Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Elsevier hereby grants permission to make all its COVID-19-related research that is available on the COVID-19 resource centre - including this research content - immediately available in PubMed Central and other publicly funded repositories, such as the WHO COVID database with rights for unrestricted research re-use and analyses in any form or by any means with acknowledgement of the original source. These permissions are granted for free by Elsevier for as long as the COVID-19 resource centre remains active.
Case Report

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

Masaru Ando¹,*, Yoshio Satonaga¹, Ryuichiro Takaki¹, Michitoshi Yabe¹, Takamasa Kan¹, Erika Omote¹, Toru Yamasaki¹, Kosaku Komiya², Kazufumi Hiramatsu²

¹Department of Respiratory Medicine, Oita Prefectural Hospital, Oita, Japan
²Department of Respiratory Medicine and Infection Diseases, Oita University Faculty of Medicine, Oita, Japan

A R T I C L E   I N F O

Article history:
Received 13 May 2022
Revised 31 August 2022
Accepted 13 September 2022

Keywords:
SARS-CoV-2 vaccine, Acute asthma exacerbation
Sensitization
Eosinophilia
Adverse reaction

A B S T R A C T

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. © 2022 The Authors. Published by Elsevier Ltd on behalf of International Society for Infectious Diseases. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/)

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 SpO₂ 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, PaO₂ of 74.0 mm Hg, and PaCO₂ 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...
positive airway pressure 10 cm H2O; expiratory positive airway pressure 5 cm H2O, FiO2 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 trifenate 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 trifenate 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 BNT16b2 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.

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

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 Yamashita: 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.

References

Colaneri M, De Filippo M, Licari A, Marseglia A, Maiocchi L, Ricciardi A, et al. COVID vaccination and asthma exacerbation: might there be a link? Int J Infect Dis 2021;112:243–6.

Ding, MA-O, Dong, XA-O, Sun, YL, Sokolowska MA-O, Akdis MA-O, van de Veen WA-O, et al. Recent advances and developments in COVID-19 in the context of allergic diseases. Clin Transl Allergy 2021;11:e12065.

Durham SR, Kay AB. Eosinophils, bronchial hyperreactivity and late-phase asthmatic reactions. Clin Allergy 1985;15:411–18.

Ibrahim H, Alkhatib A, Maysami A. Eosinophilic granulomatosis with polyangiitis diagnosed in an elderly female after the second dose of mRNA vaccine against COVID-19. Cureus 2022;14:e21179.

Korekawa A, Nakajima K, Fukushima K, Nakano H, Sawamura D. Three cases of drug-induced hypersensitivity syndrome associated with mRNA-based coronavirus disease 2019 vaccines. J Dermatol 2022;49:652–5.

Ozturk AB, Çağlayan B, Kapmaz M, Çalı̇k I, Tekin S, Iliȧs S, et al. Hypersensitivity reactions to COVID-19 vaccines: a case of Eosinophilic pneumonia following Sinovac/CoronaVac vaccination. Eur Ann Allergy Clin Immunol 2022.

Sahin U, Muñk A, Derhovanessian E, Vogler I, Kranz LM, Vormehr M, et al. COVID-19 vaccine BNT162b1 elicits human antibody and TH1 T cell responses: Nature 2020;386:794–9.

Singh AM, Busse WW. Asthma exacerbations. 2: aetiology. Thorax 2006;61:809–16.

Thomas SJ, Moreira ED, Jr Kitchin N, Absalon J, Gurtman A, Lockhart S, et al. Safety and efficacy of the BNT162b2 mRNA Covid-19 vaccine through 6 months. N Engl J Med 2021;385:1761–73.

Uzer F, Cilli C. Acute asthma exacerbation after SARS-CoV-2 vaccine (Sinovac®): a case report. Med Gas Res 2022;12:67–8.