Case Report

Suspected Anaphylactic Reaction Following Second Dose of the Pfizer-BioNTech (BNT162b2) Coronavirus Vaccine in a Geriatric Female

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Abstract

Description

Anaphylaxis is a rare but serious adverse reaction that can occur following mRNA-based vaccination against coronavirus (COVID-19). This is a case of a geriatric patient presenting with hypotension and an urticarial rash with bullous lesions following a syncopal episode with incontinence. She received the second dose of the Pfizer-BioNTech (BNT162b2) COVID-19 vaccine three days prior, and first developed the skin abnormalities the morning after receiving the vaccine. She had no past history of anaphylaxis or allergies to vaccinations.

Her presentation met the diagnostic criteria for anaphylaxis, according to the World Allergy Organization: she had acute onset illness involving the skin and was hypotensive with symptoms suggestive of end-organ dysfunction. The latest literature published on anaphylaxis to mRNA-based COVID-19 vaccination indicates that this is an extremely rare complication. From December 14, 2020, to January 18, 2021, 9 943 247 doses of the Pfizer-BioNTech vaccine and 7 581 429 doses of the Moderna vaccine were administered in the United States. Sixty-six of these patients met anaphylaxis criteria. Of these cases, 47 received the Pfizer vaccine and 19 received the Moderna vaccine. Unfortunately, the mechanisms of these adverse reactions remain poorly understood, although it is postulated that particular vaccine components such as polyethylene glycol or polysorbate 80 may be the underlying triggers.

This case demonstrates the importance of recognizing anaphylactic signs and symptoms, as well as proper patient education about the benefits and potential, albeit rare, adverse effects, of vaccination.

Keywords

COVID-19 vaccines; COVID-19 vaccines/adverse effects; BNT162 vaccine; anaphylaxis; hypersensitivity; vaccination; drug-related side effects and adverse reactions; vaccine reaction

Introduction

Vaccines play crucial roles in public health by limiting or even eradicating infectious diseases in populations. If most individuals are vaccinated, the entire population can be protected through herd immunity, including those who cannot be vaccinated or are immunocompromised.[1] Amid the COVID-19 pandemic, the swift advent of Food and Drug Administration (FDA)-approved COVID-19 vaccination has revolutionized healthcare and the safety of patients from diverse backgrounds. The Pfizer-BioNTech BNT162B2 mRNA and Moderna mRNA-1273 COVID-19 vaccines received emergency authorization for use by the United States (US) FDA in December 2020.[2] Public education regarding the safety profile of vaccination and its rare but possible adverse effects is an important pillar upholding community health. A vaccine adverse event can be local or systemic, instantaneous or relatively gradual. Anaphylaxis is one of these potential adverse outcomes and is a life-threatening, immediate, systemic reaction associated with immune reactions but can be non-immune mediated or idiopathic in etiology.[1] This case documents an anaphylac-

tic reaction following the second dose of the Pfizer-BioNTech COVID-19 vaccine in a geriatric female, with a discussion on the current literature describing such reactions to mRNA-based COVID-19 vaccination and the latest research investigating this phenomenon.

Case Description

The patient was a 66-year-old Hispanic female with type 2 diabetes mellitus and hyperlipidemia who presented to the emergency department after an episode of syncope and an unwitnessed fall. She had an episode of urinary and fecal incontinence, which she noticed when she regained consciousness. She has never had a syncopal episode prior to this incident. On initial presentation, her heart rate was 98 beats per minute, her oxygen saturation was 100% on room air, and her blood pressure was 74/40 mmHg. Upon physical examination, she had diffuse urticaria on her chest, abdomen, and face, as well as bullous lesions, some ruptured, on her extremities **(Figure 1)**. She had received the second dose of the Pfizer-BioNTech COVID-19 vaccine 3 days prior to the syncopal episode. The morning after receiving the vaccination, she developed urticaria and bullous lesions, which did not improve with oral antihistamines. She had no history of allergies or adverse reactions to other types of vaccinations and only experienced minor fatigue and chills after receiving the first dose of the Pfizer-BioNTech COVID-19 vaccine. Prior to the onset of symptoms, she had not consumed any new foods or medications for the past several months and endorsed good hydration. The second dose of the Pfizer-BioNTech COVID-19 vaccine was the only new medical therapy recently introduced. She had no known sick contacts, and no change in daily activity, clothing, linens, body wash, or laundry detergent. She denied recent travel, outdoor activity, or encounters with chemical or environmental substances. She does not own any pets and denied recent animal exposure or insect bites.

Complete blood count was significant for hemoglobin of 11.1 g/dL and a hematocrit of 28.6% but was otherwise unremarkable. We found she had an acute kidney injury, with a creatinine of 2.04 mg/dL (baseline creatinine is approximately 0.80) and an estimated glomerular filtration rate of 24. Her chest x-ray and computed brain tomography showed no abnormalities. We also performed a cardiac workup during her hospital course. Her troponin I was elevated on admission, 0.111 ng/mL, and decreased to 0.050 within 24 hours of admittance. Her electrocardiogram showed tachycardia and nonspecific ST segment abnormalities. The echocardiogram was unremarkable. Her cardiac catheterization showed patent coronary arteries.

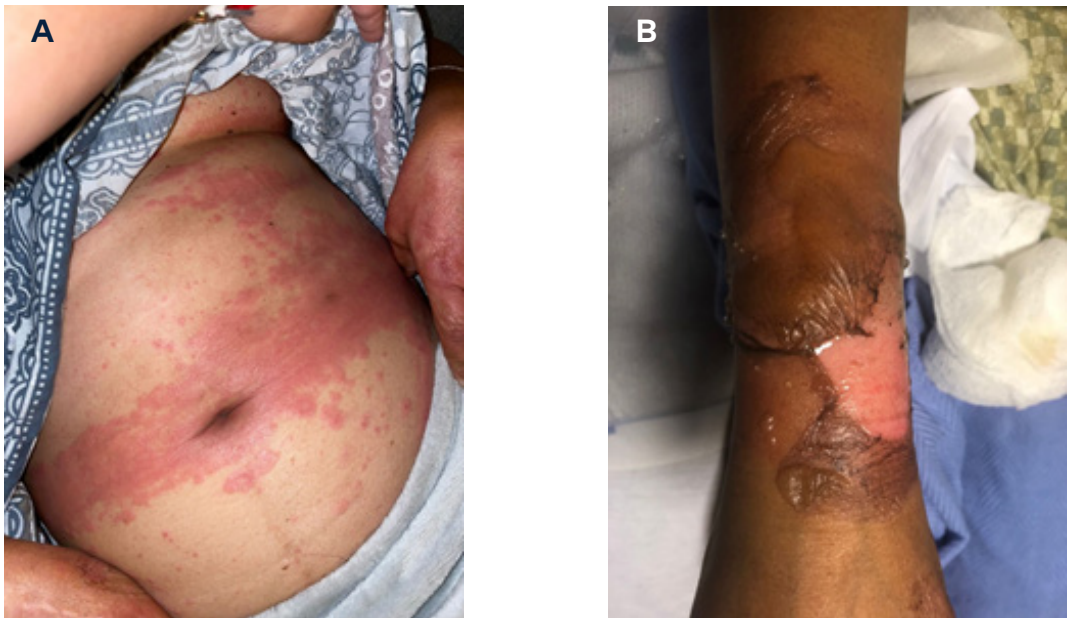

Figure 1. A. Diffuse urticaria is shown following the second dose of the Pfizer-BioNTech COVID-19 vaccine. B. Ruptured bullae shown on an upper extremity following the second dose of the Pfizer-BioNTech COVID-19 vaccine.

We treated her with intravenous fluids, methylprednisolone, famotidine, and diphenhydramine. Her vital signs stabilized, renal function returned to baseline, and her rash significantly improved within a couple of days of initiating treatment. We discharged her while she was on oral famotidine, diphenhydramine, and prednisone. At her follow-up appointment a few weeks later, the patient's rash was completely resolved, and she reported no further episodes of lightheadedness or syncope.

Discussion

This case appears to be a rare instance of an anaphylactic reaction that occurred following the administration of the second dose of the Pfizer-BioNTech COVID-19 vaccination. Anaphylaxis is an acute reaction involving multiple organ systems and potentially leading to death. Anaphylaxis primarily affects the pulmonary, cardiovascular, and/or mucocutaneous systems. Some classic manifestations include angioedema, wheezing, hypovolemia, distributive shock, urticaria, pruritis, and flushing.[3] Other associated signs and symptoms may include dizziness, confusion, syncope, seizures, nausea, vomiting, diarrhea, and urinary or fecal incontinence. The mechanism of anaphylaxis is complex and multifactorial. The traditional pathway involves mediators such as interleukin-4, interleukin-5, and B-cells producing IgE, which forms IgE-antigen complexes with the receptors on mast cells and basophils.[3] This crosslinking then triggers degranulation of the mast cells and basophils, thereby releasing both preformed (eg, histamine, tryptase, chymase, heparin, carboxypeptidase, tumor necrosis factor alpha) and newly synthesized (eg, leukotrienes, platelet-activating factor, vascular endothelial growth factor) mediators that cause the severe and variable presentations of anaphylaxis.[3]

The second dose of the Pfizer-BioNTech COVID-19 vaccine was considered a potential trigger of our patient's symptoms after a thorough history was collected. In addition to genetic disorders predisposing some to anaphylaxis, numerous possible causes of anaphylaxis are found in daily life, including but not limited to various foods, medications, animals, exercise, textiles, and hormones.[3] Thus, we attempted to collect extensive information from the patient to formulate an appropriate history of her present illness, inquiring about variables such as her living situation, diet, medication regimen, and travel history, among others. Although gathering a detailed timeline on these variables from the past few days and the last several weeks and months was challenging, the patient fervently denied any lifestyle or medical changes to the best of her knowledge. Receiving the Pfizer-BioNTech COVID-19 vaccine was the only recent possible trigger she could recall. Thus, the vaccination was considered a potential cause of anaphylaxis, though there is insufficient information to conclude it was the sole or definitive trigger of her symptoms.

Despite this broad spectrum of manifestations, the diagnosis of anaphylaxis is based on the guidelines outlined by the World Allergy Organization (WAO). According to the WAO, there is a high likelihood of anaphylaxis if the patient presents with acute onset (minutes to hours) illness involving the skin and/or mucosa with at least one of the following: respiratory compromise, reduced blood pressure or associated symptoms reflecting end-organ dysfunction, or severe gastrointestinal symptoms.[4] Even without skin manifestations, a patient can also meet the WAO criteria for likely anaphylaxis if they present with acute onset hypotension, bronchospasm, or laryngeal involvement after being exposed to a known or probable allergen.[4] This specific patient met the WAO criteria for anaphylaxis, as she developed acute skin manifestations within hours of vaccination and presented with hypotension and symptoms of end-organ dysfunction (syncope, incontinence).[4] Of note, systemic vasovagal reactions can sometimes present similar characteristics at first glance, but this patient's comprehensive clinical picture was more consistent with a true anaphylactic reaction. Systemic vasovagal reactions almost always occur immediately or within 30 minutes after exposure to a trigger.[1] Additionally, vasovagal reactions are associated with a brief duration of hypotension that swiftly resolves when supine, loss of consciousness that also quickly improves with positional changes, and bradycardia.[1] In contrast, this patient's reaction did not occur within 30 minutes of vaccination. She was tachycardic, and her hypotension and loss of consciousness were not transient nor influenced by position. Moreover, her skin manifestations, including erythematous, urticarial, and pruritic rashes, were not systemic vasovagal reactions.[1]

Anaphylaxis is a severe, life-threatening adverse event of vaccination. However, the latest data suggests the rates of anaphylactic reactions to mRNA COVID-19 vaccination, for both Pfizer and Moderna products, are low and should not deter the general population from receiving the benefits of vaccination. From December 14, 2020, to January 18, 2021, almost 10 million doses of the Pfizer-BioNTech vaccine and over 7 and a half million doses of the Moderna vaccine were administered in the US.[5] During this period, 66 cases reported to the Vaccine Adverse Event Reporting System (VAERS) met the Brighton Classification criteria for either level 1, 2, or 3 anaphylaxis.[6] Of the 66 cases reported to VAERS, 47 had received the Pfizer vaccine, and 19 had received the Moderna vaccine.[5] The median duration of time to symptom onset was approximately 10 minutes for both vaccines. Of the reported cases meeting the criteria, 32% had a previous episode of anaphylaxis secondary to other exposures. Of the 47 cases who had anaphylaxis to the Pfizer-BioNTech vaccine, the median age was 39, and 44 (94%) were female. Furthermore, 36 (77%) had a prior history of allergic reactions, and 16 (34%) had at least one previous episode of anaphylaxis.[5]

Studies looking specifically at the 2-dose series of the Pfizer-BioNTech COVID-19 vaccination have shown it to be highly effective and safe for the majority of the population. In Polack et al.'s multinational, placebo-controlled trial published in December 2020, 21 720 participants received both doses of the BNT162b2 Pfizer vaccine (21 days apart), and 21 728 received a placebo.[7] Among the 21 720 who were vaccinated, 8 cases of COVID-19 occurred at least 7 days after receiving the second dose. Of the 21 728 who received a placebo, 162 cases of COVID-19 were found.[7] The FDA defines cases of severe COVID-19 as confirmed COVID-19 with at least 1 of the following characteristics: clinical signs at rest reflective of severe systemic disease, signs of shock, respiratory failure, marked acute renal, neurologic or hepatic dysfunction, admission to the intensive care unit, or death.[1] There were 10 cases of severe COVID-19 infection, with 9 coming from the placebo group.[7] Two vaccine recipients and 4 placebo recipients died. However, the investigators did not find any deaths related to the vaccine, placebo, or COVID-19 illness.[7] Within 7 days of receiving the vaccine, less than 1% reported severe pain. Most of the local reactions reported were mild-moderate and resolved within 2 days; no grade 4 local reactions were reported.[7] Another multisite US study examined the safety of the second dose of the Pfizer or Moderna vaccination in patients who had an adverse reaction to the first dose. There were 189 participants total, including 130 (69%) receiving Moderna and 59 (31%) receiving Pfizer-BioNTech.[8] All 159 participants who received the second dose of the vaccine were found to tolerate the dose, even the 19 who had a reported reaction meeting anaphylaxis criteria after their first dose.[8] Although 32 (20%) had immediate reactions, they were mild or resolved promptly with antihistamine therapy.[8]

Unfortunately, the underlying mechanism and particular trigger of anaphylaxis in these select patients are poorly understood. Further research is needed before a definitive culprit can be identified. In Warren et al.'s case series involving 22 individuals who had a suspected allergic reaction to COVID mRNA vaccines, skin prick testing was performed with either polyethylene glycol (PEG) or polysorbate 80 (P80), known components of the mRNA vaccines.[9] Among the 11 patients who underwent skin prick testing, zero were positive to PEG or P80, and 1 out of 10 (10%) were positive to the same manufacturer of vaccine they had received.[9] However, these same 11 participants also underwent basophil activation testing; 10 of 11 (91%) had positive results to PEG, and 11 of 11 (100%) were positive to the component used in the respective vaccine administered.[9] These patients were found to have elevated levels of IgG to PEG but no significant elevations in baseline IgE levels. These results suggest that patients who experience severe allergic reactions to the COVID-19 mRNA vaccines may have an allergy to PEG or P80.[9] Furthermore, the immunoglobulin studies performed in this trial suggest that a significant proportion of documented anaphylactic reactions to the COVID-19 vaccines can be attributed to reactions to PEG in particular and may, in fact, be mediated through non-IgE-related mechanisms, such as IgG-mediated complement-activated-related pseudoallergy.[9] PEG is a hydrophilic polymer that is an excipient in various products used in everyday life and has recently had increasing recognition

in the literature as a hidden high-risk allergen. P80 can also induce similar reactions, as it shares a chemical moiety with PEG.[10]

Although the overall rates of suspected severe adverse reactions to the COVID-19 vaccination are low, patients who are at higher risk of such complications should be identified and provided the appropriate safety precautions. To screen for populations at risk of reactions to specific components of the vaccine, such as PEG or P80, skin prick or intradermal testing, immunoglobulin assays, and basophil activation testing as well as oral provocation testing can be utilized.[10] Patients at higher risk of anaphylaxis include those who have a history of hypersensitivity reactions to vaccines, anaphylaxis from any cause, mastocytosis, or severe asthma. Such patients should receive a premedication protocol and have prepared transport to a hospital if they choose to receive the vaccine.[11] Patients who develop a suspected severe allergic reaction to the first vaccination could potentially undergo desensitization with individual components of the vaccine or receive their booster vaccination in incremental doses instead, as the European Academy of Allergy and Clinical Immunology points out.[12] Such endeavors will require close collaboration and open disclosures of data between the medical field and pharmaceutical industries before they can be successfully implemented on a large scale.[12]

Conclusion

This case may be a unique instance of a suspected anaphylactic reaction following the second dose of the Pfizer-BioNTech COVID-19 vaccination in a patient who experienced minimal side effects to the first dose of the vaccine. This case demonstrates the importance of appropriately recognizing possible anaphylactic signs and symptoms and proper patient education about the benefits and potential, albeit rare, severe adverse effects of vaccination.

Further research opportunities such as assessment of the mRNA COVID-19 vaccine's long-term effects, reactions to additional boosters, and testing for other vaccine components possibly contributing to allergic responses may help expand our understanding. Correctly identifying the potential mechanisms and risk factors of adverse vaccine reactions and expanding documentation of these in the medical literature will ultimately lead to an improved public awareness of vaccination safety.[13]

In order for patients to make fully-informed decisions regarding their health amidst the COVID-19 pandemic, appropriate education must be provided on the vaccine's rare but possible adverse events, associated risk factors, and prevention efforts to strengthen patient awareness in the future. In the modern era, vaccine misinformation can be readily distributed throughout communities, especially impacting impoverished or minority populations.[13] Although severe adverse effects to vaccination are rare, it is essential to discuss and receive complete and fully informed consent. Being fully informed allows the patient to be aware and make an autonomous decision with knowledge of the benefits as well as the potential harm.[13]

Conflicts of Interest

The authors declare that they have no conflicts of interest.

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