within a ring appearance in such patients should raise the suspicion of application of topical corticosteroids and they should be counselled regarding the deleterious effects of applying such inappropriate treatments.

Acknowledgement

We thank the patients for providing informed consent for publication of the case details and images.

A. Das,[1] A. Sil,[2] S. B. Verma[3] and S. Kumar[4]
[1]*Department of Dermatology, KPC Medical College and Hospital, Jadavpur, India;* [2]*Department of Dermatology, RG Kar Medical College and Hospital, Kolkata, India;* [3]*Nirvana Skin Clinic, Vadodara, India; and* [4]*Department of Dermatology, Medical College and Hospital Kolkata, Kolkata, India*
E-mail: anupamdasdr@gmail.com
Conflict of interest: the authors declare that they have no conflicts of interest.
Accepted for publication 9 July 2021

References

1 Verma SB, Panda S, Nenoff P *et al.* The unprecedented epidemic-like scenario of dermatophytosis in India: I. Epidemiology, risk factors and clinical features. *Indian J Dermatol Venereol Leprol* 2021; **87**: 154–75.
2 Verma S. Tinea pseudoimbricata. *Indian J Dermatol Venereol Leprol* 2017; **83**: 344–5.
3 Fatima F, Das A. "Ring within a ring". *J Cutan Med Surg* 2021. https://doi.org/10.1177/1203475421998629. [Epub ahead of print].
4 Gupta V, Bhatia R, Sondhi P, Mahajan R. 'Ring-within-a-ring' appearance: morphological clue to topical steroid abuse in dermatophytosis. *J Eur Acad Dermatol Venereol* 2017; **31**: e2–3.
5 Singal A, Jakhar D, Kaur I *et al.* Tinea pseudoimbricata as a unique manifestation of steroid abuse: a clinico-mycological and dermoscopic study from a tertiary care hospital. *Indian Dermatol Online J* 2019; **10**: 422–5.
6 Verma S, Hay RJ. Topical steroid-induced tinea pseudoimbricata: a striking form of tinea incognito. *Int J Dermatol* 2015; **54**: e192–3.

Severe cutaneous adverse reaction following COVID-19 vaccination and immunotherapy: a second hit?

doi: 10.1111/ced.14852

Dear Editor,

A 62-year-old woman with metastatic melanoma presented with shortness of breath 4 days after her fourth cycle of combination checkpoint inhibitor therapy (CPI) (nivolumab and ipilimumab) having previously received 12 months of treatment with adjuvant nivolumab 14 months earlier. Subsequent investigations confirmed CPI-related myocarditis. She also described new onset of symptoms consistent with Raynaud disease (RD). Her medical history included recurrent migraines for which she took propranolol. She was admitted to hospital and received two doses of intravenous methylprednisolone 500 mg and was commenced on a reducing course or oral prednisolone 1 mg/kg, with lansoprazole and co-trimoxazole prophylaxis. Blood tests initially revealed negative results for antinuclear antibody (ANA), lupus anticoagulant and anticardiolipin antibodies with normal levels of complement and rheumatoid factor. However, repeat blood tests 6 weeks later revealed a positive ANA and a very mildly positive extractable nuclear antigen (anti-SSA52/Ro autoantibody). Assessment by the rheumatology team did not identify any underlying connective tissue disease and concluded that the RD was likely to be secondary to the CPI.

The patient was discharged, but 2 weeks later she was readmitted with pyrexia, a grade 3 skin rash (70% involvement) and worsening fatigue. The features were consistent with a drug eruption, thought most likely to be secondary to co-trimoxazole, which she had been on for a week. She had also received one dose of co-amoxiclav locally for presumed infection, but the skin eruption was already present at this stage. She remained on prednisolone 50 mg daily. A skin biopsy was taken, and histopathological examination revealed nonspecific features of mild superficial perivascular inflammation. The patient was commenced on potent topical steroids, and at follow-up 7 days later the rash had almost completely resolved; prednisolone was then reduced to 40 mg, with the patient remaining on lansoprazole.

The patient received her second COVID Pfizer vaccination (BioNTech-Pfizer COVID-19 RNA vaccine) 2 weeks later, and within 2 days she had had a significant flare of her rash and presented with a further grade 3 eruption. There was no mucosal membrane involvement at that stage. Over the following 7 days, the rash worsened to grade 4 (Fig. 1), becoming erythrodermic with superficial blistering noted on the patient's thigh and chest with associated mild mucosal and eye involvement, despite her being on prednisolone 30 mg. The findings of a further skin biopsy were consistent with a drug-induced lichenoid dermatitis with scattered apoptotic bodies and lymphocytic infiltrate (Fig. 2). Direct immunofluorescence was negative. She was admitted to hospital and treated with two further doses of intravenous methylprednisolone 500 mg and her prednisolone dose was increased to 40 mg, while lansoprazole was switched to famotidine. An infective/septic screen and a viral reactivation screen, including Epstein–Barr virus, human herpesvirus (HHV)-6, HHV-7, hepatitis

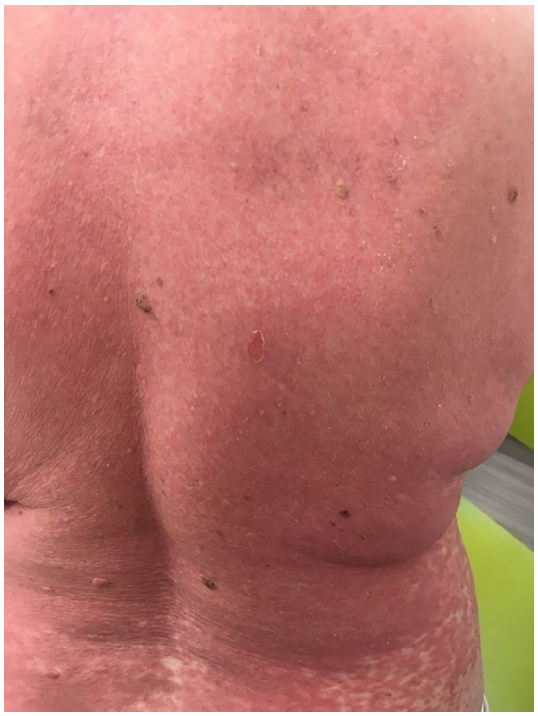

Figure 1 Image revealing grade 4 cutaneous skin toxicity (erythroderma and superficial blistering), with associated pruritis and skin tenderness.

B and C viruses, and HIV were negative. She remained systemically well throughout her admission, with subsequent slow improvement of her rash over a 2-week period.

Drug hypersensitivity reactions are the result of immune interactions with small molecular compounds or proteins used as drugs.[1] Delayed-type hypersensitivity reactions (type IV hypersensitivity) are T-cell-mediated reactions that can be CD4+ and/or CD8+ dependent, with a target allergen presented via major histocompatibility molecules to T-cell receptors.[2] Our patient had an initial drug rash that resolved on cessation of the co-trimoxazole and she then developed a more severe form of the rash after her vaccine. We postulate that our patient's original presentation was a reaction to the co-trimoxazole, during which drug-specific memory T cells were formed. The subsequent COVID-19 vaccination then caused a surge in the T-cell-driven response from skin-homing CD4+ T cells generated by the original delayed hypersensitivity reaction. This was on a background of recent CPI therapy, which in itself reduces the self-tolerance response of T cells and boosts effector T-cell responses.

Vaccinations have been reported to raise the potential of immune-related adverse events (irAEs) in patients on CPIs.[3] Skin irAEs were the most commonly reported, followed by arthritis.[4] The Pfizer vaccine has been reported to cause mild skin reactions, which are generally self-limiting.[5]An increased incidence of co-trimoxazole-induced rash in patients treated with CPIs has also been reported.[6] Current recommendations suggest that patients on CPIs can receive inactivated vaccines.[7]

This case highlights the importance of possible exacerbation of irAEs in patients on CPIs, which can occur post-vaccination, especially in the case of recent and active irAEs. This is likely to be an under-reported phenomenon. Consideration by clinicians of timing of vaccinations should therefore be given in light of active or severe irAEs in patients taking CPIs. Further work is required to elucidate drug reactions and the effect of vaccinations in patients on CPIs.

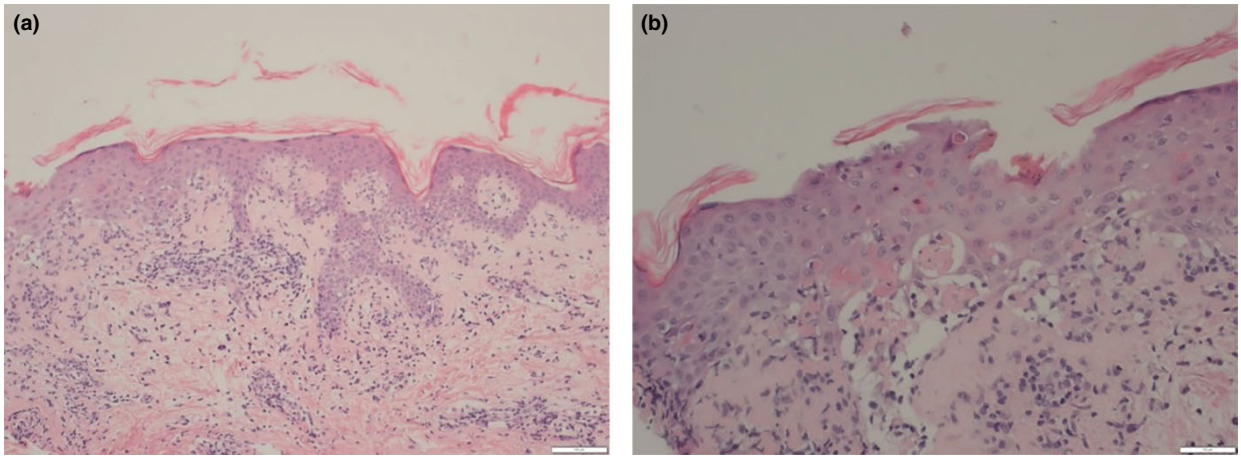

Figure 2 (a) A dense infiltrate at the dermoepidermal junction; and (b) evidence of a lichenoid infiltrate in the upper dermis with scattered apoptotic bodies. Haematoxylin and eosin, original magnification (a) × 100; (b) × 200.

Acknowledgement

We thank the patient for her informed consent for publication of her case details and images.

K. Hussain,[1] A. Kawsar,[1] J. Weir,[2] L. Au,[3] S. Turajlic,[3] J. Larkin[3] and L. Fearfield[1,3]
[1]*Department of Dermatology, Chelsea and Westminster Hospital, London, UK;* [2]*Department of Histopathology, Imperial College Healthcare NHS Trust, London, UK and* [3]*Skin and Melanoma Unit, Royal Marsden Hospital, London, UK*
E-mail: khawar.hussain1@nhs.net
Conflict of interest: the authors declare that they have no conflicts of interest.
Accepted for publication 9 July 2021

References

1 Demoly P, Adkinson NF, Brockow K *et al*. International consensus on drug allergy. *Allergy* 2014; **69**: 420–37.
2 Abbas AK. Hypersensitivity disorders. Chapter 19. In: *Cellular and Molecular Immunology*. 9th edn. (Lichtman AH, Pillai S, Abbas AK eds). Philadelphia: Elsevier, 2018.
3 Desage A-L, Bouleftour W, Rivoirard R *et al*. Vaccination and immune checkpoint inhibitors. *Am J Clin Oncol* 2021; **44**: 109–13.
4 Läubli H, Balmelli C, Kaufmann L *et al*. Influenza vaccination of cancer patients during PD-1 blockade induces serological protection but may raise the risk for immune-related adverse events. *J Immunother Cancer* 2018; **6**: 40.
5 McMahon DE, Amerson E, Rosenbach M *et al*. Cutaneous reactions reported after Moderna and Pfizer COVID-19 vaccination: a registry-based study of 414 cases. *J Am Acad Dermatol* 2021; **85**: 46–55.
6 Edwards C, Larkin J, Fearfield L *et al*. Increased incidence of co-trimoxazole induced rash in patients treated with immune checkpoint inhibitors. *Br J Dermatol* 2020; **183**(Suppl): P087.
7 Gauci M-L, Coutzac C, Houot R *et al*. SARS-CoV-2 vaccines for cancer patients treated with immunotherapies: recommendations from the French society for ImmunoTherapy of Cancer (FITC). *Eur J Cancer* 2021; **48**: 121–3.

Infective dermatitis after treatment with secukinumab

doi: 10.1111/ced.14844

Dear Editor,

A 71-year-old woman presented with a 51-year history of psoriasis vulgaris (PV). She was originally from Bahia, Brazil. Over the course of the disease she had undergone several treatments, including phototherapy, methotrexate and acitretin, but with poor response and/or intolerance. She was started on the immunobiologic, secukinumab, and 2 months after the introduction of the drug, experienced a complete improvement of psoriasis lesions. However, she developed an exudative rash.

Physical examination revealed exudation and the formation of meliceric crusts in an impetigo pattern in the periorbital, perioral, periauricular and umbilical regions (Fig. 1). Material was collected for culture and bacterioscopy, which were negative. Histopathological analysis of the umbilical lesion revealed chronic spongiotic and superficial perivascular lymphocytic dermatitis (Fig. 2).

Given the clinical condition and epidemiology, serological testing for human T-cell lymphotropic virus (HTLV)-1 was performed, which was positive. The patient was treated with trimethoprim and sulfamethoxazole, and later with doxycycline, but the lesions recurred after cessation of antibiotic therapy. During this period, she continued to use secukinumab, but the drug was withdrawn due to the inflammatory condition after she had been taking it for 6 months, The rash begin to improve gradually until there was complete resolution 3 months after secukinumab withdrawal. During this time, discrete psoriasis lesions reappeared on the trunk.

Infective dermatitis (ID) is a chronic relapsing dermatitis associated with HTLV-1. It is characterized by a chronic infection by *Staphylococcus aureus* and/or β-haemolytic *Streptococcus*, produced by a microenvironment dysregulation induced by the HTLV-1 virus. Brazil, and specifically the state of Bahia, is considered an endemic region for HTLV-1.[1] ID has a higher incidence in children, but it can start in adulthood.[1] A specific genetic background may be required for the development of ID and only a minority of patients will develop clinical manifestations.[1] Our patient had a severe erythematous and exudative dermatitis with scaling and crusting, primarily affecting the scalp, forehead, paranasal area and retroauricular areas.[1] HTLV-1 infection is also associated with more severe manifestations, such as tropical spastic paraparesis and adult T-cell leukaemia–lymphoma.[1]

Secukinumab is a fully human anti-interleukin (IL)-17A monoclonal antibody that selectively targets and neutralizes IL-17A, preventing the activation of keratinocyte proliferation, the release of inflammatory cytokines and the activation of neutrophils.[2] IL-17 is characterized by a rapid response to infectious agents, which recruits neutrophils as the first line of defence and induces the production of antimicrobial peptides. Therefore, T helper 17 responses appear to be pivotal in infections by microorganisms, as well as in chronic inflammatory diseases, including psoriasis.[3]

There have been reports of eczematous rashes developing approximately 4 months after the start of the use of anti-IL-17A monoclonal agents, characterized by intense itching that leads to treatment interruption,[4] but their descriptions do not correspond clinically to the rashes observed in this case. Treatment with immunobiologics is not entirely contraindicated in patients with HTLV-1,