Leukocytoclastic Vasculitic Rash Following Second Dose of Moderna COVID-19 Vaccine

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Abstract
The immunization against coronavirus disease (COVID-19) via vaccination serves as a significant milestone in the fight against the pandemic. Rapid introduction of various COVID-19 vaccines to stem the spread of virus has researchers scrambling to document the adverse effects left in its wake. Thus far, there have been singular examples of cutaneous vasculitis associated with COVID-19. A history of vasculitis leaves little error to miss its inclusion in diagnostic differentials. It also invokes the physiologic possibility that afflicted patients possess a more susceptible landscape for recurrence that was then triggered by the vaccine when compared with those who lack similar history. In our case report, we build on those findings with one of the first documented examples of vaccination-induced vasculitic rash in a previously asymptomatic patient.

Keywords
vasculitis, COVID-19 vaccine, autoimmune disease, coronavirus

Case Description
A 59-year-old woman with a medical history of hypertension, hyperlipidemia, prediabetes, obesity, self-reported arthritis, and coronavirus disease (COVID-19) infection in April 2020 presented to the outpatient clinic with a chief complaint of a 3-day rash. The rash had appeared on her lower extremities 1 day following the second dose administration of the Moderna COVID-19 vaccine, and subsequently spread to the lower abdomen while sparing the back. The patient lacked a history of fever, nausea, vomiting, sick contacts, recent travel, tick bites, or familial autoimmune disease. She denied rash-associated burning, draining, dryness, itchiness, or pain. Physical examination revealed diffuse, nonpalpable violaceous petechiae on the legs, pelvis, and lower abdomen (Figures 1 and 2). After an unremarkable workup and 2 days in which the rash was unresponsive to over-the-counter antihistamine, a 5-mg prednisone taper was initiated and the patient was sent home. Results from extensive testing, including antinuclear antibody (ANA), antinuclear ribonucleoprotein (anti-RNP), Sjogren's antibody, rheumatoid factor (RF), cyclic citrullinated peptide antibody (anti-CCP), double-stranded DNA antibody (anti-dsDNA), anti-Smith antibody, hepatitis panel, complement C3, and complement C4, were unremarkable.

The patient had then come to the emergency department 3 days later for rash progression to the upper abdomen, posterior left arm, and distal right arm despite adherence to the prednisone regimen (Figure 3). She also reported several hours of intermittent, localized, burning, epigastric abdominal pain. Laboratory findings were significant for elevated white blood cell count (WBC) of $17.25 \times 10^3/\mu L$, lactate of 2.3 mmol/L, and C-reactive protein of 17.7 mg/L (normal range $<5 \text{ mg/L}$). Computed tomography (CT) revealed inflammatory mesentery and circumferential thickening, concerning for ischemic bowel disease (IBD). Gastroenterology (GI) labs were notable for a weakly positive transglutaminase IgG antibody, but negative for fecal calprotectin and normal IgA. Her abdominal pain had resolved the next day without any intervention, as well as WBC and lactate. She was discharged with a prednisone taper and scheduled to repeat CT imaging with GI follow-up for her abdominal pain and dermatology for her rash.

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Unfortunately, the patient had missed her imaging and GI appointment. She was seen by the dermatology outpatient for the rash, which ultimately improved by the time she came and was subsequently not biopsied. She was advised to finish her prednisone taper.

Discussion

Vasculitis is the inflammation of blood vessels which leads to tissue destruction. Leukocytoclastic vasculitis is the most common form of small vessel vasculitis of the skin and results from immune complex deposition in the vessel wall and complement activation leading to its destruction. Leukocytoclastic vasculitis is idiopathic in up to 50% of the cases. Secondary leukocytoclastic vasculitis can be triggered by infections, most common being streptococcal upper respiratory tract infections, Mycobacterium, Staphylococcus aureus, Chlamydia, Neisseria, and HIV. Other triggers include certain drugs; autoimmune diseases such as systemic lupus erythematosus, Sjogren’s, IBD, rheumatoid arthritis, and Behçet disease; malignancies such as lymphomas and leukemias; and visceral tumors such as intestinal adenocarcinoma and lung cancer. It manifests most frequently as palpable purpura or infiltrated erythema involving the small superficial dermal vessels bilaterally on lower extremities and buttocks. In most cases, cutaneous vasculitis is a self-limited condition relieved by leg elevation, avoidance of standing, and nonsteroidal anti-inflammatory drugs. Severe diseases can be treated with systemic corticosteroids or immunosuppressants. Severe refractory diseases can be treated with plasmapheresis and intravenous immunoglobulin. A retrospective study demonstrated a good overall survival in leukocytoclastic vasculitis, but relapses remain frequent. Independent risk factors for relapse were vascular thrombosis in the biopsy, peripheral neuropathy, hepatitis, and positive antineutrophilic cytoplasmic antibody.

The temporal relationship of COVID vaccine induction with rash onset in the absence of other triggers renders the vaccine most likely responsible for our patient’s presentation.
Based on previous reports, eruptions have commenced 2 to 4 weeks after COVID infection and have been associated with a normal or mildly elevated IgA.7,8 Subsequently, cases of COVID-19 vaccine–induced vasculitis have been documented.3,10 However, most of these patients had a prior history of vasculitis. Resolution of the rash precluded a biopsy, which we deemed appropriate for the best interest of this individual patient even as it detracted from our ability to provide more definitive indictment as to the cause of her symptoms. Beyond temporal association, implication of an autoimmune rather than allergic process is furthered by failure of antihistamines to reduce our patient’s symptoms in contrast to their resolution following steroid commencement.

While determined to be incidental and noncontributory, our patient’s chronic arthritic-like symptoms and abdominal pain parallel previous literature of documented history of IBD and arthritis, and is consistent with data promoting the predisposition of those with IBD to vasculitis.11 However, concerns for ischemic colitis or IBD in the context of a benign physical examination with CT results were questionable upon abdominal pain resolution and normalization of both WBC and lactate levels the next day. Suspicion of Henoch-Schönlein purpura was diminished given a normal IgA, normal kidney function, and resolution of rash with steroid use.12 Although only weakly positive transglutaminase IgG, celiac disease could be a reason for the patient’s initial abdominal pain. However, this diagnosis was deemed unlikely in the absence of abdominal history and in the context of the patient’s age as well as the rapid resolution of her abdominal pain.

Previous reports indicated that most of the vasculitis flares occurred after the first dose of COVID vaccine. However, one can also speculate that our patient’s lack of a history of vasculitis was responsible for the delay in symptom presentation until after second dose administration. This case’s value lies in that it is one of the first to report COVID vaccine–associated vasculitis in a previously asymptomatic patient. Although biopsy was unwarranted in our case to confirm the association, the case’s addition to the literature to serve as a precautionary possibility when encountering similar presentations will facilitate the administration of prompt treatment while enabling further investigation of vaccine side effects and the vaccine’s confirmation or vindication as the culprit.

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**Ethics Approval**
Our institution does not require ethical approval for reporting individual cases or case series.

**Informed Consent**
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