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Morphoea following COVID-19 Vaccination

Dear Editor,

We would like to highlight a case of generalised morphoea after recent COVID-19 mRNA vaccination.

A 47-year-old Chinese female with no medical history or chronic medications received her second dose of Pfizer-BioNTech vaccine (Tozinameran) on 24th May 2021. 3 weeks later, she noticed a rash over her thighs, progressively spreading to her calves over the following weeks. She was otherwise well without symptoms of Raynaud's phenomenon or restriction of joint movements. Physical examination showed erythematous, indurated, hyperpigmented plaques on bilateral thighs, calves and inner arms (Figures 1a-d). Her fingers, nailfolds and face were uninvolved. Telangiectasias were not observed.

Punch biopsy was performed, which showed diffuse deposition of thickened collagen bundles throughout the dermis (Figure 2a) with loss of intercollagenous spaces. Blood vessels and eccrine glands appear shrunken and entrapped (Figure 2b). Laboratory investigations revealed elevated antinuclear antibody titres (>1:640; centromere pattern) and positive centromeric proteins (CENP A and B). Complement levels and erythrocyte sedimentation rate were normal. Anti-Scl-70 and anti-RNA polymerase were absent. Imaging studies did not reveal evidence of pulmonary fibrosis. Overall, she did not fulfil ACR/EULAR criteria for systemic sclerosis, and a diagnosis of generalised superficial morphoea was made. She declined systemic immunosuppressants or phototherapy, hence was treated with calcipotriol ointment plus mometasone cream alone. After 6 months, she showed clinical improvement, with reduced erythema and softening of skin lesions. She later was administered inactivated COVID-19 vaccine (CoronaVac) as booster, without incidents.

Morphoea had been previously reported following various different vaccines, including a case of pan-sclerotic morphoea beginning 4 weeks after the patient's second dose of Tozinameran.[1,2,3] There are several possible pathomechanisms for vaccine-induced morphoea. Firstly, vaccine-linked dysregulation of Treg cells can induce fibrogenic alterations of the dermis resulting in sclerosis.[4] Secondly, vaccine-induced autoimmunity may occur due to molecular mimicry. In genetically susceptible patients, the exposure to vaccine containing disease-related peptides and adjuvants, which may closely resemble human pathogenic peptides, can lead to immune cross-reactivity. An example of such molecular mimicry was seen in viral peptides used in the human papillomavirus vaccine and human proteins involved in the pathogenesis of SLE.[5]

Thirdly, vascular dysfunction and endothelial damage leading to overproduction of profibrotic cytokines[6] has been implicated in pathogenesis of morphoea, though in our case, histology did not reveal any vascular abnormalities. Interestingly, functional angiopathies e.g chilblains have been reported with vaccination[7] and complement-mediated destruction of cutaneous microvasculature, secondary to docking by SARS-CoV-2 spike protein in COVID-infected patients, has also been demonstrated[8].

Myriad cutaneous reaction patterns have been observed following COVID vaccination, and these include local injection site reactions, morbilliform eruptions, chilblains and pityriasis rosea-like reactions.[7] We have described herein a case of generalised morphoea with close temporal relationship to Tozinameran, suggesting possible causality. Clinicians are reminded to take a vaccination history in their evaluation of patients with recent-onset morphoea.

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Figure legends

Figure 1 Clinical photos of patient at presentation

Figure 2 (a) Haematoxlin and eosin (H&E) stain, 20x magnification. Skin biopsy specimen showing a dense dermis with sharp edges and fat boundary. Eccrine glands are located higher up than normal; (b) H&E stain, 100x magnification. Thick, closely packed, hyalinised collagen bundles surrounding blood vessels, which appear shrunken.

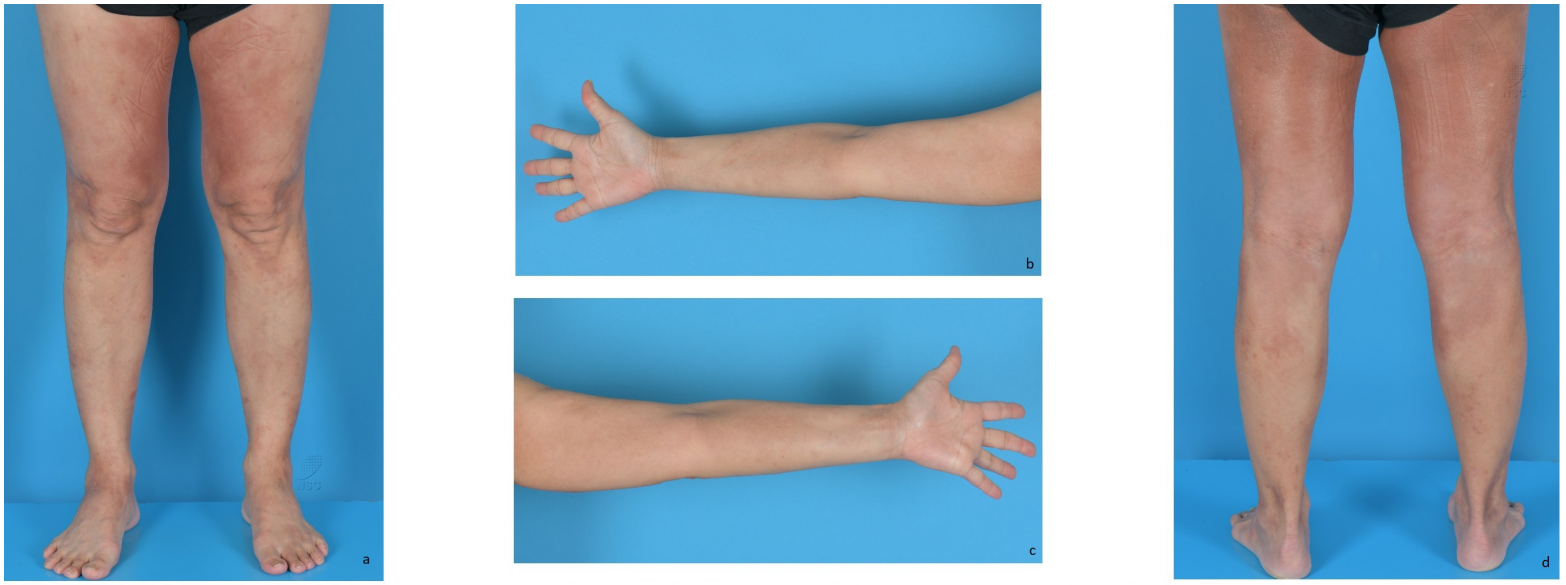

Figure 1a-d: Clinical photographs of patient at presentation.

CED_15349_Figure 1 Clinical photos - annotated.jpg

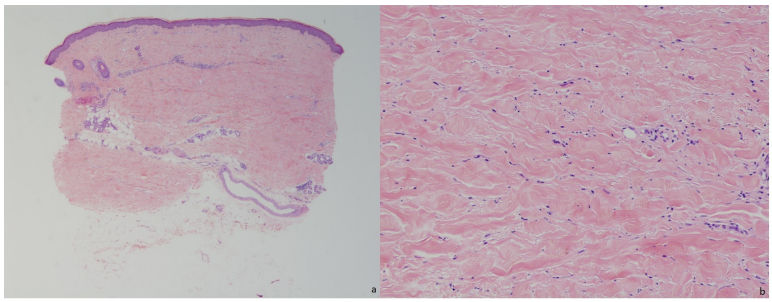

Figure 2a: Haematoxylin and eosin (H&E) stain, 20 times magnification, skin biopsy specimen showing a dense dermis with sharp edges and fat boundary. Eccrine glands are located higher up than normal.
Figure 2b: H&E stain, 100 times magnification, Thick, closely packed, hyalinised collagen bundles surrounding blood vessels, which appear shrunken

CED_15349_Figure 2 Histology photos - annotated.jpg