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CASE REPORT

Acute generalized exanthematous pustulosis associated with SARS-CoV-2 infection

Pustulose exantemática generalizada aguda associada a infecção pelo SARS-CoV-2

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Abstract

Acute generalized exanthematous pustulosis (AGEP) is characterized by the sudden onset of diffuse sterile pustules on an erythematous background. It is mainly caused by drugs and, clinically, it usually improves quickly after discontinuation of the causative agent. Viral and bacterial agents have also been reported as triggers. We present a case regarding a woman reporting flu-like symptoms, taking dipyrone, paracetamol, and azithromycin. A reverse transcriptase polymerase reaction (RT-PCR) test confirmed severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection. After 2 days, she noted the onset of erythematous plaques covered by diffuse pustules. The negative patch test reinforced the viral infection as the possible causative agent.

Keywords: Acute generalized exanthematous pustulosis. COVID-19. SARS-CoV-2.

Resumo

A pustulose exantemática generalizada aguda (PEGA) é caracterizada pelo surgimento súbito de pústulas estéreis difusas sobre fundo eritematoso na pele. É causada principalmente por medicamentos e geralmente melhora rapidamente após a interrupção do agente causador. Agentes virais e bacterianos também já foram relatados como desencadeantes. Apresentamos um caso de uma mulher com sintomas gripais, em uso de dipirona, paracetamol e azitromicina. Um teste de RT-PCR confirmou a infecção por SARS-CoV-2. Após 2 dias, notou o aparecimento de placas eritematosas cobertas por pústulas difusas. O teste de contato negativo reforçou a infecção viral como provável agente causador.

Palavras-chave: Pustulose exantematosa aguda generalizada. COVID-19. SARS-CoV-2.

Introduction

Acute generalized exanthematous pustulosis is a rare disease characterized by the sudden onset of diffuse sterile pustules on an erythematous background[1,2]. It usually improves quickly after discontinuation of the causative agent, even though severe cases have been described. Viral and bacterial agents have also been reported as triggers[1-3], as well as rare additional

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Figure 1. Erythematous plaques covered by small pustules in the trunk, mainly in the inter and submammary folds, breasts, abdomen, medial part of arms and internal side of thighs.

Figure 2. Erythematous plaques covered by small pustules in the medial part of arms and back.

causes, such as contact with mercury and spider bites[2]. However, the main triggering factors are drugs, such as antibiotics, hydroxychloroquine, terbinafine, diltiazem, and fluconazole. The period from drug exposure to the reaction onset is approximately 48 h, with antibiotics with an average of 24 h[2].

Case report

A 35-year-old women, mixed race, reported a flu-like condition for 3 days, taking dipyrone and paracetamol for symptom control. After 2 days, she was prescribed azithromycin due to a suspected SARS-CoV-2 infection, which was confirmed later through a PCR test. On the 3rd day of symptoms, erythematous plaques covered by small pustules appeared in her trunk, mainly in the inter and submammary folds, associated with local burning, and the exanthema soon progressed to the medial part of her arms, internal side of thighs, and back (Fig. 1 and 2). Azithromycin was discontinued, and she was hospitalized and started oral prednisone 40 mg/day, with an important improvement of lesions in the following 3 days.

Histopathology showed a subcorneal and intraepidermal pustular dermatosis, with severe edema in the papillary dermis and without eosinophils, compatible with the hypothesis of AGEP.

About 1 year later, the patient was called again for diagnostic elucidation. A patch contact test was conducted with the Brazilian Standard Battery of allergens and other suspected substances (dipyrone and acetaminophen, powder mixed with vaseline at 10%, and azithromycin, powder mixed with petrolatum at 5%) with a negative result for all the substances at the readings at 2 and 4 days, therefore reinforcing that SARS-CoV-2 infection could have been the potential triggering cause.

Discussion

Acute generalized exanthematous pustulosis is a neutrophilic disease which is related to a type IV immune-mediated hypersensitivity response. After exposure to the causative agent, antigen-presenting cells cause the activation of a specific cluster of differentiation (CD)—CD4 and CD8 T cells, which migrate to the dermis and epidermis, causing apoptosis of keratinocytes, formation of epidermal vesicles, chemotaxis

of neutrophils through interleukin 8, and activation and transformation of vesicles into sterile pustules due to a prevalent Th1 and Th17 profile[1-3].

Histological findings are characterized by intracorneal, subcorneal, or intraepidermal spongiform pustules with papillary dermis edema containing neutrophilic and eosinophilic infiltrates[1].

A patch test may be used to identify the cause of AGEP when the causative drug is not clear, but although the sensitivity of these tests in AGEP is around 50%, sensitivity depends on the culprit drug, and there are no reports of positive patch tests to azithromycin or dipyrone in this setting[1,2,4].

Skin manifestations of SARS-CoV-2 infection include perniosis, morbilliform, vesicular, or urticarial rash, vasculitis, and necrotic lesions[1,5]. To date, only two cases of AGEP triggered by SARS-CoV-2 infection, with no prior use of hydroxychloroquine, have been reported in the literature[1,5,6].

Although AGEP is not commonly related to viral agents, we cannot rule out the SARS- CoV-2 infection as the main trigger, mainly after the nonreactivity of the patch test.

There is a lack of robust evidence regarding skin manifestations related to SARS-CoV-2 infection. Few case reports describe the association of AGEP with SARS-CoV-2 infection. In most reports, the patients had previously used hydroxychloroquine.

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Conflicts of interest

None.

Ethical disclosures

Protection of human and animal subjects. The authors declare that no experiments were performed on humans or animals for this study.

Confidentiality of data. The authors declare that they have followed the protocols of their work center on the publication of patient data.

Right to privacy and informed consent. The authors have obtained the written informed consent of the patients or subjects mentioned in the article. The corresponding author is in possession of this document.

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