

Correspondence

SDRIFE-like rash in COVID-19 patient: drug reaction or another cutaneous manifestation of SARS-CoV-2?

Dear Editor,

We report a particular case of skin rash in a patient with COVID-19. Symmetrical drug-related intertriginous and flexural exanthema (SDRIFE) is described as a benign and self-limiting type IV hypersensitivity due to a systemic drug that occurs in the absence of systemic involvement.^{1,2} It is hallmarked by a symmetric, well-demarcated erythema of the gluteal area and/or V-shaped erythema of the perigenital region, in addition to at least one other intertriginous area.^{1,2}

A 71-year-old woman with asthma and hypothyroidism was admitted to the emergency unit with a high fever, prostration, myalgia, dry cough, coryza, and diarrhea after returning from a cruise off the Brazilian coast. Her breathing worsened, and a chest CT showed pneumonia with moderate ground-glass pattern. A RT-PCR test and immunochromatographic assay with IgM/IgG antibodies for SARS-CoV-2 were positive. She received piperacillin/tazobactam (7 days), azithromycin (6 days), hydroxychloroquine (5 days), and oseltamivir (2 days). On the day of hospital discharge (2, 3, 3, and 8 days after completing these drug regimens, respectively) a pruritic rash in the flexures appeared: erythematous papules converging on plaques in the scalp, flexures, anterior chest, bilateral inframammary, right shoulder, back, and lower abdomen, with reported craniocaudal evolution (Figure 1a–d). A histopathological

examination showed vacuolar degeneration of the basal layer, pigmentary incontinence, and perivascular and interstitial inflammatory infiltrate that consisted of lymphocytes and eosinophils (Figure 2a,b). An RT-PCR test of a skin fragment was negative for SARS-CoV-2. Prednisone 0.5 mg/kg/day was prescribed for 7 days, which was reduced to 0.25 mg/kg/day for the following week. The lesions and pruritus have completely resolved (Figure 1e–h).

Although SDRIFE has been regularly reported in association with beta-lactams, antihypertensives, radiocontrast media, chemotherapeutic agents, and biologics,^{1,3} we could not find any specific report relating hydroxychloroquine, azithromycin, oseltamivir, and piperacillin/tazobactam to this drug eruption.^{1,2,3}

The histology of lesions in SDRIFE varies, but there is a predominance of superficial perivascular inflammatory cell infiltrates in the upper dermis.^{1,2} However, viral rashes may also cause such histopathological findings.⁴ Moreover, as in this report, many cases with less severe skin rashes have occurred later during COVID-19 treatment and had a longer duration.⁵

To our knowledge, this was the first SDRIFE-like case in a COVID-19 patient with a complete investigation for SARS-CoV-2, including skin biopsy and biomolecular analysis. It is unclear whether these skin lesions are associated with COVID-19, as a rare new skin manifestation of this disease, or are a case of SDRIFE caused by previously undescribed drug reaction.

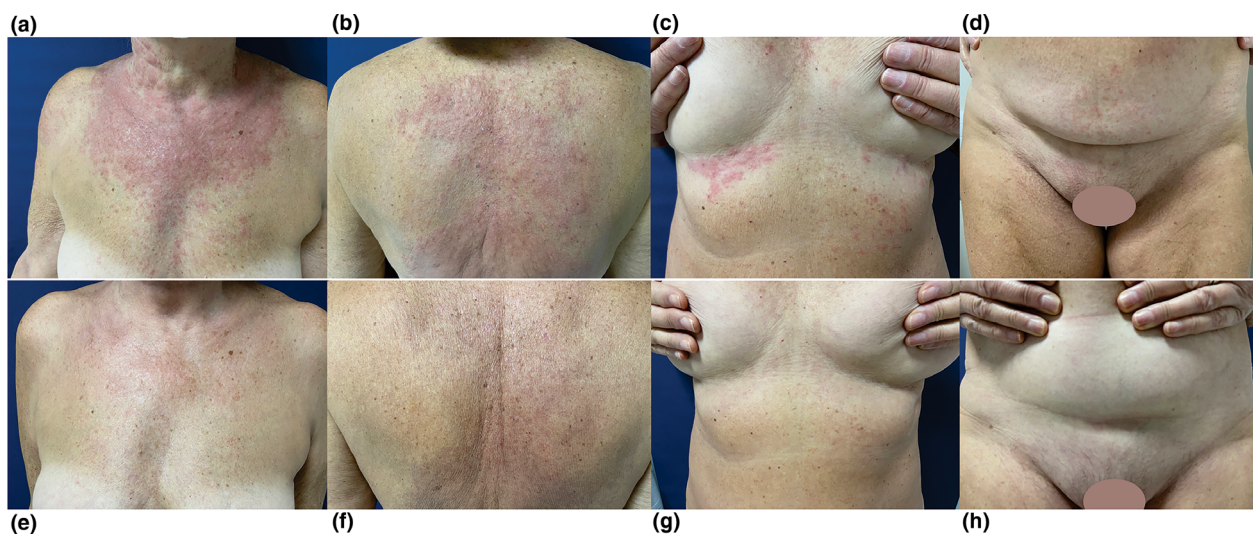


Figure 1 Maculopapular eruption affecting the flexures. (a) Anterior chest; (b) between the shoulder blades; (c) inframammary; (d) lower abdomen and pubis; (e–h) improvement in SDRIFE-like rash in the same regions after treatment

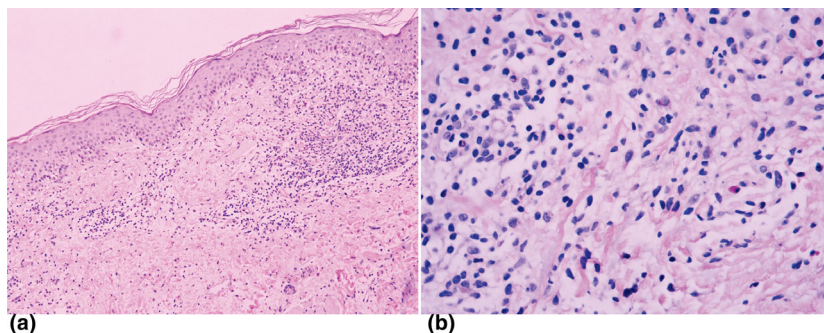



Figure 2 Histopathology of the skin eruption. (a) Vacuolar degeneration of the basal layer, dense perivascular and interstitial inflammatory infiltrate. (b) At higher magnification: lymphocytes and eosinophils predominating in inflammatory infiltrate (hematoxylin and eosin, a: $\times 10$, b: $\times 40$)

Although we found no evidence of SARS-CoV-2 on the skin, it has been found in a few of the countless recent reports.

As already described in other drug eruptions, the presence of an active viral infection may contribute to the appearance of a skin rash. Could SARS-CoV-2 also interact with drugs, triggering a SDRIFE-like rash? Further studies with more cases and follow-up time may provide an answer.

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