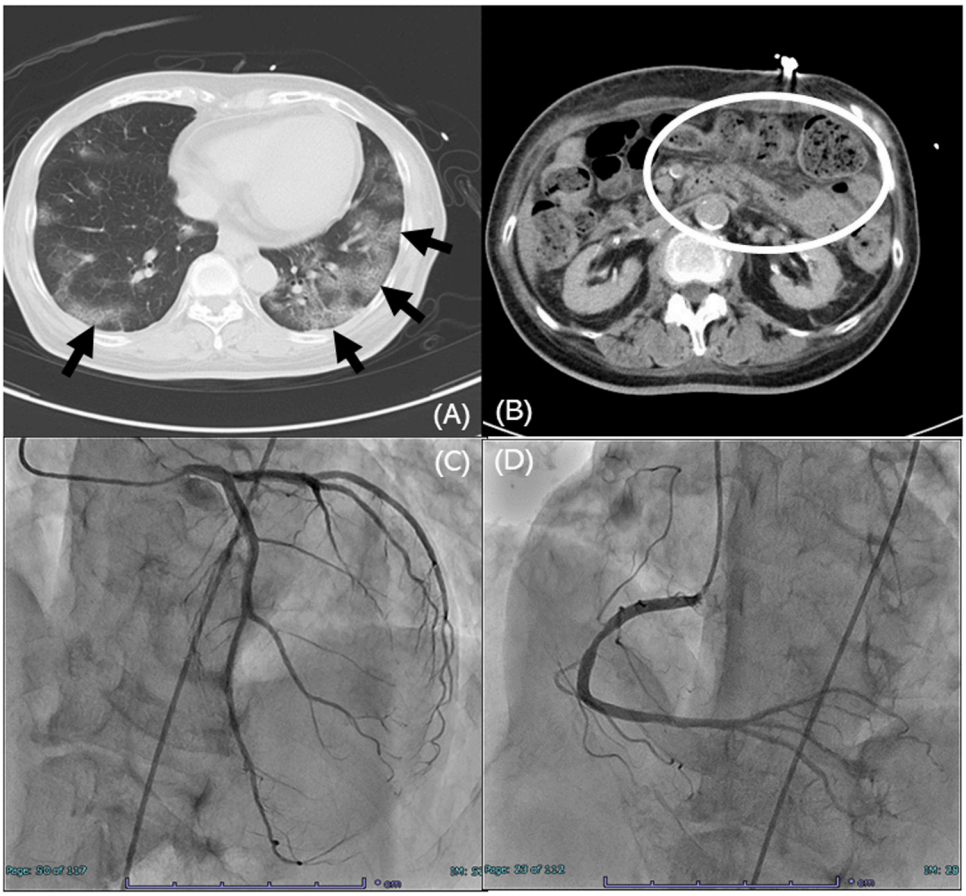

Fig. 2. Thoracoabdominal plain CT and coronary angiography on the first day. CT revealed patchy ground-glass opacities and thickening of the interlobular septa in both lungs, as well as a small amount of ascites and edema in the fatty tissue of the mesenteric membrane, suggesting COVID-19-related pneumonia and enteritis (A, B; black arrows indicate pneumonia, white circles pneumonia enteritis). No significant stenosis was observed in the left and right coronary arteries (C, D).

arteries on contrast imaging (Figs. 2B and 2C), left ventricular imaging was performed; this revealed no contraction centered on segment 1 and segment 2, and hypercontraction in other segments (Video 2). Although the strange left ventricular wall motion abnormalities were not typical, she was diagnosed with Takotsubo cardiomyopathy. The patient was admitted to the hospital for careful follow-up under isolation measures, as the CT value was low and she was in the acute to subacute stage of COVID-19 infection.

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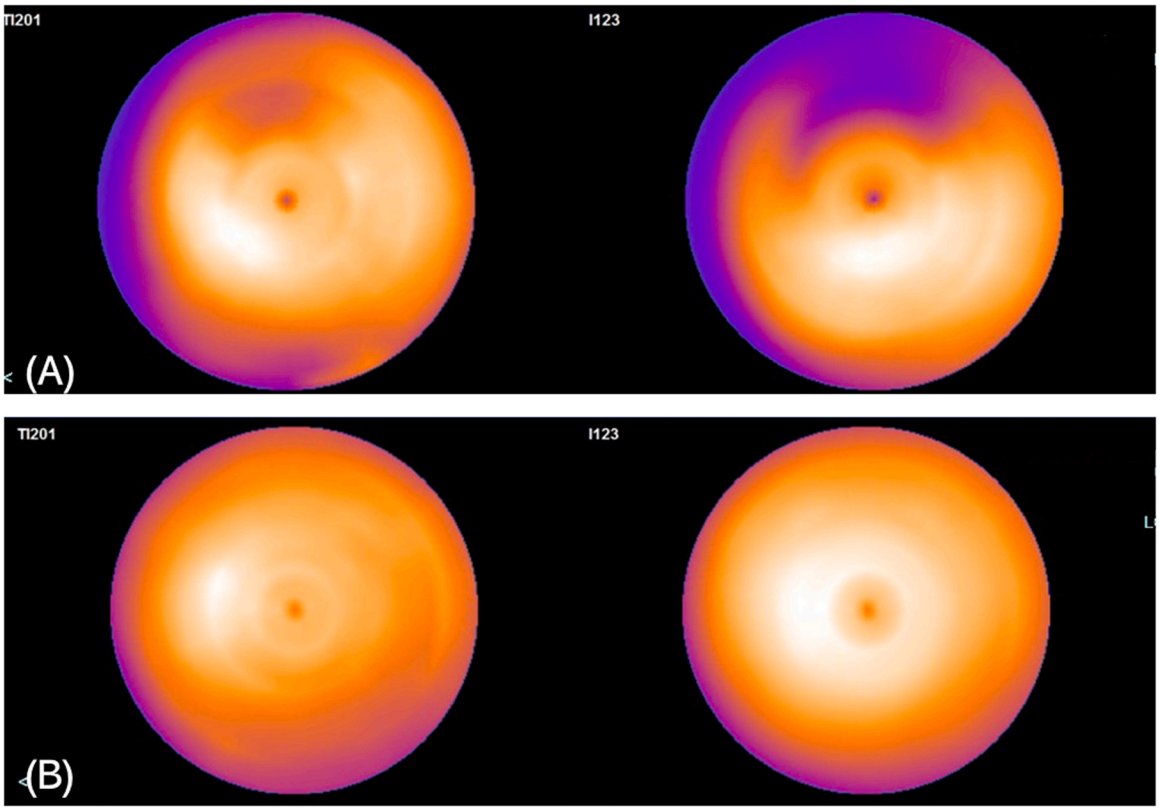

Fig. 3. Simultaneous binuclear myocardial scintigraphy of thallium and BMIPP images on the 11th day and 4 months later. A mismatch between thallium and BMIPP was observed in the anterior wall region, but not in the apical region (A). The blood flow/metabolic mismatch observed during the acute phase disappeared during the chronic phase (B).

Video Legends.

Video 1: Echocardiograms on the first day and 1 month later. The 3-chamber view showed thinning of the wall from the mid of the anterior septum to the apex of the heart, a protruding aneurysm-like left ventricular wall, and severe wall hypokinesis (A). The ventricular aneurysm-like image of reduced wall motion had disappeared (B).

Video 2: Left ventricular contrast image on the first day. No contraction was observed in segment 1 and segment 2 instead of segment 3, and hypercontraction was observed in other segments. Local wall motion abnormality resembling a giant ventricular aneurysm was observed in the left ventricle.

Bisoprolol was started because a short run was observed on the electrocardiogram monitor. An electrocardiogram on the second day showed giant negative T waves (Fig. 1B). The patient had been experiencing frequent vomiting and constipation before admission that had lasted for one week, suggesting decreased intestinal peristalsis due to enteritis; accordingly, laxatives were also administered. Thereafter, the patient continued to experience repeated nausea and vomiting, but improvement was seen around the seventh day. On the 10th day, a simultaneous binuclear myocardial scintigraphy of thallium and BMIPP showed blood flow and metabolic mismatch accumulation in the anterior wall region (Fig. 3A), which was definitively diagnosed as Takotsubo cardiomyopathy. After admission, neither COVID-19 nor Takotsubo cardiomyopathy became severe, and the patient was discharged from the hospital on the 12th day. During the acute phase, echocardiography and left ventriculography showed abnormal wall motion similar to a ventricular aneurysm, but echocardiography performed one month later showed that the wall motion abnormality had improved (Video 1B). At four months, simultaneous binuclear myocardial scintigraphy of thallium and BMIPP revealed that the mismatch accumulation had disappeared (Fig. 3B).

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Discussion

Takotsubo cardiomyopathy as a complication of COVID-19 has been previously reported [5]. Generally, however, the reason for the characteristic wall motion contraction pattern of Takotsubo cardiomyopathy is unknown. One possibility is that the apex of the heart may be more vulnerable to a sudden increase in circulating catecholamine concentrations due to it having a higher density of sympathetic β-receptors compared to the basal myocardium; alternately, the perfusion gradient from the basal to the apex myocardium may cause a local regional difference in the cardiac blood flow [6]. In patients who contract COVID-19, it is reported that Takotsubo cardiomyopathy can be caused by the release of norepinephrine from the end of the sympathetic nervous system due to the stress of infection, catecholamin-induced microvasospasm and dysfunction associated with the release of epinephrine from the adrenal medulla, or direct cardiotoxicity related to catecholamine [7]. Additionally, myalgic encephalomyelitis (ME) and chronic fatigue syndrome (CFS) can develop after being infected with COVID-19, with symptoms such as strong fatigue, gastrointestinal dysfunction, muscle pain, headache, and loss of concentration. Functionally active autoantibodies (fAABs) have been detected in ME/CFS patients that target two to seven different G protein-coupled receptors (GPCR-fAABs), including autoantibodies to β2-adrenergic receptors and muscarinic cholinergic receptors, and are reported to act as agonists for these receptors [8]. Previous reports have shown that stress cardiomyopathy (SCM) can be induced by inhaled β2-agonists and by intravenous administration of catecholamines and beta receptor agonists [9,10]. As described by Abraham et al., the neural control of the human heart is incompletely characterized, and the different ballooning patterns seen

in SCM may be related to sympathetic innervation and beta-receptors. This results from a complex interplay between body density and function, and catecholamine sensitivity [10].

In this case, the strange local wall motion abnormality can be attributed not only to the cytokine storm associated with COVID-19 infection, but also the influence of GPCR-fAABs, including ones targeting β2-adrenergic receptors. We hypothesize that these combined events may have resulted in the unique response to sympathetic nerve stimulation, which is different from normal Takotsubo cardiomyopathy, which is in the myocardium at the base of the heart.

Conclusions

Patients who develop Takotsubo cardiomyopathy in post-COVID-19 conditions may exhibit atypical wall motion abnormalities due to a cytokine storm and catecholamine receptor antibodies.

Ethical approval

This is case report, so we have informed consent.

Fundings

The authors have reported with no relationships relevant to the contents of this paper to disclose.

Informed consent

Written informed consent was obtained from the patient to publish this case report.

Author contribution

Masashi Morita contributed to patient care.
The manuscript was peer-reviewed by all authors.

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CRediT authorship contribution statement

Yoji Sumimoto: Writing – review & editing. **Munehiro Kanegawa:** Writing – review & editing. **Shiori Maeda:** Writing – review & editing. **Masashi Morita:** Writing – review & editing. **Haruyuki Kinoshita:** Conceptualization, Data curation, Formal analysis, Investigation, Methodology, Project administration, Resources, Supervision, Visualization, Writing – original draft, Writing – review & editing. **Hiroshi Sugino:** Writing – review & editing. **Takashi Shimonaga:** Writing – review & editing. **Kenji Masada:** Writing – review & editing.

Declaration of Competing Interest

No authors have any competing interests in this case.

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