Acantholytic Dyskeratosis Post-COVID Vaccination

Kevin Yang, BS, Lisa Prussick, MD,† Rebecca Hartman, MD, MPH,‡§ and Meera Mahalingam, MD, PhD, FRCPath†‖*

Abstract: Acantholytic dyskeratosis mimicking Grover disease as a cutaneous manifestation of a side effect to the Moderna (mRNA-1273) COVID vaccine is rare with only one documented case in the literature to date. Herein, we present a case of an eruptive, erythematous, vesiculopapular rash developing in a patient after the Moderna vaccine. Histopathology of a representative biopsy [x2, done 8 weeks apart] of the rash revealed similar histopathologic findings of patchy suprabasal acantholysis with dyskeratotic keratinocytes and an underlying inflammatory infiltrate of lymphocytes and neutrophils. Direct immunofluorescence was negative. In contrast to the only case previously reported in the literature, a confounding feature in our case, was that patient had a medical history significant for Grover disease, which had been successfully treated with complete resolution and seemed to be in remission. Given the temporal relationship of the onset of the rash to vaccine administration, the changes were likely vaccine-related with the caveat that, in light of the medical history, the differential diagnosis includes reactivation of Grover disease by the vaccine as a trigger factor.

Key Words: covid-19 vaccination, Grover disease, transient acantholytic dermatosis, vesiculopapular lesions

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INTRODUCTION

In the midst of the global COVID-19 pandemic, vaccinations were developed in efforts to protect the public from the virus. These included the Pfizer-BioNTech COVID-19 vaccine (BNT162b2), Moderna COVID-19 (mRNA-1273 SARS-CoV-2) vaccine, Johnson &Johnson COVID-19 vaccine, and many others.[1] In the initial safety and efficacy study for the Pfizer vaccine, the most commonly reported side effects included local pain at injection site and systemic side effects such as fatigue, headache, and fever.[2] A much smaller percentage of participants experienced local injection site redness or swelling.[2] In the preliminary report of safety data for the mRNA-1273 SARS-CoV-2 vaccine, the most common reported side effects included chills, fatigue, myalgia, headache, and pain at the local injection site.[3]

The pathogenesis for transient acantholytic dermatosis (Grover disease) is not currently well understood.[4] In a systemic review, Gantz et al[4] cited different exacerbating factors including sunlight, ionizing radiation, UV radiation, excessive perspiration, heat exposure, bedbound hospitalization, and drug therapy. Potential associated factors included malignancies, hematopoietic stem cell transplantation, solid organ transplant, and chemotherapy.[4,5] To our knowledge, developing Grover disease after any form of vaccination is rare, with only 2 documented cases from one study in the literature, of which only one was Moderna vaccine-related.[6]

Herein, we present a case of an eruptive, erythematous, vesiculopapular rash developing in a patient a few days after the Moderna vaccine. Histopathology of a representative biopsy of the rash, performed 8 weeks apart revealed similar histopathologic findings of patchy suprabasal acantholysis with dyskeratotic keratinocytes and an underlying inflammatory infiltrate of lymphocytes and neutrophils. A confounding feature in our case was that the patient had a medical history significant for Grover disease, which had been successfully treated previously with complete resolution and seemed to be in remission. There were no flares in over a year and no changes in medication or treatment during that time. Given this and the temporal relationship of the onset of the rash to vaccine administration, the changes were likely vaccine-related with the caveat that, in light of the medical history, the differential diagnosis included reactivation of Grover disease by the vaccine acting as a trigger factor.

CASE PRESENTATION

A 74-year-old man presented to the dermatology clinic in early March 2021 with a new red, itchy rash on the chest of a "few weeks" duration and which on examination were pink scaly and crusted papules. He was prescribed a high potency topical steroid (betamethasone 0.05% ointment, twice daily 3 times per week) and calcipotriene 0.005% cream (twice daily when not using topical steroids). No biopsy was performed. One month later, he presented again to the dermatology clinic in April 2021, because the rash had spread to involve the abdomen and he did not have any relief from the pruritus. On examination, there were multiple vesicles and nonfollicular centered erythematous papules with minimal white scale (more on the abdomen than chest, Fig. 1), a well-defined erythematous nonscaly patch approximately 4 cm in size (bilateral antecubital fossae) and an erythematous somewhat annular patch involving both axillae (R > L, Fig. 2). At that time, the clinical differential for the rash on the chest was Grover disease versus a hypersensitivity reaction. Of note, there were no recent changes to the patient's medications, and he denied any use of over-the-counter medications

From the *Tufts University School of Medicine, Boston, MA; †Department of Dermatology, Tufts University School of Medicine, Boston, MA; ‡Department of Dermatology, Brigham and Women's Hospital, 221 Longwood Ave, Boston, MA; §Dermatology Section, Department of Medicine, VA Integrated Service Network 1 (VISN-1), Jamaica Plain, MA; and ‖Dermatopathology Section, Department of Pathology and Laboratory Medicine, VA Consolidated Laboratories, West Roxbury, MA.

The authors declare no conflicts of interest.

Correspondence: Meera Mahalingam MD, PhD, FRCPath, Dermatopathology Section, VA-Integrated-Service-Network-1 (VISN1) Department of Pathology and Laboratory Medicine (113) 1400 VFW Pkwy, West Roxbury MA 02132 (e-mail: me@meeramahalingam.com).

or supplements. However, he had received his first dose of the Moderna COVID vaccine in January 2021, and his second dose 32 days later in late February 2021. Of clinical significance, he reported worsening pruritus and appearance of the rash following his second dose of the Moderna COVID-19 vaccine. A shave biopsy of the rash from the abdomen was performed, which revealed patchy suprabasal acantholysis with an underlying inflammatory infiltrate composed of lymphocytes and neutrophils (Fig. 3), findings which in the context of the clinical presentation generated a differential diagnosis of Grover disease versus, given the neutrophils, a vesiculopapular eruption secondary to the vaccine. He was restarted on clobetasol 0.05% ointment BID and calcipotriene 0.005% cream BID.

His past medical history was significant for presumptive Grover disease [diagnosis not confirmed by biopsy] for which he was treated with triamcinolone 0.01% cream BID with complete resolution of the rash, nonmelanoma skin cancer (BCC x3) completely excised surgically, JAK2+ myelofibrosis, atrial fibrillation, hypertension, deep vein thrombosis, Barrett esophagus, and gout.

He came back to the dermatology clinic in June 2021 because the rash seemed to be spreading to involve the back although, the itch seemed to have decreased. A second biopsy of the rash from the back was performed, which revealed features similar to those seen in the initial biopsy of an acantholytic dermatosis (although no neutrophils were present). A biopsy submitted for direct immunofluorescence was negative. He was asked to continue clobetasol ointment BID as needed for the itch. He came back for a follow-up visit to the dermatology clinic in July 2021 with amelioration of the rash and clobetasol ointment was discontinued and triamcinolone cream was started.

DISCUSSION

Although a spectrum of cutaneous reactions have been reported after mRNA COVID vaccines, in frequency, site-related reactions seem the most common followed by urticarial, and morbilliform lesions.[7] The presence of a vesicular rash developing after COVID-19 vaccination seems relatively rare.[6,8] In studying the efficacy and safety of the mRNA-1273 SARS-CoV-2 vaccine, Baden et al[8] reported only 3 cases of vesicular rashes among the 15,185 patients given the vaccine. McMahon et al evaluated 414 skin reactions to the Moderna and Pfizer Covid-19 vaccines and found only 1 case of a vesicular rash reported as a consequence of a second dose of mRNA-1273 administration.[7] Of note, biopsies were not performed in either of these studies.[7,8] In their study of 22 patients, Magro et al[6] described 2 patients who presented clinically with a papulovesicular eruption such as in our case, and both cases [Patient #6 and #14] had taken the Moderna vaccine. Of the Moderna-vaccinated patients, only one case [patient #14] demonstrated histopathology similar to our case ["acantholytic dyskeratosis with suprabasilar clefting and subepithelial neutrophilia"] after the second dose of the vaccine.[6] Of note, although another patient from the same series [Patient #9] also showed similar biopsy findings, the clinical presentation was that of a papular rash and the vaccine received was not specified.[6] To the best of our knowledge, these are the only cases in the literature of a Grover disease-like response to a vaccination.[6] However, unlike our patient, these cases did not have a medical history significant

FIGURE 1. Clinical presentation and close-up of biopsy site [inset].

FIGURE 2. Clinical presentation of erythematous somewhat annular rash involving the axillae.

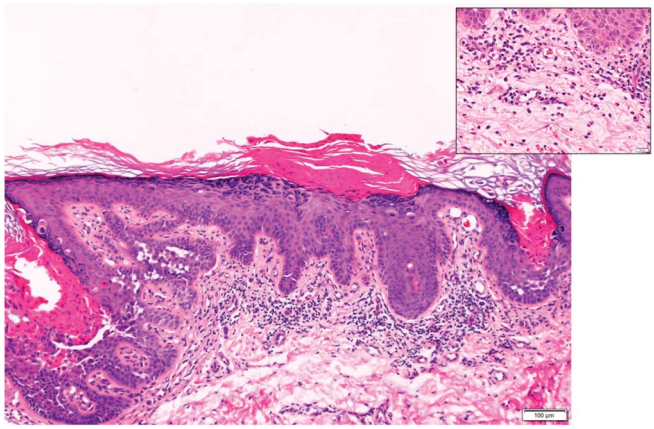

FIGURE 3. H&E of shave biopsy of rash from patient's abdomen showing patchy acantholytic dyskeratosis with an underlying inflammatory infiltrate composed of lymphocytes and neutrophils [inset].

for Grover disease, although this was never biopsy-confirmed in our patient.[6]

Nonetheless, given the medical history in our case, the differential diagnosis included a flare of Grover disease postvaccination. Favoring this theory, flares of other entities with differing pathologies triggered following COVID-19 vaccination have been previously reported in the literature.[9–13] Elbaek et al[9] described a case of a flare-up of Darier disease 2 days after receiving the Vaxzevria COVID-19 vaccination. Niebel et al and Joseph et al both described cases of triggered flares of subacute cutaneous lupus erythema, 4 and 10 days after receiving the Pfizer and Moderna COVID-19 vaccines, respectively.[10,11] Rodriguez-Jimenez et al recently described a case series of 5 patients with varicella zoster reactivation approximately 5 days after receiving the Pfizer COVID-19 vaccination and the authors also postulated that the vaccine played an immunologic role in allowing the varicella zoster virus to escape its latent phase.[12] Furer et al[13] described 6 autoimmune inflammatory rheumatic disease patients who experienced reactivation of herpes zoster after their Pfizer COVID-19 vaccination and developed vesicular rashes approximately 8 days later. In one report of drug-induced Grover disease describing 3 clinical trial patients treated with interleukin-4, the authors suggested that the etiopathogenesis may be because of increased production of B-cell antibodies or increased activation of plasminogen.[14]

Gianotti et al[15] described 2 COVID-19 patients who developed diffuse maculopapular rashes and biopsy findings of dyskeratotic keratinocytes with acantholytic clefts, findings suggestive of Grover disease. Our patient was tested and found to be COVID-negative. Notably, there is a tendency to limit the diagnosis of Grover disease to cases without a triggering factor. This suggests that there may potentially be a higher number of undiagnosed Grover disease-like lesions postvaccination.

In conclusion, to the best of our knowledge, this is the second case of acantholytic dyskeratosis post-Moderna vaccine. In contrast to the only case previously reported in the literature, a confounding feature in our case, was the medical history of Grover disease, given which the differential diagnosis also includes reactivation of Grover disease by the Moderna vaccine. In our patient, the absence of flares over the past year and the temporal relationship of the onset of the rash to vaccine administration argued in favor of the changes being likely vaccine-related.

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