


Acknowledgement

We thank Dr A. Barve, Consultant Dermatologist, Thane, India for his contribution to the refinement of these techniques.

T. Vishwanath,¹  A. Kumar Bose,¹ S. Mahajan,¹ S. Chikhalkar,¹ P. Gole,¹ V. Kharkar¹ and H. Balaji¹

¹Department of Dermatology, Seth GS Medical College and KEM Hospital, Mumbai, India

E-mail: harishbalaji35@gmail.com

Conflict of interest: the authors declare that they have no conflicts of interest.

Accepted for publication 20 July 2021

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Induction and exacerbation of subacute cutaneous lupus erythematosus following mRNA-based or adenoviral vector-based SARS-CoV-2 vaccination

doi: 10.1111/ced.14858

Dear Editor,

Evidence is accumulating that COVID-19 vaccines might induce or exacerbate autoimmune rheumatic diseases. The currently available COVID-19 vaccines include mRNA and recombinant adenoviral vector vaccines, both encoding SARS-CoV-2 spike protein production as the primary target for neutralizing antibodies.¹ We report a case of subacute cutaneous lupus erythematosus (SCLE) following mRNA vaccination with the Pfizer mRNA vaccine BNT162b2, and summarize the current literature on CLE occurring after COVID-19 vaccination.

A 79-year-old man was admitted to our department with a widespread annular and papulosquamous exanthema on his trunk and lower legs, occurring concomitantly with mild malaise and fatigue (Fig. 1a–c). There were no potential trigger factors for his skin lesions such as recent (viral or bacterial) infections, ultraviolet light

exposure or new drug intake. However, he had received the first dose of BNT162b2 mRNA vaccine 10 days before onset of the exanthema.

Histopathological examination of a skin biopsy taken from the patient's chest revealed features of CLE, including vacuolar interface dermatitis, dense dermal lymphocytic infiltrates, and mild mucin deposition (Fig. 1d,e).

Laboratory investigations showed normal blood cell count and serum chemistry, but increased titres (1 : 320; normal < 1 : 160) for antinuclear antibodies (ANA), positivity for anti-Ro/SSA (60 kDa) and anti-La/SSB antibodies, and a slightly increased rheumatoid factor (18 U/mL; normal < 14 U/mL). All other extractable nuclear antigens were negative, and review of organ systems (chest radiography, abdominal ultrasonography, heart echography) was unremarkable.

Based on these findings, a diagnosis of vaccine-induced SCLE was made, and treatment with hydroxychloroquine 200 mg twice daily and tapered intravenous glucocorticosteroid therapy beginning at 150 mg daily was initiated, resulting in a complete clearance of all skin lesions within 4 weeks.

SCLE is a distinct subtype of CLE with typical clinical (annular and/or papulosquamous cutaneous lesions symmetrically located in sun-exposed areas) and serological (anti-Ro/SSA antibodies) characteristics. Various external factors including drugs and vaccines are known to induce disease flares in CLE, especially in SCLE.² To our knowledge, three similar cases of post-vaccination CLE have been reported.^{3–5} All were classified clinically as SCLE, and all occurred within 10 days after application of the first vaccination dose and rapidly responded to treatment with systemic corticosteroids (Table 1).

Both mRNA and adenoviral vaccines elicit immunity to SARS-CoV-2 by production of high levels of spike proteins. Additionally, they trigger innate sensors by intrinsic adjuvant activity, resulting in production of type 1 interferons (IFNs),¹ which play an important role in the pathogenesis of various autoimmune rheumatic diseases through elevated levels of nuclear antigen-containing immune complexes. The elevated levels of nuclear antigen-containing immune complexes might enhance production of type 1 IFNs, which in turn further disturbs B- and T-cell tolerance mechanisms, promoting production of ANAs.⁶ The type 1 IFN pathway is also a major component of CLE pathogenesis, and correlates with disease activity.² Interestingly, among ANA-positive clinically asymptomatic patients, anti-Ro/SSA and/or anti-La/SSB antibodies were associated with an elevated IFN signature and the lupus-risk variant IRF5.⁶ These findings might explain why all of the reported post-vaccination lupus cases had Ro/SSA-positive SCLE (Table 1).

A recently published register-based study on 414 skin reactions following mRNA-based COVID-19 vaccination revealed that most cutaneous adverse effects were large local reactions and local injection site reactions as well as

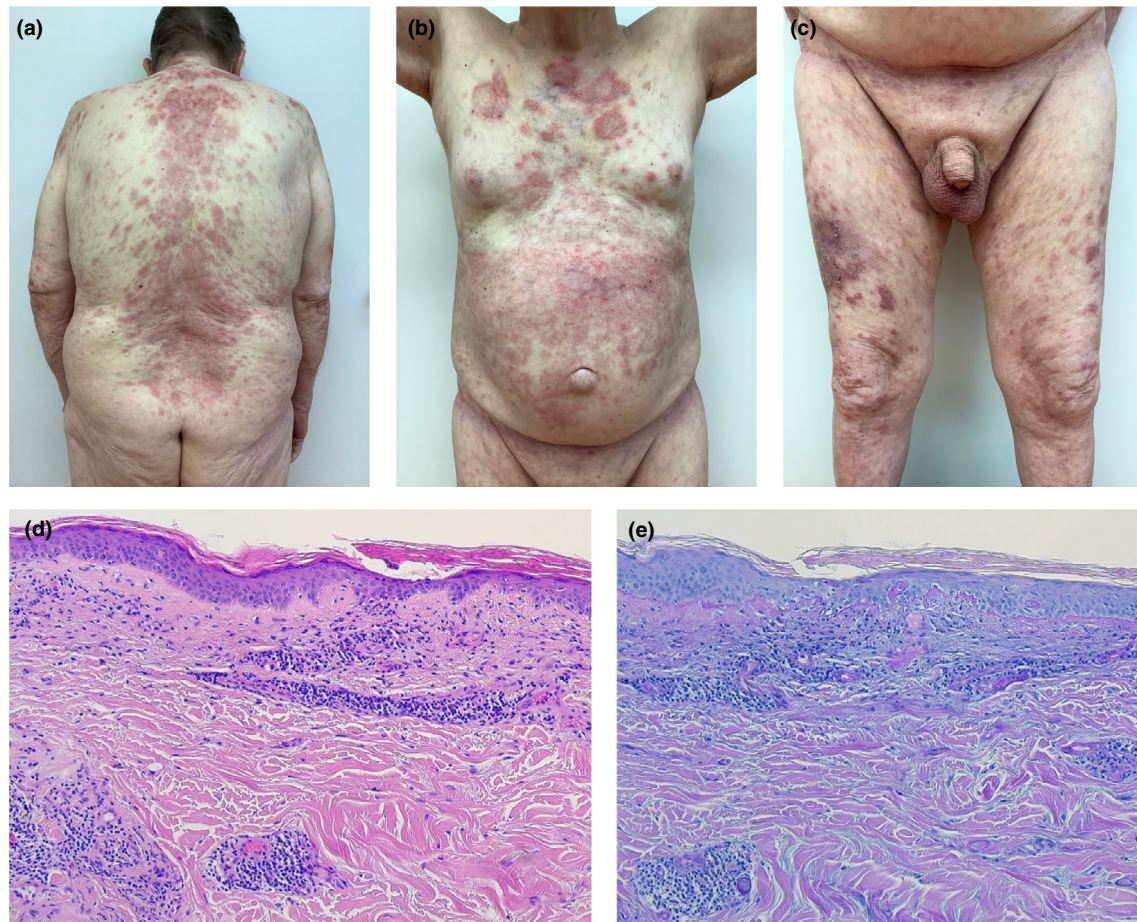


Figure 1 Clinical findings of a patient with induction of subacute cutaneous lupus erythematosus following mRNA vaccination with BNT162b2: (a) widespread erythematous papules and plaques located on the upper and lower back; (b) annular papulosquamous plaques on the upper chest and confluent macules on the abdomen; and (c) additional papulosquamous plaques on the legs. Histopathological analysis showed (d) characteristic features of subacute cutaneous lupus erythematosus, with mild vacuolar interface dermatitis and dense superficial and deep dermal lymphocytic infiltrates (haematoxylin and eosin, original magnification $\times 100$). (e) Dermal mucin deposition characteristic for cutaneous lupus erythematosus (Alcian blue staining, original magnification $\times 100$).

urticarial and morbilliform eruptions. Less frequently seen reactions included chilblains, cosmetic filler reactions, herpes zoster or herpes simplex flares, and pityriasis rosea-like reactions. Only two patients had cutaneous vasculitis. Lupus-like skin lesions or lupus deterioration were not reported.⁷

Strong agreement exists that all patients with autoimmune rheumatic diseases should be vaccinated against COVID-19. However, SARS-CoV-2 vaccination should be considered as a potential trigger of disease flares, especially in individuals with certain ANA constellations (e.g. anti-Ro/SSA and anti-La/SSB antibodies) predisposing for CLE.

A. Kreuter,¹ M. J. Licciardi-Fernandez,¹ S.-N. Burmann,¹ B. Burkert,¹ F. Oellig² and A.-L. Michalowitz¹

¹Department of Dermatology, Venereology and Allergology, HELIOS St Elisabeth Hospital Oberhausen, University Witten/Herdecke,

Witten, Germany and ²Institute of Pathology, Mülheim an der Ruhr, Germany

E-mail: alexander.kreuter@helios-gesundheit.de

Conflict of interest: the authors declare that they have no conflicts of interest.

Accepted for publication 20 July 2021

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Table 1 Patient details.

	Patient			
	1	2	3	4
Reference	Gambichler <i>et al.</i> , 2021 ³	Niebel <i>et al.</i> , 2021 ⁴	Kreuter <i>et al.</i> , 2021 ⁵	Present case
Sex	F	F	F	M
Age, years	74	73	62	79
SCLE subtype	Annular	Papulosquamous	Papulosquamous	Annular and papulosquamous
Histopathology results	Vacuolar interface dermatitis, dermal lymphocytic infiltrates, basal dyskeratoses	Not reported	Vacuolar interface dermatitis and dense dermal lymphocytic infiltrates	Mild vacuolar interface dermatitis and dense superficial and deep dermal lymphocytic infiltrates
DIF results	Negative	Not reported	Positive	Negative
Location of SCLE	Trunk, arms, legs	Back and chest	Back, chest, lower arms, dorsal hands	Trunk and legs
Type of COVID vaccine	mRNA (BNT162b2)	mRNA (BNT162b2)	Adenoviral (AZD1222)	mRNA (BNT162b2)
Onset of skin lesions after vaccination, days ^a	1	10	10	10
Induction or exacerbation of SCLE	Induction	Exacerbation (SCLE diagnosed in 2005)	Exacerbation (transition of SCLE into SLE)	Induction
Antibody profile	ANA (1 : 640), Ro, La	Ro	ANA (1 : 640), Ro, La	ANA (1 : 320), Ro, La
Other abnormal blood findings	Not reported	Not reported	Increased anti-dsDNA antibodies, leucocytopenia, C3/C4-hypocomplementaemia	Elevated RF
Other medication	Pantoprazole	Hydroxychloroquine	Hydroxychloroquine	Pantoprazole, metoprolol, ramipril, finasteride
Treatment of SCLE	Tapered systemic prednisolone, beginning at 150 mg/day	Tapered systemic prednisolone, beginning at 60 mg/day	Tapered systemic prednisolone, beginning at 250 mg/day	Tapered systemic prednisolone, beginning at 150 mg/day

ANA, antinuclear antibodies; C3/C4, complement C3/C4 deficiency (C3 range 90–180 mg/dL), (C4 range 10–40 mg/dL); DIF, direct immunofluorescence; dsDNA, double-stranded DNA; La, anti-La antibody; RF, rheumatoid factor; Ro, anti-Ro antibody; SCLE, subacute cutaneous lupus erythematosus; SLE, systemic lupus erythematosus. ^aAll patients developed skin lesions after their first dose.

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Incomplete excision of basal cell carcinoma: combining multidisciplinary data gives a better overall understanding of risk

doi: 10.1111/ced.14863

Dear Editor,

A recent systematic review and meta-analysis¹ identified an overall rate of incomplete basal cell carcinoma (BCC) excision of 11%, rising to 20% for excisions attempted in primary care. The spectrum of cases treated by a single