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CLINICAL LETTER

mRNA COVID 19 vaccine-induced recall dermatitis after topical imiquimod

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Dear Editors,

Numerous cutaneous reactions provoked by SARS-CoV2 vaccines have been documented since the implementation of large COVID-19 immunization campaigns, ranging from local responses such as "COVID arm" to systemic reactions including urticaria and/or angioedema, and maculopapular, papulovesicular, purpuric and pityriasis rosea-like eruptions.[1] However, more uncommon dermal reactions such as skin necrosis,[2] bullous drug reaction,[3] and radiation recall dermatitis,[4] have also been linked to COVID-19 vaccination.

The recall phenomenon is typically associated with prior radiotherapy and reflects a delayed local inflammatory process arising in previously exposed areas, triggered predominantly by anti-cancer systemic therapies such as intravenous cytotoxic agents.[5]

To our knowledge, this case report describes the first presentation of recall dermatitis after local imiquimod therapy.

A 61-year old male patient presented with periorbital, frontal and parietal erythema associated with mild swelling 5 days after the administration of the third dose of the Moderna mRNA SARS-CoV-2 vaccine.

One month earlier the patient had completed treatment with topical imiquimod cream (Zyclara 3,75% cream, MEDA Pharma, Sweden) for 14 and 7 consecutive days each for actinic keratoses on the scalp, forehead and temples as well as the left zygomatic area. A few days after both treatments with imiquimod the patient developed the expected inflammatory reaction in the area of the former actinic keratoses. The skin lesions had completely healed by the time he received the booster vaccine. Five days after the inoculation, sharply demarcated erythematous, infiltrative, pruriginous plaques with focal desquamation appeared at the area of previous imiquimod application (Figures 1, 2). The patient denied the application of any topical agent or the initiation of any systemic therapy prior to onset of the skin lesions and he reported no skin reaction after the first two doses of the vaccine.

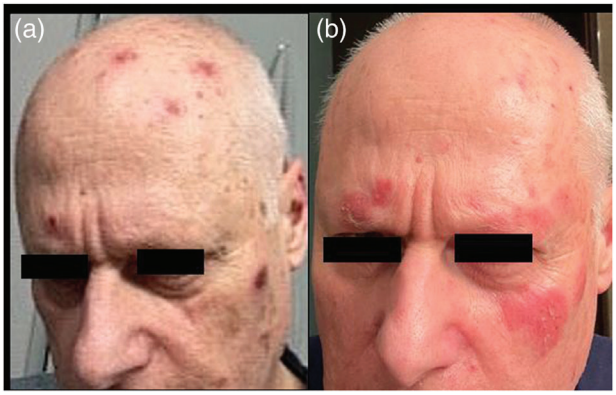

FIGURE 1 (a) Clinical features after second topical treatment with imiquimod (b). Recall dermatitis 5 days after inoculation with the third mRNA SARS CoV-2 vaccine.

The erythema was most pronounced two weeks after the onset of the symptoms and subsequently subsided. The patient was unable to visit a dermatologist and used only a moisturizing cream to treat the skin lesions.

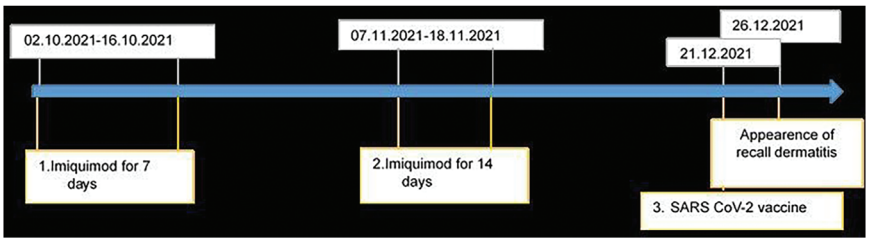

FIGURE 2 Timeline showing the course of the disease.

Imiquimod is a Toll-like receptor (TLR) 7 agonist, which stimulates the secretion of local cytokines, such as interferon (IFN)-α, tumor necrosis factor α and interleukin-12, thus augmenting the innate immune response. Furthermore, it promotes the adaptive immunity via migration and activation of Langerhans cells in the skin, which promotes the emergence of IFN-γ producing Th1 cells.[6] The antiviral and antitumor properties of imiquimod are largely attributable to its ability to induce type 1 IFN production by activation and recruitment of plasmacytoid dendritic cells (PDCs) to the treatment area.[7,8]

Like imiquimod mRNA SARS-CoV-2 vaccines also trigger TLR7 provoking the release of multiple pro-inflammatory cytokines.[9] We hypothesize that the mRNA SARS-CoV-2 vaccine re-activated resident innate immune cells in the skin previously recruited by imiquimod through stimulation of the TLR7 causing a recall reaction at sites of formerly inflamed skin.

Our case is notable for being the first reported case of recall dermatitis associated with topical imiquimod treatment. Dermatologist should be aware of the potential appearance of recall dermatitis after SARS CoV-2 vaccine in patients previously treated with this therapy.

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CONFLICT OF INTEREST

None.

REFERENCES

1. Catala A, Munoz-Santos C, Galvan-Casas C, et al. Cutaneous reactions after SARS-CoV-2 vaccination: a cross-sectional Spanish nationwide study of 405 cases. *Br J Dermatol*. 2022;186(1):142-152.
2. Gallo-Pineda G, Navarro-Navarro I, Viedma-Martinez M,, et al. Skin necrosis after COVID-19 vaccines. *J Dtsch Dermatol Ges*. 2022;20(12):1654-1656.
3. Irmer ML, Nast A, Ghoreschi F, et al. Severe bullous drug reaction after COVID-19 mRNA vaccination. *J Dtsch Dermatol Ges*. 2022;20(11):1509-1511.
4. Liu J WJ, Gomez C. Radiation recall after the COVID-19 vaccine: two cases and a review of the literature. *Appl Rad Oncol*. 2021;10(4):30-33.
5. Ristic B. Radiation recall dermatitis. *Int J Dermatol*. 2004;43(9):627-631.
6. Urosevic M, Dummer R. Role of imiquimod in skin cancer treatment. *Am J Clin Dermatol*. 2004;5(6):453-458.
7. Gilliet M, Conrad C, Geiges M, et al. Psoriasis triggered by toll-like receptor 7 agonist imiquimod in the presence of dermal plasmacytoid dendritic cell precursors. *Arch Dermatol*. 2004;140(12):1490-1495.
8. Urosevic M, Dummer R, Conrad C, et al. Disease-independent skin recruitment and activation of plasmacytoid predendritic cells following imiquimod treatment. *J Natl Cancer Inst*. 2005;97(15):1143-1153.
9. Teijaro JR, Farber DL. COVID-19 vaccines: modes of immune activation and future challenges. *Nat Rev Immunol*. 2021;21(4):195-197.