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Outcomes of allergic-type reactions after messenger RNA coronavirus disease 2019 vaccination at 3 military medical centers

In response to the global coronavirus disease 2019 (COVID-19) pandemic, 2 messenger RNA (mRNA) COVID-19 vaccines were developed and authorized for use.[1,2] Adverse events following immunization (AEFI) have occurred after receipt of these vaccines to include anaphylaxis that is estimated to occur at a rate of 2.5 to 11 cases per 1 million doses.[3] Several studies have found tolerance to vaccine challenge in these individuals, suggesting the reactions are likely not immunoglobulin (Ig)E driven.[4,5] The Centers for Disease Control and Prevention now considers nonsevere, immediate, allergic-type reactions after a dose of a COVID-19 vaccine a precaution, not a contraindication, to a subsequent dose of the same vaccine.[6] To further support the growing evidence of second dose tolerance after first dose reaction, we describe the evaluation and outcome of patients referred to 3 Military Health System allergy clinics for consultation for suspected allergic reactions after mRNA COVID-19 vaccination.

This is a multicenter retrospective review of patients referred to the Allergy Clinics of the Walter Reed National Military Medical Center, Naval Medical Center Portsmouth, and Womack Army Medical Center, from January 2021 to November 2021 for AEFI after receipt of either mRNA COVID-19 vaccine. Those with at least 1 symptom consistent with an immediate hypersensitivity reaction within 24 hours of the first dose were included. The likelihood of anaphylaxis was based on the Brighton Collaboration Criteria used to determine the level of certainty of anaphylaxis.[7] Evaluation and determination of testing, vaccine challenge, or vaccine avoidance was based on the risk assessment of the evaluating allergist. Skin testing was performed to the Pfizer-BioNTech COVID-19 vaccine, polyethylene glycol, and polysorbate. In most of the cases, the vaccine and component testing were done with full-strength prick test followed by 1:100 dilution intradermal.[8] Vaccine challenge was offered to most patients at full dose, except for 3 patients who received split dosing at the discretion of the treating allergist. Premedication was not routinely used. The institutional review board at the Walter Reed National Military Medical Center determined this study as exempt from review.

There were 391 patients referred for concern of an AEFI after either mRNA COVID-19 vaccine. A total of 65 patients met the inclusion criteria. Most of the patients included in the study were of female sex (78%), and the mean age was 42 (13-78) years. In addition, 58 (88%) of the patients received the Pfizer-BioNTech COVID-19 vaccine. Furthermore, 27 (42%) patients met the Brighton levels 1 to 3 classifications (Table 1). The primary symptoms reported were sensation of throat closure (45%), pruritus (31%), lightheadedness (30%), flushing (27%), urticaria (24%), shortness of breath (19%), nausea (16%), angioedema (9%), tachycardia (4%), hoarse voice (4%), or a combination. A total of 26 (40%) patients underwent skin prick testing. There was 1 patient (4%) whose skin test result was positive to the Pfizer COVID-19 vaccine on intradermal testing at 1:100, but all other skin testing results were negative; this patient was advised against the second dose. In terms of second dose recommendations, 7 (11%) were advised against by the allergist, 5 (8%) declined, and 53 (82%) underwent vaccine challenge. Moreover, 47 (89%) who underwent vaccine challenge had no symptoms, whereas 6 (11%) experienced recurrence of symptoms. One patient received a 10% dose and within minutes developed throat clearing, sensation of throat closure, ear fullness, but with normal vitals and received epinephrine with quick resolution of symptoms. The remaining 90% of the vaccine dose was withheld. Two patients had mild self-resolved pruritus and urticarial rash. Three described isolated throat closure sensation with normal vitals and no respiratory distress; real-time laryngoscopy result revealed pharyngeal muscle tension without evidence of edema most consistent with vocal cord dysfunction.

Table 1
Characteristics and Second Dose Outcomes of Subjects With Possible Allergic Reaction to mRNA COVID-19 Vaccines

Characteristics	n (% total or range)
Subjects (n = 65)	
Age, average	42 (13-78)
Sex	
Female	51 (78)
Male	14 (22)
Vaccine	
Pfizer	57 (88)
Moderna	8 (12)
Received epinephrine	15 (23)
Met Brighton classification	27 (42)
Brighton level 1	2 (3)
Brighton level 2	22 (34)
Brighton level 3	3 (5)
Skin testing (n = 26)	
Reactive	1 (4)
Non-reactive	25 (96)
Second dose outcome (n = 65)	
Provider advised against	7 (11)
Patient declined	5 (7)
Vaccine challenge	53 (82)
No reaction	47 (88)
Immediate allergic symptoms	6 (12)[a]

Abbreviations: COVID-19, coronavirus disease 2019; mRNA, messenger RNA.
[a]One subject was treated with epinephrine after administration of 10% dose with quick symptom resolution. Two patients had mild self-resolved pruritus and urticarial rash. Three experienced sensation of throat closure and real-time laryngoscopy revealed pharyngeal muscle tension without evidence of edema.

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Our study revealed that nearly 90% of patients with first-dose allergic symptoms tolerated the second dose with no recurrence of symptoms and all but one had symptoms that were mild and self-limited. Most of the reactions in our study were self-reported symptoms without objective findings of anaphylaxis. A few examples of this were illustrated in the 3 patients with sensation of throat closure after vaccine challenge with evidence of vocal cord dysfunction on real-time laryngoscopy without respiratory distress or vital sign abnormalities. This is particularly relevant given the primary symptom patients in our study reported was sensation of throat closure.

The role for skin testing seems to be limited as 96% of the patients had negative skin test results and almost 88% of the patients tolerated the vaccine challenge; hence, these cases do not seem to be IgE-mediated.[9] One patient did have a positive intradermal test at 1:100 concentration of the mRNA vaccine. She was advised against receiving the second dose; therefore, it is not clear whether she truly has allergy or only sensitized as there have been published data of patients with both a clinical allergic reaction and positive skin testing result who tolerated a subsequent dose.[10] This is further illustrated by the patient with objective signs of an allergic reaction on vaccine challenge and received epinephrine, but had skin test negative result.

Despite the rarity of IgE-mediated allergy to the mRNA COVID-19 vaccines and growing evidence of second-dose tolerance, 12 (18%) of the patients in our cohort either declined or were advised against receiving the second dose. However, as the vaccination campaign progressed, more patients who presented with similar clinical concerns were offered a vaccine challenge highlighting the important role of an allergist in improving patient comfort after allergic-type reactions to these vaccines.

Nearly half of the cohort met the Brighton criteria for vaccine anaphylaxis. More patients in this group who received epinephrine as part of the treatment for their index reaction were advised against receiving the second dose and were skin tested. However, the vast majority of this cohort, at all levels of certainty of vaccine anaphylaxis, tolerated the vaccine challenge without recurrence of symptoms or had mild self-resolved symptoms.

In summary, this study reveals that most patients with reported symptoms of allergic reactions to the mRNA COVID-19 vaccines can tolerate the second dose. Skin testing does not seem to be effective at predicting second dose reactions. These reactions can lead to vaccine hesitancy and incomplete vaccination; hence, these studies are critical to supporting the vaccination effort. Further studies are needed to understand mechanisms of AEFI after mRNA COVID-19 vaccinations.

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Acute increases in total serum tryptase unassociated with hemodynamic instability in diffuse cutaneous mastocytosis

Mastocytosis is associated with an accumulation of mast cells (MCs) in 1 or more organ systems. It is classified into the following 2 major variants: cutaneous mastocytosis (CM) and systemic mastocytosis (SM). CM is characterized by mastocytosis limited to the skin, whereas SM involves MC accumulation in at least 1 noncutaneous organ system with or without skin involvement. In pediatric patients, CM accounts for approximately 90% of all cases.[1] Subtypes include maculopapular cutaneous mastocytosis, formerly termed urticaria pigmentosa, diffuse cutaneous mastocytosis (DCM), and mastocytoma.

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