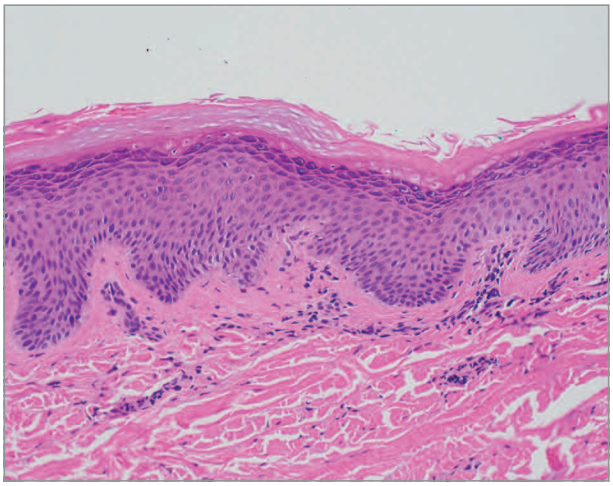
Figure 2. Punch Biopsy of an Eczematous Plaque on the Hand



Specimen reveals spongiotic psoriasiform dermatitis with background eosinophils (hematoxylin-eosin; original magnification ×200).

diagnostic and therapeutic challenge. Cytotoxic T-lymphocyte antigen–4 is expressed on regulatory T cells and binds ligands CD80 and CD86 on antigen-presenting cells to halt T-lymphocyte activation.[2] When dysfunctional, the T-cell activation leads to lymphoproliferation and autoimmunity and clinically presents with common recurrent infections, such as sinus, ear, respiratory (61%), hypogammaglobinemia (84%), autoimmune cytopenias (62%), gastrointestinal symptoms (59%), endocrinopathies (33%), neurological features (including headaches) (29%), and arthritis (14%).[1,2] Nonmalignant T-cell lymphoproliferation, such as hepatosplenomegaly, lymphadenopathy, and lymphocytic lung infiltrates, can be seen in 73% of patients.[1,3] Symptom onset occurs at a mean age of 11 years, but disease manifestations may occur as late as age 50 years.[3] Treatment of CTLA-4 haploinsufficiency includes management of autoimmune symptoms with standard therapies. Abatacept, a fusion protein comprising human CTLA-4 that is linked to a modified Fc portion of IgG1, acts as a selective T-cell costimulation modulator that can be useful in disease regulation.[1]

Cytotoxic T-lymphocyte antigen–4 haploinsufficiency cutaneous findings are still poorly characterized, despite being present in 56% of patients.[3] Atopic dermatitis (AD) is the most commonly described skin comorbidity, with recent reports of vitiligo, psoriasis, and alopecia.[3] Cytotoxic T-lymphocyte antigen–4 variations have been associated with childhood AD and the severity of AD symptoms, and it can be the initial presenting symptom in 2% of patients.[4] Similarly, CTLA-4 variations have been associated with AA in European populations and psoriasis in Eurasian populations.[5,6] This case highlights the occurrence of novel immunodeficiency syndromes and alerts dermatologists to the clinical constellation of chronic relapsing skin diseases, frequent respiratory infections, and autoimmune conditions.

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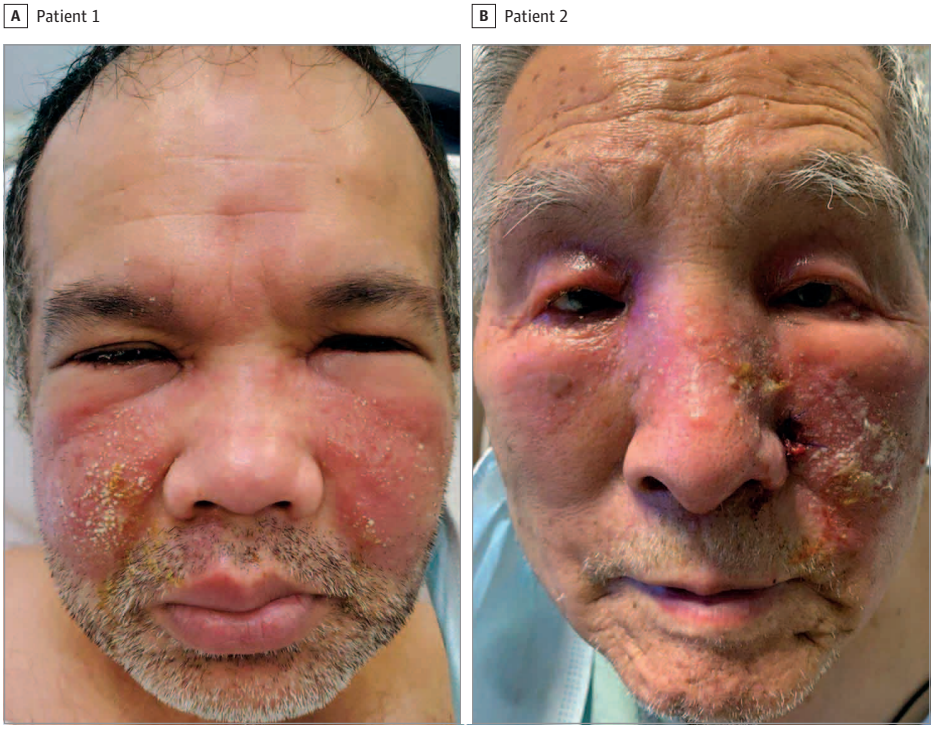
Association of Facial Pustular Neutrophilic Eruption With Messenger RNA–1273 SARS-CoV-2 Vaccine

Multiple cutaneous reactions to the messenger RNA (mRNA)-1273 SARS-CoV-2 vaccine have been reported, including immediate injection site reactions,[1-3] delayed injection site reactions,[1-4] and localized facial/lip swelling in prior dermal filler injection sites.[2,3] We report a facial eruption that developed within 24 hours after receiving the mRNA-1273 vaccine in 2 patients without a history of known allergies, rosacea, facial/dental fillers, or prior SARS-CoV-2 infection.

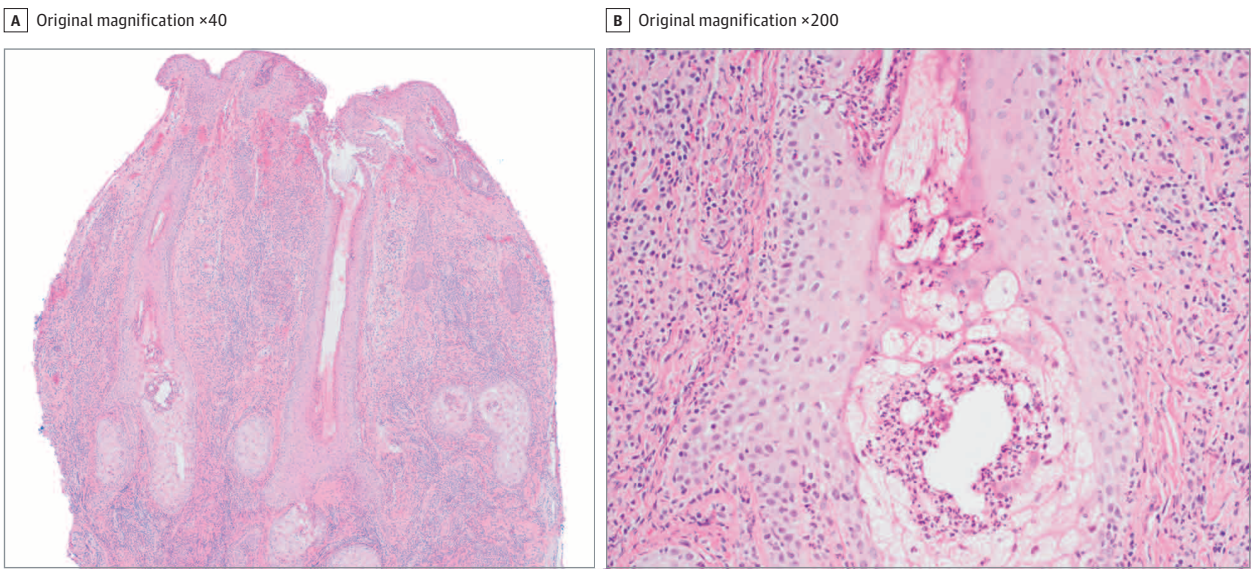
Report of Cases | *Patient 1.* A previously healthy man in his 50s presented to our department 4 days after receiving his initial dose of the mRNA-1273 vaccine. Within 24 hours after receiving his vaccination, the patient noticed chills and facial swelling that developed into painless, nonpruritic erythema. At presentation, he did not have a fever and had a leukocytosis with neutrophil predominance. On examination, there were bilateral edematous, erythematous, well-demarcated plaques of the central face and eyelids with numerous punctate monomorphic pustules and crust (**Figure 1**A). The clinical differential diagnosis included acute localized exanthematous pustulosis, neutrophilic dermatosis, rosacea fulminans, *Demodex* folliculitis, and a skin and soft tissue infection. Cephalexin and halobetasol,

Figure 1. Clinical Images of Facial Pustular Neutrophilic Eruption Associated With Messenger RNA (mRNA)–1273 SARS-CoV-2 Vaccine



Edematous, erythematous, well-demarcated plaques with overlying punctate monomorphic pustules and crusting on the central face and eyelids at 4 days after administration of an mRNA-1273 vaccine in patient 1 (A) and 5 days after vaccination in patient 2 (B).

Figure 2. Histopathologic Images of Facial Pustular Neutrophilic Eruption Associated With Messenger RNA (mRNA)–1273 SARS-CoV-2 Vaccine



Hematoxylin-eosin–stained lesional specimens from patient 1. A, Interstitial and intrafollicular infiltrate composed mostly of neutrophils with some admixed lymphocytes and plasma cells that are present in the superficial and deep dermis. There is follicular dilatation and plugging. B, High magnification demonstrating neutrophils with prominent involvement of hair follicles.

0.05%, ointment was prescribed. Cephalexin use ended 3 days later when a bacterial culture from a pustule did not reveal a causative organism. Histopathology results revealed an infiltrate of neutrophils interstitially and within intact follicular epithelium with negative infectious stains. (**Figure 2**, A and B). The rash cleared within 7 days. The patient received the second vaccine dose as scheduled without recurrence.

Patient 2. A previously healthy man in his 80s presented to our department 5 days after receiving his second dose of the mRNA-1273 vaccine. He had not had a reaction after the first dose. Within 24 hours of receiving his vaccination, the patient noticed swelling, predominantly of the central face and eyelids, with worsening swelling, pain, and erythema over the next several days. He had weakness, malaise, and subjective fevers. At presentation, he did not have a fever, had tachycardia, and had a leukocytosis with neutrophil predominance. On examination, there were erythematous, edematous plaques spanning the eyelids, cheeks, and nasal dorsum; during the course of 24 hours, monomorphic submillimeter follicularly based pustules and crust emerged within the erythema (Figure 1B). Given the same clinical differential diagnosis as patient 1, he was prescribed vancomycin and piperacillin/tazobactam and tacrolimus, 0.1%, ointment. His systemic symptoms resolved within 24 hours. When infectious workup results did not reveal an obvious infection, antibiotics were narrowed to doxycycline and continued for an additional 5 days while awaiting histopathology results. Bacterial culture from a pustule did not reveal a causative organism. Histopathology results showed similar findings to patient 1. The rash completely resolved 10 days later.

Discussion | The clinical presentation of a facial rash with pustules and the shared histopathologic findings of a dense neutrophilic infiltrate interstitially and within intact follicular epithelium support a facial pustular neutrophilic eruption as the reaction pattern. The differential diagnosis can be narrowed to rosacea fulminans, neutrophilic dermatosis, and skin and soft tissue infection. The abrupt onset of facial erythema, edema, and pustules may be consistent with rosacea fulminans, although the lack of nodules, papules, and cysts and occurrence in 2 older men go against this diagnosis.[5] The abrupt onset of marked edema and pustules fits well for a neutrophilic dermatosis, although negative tissue cultures are a diagnostic criterion. It is unclear if this facial eruption in the setting of the mRNA-1273 vaccine represents a distinct entity or an unmasking of a dermatologic condition in a predisposed individual. It is also notable that for patient 2, the eruption occurred after the second dose only, which has been reported elsewhere.[3] Reassuringly, this facial pustular neutrophilic eruption resolved within 7 to 10 days and without serious sequelae. This is consistent with evidence that most cutaneous reactions that are associated with the mRNA SARS-CoV-2 vaccines are generally self-limited and minor.[3]

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