

## BRIEF ARTICLE

**Aquagenic Urticaria in an Adolescent Following COVID-19 Vaccination**John T. Broderick, BS<sup>1</sup>, Thomas D. Selby, MD<sup>1</sup>, Julian Trevino, MD<sup>1</sup><sup>1</sup>Department of Dermatology, Wright State University Boonshoft School of Medicine, Fairborn, OH**ABSTRACT**

A subset of patients receiving COVID-19 vaccinations develops cutaneous reactions. The majority are delayed hypersensitivity reactions that resolve spontaneously without treatment. More rarely, cutaneous manifestations such as urticaria, vasculitis, and morbilliform eruptions have been reported. Aquagenic urticaria is a form of chronic inducible urticaria caused by skin contact with water. Characteristic 1-2mm folliculopapular urticarial papules appear 20-30 minutes following water exposure and spontaneously resolve within 30-60 minutes of water removal. A water provocation test is the gold standard of diagnosis. The mainstay of treatment is 2<sup>nd</sup> generation H1 antihistamines taken before water exposure. We report the development of aquagenic urticaria in a 12-year-old African American male patient after receiving the Pfizer-BioNTech mRNA COVID-19 vaccine.

**INTRODUCTION**

Over 600 million doses of the COVID-19 vaccine have been administered in the United States.<sup>1</sup> Close to 96% of doses administered have been mRNA vaccines from Pfizer-BioNTech and Moderna.<sup>1</sup> These safe and effective vaccines have been associated with cutaneous reactions in a subset of patients. The most common cutaneous reactions are delayed injection site reactions involving redness, swelling, pain, or induration that occur within 7 days following vaccination.<sup>2,3</sup> Most reactions are self-limiting and do not require treatment. More rare vaccine reactions include urticaria, morbilliform eruptions, pityriasis rosea, and vasculitis.<sup>2,3</sup> In one large review of 40,640 patients who received mRNA vaccines, urticaria involving itchy wheels occurred in 0.3% of patients after the first vaccine dose

and in 0.6% of patients after the booster.<sup>4</sup> Most urticarial reactions have been delayed hypersensitivity reactions, occurring at least 4 hours after injection, and have been symptomatically managed with antihistamines.<sup>5</sup> Chronic spontaneous urticaria lasting >6 weeks has been reported but these reactions were not associated with specific exacerbating factors.<sup>6,7</sup> Aquagenic urticaria (AU) is a unique type of urticaria caused by skin contact with water. We present the first reported case of aquagenic urticaria induced by the COVID-19 vaccine from our review of the available literature.

**CASE REPORT**

A 12-year-old African American male with a history of atopic dermatitis and herpes labialis received the first dose of the Pfizer-BioNTech COVID-19 vaccine on Aug 3, 2021

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and developed shortness of breath and throat swelling requiring Epipen administration and hospital monitoring. The following week, the patient started developing hives on his trunk, arms, legs, and face after showering, regardless of water temperature. The hives started minutes after showers and resolved within 20-60 minutes. The patient endorsed pruritis and discomfort but denied wheezing, shortness of breath, throat or lip swelling, and vomiting. A water challenge test was positive with small erythematous to violaceous papules consistent with urticaria in his Fitzpatrick type V skin were noted in the test area with the patient reporting subjective symptoms of burning and pruritis (**Figure 1**). Dermatographism was negative.



**Figure 1.** Water provocation test performed according to expert consensus.<sup>8</sup> **a)** A towel was soaked in room temperature water and placed on the left posterior shoulder for 20 minutes. **b)** 1-2mm erythematous papules (black arrows) were noted in the test area with the patient reporting symptoms of burning and pruritis.

On follow-up, the patient reported a decreased duration of the hives on 20mg BID of cetirizine but the urticaria persisted following showers. Narrow-band UVB phototherapy was trialed, but the patient was unable to tolerate due to post-treatment migraine. Other treatment options including: dupilumab, omalizumab, and  $\beta$ -alanine

supplementation were discussed but further treatment was deferred at that time. At 10 months post-vaccination, the patient reported marked improvement. The hives were occurring sporadically and in fewer numbers.

## DISCUSSION

Aquagenic urticaria is a rare dermatologic reaction that involves development of hives following exposure to water. Chronic inducible urticaria is the consistent development of hives following exposure to triggers including cold, sunlight, sweat, and water.<sup>8</sup> AU has a 1-2 mm folliculopapular urticarial appearance that is very similar to the pattern seen in cholinergic urticaria.<sup>3</sup> Wheals are commonly seen on the trunk and upper extremities 20-30 minutes following exposure to water and spontaneously resolve within 30-60 minutes after water removal.<sup>9</sup> AU occurs regardless of water temperature and pH.<sup>8</sup> Interestingly, AU is often localized to certain areas of the body even when there is whole body contact with water.<sup>10</sup> The condition causes pruritus and rarely has associated symptoms of headache, wheezing and shortness of breath, and angioedema.<sup>9,10</sup> The diagnosis can usually be made from patient history, but it can be difficult to delineate between cholinergic urticaria if the hives occur following sweating. The gold standard diagnostic test is a water provocation test.<sup>8</sup> The mechanism of AU is thought to be related to mast cell degranulation and release of histamine.<sup>9</sup> Thus, the mainstay of treatment is with 2<sup>nd</sup> generation H1 antihistamines taken before water exposure.<sup>9,10</sup> Greater treatment success has been achieved using antihistamine doses up to 4 times of standard dosing.<sup>10</sup> For symptoms refractory to antihistamines, other options to consider are barrier creams, omalizumab, dupilumab, and UV light therapy.<sup>9</sup>

The reported cutaneous reactions for COVID-19 are similar to those reported in other vaccines.<sup>3</sup> Polyethylene glycol (PEG) and polysorbate 80 are components that have been identified as possible allergic triggers in other vaccines.<sup>3</sup> PEG is present in both Pfizer and Moderna; polysorbate 80 is a component of the Oxford/AstraZeneca and Johnson & Johnson vaccines. Of note, the patient's symptoms started to resolve around 10 months post-vaccination. It has been shown that COVID-19 antibodies induced by disease and vaccination decrease over time.<sup>11</sup> The improvement of our patient's symptoms could be correlated with waning antibodies generated from the initial vaccination. Cutaneous reactions to COVID-19 mRNA booster vaccinations have been reported, including reactions in patients that did not have cutaneous reactions to primary vaccine doses.<sup>12</sup> We predict similar symptoms in response to a booster vaccination because of activation of memory B cells and production of antibodies. We recommended against a booster dose in our patient due to prior anaphylactic reaction.

Dermatologists serve an important role in identifying new adverse cutaneous reactions as mass vaccination efforts with booster vaccines continues. They can accurately interpret skin reactions and provide guidance regarding further vaccination. A standardized grading scale for COVID-19 vaccine-associated cutaneous reactions was recently proposed and utilizes the FDA's Toxicity Grading Scale for local reactions and the NCI's Common Terminology Criteria for Adverse Events (CTCAE) for generalized reactions.<sup>13</sup> Most occurrences are acute self-resolving local injection site reactions, and these patients should be encouraged to continue to receive booster doses per CDC recommendations. Chronic dermatologic manifestations should be treated according

to the standard of care, and symptoms may improve as vaccine-induced immunity wanes over time. Current CDC guidelines recommend referral to an allergist if a patient has a vaccine reaction within 4 hours of administration or severe symptoms.<sup>14</sup> Patients with a suspected IgE-mediated immediate hypersensitivity reaction may benefit from skin testing using PEG or polysorbate to help guide future vaccination decisions.<sup>15</sup> Patients with delayed hypersensitivity reactions should consult with an allergist to discuss risk/benefits of future doses but there are no current guidelines recommending for or against receiving booster doses.<sup>15</sup>

## CONCLUSION

We present the first reported case of aquagenic urticaria following COVID-19 vaccination in a skin of color patient and propose a possible mechanism for waning symptoms. There were no other associated medications or illnesses to explain the onset of symptoms. This case demonstrates a new adverse event that should be included in vaccine monitoring.

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