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Exacerbation of Lupus Erythematosus Panniculitis After Administration of COVID-19 mRNA Vaccine

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Sir,

Little is known about the safety of COVID-19 vaccines in patients with autoimmune and inflammatory skin diseases such as cutaneous lupus erythematosus. Herein, we describe a patient with lupus erythematosus panniculitis who developed disease flare after the second dose of COVID-19 mRNA vaccine.

A 28-year-old female presented with erythematous plaque on the nasal dorsum and left side of her face. The first manifestation of the disease was nine years ago, as a small erythematous nodule on her nasal dorsum. The

patient had a history of hypothyroidism and rhinoplasty, and her father had familial Mediterranean fever. A biopsy performed at that time was non-diagnostic and after eight months of prednisolone treatment her lesions regressed. In 2019, indurated plaques appeared on the face, ears, right supraclavicular and left deltoidal areas without any skin surface changes. She was diagnosed with morphoea, and she used hydroxychloroquine irregularly for one year. Under hydroxychloroquine therapy, the extent and severity of her lesions decreased and lipoatrophy on the affected sides appeared. In September 2021, 10 days after the second dose of BNT162b2 mRNA COVID-19 (Biontech/Pfizer) vaccine, erythematous induration spread towards of her left cheek and left side of her nose. There was no history of any other drug use, infection, or sun exposure that could have caused her disease flare. On physical examination, oedema in the left infraorbital region, erythematous-livid coloured induration on the left maxillary and left mandibular region were observed [Figure 1a]. The patient also had lipoatrophy on the right suprascapular and left deltoidal areas [Figure 1b and c]. An examination of punch biopsy tissue of the lesion revealed lymphocytic lobular panniculitis [Figure 1d]. Laboratory test results showed normal levels of blood cell counts, urinalysis, CRP, erythrocyte sedimentation rate, and renal and liver function. Serological study found low grade antinuclear antibodies (ANA; >1/100 to <1/320, granular pattern) and borderline positivity for AntiRNP/Sm. Based on the clinical, histopathological and laboratory findings, the patient was evaluated as lupus erythematosus panniculitis (LEP), and systemic involvement was not detected. The patient was started on hydroxychloroquine 200 mg twice a day and prednisolone 0.5 mg/kg per day. After three weeks of treatment, oedema, erythema, and induration of the lesions significantly decreased, and gradual prednisolone dose tapering was administered [Figure 1e].

LEP is an uncommon variant of cutaneous lupus erythematosus, characterized by a tender, erythematous subcutaneous induration that usually occurs on the upper arms, face, trunk, buttocks, and thighs. Although the exact aetiology of LEP is not known, it is reported that the history of trauma on the lesion area may be a triggering factor.[1] Additionally, environmental factors such as medications and vaccines can exacerbate cutaneous lupus erythematosus.[2] In the literature, three cases of subacute cutaneous lupus erythematosus (SCLE) and one case of Rowell syndrome induction and three cases of pre-existing SCLE exacerbation after COVID-19 vaccination have been reported [Table 1].[2–8] In one of them, transition of SCLE into systemic lupus erythematosus was observed which responded to prednisolone treatment within seven days.[3] To the best of our knowledge, no case of exacerbation of LEP have been reported after the administration of COVID-19 vaccine.

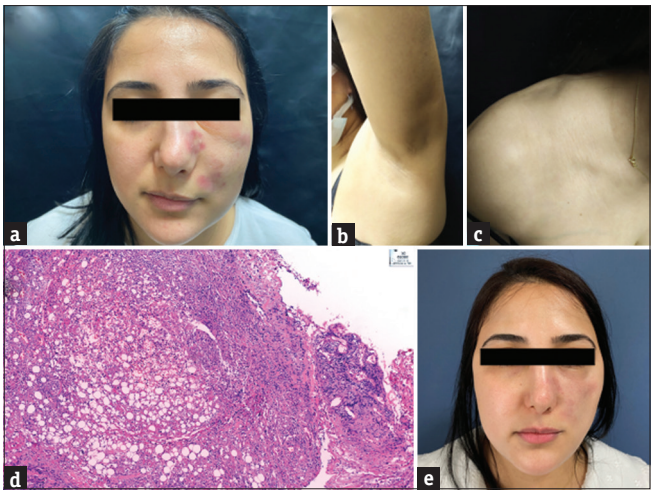


Figure 1: (a) Patient photograph at admission, showing oedema in the left infraorbital region, erythematous-livid coloured induration on the left maxillary and left mandibular region. (b and c) Lipoatrophy on the right suprascapular and left deltoidal areas. (d) Punch biopsy tissue of the lesion showing subcutaneous lymphocytic lobular panniculitis, haematoxylin and eosin (H and E), 10× original magnification. (e) Patient photograph after three weeks of prednisolone and hydroxychloroquine treatment showing improvement of the oedema, erythema, and indurated lesions

BNT162b2 mRNA vaccine, which is administered in two doses, acts by both humoral and cellular immunity. After the second dose, there is a significant increase in neutralizing antibody levels, while the antigen-specific response of IFNγ by $CD4^+$ and $CD8^+$ T cells is also observed.[9]

We think that there is a relationship between vaccination and the flare of skin lesions of our patient who was misdiagnosed with morphoea profunda priorly. The absence of reaction in the vaccine injection area and the exacerbation of pre-existing lesions suggest that the vaccine caused the disease flare by stimulating the systemic immune response. Although there is a possibility of disease flare, the American Association of Rheumatology recommends vaccination for patients with autoimmune and inflammatory rheumatological diseases due to risk of severe COVID-19 infection.[10] Since facial lipoatrophy is a difficult complication of LEP, we want to emphasize that exacerbation may be observed in these patients after SARS-CoV-2 vaccine administration.

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The patient in this manuscript has given written informed consent for the publication of her case details.

Author contributions

Ceylan Avcı wrote the first draft of the manuscript. Ceylan Avcı and Nilüfer Diana Şirin prepared the figure and table. Banu Lebe evaluated the punch biopsy tissue of the lesion and supplied the photograph. Ceylan Avcı, Turna İlknur and Sevgi Akarsu were directly involved in

Table 1: Patient characteristics of cutaneous lupus erythematosus triggered or exacerbated after COVID-19 vaccine administration

Reference	Sex/Age (years)	Cutaneous lupus erythematosus subtype	ANA and other antibody profile	Systemic involvement of lupus	COVID-19 vaccine subtype	Interval between the vaccination and onset of skin lesions	Induction	Exacerbation
Kreuter *et al.*[2]	F/62	SCLE* (papulosquamous subtype)	Previously elevated ANA and positivity for Anti-Ro/SSA; after vaccination positive anti-dsDNA, reduced C3 and C4 levels	+	First dose, adenovirus (AZD1222)	10 days	-	+(SLE** return from SCLE)
Kreuter *et al.*[3]	M/79	SCLE (annular and papulosquamous)	Elevated ANA (1/320), positivity for Anti-Ro/SSA and Anti-La/SSB, elevated RF (18U/mL)	-	First dose, mRNA (Pfizer/BioNTech; BNT162b2)	10 days	+	-
Gambichler *et al.*[4]	F/74	Rowell syndrome	Elevated ANA (1/640), positivity for Anti-Ro/SSA and Anti-La/SSB	-	First dose, mRNA (Pfizer/BioNTech; BNT162b2)	1 day	+	-
Niebel *et al.*[5]	F/73	SCLE (papulosquamous subtype)	Elevated anti-Ro/SSA antibodies	-	First dose, mRNA (Pfizer/BioNTech; BNT162b2)	10 days	-	+ (SCLE diagnosis: 2005)
Rechtien *et al.*[6]	F/24	SCLE	Elevated ANA, reduced C3 and C4 levels, positive anti-dsDNA and antiSM antibodies, after vaccination newly detected anti LA and anti-Histone antibodies	History of SLE and lupus panniculitis since age 15	First dose, mRNA (Pfizer/BioNTech; BNT162b2)	4 days	+	-
Zengarini *et al.*[7]	F/30	SCLE	Elevated anti-dsDNA, complement consumption, positive anti-sm and anti -nRNP antibodies, Anti-Ro/SSA	-	Second dose, mRNA (Pfizer/BioNTech; BNT162b2)	10 days	+	-
Joseph *et al.*[8]	F/54	SCLE	Prior labs; Elevated ANA (1/1280), anti-sm, anti-dsDNA	-	First dose, mRNA (Moderna)	4 days	-	+

SCLE*: Subacute cutaneous lupus erythematosus, SLE**: Systemic lupus erythematosus

the treatment of the patient. All authors added critical intellectual content and read and approved the final version of the manuscript.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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