Funding sources

No funding was received for the following work.

S. Cretu,[1,2,*,†] M. Dascalu,[3,†] S.R. Georgescu,[1,4] C.M. Salavastru[1,5]

[1]Carol Davila" University of Medicine and Pharmacy, Bucharest, Romania, [2]Dermatology PhD Student, Dermatology Research Unit, Colentina Clinical Hospital, Bucharest, Romania, [3]Department of Computer Science, Polytechnic University of Bucharest, Bucharest, Romania, [4]Dermatology Department, "Victor Babes" Clinical Hospital for Infectious Diseases, Bucharest, Romania, [5]Pediatric Dermatology Department, Colentina Clinical Hospital, Bucharest, Romania

*Correspondence: S. Cretu. E-mail: stefana.spiridon@drd.umfcd.ro

[†]These authors contributed equally to this work.

References

1 Foo CCI, Goon ATJ, Leow Y-H, Goh C-L. Adverse skin reactions to personal protective equipment against severe acute respiratory syndrome – a descriptive study in Singapore. *Contact Dermatitis* 2006; **55**: 291–294.
2 Daye M, Cihan FG, Durduran Y. Evaluation of skin problems and dermatology life quality index in health care workers who use personal protection measures during COVID-19 pandemic. *Dermatol Ther* 2020; **33**: e14346. https://doi.org/10.1111/dth.14346
3 Long H, Zhao H, Chen A, Yao Z, Cheng B, Lu Q. Protecting medical staff from skin injury/disease caused by personal protective equipment during epidemic period of COVID-19: experience from China. *J Eur Acad Dermatol Venereol* 2020; **34**: 919–921.
4 Techasatian L, Lebsing S, Uppala R *et al*. The effects of the face mask on the skin underneath: a prospective survey during the COVID-19 pandemic. *J Prim Care Community Heal* 2020; **11**: 215013272096616.
5 Yu J, Chen JK, Mowad CM, Reeder M, Hylwa S. Occupational dermatitis to facial personal protective equipment in health care workers: a systematic review. *J Am Acad Dermatol* 2020; **84**: 486–494.
6 Teo WL. The "Maskne" microbiome – pathophysiology and therapeutics. *Int J Dermatol* 2021; **60**: 799–809.
7 Metin N, Turan Ç, Utlu Z. Changes in dermatological complaints among healthcare professionals during the COVID-19 outbreak in Turkey. *Acta Dermatovenerologica Alpina, Pannonica Adriat* 2020; **29**: 115–122.
8 Gheisari M, Araghi F, Moravvej H, Tabary M, Dadkhahfar S. Skin reactions to non-glove personal protective equipment: an emerging issue in the COVID-19 pandemic. *J Eur Acad Dermatol Venereol* 2020; **34**: e297–e298.
9 Masters NB, Shih SF, Bukoff A *et al*. Social distancing in response to the novel coronavirus (COVID-19) in the United States. *PLoS One* 2020; **15**: e0239025.
10 Dimock M. Defining generations: Where Millennials end and Generation Z begins. 2019. Available at: https://www.pewresearch.org/fact-tank/2 (last accessed: 1 June 2021)

DOI: 10.1111/jdv.17679

SARS-CoV-2 mRNA vaccine injection site pseudolymphoma

Dear Editor,

A healthy 68-year-old female presented with an erythematous nodule on the outer aspect of her left arm (Fig. 1a,b). The location of the nodule coincided with the injection site of the second dose of the Pfizer-BioNTech (Pfizer, Inc., New York City, NY, USA) SARS-CoV-2 mRNA vaccine, administered three months before. The nodule was preceded by a pruritic macule which emerged a week after inoculation, and which steadily evolved to the lesion with which the patient presented. The patient had not experienced any side effects related to the administration of the first vaccine dose, which she had received 3 weeks before in the ipsilateral arm. Dermoscopic evaluation of the nodule revealed

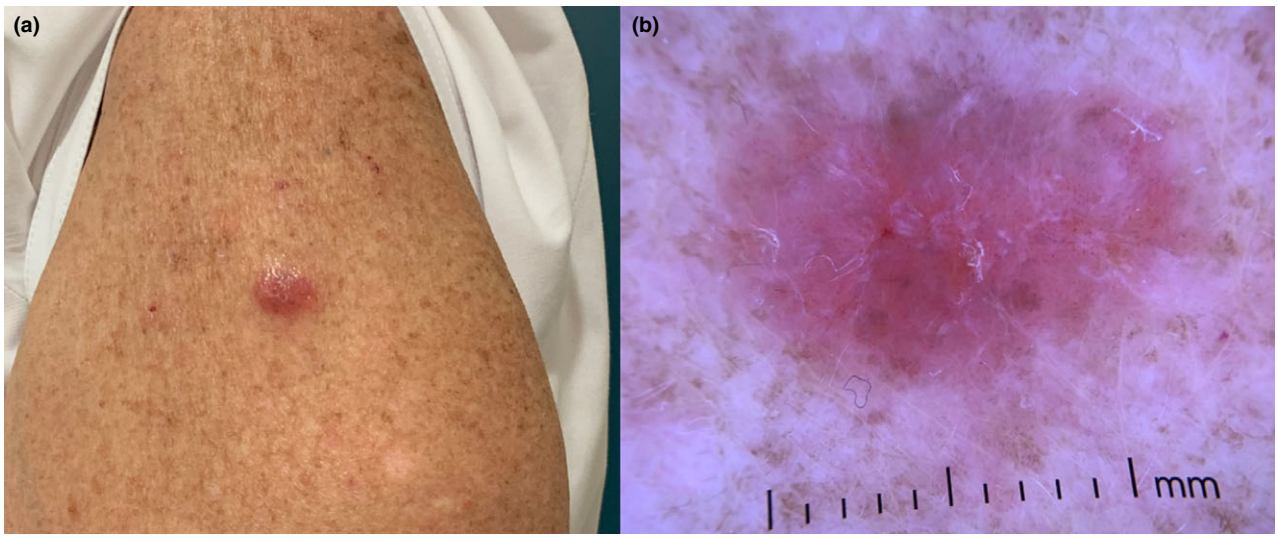

Figure 1 (a) Erythematous nodule on the patient's left arm as observed clinically. (b) Dermoscopic evaluation of the nodule revealed dotted vessels on an erythematous background and shiny white lines.

dotted vessels and shiny white lines on an erythematous background.

Histological examination of the excised nodule revealed a wedge-shaped, nodular infiltrate of small mature lymphocytes and rare blasts, extending from the superficial dermis to the subcutis, being denser in the superficial dermis (Fig. 2a). Occasional lymphocytes extended into the basal layers of the epidermis with associated basal cell vacuolar damage, Civatte body formation and spongiosis, in keeping with an interface (Fig. 2a,b). Immunohistochemistry revealed a mixture of B and T cells (Fig. 2c,d) with a predominance of T cells and with a low Ki67 index. The T cells expressed all T cell antigens. No light chain restriction was identified in the B-cells.

Based on clinical and histological features, a diagnosis of cutaneous pseudolymphoma was made.

Vaccination site-associated pseudolymphoma (also referred to as lymphoid hyperplasia and lymphocytoma cutis) is an exceedingly rare – albeit documented – phenomenon.[1] Reactions at the mRNA SARS-CoV-2 injection site have been reported in up to 84.2% of vaccinated patients, with erythema being the commonest.[2] Development of pseudolymphoma at the SARS-CoV-2 injection site is however previously undescribed. The acute or delayed occurrence of cutaneous pseudolymphoma has been reported at the injection site of Hepatitis A, Hepatitis B,[1] quadrivalent human papilloma virus,[3] early summer time meningoencephalitis and tetanus vaccination.[4] Subcutaneous

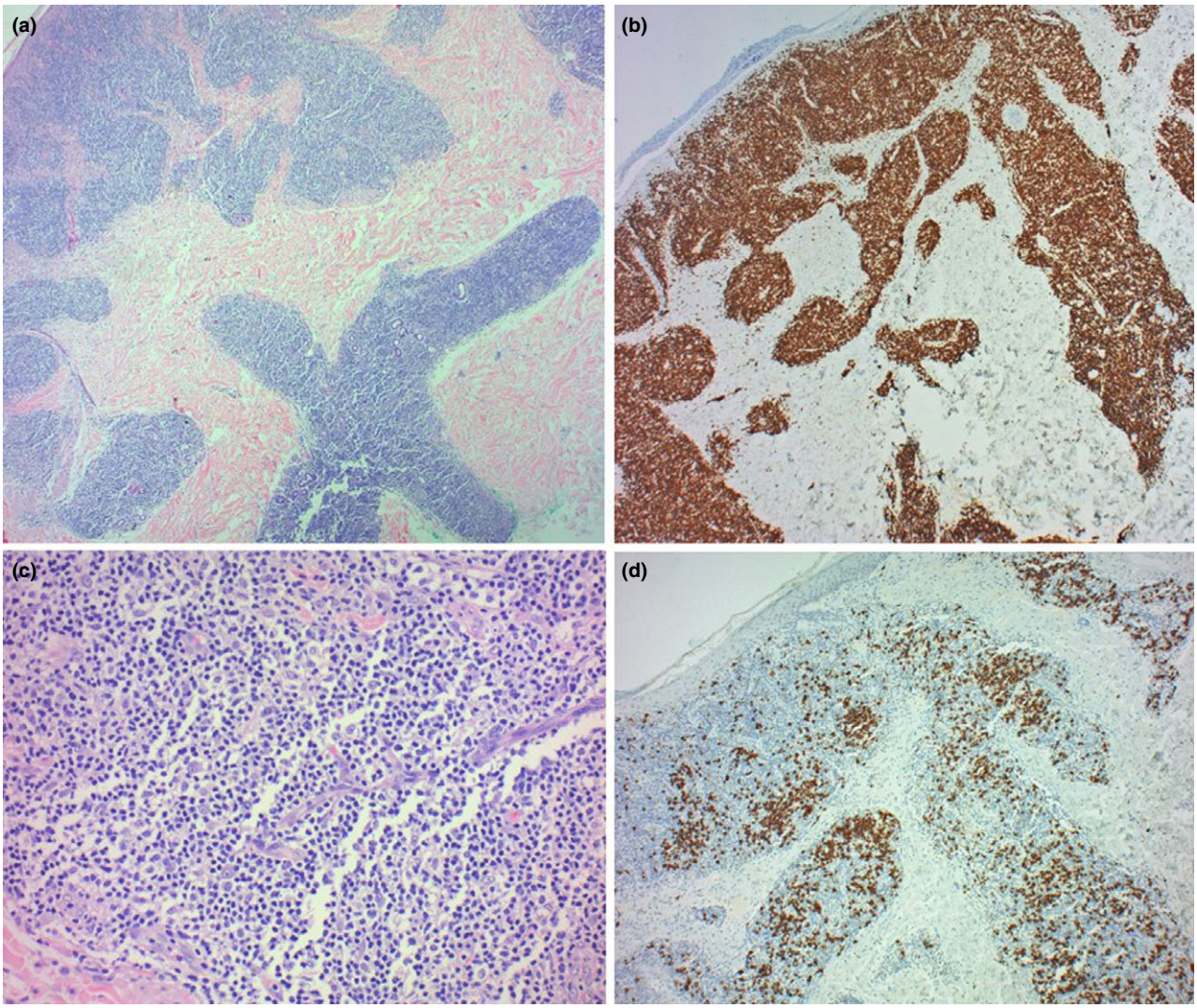

Figure 2 (a) Nodular lymphoid infiltrate extending from the superficial dermis to the deep dermis, with a focal interface at the basal layers of the epidermis. (H&E, x100). (b) Polymorphous infiltrate with a predominance of small mature lymphocytes. (H&E, x 200). Immunohistochemistry shows a mixture of B and T cells, highlighted by CD3 (c) and CD20 (d) respectively, with a predominance of T cells (x100).

papules, nodules and erythematous patches can be presenting signs of vaccine-associated cutaneous pseudolymphoma.[4] The patient in this case had received various vaccinations throughout her lifetime, including the influenza vaccine on a yearly basis but had not experienced any localized or systemic side effects. It has been proposed that cutaneous pseudolymphoma may represent a reaction to vaccine adjuvants such as aluminium hydroxide.[1] This adjuvant is not found in the Pfizer-BioNtech SARS-CoV-2 mRNA vaccine.[5]

By flagging this unique adverse drug reaction, we hope to broaden physician's repertoire of differential diagnoses when presented with SARS-CoV-2-related injection site reactions.

Acknowledgement

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

Authors contributions

All authors contributed equally to the conceptualizing, drafting and revising of the submitted text.

Conflict of interest

None of the authors have any relevant conflicts or funding to disclose.

Data availability statement

The data that support the finds of this manuscript are available from the corresponding author, DM, upon reasonable request.

D. Mintoff,[1,2,*] L. Scerri,[1] A. Betts[3]

[1]Department of Dermatology, Mater Dei Hospital, Msida, Malta, [2]Department of Pathology, Faculty of Medicine and Surgery, University of Malta, Msida, Malta, [3]Division of Histopathology, Department of Pathology, Mater Dei Hospital, Msida, Malta

*Correspondence: D. Mintoff. E-mail: dillon.mintoff@gov.mt

References

1 Maubec E, Pinquier L, Viguier M *et al*. Vaccination-induced cutaneous pseudolymphoma. *J Am Acad Dermatol* 2005; **52**: 623–629.
2 Baden LR, El Sahly HM, Essink B *et al*. Efficacy and safety of the mRNA-1273 SARS-CoV-2 vaccine. *N Engl J Med* 2021; **384**: 403–416.
3 Ramos Pinheiro R, Duarte B, João A, Lencastre A. Cutaneous pseudolymphoma following quadrivalent human papillomavirus vaccination - a rare adverse event. *J Dtsch Dermatol Ges* 2018; **16**: 465–467.
4 Cerroni L, Borroni RG, Massone C, Chott A, Kerl H. Cutaneous B-cell pseudolymphoma at the site of vaccination. *Am J Dermatopathol* 2007; **29**: 538–542.
5 Pfizer, Inc. Vaccine information fact sheet for recipients and caregivers about comirnaty (COVID-19 vaccine, mRNA) and Pfizer-BioNTech COVID-19 vaccine to prevent coronavirus disease 2019 (COVID-19). 2021. https://www.fda.gov/media/144414/download.

DOI: 10.1111/jdv.17680

Pfizer-BioNTech SARS-CoV-2 mRNA vaccine-associated erythema multiforme

Dear Editor,

A 38-year-old healthy gentleman was referred for a dermatology review in view of a vesicobullous eruption. General examination revealed multiple, generally distributed targetoid lesions with central bullae as well as a superficial ulcer on the hard palate (Figure 1). The lesions were tender to touch but otherwise asymptomatic. Nikolsky sign was negative. Examination of other mucosae was normal. The patient denied a history of recent illness or foreign travel and had not been on any regular or as required medication. The patient had received the first dose of the Pfizer-BioNTech SARS-CoV-2 mRNA vaccine two days prior to onset of the cutaneous eruption. The clinical impression was of bullous erythema multiforme (EM) secondary to the Pfizer-BioNTech SARS-CoV-2 mRNA vaccine. An excisional biopsy of a bulla on the left forearm was performed.

Histology (Figure 2) showed centrally crusted epidermis with a predominantly basket weave keratin pattern and with central hypergranulosis. A predominantly perivascular lymphocytic and histiocytic infiltrate was present in the upper dermis. Lymphocytes extended into the basal layers of the epidermis with prominent associated basal cell vacuolar damage, Civatte body formation and pigment incontinence. Occasional apoptotic keratinocytes were also seen in all layers of the epidermis. Subepidermal clefting was also noted. These features were consistent with the clinical impression of bullous EM. The patient was treated with prednisolone 40 mg daily for five days and most lesions resolved within seven days.

To date, there have been three cases of EM related to the SARS-CoV-2 vaccine, two with the Moderna vaccine and another with Coronavac vaccine.[1,2] To the best of our knowledge, this is the first case of EM associated with the Pfizer-BioNTech Covid vaccine. EM is a self-limiting, cutaneous type IV hypersensitivity reaction. Cases of bullous EM are more likely to require active treatment. Drug-associated EM accounts for <10% of cases.[3] The drugs most commonly associated with EM are anti-epileptics, antibiotics (particularly cephalosporins and penicillin), anti-fungals and allopurinol. EM in the context of the MMR, Influenza, DPT and Hepatitis B vaccines has also been reported.[4]

Cutaneous adverse drug reactions have been reported in association with COVID mRNA vaccines. Out of 19,485 individuals vaccinated with the Pfizer-BioNTech COVID mRNA vaccine in Trieste in January 2021, 44 individuals developed a cutaneous adverse reaction.[5] The commonest cutaneous reactions are localized and included erythema and oedema at the injection site.