A case of takotsubo cardiomyopathy triggered by asthma exacerbation after mRNA-based vaccination for coronavirus disease 2019

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Abstract

Recent studies have reported that coronavirus disease-2019 (COVID-19) vaccination can exacerbate asthma. Status asthmaticus sometimes induces takotsubo cardiomyopathy. We present a case of takotsubo cardiomyopathy triggered by asthma exacerbation after the mRNA-based vaccination. Therapies for status asthmaticus resulted in prompt improvement of respiratory failure and cardiac-apex ballooning.

Case report

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ABSTRACT

Recent studies have reported that coronavirus disease-2019 (COVID-19) vaccination can exacerbate asthma. Status asthmaticus sometimes induces takotsubo cardiomyopathy. We present a case of takotsubo cardiomyopathy triggered by asthma exacerbation after the mRNA-based vaccination. Therapies for status asthmaticus resulted in prompt improvement of respiratory failure and cardiac-apex ballooning.

Key Clinical Message

In patients with asthma, mRNA-based COVID-19 vaccination can trigger asthma exacerbation and takotsubo cardiomyopathy; therefore, adequate asthma control is essential for asthma patients receiving the vaccination.

KEYWORDS: COVID-19 vaccine, asthma exacerbation, takotsubo cardiomyopathy, mRNA-based vaccination

1 INTRODUCTION

The coronavirus disease 2019 (COVID-19) pandemic has affected people's lifestyles, and vaccines have been administered worldwide.

Most COVID-19 vaccines are mRNA-based and are highly effective; however, their adverse reactions have not been entirely clarified. Common side effects include fever, fatigue, headache, or local pain. However, some studies have reported that COVID-19 vaccination exacerbates asthma [1]. In addition, anaphylaxis, takotsubo cardiomyopathy (TTC), myocarditis, and pericarditis have been reported to occur rarely [2]. Therefore, attention should be paid to the emergence of severe side effects after COVID-19 vaccination.

TTC is an acute, reversible myocardial injury induced by emotional or physical stress. Risk factors for TTC include female sex, menopause, and psychiatric disorders. While natural disasters and negative and positive emotions are mental causes, physical causes include trauma, surgery, medications, or intoxication. Respiratory disorders including pneumothorax, chronic obstructive pulmonary disease exacerbation, and bacterial or viral infections; chemotherapy for cancer; and invasive procedures such as bronchoscopy or intubation have been reported as triggers of TTC in patients with respiratory diseases. Moreover, asthma exacerbation and its therapies, such as short- acting β2 agonists (SABAs), adrenaline, or intubation are known to cause TTC [3,4,5]. Fatal complications of TTC include cardiogenic shock, systemic embolism, and heart rupture; hence, TTC should not be missed. However, because respiratory problems often cause dyspnea or chest pain, TTC is difficult to diagnose [6,7].

Here, we report our experience of COVID-19 vaccine-induced asthma exacerbation and TTC in a patient with bronchial asthma.

2 CASE PRESENTATION

2.1 Case history / examination

A 70-year-old Japanese woman with a medical history of bronchial asthma, rheumatoid arthritis, and hypertension had been prescribed a fluticasone-vilanterol combination inhaler for asthma and tacrolimus, iguratimod, and golimumab for rheumatoid arthritis. She had not experienced asthma exacerbation during the previous decade. She was a never-smoker with pollen allergy and had no history of drug allergies. Although she had a slight cough and dyspnea for a few days, she received the second dose of the mRNA-based COVID-19 vaccine BNT162b2 (Pfizer-BioNTech) and took acetaminophen to prevent fever. Approximately 12 h after vaccination, her respiratory symptoms worsened, and the patient was transported to our emergency room by ambulance. The percutaneous oxygen saturation (SpO_2) was 86% (reservoir mask O_2, 15 L/min). Physical examination revealed decreased respiratory sounds and a silent chest. Wheezing emerged after nebulization with the SABA procaterol. The patient had no edema, rash, or aggravation of joint symptoms.

The initial blood test showed an increased white blood cell count with eosinophilia, a negative C-reactive protein test, and increased total immunoglobulin (Ig)E. Arterial blood gas analysis before intubation revealed acute hypercapnic respiratory failure **(Table 1).** A 12-lead electrocardiogram demonstrated sinus rhythm with ST elevation (V2-V5, **Figure 1**), but the creatine kinase MB and troponin I levels were not elevated. Chest radiography and thoracoabdominal contrast-enhanced computed tomography revealed no acute pulmonary abnormalities. Bronchial wall thickening and a calcified nodule were detected in the lower lobe of the right lung. Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) nucleic acid test results were negative. In the emergency department, she had a depressed level of consciousness; therefore, endotracheal intubation was performed, and intravenous corticosteroids were administered. To rule out cardiogenic disease, coronary angiography was performed, which revealed no significant coronary artery disease. However, left ventriculography and ultrasonic cardiography revealed apical akinetic expansion (apical ballooning) and severe hypokinesia of the mid-ventricular segments, with slightly reduced systolic function (ejection fraction, 47%,**Figure 2,3**).

2.2 Differential diagnosis

Otolaryngological examination to investigate other comorbidities related to asthma exacerbation revealed that the patient had no eosinophilic sinusitis but had bilateral chronic sinusitis and right secretory otitis media, which were treated with antibiotics. Other infections were excluded, and there were no significant bacterial findings. Serum aspergillus/cryptococcal/candida-mannan antigen and β-D-glucan tests were negative. Although the patient had oral candidiasis, it was not a cause of asthma exacerbation. The SARS-CoV-2 nucleic acid test results were negative.

Computed tomography showed no signs of pneumonia, exacerbation of interstitial pneumonitis, pulmonary embolism, or acute respiratory distress syndrome.

She had acetaminophen after COVID-19 vaccination; however, she did not have a history of allergy to drugs, including nonsteroidal anti-inflammatory drugs (NSAIDs). In addition, the patient did not have any obvious contact with potential allergens. Anaphylaxis was considered in the differential diagnosis, but other cutaneous and mucosal symptoms were absent.

She had not experienced asthma exacerbation during the previous decade. Accordingly, her adherence was not the cause of the asthmatic crisis. In this case, we did not administer adrenaline before the diagnosis of TTC; hence, adrenaline use was not involved in the onset of TTC.

Therefore, we consider that her status asthmaticus was enhanced by the COVID-19 vaccination and not by infection, allergic reactions, or medication.

2.3 Outcome and follow-up

The patient was treated with procaterol, systemic corticosteroids, leukotriene receptor antagonists, and aminophylline for status asthmaticus and with heparin for TTC. Adrenaline was used after the diagnosis of

TTC. The respiratory status improved promptly, and she was extubated on day 2 and discharged on day 10. During hospitalization, ST changes in the electrocardiogram were typical for TTC; ST elevation normalized within few days and a deep negative T wave developed in a week. After asthma therapy and extubation, the fractional exhaled nitric oxide level was 10 ppb, and spirometry showed an almost normal pattern.

The patient was discharged with instructions to follow up as an outpatient and was prescribed an inhaled corticosteroids/long-acting β agonists/long-acting muscarinic antagonist combination, leukotriene receptor antagonists, and the therapeutic anti-IgE antibody omalizumab. Her outpatient course was stable.

3 DISCUSSION

TTC is an acute reversible myocardial injury first reported by Sato et al. in 1990. The term "takotsubo" means an octopus fishing pot in Japanese that has a round bottom and a narrow neck, and it is similar to the shape of the heart in TTC. TTC is triggered by emotional (negative and positive) or physical stress, including asthma exacerbation. Symptoms similar to those of myocardial infarction have been observed in patients with TTC, without coronary artery stenosis [3,8,9].

The pathophysiology of stress cardiomyopathy is unclear and may involve several mechanisms. One pathway involves high circulating catecholamines released by the sympathetic nerves under stress, including respiratory diseases. Sato et al. showed that microvascular dysfunction and coronary artery spasms cause TTC.

As most patients with TTC are postmenopausal women, estrogen deprivation has been proposed as a cause in several hypotheses [20], whereas some studies have reported abnormalities in the central autonomic nervous system [10].

Although TTC has a good prognosis, patients with TTC sometimes develop heart failure, arrhythmia, systemic embolism, cardiogenic shock, and cardiac rupture, which might be fatal. Underlying diseases triggering TTC increase mortality (12.2% vs. 1.1% in patients without preexisting diseases) [6]. Our patient did not have cardiac complications; however, adequate treatment for asthma was required.

Dyspnea is a common symptom in respiratory illnesses and TTC; therefore, electrocardiography and echocardiography should be performed before the use of SABAs or adrenaline.

Infection with SARS-CoV-2, a novel virus that was first reported in Wuhan, China in 2019, might trigger asthma flare-up; however, the SARS-CoV-2 polymerase chain reaction test of the patient was negative, indicating that she was not infected with SARS-CoV-2. COVID-19 aggravates many diseases; therefore, vaccines have been developed and implemented rapidly worldwide to reduce the risk of progression and death. mRNA-based COVID-19 vaccines are effective and safe. Nonetheless, adverse events associated with the vaccines are not completely understood. Almost all COVID-19 vaccines used in Japan are mRNA-based.

TTC has been reportedly triggered by mRNA-based COVID-19 vaccines [11,12,13] or the influenza vaccine [12,14]. However, our patient had status asthmaticus, and the vaccination did not seem directly of TTC, despite her symptoms being common to both diseases.

Colaneri et al. reported a case of asthma exacerbation triggered by an mRNA-based COVID-19 vaccine [1]. mRNA-based vaccines promote secretion of type I interferons and that increased interferon-I production is associated with asthma exacerbation [15,16]. Nappi et al. reported a case in which two doses of the adenovirus-vectored vaccine ChAdOx1 (Astra Zeneca) progressively worsened asthma and a subsequent dose of the COVID-19 vaccine mRNA-1273 (Moderna) triggered eosinophilic granulomatosis with polyangiitis [17]. Regardless of the type of vaccine, COVID-19 vaccination itself may exacerbate asthma.

Hence, we concluded that the mRNA-based vaccine enhanced asthma exacerbation and TTC onset in our patient. However, our study was limited because the relationship between asthma exacerbation and mRNA-based COVID-19 vaccines is currently difficult to demonstrate directly. Thus, more reports and further studies are required.

Between February 17, 2021, and July 25, 2021, 74,137,348 patients received the BNT162b2 vaccine in Japan. Among these, 219 (0.0003%) cases of asthma attacks were reported to the Japanese Ministry of Health, Labour, and Welfare, which indicates a low incidence [18].

Pfaar et al. reported that patients taking biologicals for asthma do not have an increased risk of allergic reactions following COVID-19 vaccination [19].

4 CONCLUSION

The mRNA-based COVID-19 vaccination can trigger asthma exacerbation and TTC in patients with asthma control. The combination of COVID-19 vaccination and adequate asthma control is essential for patients with bronchial asthma during the SARS-CoV-2 pandemic.

AUTHOR CONTRIBUTIONS

Y. Tachibana, T. Yamada, and T. Tsuji conceived and presented the idea. Y. Tachibana wrote the manuscript in consultation with T. Tsuji, T. Yamada and K. Takayama. J. Murai collected the data. K. Jinno, S. Matsumoto, A. Sasada, S. Goda, A. Omura, S. Shiotsu, T. Yuba, C. Takumi, and N. Hiraoka contributed to the interpretation. All authors provided critical feedback and helped to complete the manuscript.

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DECLARATION OF INTEREST

None.

CONSENT

Written informed consent for publication of clinical data was obtained from the patient.

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