



## Chronic, Diffuse Erythema Multiforme Following Third Dose of an mRNA SARS-CoV-2 Vaccine

Michael Yi<sup>1\*</sup>, Jaasrini Reddy Vellore<sup>2</sup>, Panagiotis Koutsoupas<sup>3</sup> and Manish Trivedi<sup>3</sup>

<sup>1</sup>Geisinger Commonwealth School of Medicine, USA

<sup>2</sup>Rowan School of Osteopathic Medicine, USA

<sup>3</sup>AtlantiCare, USA

### Abstract

Erythema Multiforme (EM) is a benign hypersensitivity reaction characterized by multiple, erythematous, targetoid papules that appear most often symmetrically across the extremities. Histologically, the epidermis usually shows apoptotic keratinocytes, spongiosis, and hydropic changes. EM is associated with infections such as HSV and *Mycoplasma pneumoniae* and rarely with vaccinations and medications. It is an acute, self-limited disorder that resolves within 2 to 6 weeks. Recent studies report a variety of cutaneous findings status post mRNA COVID-19 vaccination with EM encompassing 1.1% of cutaneous findings. We report a case of a 39 y/o healthcare worker who developed acute erythema multiforme 10 days after receiving the third dose of the Moderna COVID-19 vaccine without prior adverse reactions to the first two doses. The diagnosis was made clinically, and the patient course was followed for 8 weeks without complete resolution.

### Introduction

There is no doubt that the mRNA and adenoviral-vector-based COVID-19 vaccines protect individuals from the majority of COVID-19 strains and decrease the chances of severe complications of COVID-19. In a single-blind, multinational trial, the BNT162b2 mRNA COVID-19 vaccine (Pfizer and Biotech) was found to be 95% effective in preventing COVID-19 [1]. The interim efficacy results of the Johnson & Johnson attenuated adenovirus vector vaccine has been shown to be 76% to 83% effective at preventing COVID-19 infections 14 days post-vaccination [2]. With the advent of the Omicron variant, there have been numerous pushes for a booster shot to maintain immunity, but there have been little to no reports on acute, novel adverse effects following an mRNA COVID-19 booster shot. Numerous cutaneous manifestations have already been associated with the Moderna mRNA COVID-19 vaccination 2-shot series. These include urticaria, erythromelalgia, pernio, petechiae, and pityriasis rosea among others [3]. There have also been reported cases of erythema multiforme associated with the COVID-19 vaccine. One report of 414 cases has shown that in those that had cutaneous findings following the first dose, only 43% had another cutaneous finding following the second dose [3]. Additionally, the report noted that cutaneous findings were less severe and quicker to resolve when associated with the second vaccination shot [3]. We present a case of chronic, diffuse erythema multiforme after receiving the Moderna mRNA COVID-19 booster shot without any prior cutaneous reactions.

### Case Presentation

A healthy 39-year-old female healthcare worker presented to the Emergency Department with diffuse erythema and pruritus that began one night prior to the visit. The symptoms started with mild itching of the arms and chest but progressed overnight to diffuse hives covering the chest, bilateral upper extremities, and back. The patient complained solely of cutaneous issues and denied chest pain or discomfort, shortness of breath, difficulty with breathing, or throat swelling. The patient denied any changes to her daily routine, including any new soaps, lotions, or detergents. She also denied consumption of any new medications or food and noted a previously known allergic reaction to kiwis. She also reported being outdoors raking leaves in the hours immediately prior to the onset of hives. The patient also received the third Moderna mRNA COVID-19 booster shot 10 days prior to the onset of symptoms, with no prior cutaneous manifestations associated with the Moderna vaccination 2-dose series. She was discharged on suspicion of allergic reaction and prescribed oral prednisone 20 mg daily for 5 days and Benadryl as needed. Two days after the initial presentation, the patient returned to the emergency department and was admitted with worsening symptoms and

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#### \*Correspondence:

Michael Yi, Geisinger Commonwealth School of Medicine, AtlantiCare Mainland Campus, 65 W. Jimmie Leeds Road, Pomona, New Jersey, 08240, USA, Tel: 2676321735; E-mail: mxy5128@gmail.com

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**Figure 1:** Erythematous, targetoid lesions on the lower extremities.



**Figure 2:** Erythematous, targetoid lesions on the upper peripheral extremities.

shortness of breath. Physical exam noted urticaria, dermatographism, angioedema, and maculopapular, erythematous, targetoid lesions diffusely over the upper and lower extremities, face, lips, and throat (Figure 1, 2). The patient was started on oral Zyrtec and daily, oral prednisone. On day two of admission, the oral Zyrtec was changed to IV Benadryl and the oral prednisone was changed to IV Solu-Medrol due to lack of significant improvement. Physical exam indicated erythema multiforme and spontaneous angioedema. No additional pathology workup was performed due to the clinical picture. The patient was maintained on this regimen for 2 days with improvement of cutaneous symptoms and discharged for outpatient follow-up with daily, oral prednisone. Eight weeks following out-patient therapy, the patient continues to report flares of diffuse erythema multiforme after multiple attempts to taper off the daily, oral prednisone.

## Discussion

Erythema Multiforme (EM) is a benign hypersensitivity reaction characterized by multiple, erythematous, targetoid papules that appear

most often symmetrically across the extremities. Histologically, the epidermis shows apoptotic keratinocytes, spongiosis, and hydropic changes [4]. It is an acute, self-limiting disorder that usually resolves within 2 to 6 weeks [5]. EM is also a known, rare cutaneous manifestation associated with HSV, *Mycoplasma pneumoniae*, adverse drug reactions, and to a lower degree, vaccinations since the establishment of the Vaccine Adverse Event Reporting System (VAERS) in 1990 [6]. In a study of adverse events to vaccinations in 466,027 participants from 1999-2017, 0.2% had reported erythema multiforme [6]. In another study of 414 patients who received the Moderna or Pfizer mRNA COVID-19 vaccination, EM encompassed 1.1% of cutaneous findings [3]. Of the reported EM findings, all were resolved over the course of 3 to 4 days with topical steroids, oral antihistamines, and pain medication [3]. Second-dose reactions were also less severe and more likely to resolve quickly, and no severe reactions were recorded [3]. In the case of cutaneous reactions to the Moderna mRNA COVID-19 vaccine, it is hypothesized that a possible etiology is a delayed-type hypersensitivity reaction to polyethylene glycol [3].

## Conclusion

Erythema multiforme is an acute condition that generally resolves within weeks. We report a case of a 39 y/o healthcare worker who developed chronic erythema multiforme 10 days after receiving the third dose/booster shot of the Moderna COVID-19 vaccine without prior adverse reactions to the first two doses. Previous reports have hypothesized that cutaneous reactions associated with mRNA second-dose vaccinations are less severe and quicker to resolve. Nonetheless, clinicians should be aware of this unique, chronic cutaneous reaction to the COVID-19 vaccination even after the booster dose and this should not discourage physicians from recommending the booster.

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