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LETTERS TO THE EDITOR

Possible case of mRNA COVID-19 vaccine-induced small-vessel vasculitis

To the Editor,

Coronavirus disease (COVID-19) is a hyperinflammatory, multisystemic viral infection that is mainly characterized by immune system dysregulation, complement activation, and coagulation cascade induction.[1] DNA/RNA-based vaccines, non-replicating viral vector vaccines, and inactivated vaccines are now being applied worldwide in an effort to develop an efficacious immune response against COVID-19. Local injection site reactions, urticaria, morbilliform eruption, and erythromelalgia are among the reported cutaneous side effects of mRNA COVID-19 vaccine.[2] Herein, we would like to report a possible association between mRNA COVID-19 vaccine and the development of cutaneous vasculitis.

A 57-year-old woman with a history of epilepsy, bipolar disorder, and depression was consulted to us due to the appearance of widespread erythematous eruption involving the trunk and extremities. Upon questioning, it was learnt that lamotrigine was started 1 month ago, for epilepsy. Additionally, she had the first dose of mRNA COVID-19 vaccine 1 week ago. Dermatologic examination showed erythematous-confluent papules and plaques involving the trunk and extremities (Figure 1). Our pre-diagnoses were maculopapular drug eruption and small-vessel vasculitis (SVV). A 4-mm punch biopsy was taken from the trunk, which showed inflammatory infiltrate in the perivascular and interstitial area along with erythrocyte extravasation and fibrin deposition (Figure 2). SVV was the final diagnosis. Even though we cannot totally exclude the possibility of lamotrigine-induced SVV, we believe that the most probable diagnosis was COVID-19 vaccine-induced SVV, considering the short time (7 days) between the vaccination and the start of the rash. Upon questioning, she did not report to have any systemic symptoms and there was no history of recent infection. Biochemistry results, urinalysis, chest X-ray, and stool guaiac test were within the normal limits. Rheumatologic markers were all negative; there was only mild eosinophilia. The patient was started on 40 mg/day oral prednisolone, 20 mg/day cetirizine, and topical clobetasol propionate ointment. She showed dramatic response to the treatment within a week; lamotrigine was discontinued and changed to levetiracetam. Since we were not able to totally exclude the possibility of lamotrigine-induced vasculitis, lamotrigine was immediately interrupted and changed to levetiracetam. In order to avoid further aggravation or systematization of vasculitis, lamotrigine was never reintroduced. An evidence-based guide to SARS-CoV-2 vaccination of patients on immunotherapies by Gresham et al[3] suggested that high dose regimens of systemic prednisone (>20 mg/day) are associated with diminished seroconversion rates and/or attenuated immune response and humoral response. Therefore, we advised our patient to have the second dose of mRNA COVID-19 vaccine. The patient had responded to oral prednisolone treatment, which was tapered off 10 mg every week and cessated in a month. However, 1 month later, the second dose of mRNA COVID-19 vaccine was administered and flare-up of previous vasculitic eruption was observed which responded to topical corticosteroid treatment.

Maculopapular rash, papulovesicular eruption, livedo reticularis, vasculitis, and chilblain-like lesions have all been associated with COVID-19.[4] Recently, both inactivated and mRNA-based COVID-19 vaccines are implicated in the development of urticaria, maculopapular rash, injection site reactions, herpes zoster, chilblain, cutaneous vasculitis, erythema multiforme, and pityriasis rosea.[2,5] The overall impression is that COVID-19 vaccines are generally well tolerated and cause self-limited cutaneous reactions.[5] Even though cutaneous reactions are typically mild, Cohen et al.[6] reported a case of leukocytoclastic vasculitis flare after the administration of mRNA COVID-19 vaccine similar to our case. Even though, we cannot totally exclude the possibility of lamotrigine-induced vasculitis; there has been, to our knowledge, no reported association between lamotrigine and vasculitis. In addition, considering the short time interval between COVID-19 vaccine administration and the onset of cutaneous rash in our case, SVV seems to be associated with mRNA COVID-19 vaccination. In line with the case reported by Cohen et al.,[6] our patient did not show any systemic involvement and dramatic resolution was observed after systemic corticosteroid administration. The hyperinflammatory state secondary to COVID-19 may promote the development of antibodies against vaccine-related antigens, thereby causing immune complex deposition and manifestations of vasculitis.[6]

All in all, we would like to report to a possible case of mRNA COVID-19 vaccine-induced cutaneous vasculitis, which showed dramatic response to systemic corticosteroids without any systemic involvement. COVID-19 vaccines, just like the disease itself, may have tolerable and transitory cutaneous side effects including limited cutaneous vasculitis.

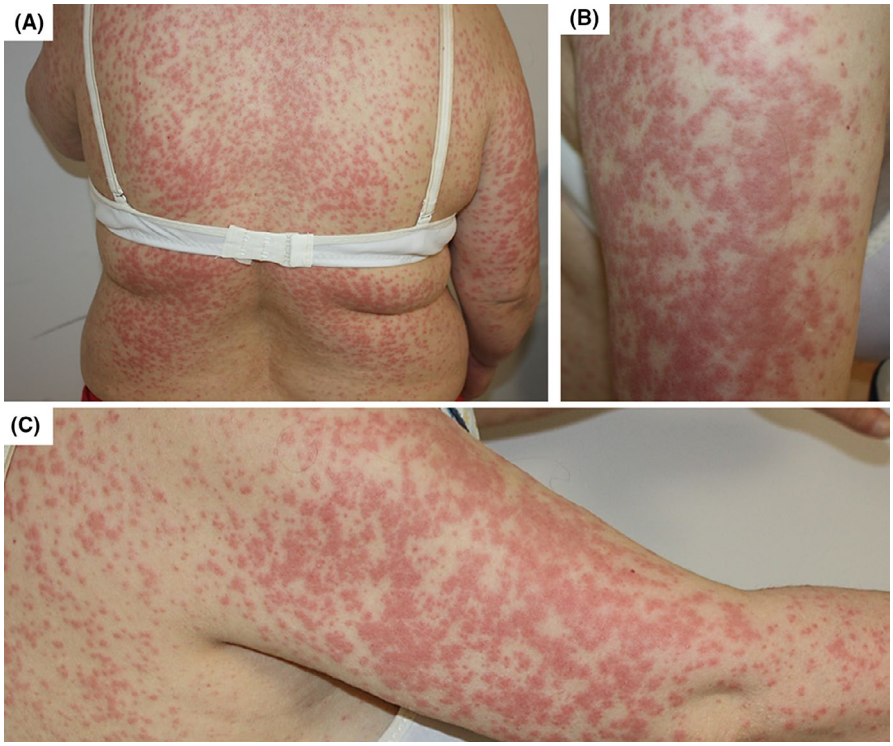

FIGURE 1 Dusky red, palpable, confluent papules and plaques involving the trunk (A) and upper arms (B, C)

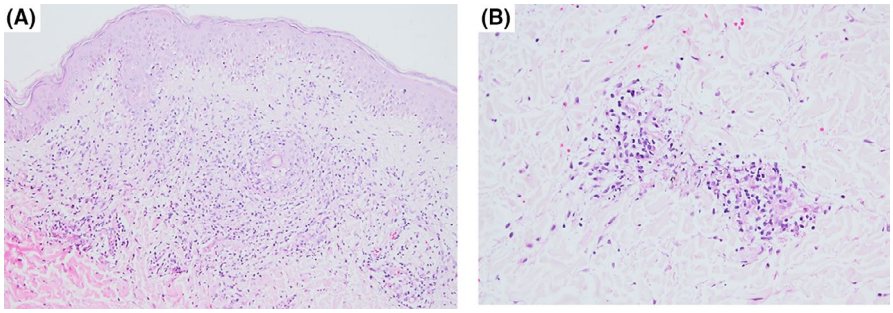

FIGURE 2 Basal vacuolar change and lymphocyte exocytosis in the epidermis with moderate inflammation around vessels in the superficial dermis (A) (H&E×200). Mixed inflammatory infiltrate attacking the small-vessel walls, endothelial injury, perivascular nuclear dust, and erythrocyte extravasation (B) (H&E×200)

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CONFLICT OF INTEREST

We declare that there is no conflict of interest for all authors in this work.

AUTHOR CONTRIBUTIONS

Ecem Bostan involved in conceptualization, visualization, and writing—original draft. Fethi Zaid involved in conceptualization and data curation. Neslihan Akdogan involved in conceptualization, supervision, and writing—review and editing. Ozay Gokoz involved in conceptualization, data curation, supervision, and editing.

ETHICAL APPROVAL

The authors declare that no ethical approval was needed for the presentation of the case.

DATA AVAILABILITY STATEMENT

Data sharing is not applicable to this article as no new data were created or analyzed in this study.

INFORMED CONSENT

Informed consent and permission for publication of medical images were taken from the patient.

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