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CASE REPORT

Cutaneous lupus erythematosus flare with vitiligo-like depigmentation following the AstraZeneca COVID vaccine

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Key words: cutaneous lupus; COVID-19; vaccine.

INTRODUCTION

The recent COVID-19 pandemic has had a profound impact on global health. The importance of clinician awareness of the dermatological manifestations of the disease is paramount. 1 In addition, the onset of vaccination programs to combat the disease is uncovering further cutaneous eruptions and systemic reaction patterns. 2 We present a case of cutaneous lupus in a patient with underlying secondary Sjögren’s syndrome following the Oxford–AstraZeneca COVID-19 vaccine (AZD1222), review the literature and highlight the potential for systemic lupus erythematosus or cutaneous lupus erythematosus (CLE) flare following COVID vaccination.

CASE REPORT

A 51-year-old gentleman with a diagnosis of systemic lupus erythematosus (positive dsDNA [anti double stranded DNA] and ANA titers) with overlapping features of Sjögren’s disease (parotid swelling, Ro and La antibody positivity, recurrent pleuropericardial effusions, and bronchiectasis) managed with hydroxychloroquine and azathioprine presented to dermatology in April 2021 with a widespread pruritic eruption. Onset was 1 week after receiving the Oxford–AstraZeneca COVID-19 vaccine (AZD1222) (January 2021), with subsequent exacerbation 4 days after the second dose, 2 months later; managed by his family physician with prednisolone 30 mg for 5 days. The patient was not started on any new medications prior to the onset of the eruption and had not displayed cutaneous lupus features in the past.

On presentation, he exhibited indurated, flat-topped papular lesions on the scalp, dorsal hands, ears and erythematous, polycyclic, annular lesions on the arms, back, scalp and trunk suspicious for discoid, and subacute CLE, respectively (Fig 1, A–D). Palmar perniosis was noted.

Punch biopsies from the back and dorsa of the hand demonstrated features consistent with CLE including vacuolar interface dermatitis with pigmentary incontinence, apoptotic keratinocytes, and an inflammatory lymphocytic infiltrate in the superficial dermis (Fig 2, A and B). Direct immunofluorescence from a non–sun-exposed site on the back revealed immunoglobulin G anti-nuclear antibodies throughout the epidermis (red) with C3 deposition (green) in the basement membrane (Fig 3, A). An

Abbreviations used:
ANA: antinuclear antibody
Anti-dsDNA: anti-double stranded DNA
Anti-Sm: anti-Smith
CLE: cutaneous lupus erythematosus
IFN: interferon
MCTD: mixed connective tissue disease
RS: Rowell’s syndrome
SCLE: subacute cutaneous lupus erythematosus
SLE: systemic lupus erythematosus
TLR: toll-like receptors

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autoimmune screen revealed positive ANA titers, as previously. Anti-Ro/SSA and anti-Sm antibodies (anti Smith antibody) were positive, in keeping with the patient's history of Sjögren's-like features, as well as a chronically raised erythrocyte sedimentation rate and neutropenia. His renal function was unremarkable. He reported no systemic symptoms.

A diagnosis of Oxford-AstraZeneca COVID-19 vaccine (AZD1222) induced CLE was made in view of the clinical features, histology, direct immunofluorescence, and antibody profile. Hydroxychloroquine dosage was increased from 200 mg to 400 mg and azathioprine from 100 mg to 150 mg daily. At 6 months, the acute eruption had resolved leaving widespread post-inflammatory hypopigmentation with areas of vitiligo-like post inflammatory depigmentation (Fig 1, E-G). At further follow-up there is evidence for repigmentation within some of the lesions.

DISCUSSION

Cutaneous eruptions following COVID-19 infection are not uncommon. Although the exact incidence is yet to be ascertained, cutaneous manifestations have been reported in up to 20% of cases and can encompass a wide range of morphologies including urticarial, morbilliform, papulovesicular, chilblain-like, livedoid, and vasculitic. Far less commonly (<0.5% of cases), a wide range of cutaneous eruptions have also been reported post-COVID-19 vaccination but these are more often associated with the mRNA vaccines (BNT162b2 Pfizer-BioNTech and mRNA-1273 Moderna). Pityriasis rosea, urticaria, and chilblain-like lesions are the most frequently observed morphologies (0.1% to 0.4% of cases); whereas, morbilliform and petechial eruptions (<0.1% of cases) have been associated with adenoviral vector vaccines.

CLE following COVID-19 vaccination is uncommon. Our case is only the second reported after exposure to the Oxford–AstraZeneca adenoviral vaccine (AZD1222), with the majority of remaining cases reported after exposure to the Pfizer mRNA vaccine (BNT162b2). The summary of CLE eruptions occurring post-COVID vaccination is summarized in Table I. The postulated mechanism behind CLE eruption following COVID-19 vaccination involves increased Type 1 interferon (IFN) secretion. In the pathogenesis of cutaneous lupus this is triggered by the binding of immune complexes to toll-like receptors on dendritic cells. Both mRNA and adenoviral COVID-19 vaccines trigger innate sensors leading to Type 1 IFN secretion, resulting in cytokine and chemokine cascades, T-cell activation, and a lichenoid tissue reaction (Fig 3, B). Interestingly, the majority of cases are associated with anti-Ro and anti-La antibodies, which are often newly positive. Anti-Ro antibodies are encountered in up to 70% of non-vaccine associated subacute CLE cases. Furthermore, anti-Ro and/or anti-La positivity is also associated with an increased IFN signature.

The vitiligo-like depigmentation is an unusual and interesting feature with some evidence of repigmentation at follow-up. Cases of vitiligo post-COVID vaccination have been reported in the literature and may again be related to type 1 IFN production which is also an early phase in vitiligo pathogenesis.

In summary, we present a case of CLE following the Oxford–AstraZeneca COVID-19 vaccine
Fig 2. Histological features consistent with cutaneous lupus. A, low power magnification reveals mild inflammatory predominantly lymphocytic infiltrate in the superficial dermis with pigmentary incontinence. There is mild irregular acanthosis of the epidermis with a plugged follicle on the right. (hematoxylin and eosin, ×40). B, at higher magnification there is further evidence of an interface dermatitis with prominent vacuolar degeneration of the basal epidermis with several apoptotic keratinocytes. There is marked pigmentary incontinence in the superficial dermis with a mild, mainly lymphocytic inflammatory infiltrate. (hematoxylin and eosin, ×200).

Fig 3. A, direct immunofluorescence reveals immunoglobulin G antibodies throughout the epidermis (red) with C3 deposition (green) in the basement membrane consistent with connective tissue disease. B, postulated mechanism of vaccine-induced cutaneous lupus. COVID-19 vaccines trigger innate sensors which lead to type 1 interferon secretion, resulting in the activation of cytokine and chemokine cascades. T-cell activation ensues followed by a lichenoid tissue reaction. TLRs, Toll-like receptors.
### Table I. Summary of reported cutaneous lupus reactions occurring post-COVID vaccination

| Patient | Age (years) | Sex | Autoimmune disease history | COVID vaccine type | CLE subtype | Induction or exacerbation of CLE | Onset of skin lesions post-vaccine (days) | Antibody profile | Reference |
|---------|-------------|-----|-----------------------------|--------------------|-------------|---------------------------------|------------------------------------------|----------------|-----------|
| 1       | 74          | F   | Nil                         | mRNA (BNT162b2)    | SCLE        | Induction                       | 1                                        | ANA (1:640)    | Gambichler et al\(^5\) |
| 2       | 73          | F   | SCLE                        | mRNA (BNT162b2)    | SCLE        | Exacerbation                    | 10                                       | Anti-Ro, anti-La | Niebel et al\(^6\) |
| 3       | 62          | F   | SCLE                        | Adenoviral (AZD1222) | SCLE        | Exacerbation and systemic transformation | 10                                       | ANA (1:640)       | Kreuter et al\(^4\) |
| 4       | 54          | F   | SCLE                        | mRNA-1273 (Moderna) | SCLE        | Exacerbation                    | 4                                        | ANA (1:1280)    | Joseph et al\(^15\) |
| 5       | 70          | M   | Nil                         | mRNA (BNT162b2)    | SCLE        | Induction                       | 10 wk                                    | ANA (1:540)  | Liu et al\(^10\) |
| 6       | 79          | M   | Nil                         | mRNA (BNT162b2)    | SCLE        | Induction                       | 10                                       | ANA (1:320)       | Kreuter et al\(^7\) |
| 7       | 30          | F   | Primary biliary cholangitis | mRNA (BNT162b2)    | SCLE        | Induction                       | 10                                       | Anti-dsDNA, anti-Sm, anti-nRNP, anti-Ro, anti-La | Zengarini et al\(^11\) |
| 8       | 41          | M   | MCTD                        | mRNA (BNT162b2)    | RS          | Induction                       | 4                                        | Speckled ANA | Niebel et al\(^12\) |
| 9       | 22          | F   | Hypothyroidism              | mRNA-1273 (Moderna) | Drug-induced SCLE mimicking RS | Induction | 10                             | ANA (1:80) | Niebel et al\(^12\) |
| 10      | 24          | F   | SLE                          | mRNA (BNT162b2)    | SCLE        | Induction                       | 14                                       | Anti-dsDNA, anti-Sm, anti-histone | Rechtien et al\(^8\) |
| 11      | 33          | F   | Nil and Sjogren’s overlap   | mRNA (BNT162b2)    | SCLE        | Induction                       | 1                                        | Antinuclear antibody | Rose et al\(^9\) |
| 12      | 51          | M   | SLE and Sjogren’s overlap   | Adenoviral (AZD1222) | DLE and SCLE | Induction                       | 7                                        | ANA (1:1280) | Present case |

ANA, Antinuclear antibody; Anti-dsDNA, anti-double stranded DNA; anti-Sm, anti-Smith antibody; F, Female; M, Male; MCTD, mixed connective tissue disease; SCLE, subacute cutaneous lupus erythematosus; SLE, systemic lupus erythematosus; RS, Rowell’s syndrome.
(AZD1222) with subsequent vitiligo-like depigmentation. Decisions as to further vaccination were made on a personalized risk benefit analysis and a subsequent dose of Pfizer mRNA vaccine (BNT162b2) was well tolerated.

Conflicts of interest
None disclosed.

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