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Case Report

# Acute asthma exacerbation due to the SARS-CoV-2 vaccine (Pfizer-BioNTech BNT162b2 messenger RNA COVID-19 vaccine [Comirnaty®])

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ABSTRACT

The messenger RNA vaccine against SARS-CoV-2 is effective at preventing COVID-19-associated hospitalization, and the Centers for Disease Control and Prevention has recommended vaccination for all eligible individuals. We demonstrate a case involving a patient who developed a life-threatening acute asthma exacerbation after receiving their third dose of the BNT16b2 vaccine. Because eosinophilia was observed after the second inoculation, it was considered likely that the patient had been sensitized to the BNT16b2 vaccine. Theoretically, the SARS-CoV-2 vaccine could trigger the exacerbation of asthma. It should be recognized that repeated SARS-CoV-2 vaccination may be a risk factor for the acute exacerbation of asthma.


## Introduction

The most common adverse reactions of the Pfizer-BioNTech BNT162b2 messenger RNA (mRNA) COVID-19 vaccine (Comirnaty®) were local reactions at the injection site, fatigue, headache, muscle pain, chills, joint pain, and fever (Thomas *et al.*, 2021). A serious allergic reaction involved anaphylaxis, but the incidence was very low, and other allergic reactions have been uncertain. We herein report a patient who developed acute asthma exacerbation after receiving the third dose of the BNT16b2 vaccine, who was considered likely to have been sensitized to the BNT16b2 vaccine during repeated vaccination.

## Case presentation

A female patient aged 55 years was transported to the emergency department for sudden shortness of breath. She had previously visited the Department of Cardiovascular Surgery due to hypertension and for postoperative checkups. She had been diagnosed with Marfan syndrome and had repeated aortic dissection, undergoing replacement surgery of the aortic arch, aortic root, and descending aorta. The second dose of the BNT16b2 vaccine had been administered 8 months before this most recent presentation, and a booster dose of the same vaccine had been administered 1 day before she visited our emergency department.

She had felt throat discomfort and chest oppression after receiving the second shot. She had never experienced severe side effects due to any vaccination before. On presentation, her blood pressure was 193/107 mm Hg, pulse was 112 beats/min, and regular respiratory rate was 35 breaths/min. Her body temperature was 36.3°C. Her $SpO_2$ was 94%, breathing supplemental oxygen at a rate of 10 l/min through a reservoir mask, and a blood gas analysis revealed a pH 7.36, $PaO_2$ of 74.0 mm Hg, and $PaCO_2$ of 56.0 mm Hg. She was unable to lie down and remained in an orthopneic position.

A physical examination indicated wheezing in both lungs, with no heart murmur. Laboratory tests revealed an elevated white blood cell count (10,240/μl), elevated eosinophil count (1980/μl; 19.4%), and mildly elevated C-reactive protein level (0.31 mg/dl). High-resolution computed tomography (CT) demonstrated diffuse and marked bronchial wall thickening and mediastinum lymph node swelling (Figure 1a). She was suspected of having an acute exacerbation of asthma caused by the BNT16b2 vaccine booster dose.

Noninvasive positive airway pressure ventilation was initiated with the following settings: spontaneous/timed mode, inspiratory

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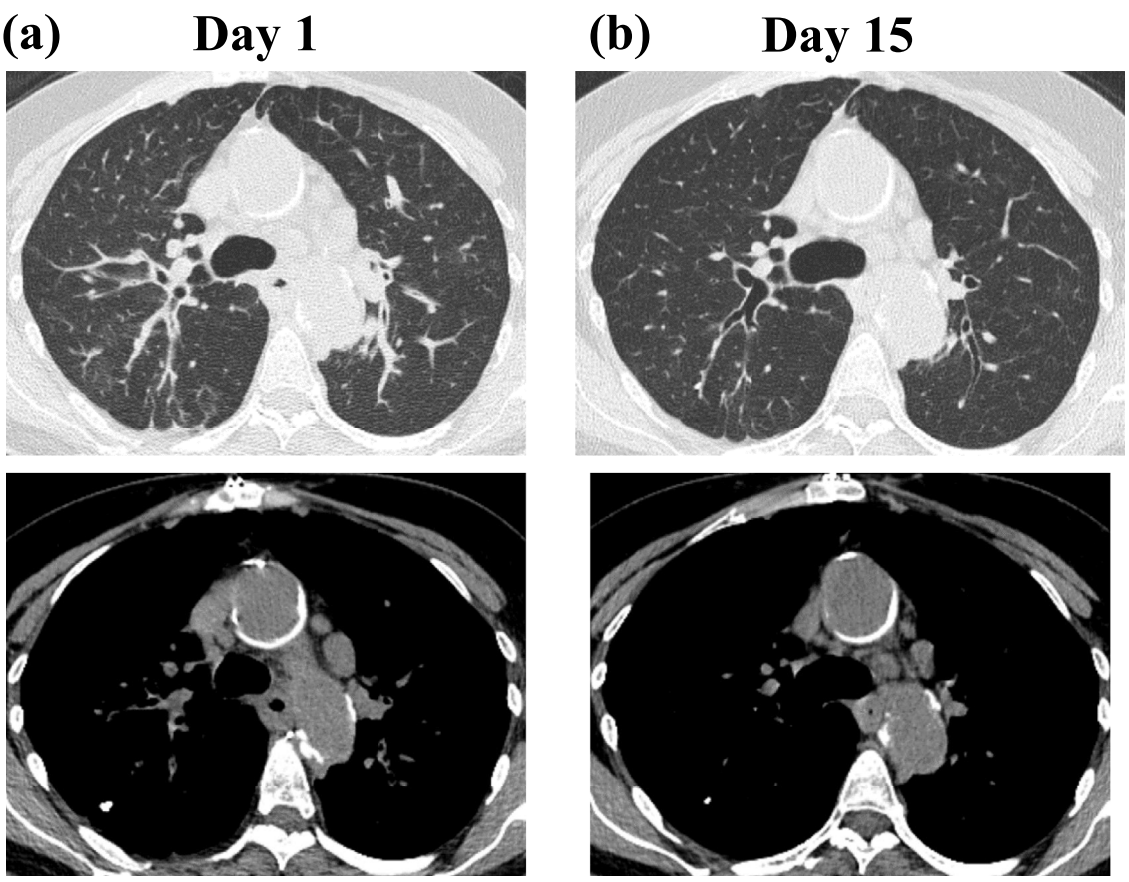


**Figure 1.** (a) High-resolution computed tomography on admission demonstrated diffuse and marked bronchial wall thickening and mediastinum lymph node swelling. (b) High-resolution computed tomography performed on day 15 after admission revealed improvement of the bronchial wall thickening and a reduction in the size of mediastinal lymph nodes.

positive airway pressure 10 cm $H_2O$; expiratory positive airway pressure 5 cm $H_2O$, $FiO_2$ 70%. Methylprednisolone (125 mg) and aminophylline (250 mg) through intravenous drip were initiated, and subsequently, methylprednisolone (60 mg) was repeated every 6 hours. The next day, her symptoms had dramatically improved, so noninvasive positive airway pressure ventilation and intravenous methylprednisolone were ceased. Inhaled fluticasone furoate/vilanterol trifenatate at 200/25 μg and oral montelukast at 10 mg was started. In addition, oral aminophylline at 200 mg twice daily was added for 6 days starting on the second day, and 30 mg of prednisolone was administered for 5 days on the third day. Because shortness of breath and wheezing were not observed, she was discharged on the seventh day. High-resolution CT performed on day 15 after admission revealed an improvement in the bronchial wall thickening and reduction in mediastinal lymph node sizes (Figure 1b).

According to the patient's medical record, the eosinophil absolute counts and percentage were normal 83 days before the first dose of the vaccine (270/μl; 3.8%). An elevated white blood cell count (12,700/μl) was initially noted 20 days after the second dose, and an elevated eosinophil count and the percentage were noted 84 days after the second dose (4590/μl; 37.7%); both spontaneously decreased 175 days after the second dose (1170/μl; 16.4%). However, the count increased again on the day after the third dose (1980/μl; 19.4%). After discharge, the Fractioned exhaled nitric oxide (FeNO) level was elevated (275 parts per billion). She was diagnosed with bronchial asthma with mild chronic sinusitis and has continuously been treated with inhaled fluticasone furoate/vilanterol trifenatate and montelukast. At the time of writing this report, she has not experienced any further acute exacerbation.

## Discussion

The recent approval of novel mRNA SARS-CoV-2 mRNA vaccines has provided hope that we may finally be able to end the COVID-19 pandemic. One of the obstacles to the delivery of these vaccines is concern that they may trigger the exacerbation of asthma. However, allergic reactions to vaccines are uncommon. To the best of our knowledge, this is the second case report of a patient with acute exacerbation triggered by the BNT162b2 vaccine.

The BNT162b2 vaccine elicits high levels of specific clusters of differentiation 4+ T cells that primarily produce T helper 1 cytokines, as opposed to T helper 2 (Th2) cytokines (Sahin *et al.*, 2020). Th2-type disorders after inoculation are thought to be uncommon, but several case reports of Th2-type disorders with eosinophilia, such as acute eosinophilic pneumonia, drug rash with eosinophilia and systemic symptoms, and eosinophilic granulomatosis with polyangiitis (EGPA), have been published in the wake of nationwide immunization (Ibrahim *et al.*, 2022; Korekawa *et al.*, 2022; Ozturk *et al.*, 2022). Polyethylene glycol has been identified as a potential trigger of allergic reaction and is an integral part of the micellar delivery system of the BNT162b2 vaccines containing mRNA coding the spike protein of SARS-CoV-2, but the pathological mechanisms involved are not fully understood (Ding *et al.*, 2021).

Eosinophilia was observed on the day after the third dose. As mentioned previously, the development of Th2-type disorders with eosinophilia after mRNA COVID-19 vaccinations has been reported. In particular, it is well known that EGPA develops in the disease course of bronchial asthma. The clinical manifestations are involved with severe asthma, allergic rhinitis, and blood and tissue eosinophilia, as well as cardiac, gastrointestinal, skin, renal involve-

ment, and peripheral neuropathy. Similarly, in the present case, extrapulmonary involvements were not detected, peripheral neuropathy was not observed, and chest CT revealed no pulmonary infiltration. Moreover, the patient's serum was negative for antineutrophil cytoplasmic antibodies (MPO-ANCA/PR-3ANCA). Thus, we excluded the probability of vaccine-induced EGPA.

There have been only two case reports related to asthma exacerbation after the receipt of a SARS-CoV-2 mRNA vaccine. Uzer and Cilli (2022) reported a female patient aged 76 years who complained of shortness of breath and was diagnosed with acute asthma exacerbation and drug-induced pneumonitis 1 day after inoculation with a SARS-CoV-2 vaccine (CoronaVac, Sinovac®). Colaneri *et al.* (2021) reported a female patient aged 28 years who developed asthmatic symptoms, such as worsening of respiratory symptoms, with mild dyspnea during physical activity, mainly at night, 3 weeks after receiving the second dose of the BNT162b2 vaccine.

There are many etiologies of acute exacerbation in which antigens are the essential factors. Asthma exacerbation is associated with both inflammatory and immunological cell infiltration, as well as, presumably, their activation. When allergens drive the process, T cells in the lung appear to orchestrate an immune response with a strong Th2 component. Allergen-induced asthmatic reactions evoke an interleukin-5 response, with increased eosinophil recruitment and degranulation (Singh and Busse, 2006). In previous examinations, elevated numbers of blood eosinophils were observed after specific antigen exposure in patients with asthma (Durham and Kay, 1985). Because eosinophilia had been observed and the patient complained of throat discomfort and chest oppression after the second inoculation, it was considered likely that she had been sensitized to the BNT16b2 vaccine and that she was experiencing bronchial asthma. Furthermore, it is speculated that an excessive immune reaction against the BNT162b2 vaccine resulted in a life-threatening asthma exacerbation after the booster shot.

In conclusion, the recent availability of vaccines against COVID-19 has the potential to dramatically reduce the risk of the disease and related exacerbation in patients with severe respiratory diseases. However, there is also a theoretical risk that the SARS-CoV-2 vaccine could trigger an asthma exacerbation. Physicians should be aware of the risk of acute exacerbation in patients with asthma after SARS-CoV-2 vaccine inoculation.

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## Ethical approval

Ethical approval was not required.

## Author contributions

Masaru Ando: corresponding author, drafting the article, conception and design, and interpretation of data.; Yoshio Satonaga, Ryuichiro Takaki, Michitoshi Yabe, Takamasa Kan, Erika Omote, and Toru Yamasaki: investigation; Kosaku Komiya: revising draft for important intellectual content; Kazufumi Hiramatsu: revising draft for important intellectual content and final approval for submission.

## Declarations of competing interest

The authors have no competing interests to declare.

## Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.ijid.2022.09.019.

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