Correspondence

Detection of SARS-CoV-2 in a case of DRESS by sulfasalazine: could there be a relationship with clinical importance?

Dear Editor,

Drug reaction with eosinophilia and systemic symptoms (DRESS) is a hypersensitivity syndrome that includes severe skin rash, fever, lymphadenopathy, hematologic changes with eosinophilia, atypical lymphocytes, and possible involvement of other organs, such as liver and kidneys.[1] It's a potentially life-threatening condition that usually appears within 2 months of initiation of a new drug.[1,2] Diagnosis relies on clinical and laboratory findings and on use of the RegiSCAR scoring system.[1,2] There is evidence that the disease occurs in genetically predisposed people after ingestion of a related drug, such as sulfonamides.[2] Reactivation of some viruses and the immunological response that follows it are involved mechanisms.[2] We report a case of DRESS associated with COVID-19.

A 20-year-old woman presented to the emergency department with a morbilliform, erythematous-violaceous rash, fever (38.5 °C), lymphadenopathy, pruritus, myalgia, and arthralgia that started 14 days after initiation of sulfasalazine treatment for ulcerative colitis. Exanthema appeared on her face and spread to the trunk and upper and lower extremities (with follicular accentuation—Fig. 1) 4 days before admission, when she stopped sulfasalazine on her own. A nasopharyngeal swab was collected for PCR for SARS-CoV-2, a routine hospital procedure because of local epidemic. The test was positive.

The symptoms became more severe, with worsening liver function, lip erosion, facial and acral edema, purple macules in the plantar regions, and digital pulps (resembling chilblain-like acral lesions) (Fig. 2).

Blood tests showed significant leukocytosis (28,020/μl), lymphocytosis (9,807/μl), 13% of atypical lymphocytes, eosinophilia (2,522/μl), elevated lactate dehydrogenase (1,378 U/l), and elevated erythrocyte sedimentation rate, C-reactive protein, and D-dimers (1,440 ng/ml). Transaminase levels were elevated to 7-fold the upper limit of normal (ALT 403 iU/l and AST 350 iU/l). Antinuclear antibodies, blood cultures, and serologic test results for HIV, HCV, HBV, toxoplasmosis, syphilis, CMV, and EBV were negative. Histopathology of the rash revealed spongiosis, intense vacuolar degeneration of the basal layer and lymphoid infiltrate in the dermo-epidermal interface, and presence of rare eosinophils, without vasculitis (Fig 1). Based on clinical, laboratory, and histopathologic features and a RegiSCAR score >5, both DRESS and COVID-19 were diagnosed.

Numerous skin rashes have been reported in SARS-CoV-2 infection.[3] In the present case, the patient had concurrent diagnoses of DRESS and COVID-19. Supportive and corticosteroid therapy was performed, and she recovered and was discharged.

Up to 60% of patients with DRESS have evidence of simultaneous viral infection and, considering the current state of knowledge about drug–virus interaction, there is a high possibility that strong drug reactions of type IVc and IVd may reactivate viruses.[4]

Paradoxical worsening of symptoms in DRESS has been the subject of recent studies. Although there is no consensus, a relationship between the disease and viral reactivation has been suggested to contribute to higher severity, especially reactivation of viruses belonging to the Betaherpesvirinae subfamily (HHV-6, EBV, HHV-7, and CMV).[1,2] However, according to Rojeau and Dupin, it is possible that the severity of DRESS caused by viral reactivation is related to other individual factors, particularly a preserved immune system.[4]

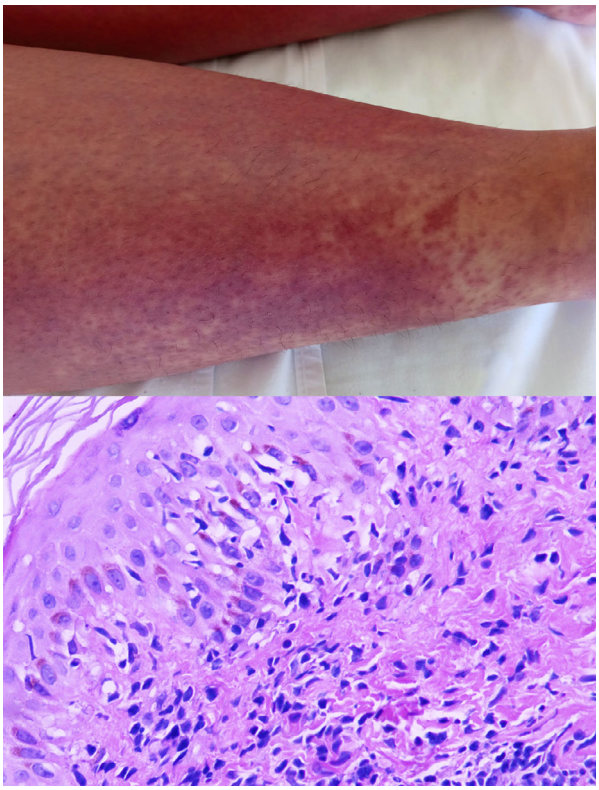

Figure 1 Erythematous-violaceous rash, with follicular accentuation (above). Histopathology (hematoxylin and eosin, ×200): vacuolar degeneration of the basal layer, lymphoid infiltrate in the dermo-epidermal interface (below)

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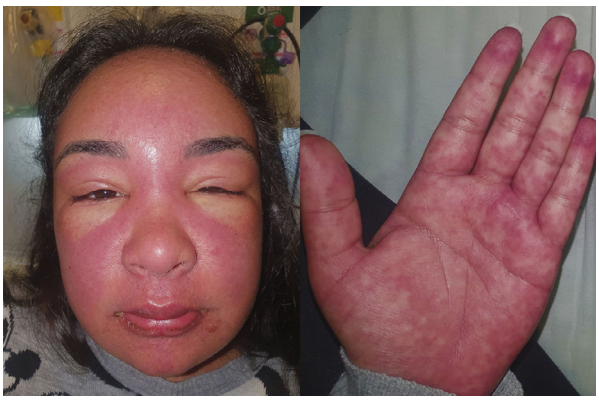

Figure 2 Facial erythema and edema (left). Digital pulps: erythema-purpuric macules (right)

Regarding the pathomechanism of DRESS and COVID-19 coexistence, it is important to remember the high-serum TNF-α levels in patients with DRESS and viral reactivation, suggesting that TNF-α might play an important role in viral reactivation and disease worsening.[1] Also, patients with DRESS and viral infection displayed a decreased number of plasmacytoid dendritic cells (pDCs) in circulation and accumulation in the skin.[1] The pDCs play a key role in the response to viral infection by producing cytokines such as IFN-γ,[1] and available data show that IFN-γ produced by pDCs, as well as related inflammatory cytokines, play a protective role against COVID-19.[5]

The subject of DRESS and viral reactivations remains with non-definitive conclusions, and this report adds a new topic: SARS-CoV-2 infection in the current pandemic.

Acknowledgment

The patient authorized the release of the photos and the clinical case for scientific purposes. This article contains a small case report and respects the ethical principles for medical research.

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