Erythema nodosum after COVID-19 vaccination in a pediatric patient

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INTRODUCTION

Over the past year, vaccinations against SARS-CoV-2 have been authorized across the world to mitigate the effects of the COVID-19 pandemic. These vaccines have proven safe and effective, though side effects and adverse reactions do occur.[1] Several dermatologic reactions following COVID-19 vaccination have been reported in adults.[2,3] As vaccination eligibility is extended to the pediatric population, further characterization of the spectrum of cutaneous reactions in this population is needed. We describe a case of erythema nodosum following COVID-19 vaccination in a pediatric patient.

CASE REPORT

A previously healthy 17-year-old female presented to the pediatric urgent care clinic with multiple days of tender, erythematous nodules on her bilateral lower extremities. In the 2 days prior to presentation, she had noticed them enlarging and becoming increasingly painful. She denied any preceding traumatic events, including falls or direct trauma to the legs. She denied fevers or recent infections. There were no ill contacts reported in the home or at school. No known contacts had similar lesions.

Three weeks prior to presentation, the patient had received her second dose of the Pfizer-BioNTech COVID-19 vaccine. She reported a 1-day period of malaise the day after her vaccination, but since that time, she had been in her usual state of health. The patient had not experienced any side effects following her first dose of the vaccine. She had no known recent history of streptococcal pharyngitis or new drug exposures. Her past medical history was negative for known systemic infections or inflammatory conditions including tuberculosis, sarcoidosis, or inflammatory bowel disease.

Abbreviation used:

EN: erythema nodosum

On the physical examination, numerous tender, warm, erythematous nodules with a diameter of 2-3 centimeters were noted across the anterior tibial surfaces, bilaterally (Fig 1). There was also a single similar lesion on her left forearm. There were no other notable findings on physical examination. The patient's vital signs were within the normal limits.

Laboratory testing was notable for an elevated erythrocyte sedimentation rate of 37 mm/hr (reference range, <25 mm/hr) as well as elevated C-reactive protein at 1.7 mg/dL (reference range, <0.8 mg/dL). Complete blood count with differential was within the normal ranges. Antistreptolysin-O titers were not elevated, and interferon-gamma release assay was negative. Given the high clinical suspicion for erythema nodosum (EN), a biopsy was not performed. With the temporal association and otherwise negative workup for common underlying etiologies of EN, the patient's recent COVID-19 vaccination was hypothesized as the likely trigger for the onset of EN. At the time of follow-up 1 week later, the patient's skin lesions had nearly resolved (Fig 2) with rest and nonsteroidal anti-inflammatory medications; her erythrocyte sedimentation rate remained elevated at 56 mm/hr, though her C-reactive protein level had normalized.

DISCUSSION

EN is a septal panniculitis thought to be a delayed-type hypersensitivity reaction. EN may be accompanied by systemic symptoms such as fever, malaise, and arthralgias, though this is less common in

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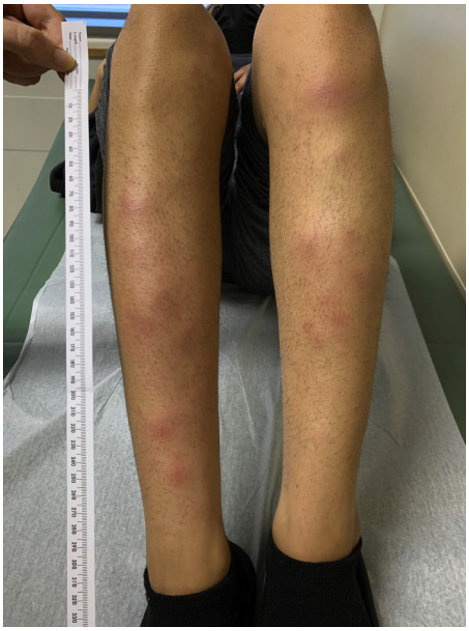

Fig 1. Erythema nodosum (EN) on the anterior aspect of the bilateral lower extremities at the first clinic visit.

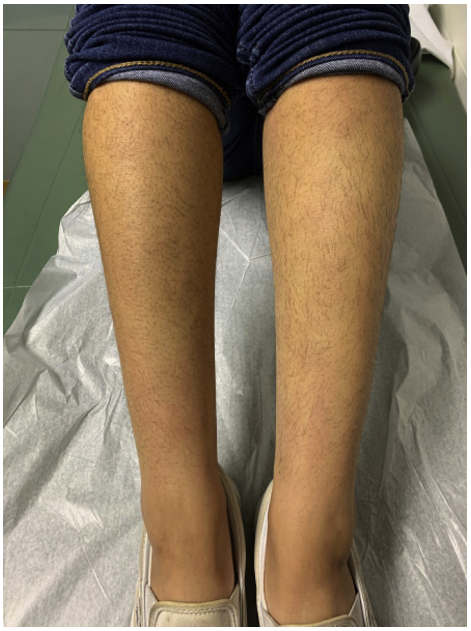

Fig 2. Erythema nodosum (EN) on the bilateral lower extremities at clinical follow-up 1 week after the first clinic visit.

pediatric patients. EN is often idiopathic but is also known to occur in the setting of infections, systemic inflammatory conditions, medication use, pregnancy, and malignancy, among other conditions.[4] In the pediatric population, group A β -hemolytic streptococcal infection is the most common trigger.[5] Regardless of etiology, the condition is generally self-limiting within 3-6 weeks and resolves without long-term sequelae such as scarring or atrophy.[4] Diagnosis is based on clinical presentation, but if presentation is atypical, skin biopsy can be considered.[5] We based our diagnosis of EN on the classic clinical presentation and discussion with an on-site pediatric dermatologist. Biopsy was deferred in our pediatric patient given the typical clinical findings and course, and following consideration that biopsy would not likely change management.[6]

The workup involves evaluating for common underlying etiologies including tuberculosis (chest x-ray or interferon-gamma release assays), *Streptococcus* (antistreptolysin-O titers), and malignancy (complete blood count). In the case of our patient, none of these tests revealed an identifiable cause. Since vaccine-related reactions may occur up to 6 weeks following inoculation according to the Center for Disease Control's timeline for monitoring of COVID-19 vaccine safety,[7] we considered our patient's recent COVID-19 vaccination to be the most likely underlying etiology of her EN. Furthermore, vaccine-associated EN has been described previously up to 30 days after the administration of other vaccines.[8]

Although the majority of EN cases are idiopathic, EN has been described following several different vaccinations. EN has occurred following tetanus, diphtheria, and acellular pertussis; bacille Calmette-Guérin; hepatitis B; human papillomavirus; rabies; small pox; typhoid; and cholera vaccines.[8] More recent reports have noted EN following COVID-19 vaccination in the adult population.[2,3] Vaccine-related EN is generally assumed to represent a reaction to the infectious antigen present in the vaccine, but it could theoretically also represent a response to vaccine adjuvants. To the best of our knowledge, EN following COVID-19 vaccination has not yet been described in the pediatric population.

Our patient developed EN following her second dose of the COVID-19 vaccine. Of the 2 doses of the Pfizer-BioNTech COVID-19 vaccines, the second dose appears to generate more systemic side effects than the first dose, possibly due to a more robust immunological response.[9,10] The presentation of EN and other cutaneous reactions after second (and even third) doses of other vaccines has indeed been previously described in the literature.[8]

As eligibility for COVID-19 vaccination expands to include younger patients, we sought to raise awareness and consideration of EN as a dermatologic reaction among pediatric patients, as it has been noted among adult patients. Pediatric providers should be cognizant of this dermatological diagnosis to counsel patients and families accordingly. Finally, although EN can be alarming or uncomfortable for

patients, it is most frequently self-limiting and resolves with supportive measures.[4] The benefits of vaccination against COVID-19 continue to outweigh the risks for the vast majority of patients.[1]

Conflicts of interest

None disclosed.

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