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CASE REPORT

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A case of acute generalized exanthematous pustulosis following COVID-19 infection and remdesivir

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Key Clinical Message

We report a challenging AGEP case following COVID-19 infection and a history of remdesivir use. Our study highlights the importance of considering history of COVID-19 and remdesivir as possible causative factors when visiting new-onset AGEP patients.

KEYWORDS

acute generalized exanthematous pustulosis, adverse reaction, AGEP, COVID-19

JEL CLASSIFICATION

Dermatology

1 | INTRODUCTION

In the COVID-19 era, cases of acute generalized exanthematous pustulosis (AGEP) after COVID-19 infection and the use of COVID-19 medications such as hydroxychloroquine (HCQ) and cefepime have been reported.[1–3] Herein, we report a challenging case that presented with AGEP following COVID-19 infection and a history of remdesivir use.

2 | CASE PRESENTATION

A 65-year-old female with a 3 days history of widespread pruritic pustules presented to our clinic (Figures 1 and 2). The patient had a prior history of diabetes mellitus controlled with metformin and gliclazide, hyperthyroidism controlled with methimazole, and hypertension for which she was taking losartan and amlodipine. She was taking all these medications for the last 3 years. Four months before presentation, she had received the second dose of Pfizer vaccine.

One week before presentation to our hospital, she had fever and cough and she was diagnosed with COVID-19 infection initially based on her symptoms and had received two doses of remdesivir in another hospital. One day after the second dose of remdesivir, the lesions first emerged as maculopapular erythematous lesions and pustules on her upper limbs and then rapidly progressed to the whole body. Of note, by presenting to our clinic, the patient was afebrile with mild respiratory symptoms and mild reticulation observed in chest CT scan. We suspected remdesivir as the culprit for AGEP and according to the mild respiratory symptoms, we discontinued remdesivir. The only abnormal findings in the laboratory examination were leukocytosis (WBC:14000), CRP:2+, and ESR:40 mm/hr (normal range 0–29 mm/hr). A skin biopsy was performed from the lesions that showed subcorneal pustules containing many neutrophils and degenerated inflammatory cells with surrounding neutrophilic spongiosis, superficial dermal inflammation composed of lymphohistiocytes, and some eosinophils with severe dermal edema (Figure 3).

The clinical and histopathological findings were compatible with AGEP due to either COVID-19 infection or

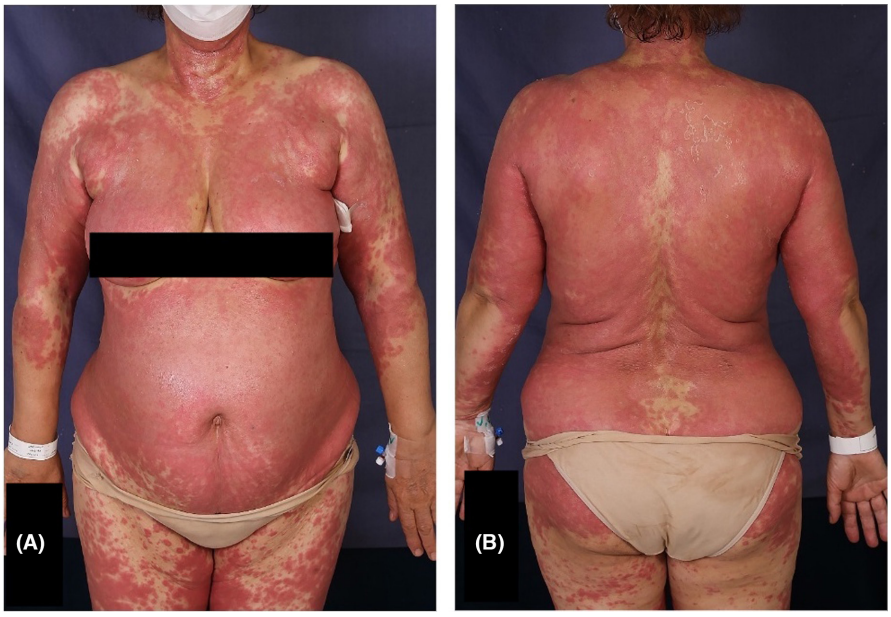

FIGURE 1 (A and B) Generalized maculopapular erythematous eruptions with scattered pustules in a 65-year-old female a few days after COVID-19 and remdesivir.

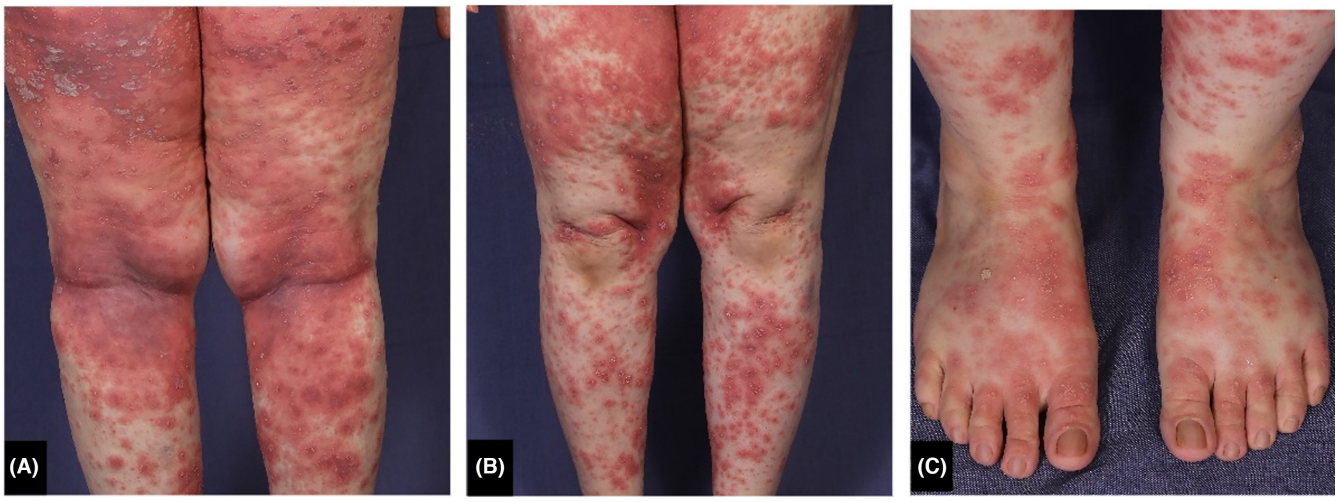

FIGURE 2 (A–C) AGEP lesions on the patient's lower limbs.

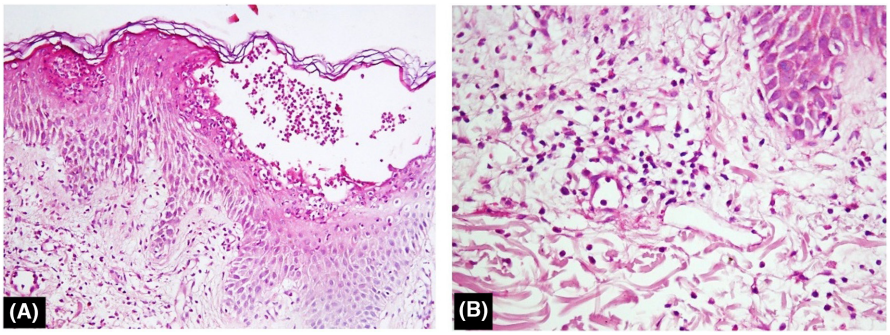

FIGURE 3 (A) Subcorneal pustule containing many neutrophils and degenerated inflammatory cells with surrounding neutrophilic spongiosis (H&E original magnification ×200), (B) Superficial dermal inflammation composed of lymphohistiocytes and some eosinophils with severe dermal edema (H&E original magnification ×400).

remdesivir (Figure 3). Prednisolone 30 mg and cyclosporin 200 mg daily was prescribed. During her hospital stay, the D-dimer level was increased from 702 to 2337 with a normal range below 500. Enoxaparin 40 mg subcutaneous was initiated. Furthermore, due to the elevated serum glucose level, insulin regular and NPH was prescribed. She

was discharged after 2 weeks of hospital stay and the prednisolone dosage was tapered in 5 mg increments once a week.

In our follow-up after discharge, she experienced two relapses with sudden eruption of pustules which were controlled by increasing the dosage of cyclosporin to 300 mg daily and prednisolone to 30 mg temporarily. Six months after the onset of AGEP, both cyclosporin and prednisolone were discontinued. Methotrexate (MTX) was initiated with a dosage of 10 mg/week and her lesions were completely resolved. After our 2 years of follow-up, she did not experience any relapses. However, she is currently taking MTX with a dosage of 7.5 mg/week.

3 | DISCUSSION

With the emergence of the COVID-19, various cutaneous adverse effects were reported to be related to the virus itself, prescribed medications, and COVID-19 vaccines.[4–6] In this study, we presented a case of AGEP following both COVID-19 infection and remdesivir who had received two dosages of Pfizer COVID-19 vaccine with a prolonged course (nearly 2 years) to be controlled. AGEP is an exanthematous condition and in most cases, it is caused by drugs and usually occurs within 48 hours of treatment initiation, but other factors such as bacterial, viral or parasitic infections can induce the disease.[7–9]

Similar to our study, Mohaghegh et al. presented the first reported case of AGEP following treatment with remdesivir 2 days after the completion of treatment in a patient with COVID-19.[1] Alzahrani et al., reported a case of AGEP in a 34-year-old male that presented with pustular rash on erythematous base 4 days after his COVID-19 was resolved. The rash started after he took azithromycin, oseltamivir, ribavirin, lopinavir, hydroxychloroquine, prednisolone, ceftriaxone, clindamycin, interferon (IFN) beta, and ceftazidime for COVID-19. In that study, it was unclear whether AGEP was developed following COVID-19 or as a drug-related reaction and he was managed with topical corticosteroids.[10] In a study done by Goyal et al., among the 33 patients diagnosed concomitantly with SARS-CoV-2 and AGEP, 16 patients (48%) were favored to have AGEP triggered primarily by COVID-19 infection and in these patients no culprit drugs were documented.[7]

Of note, cases of AGEP following COVID-19 vaccination have also been reported.

Agaronov et al., reported a case of AGEP in a young woman within a few hours after Moderna COVID-19 vaccine that took 12 days to be completely resolved.[8] Kang et al., reported a young woman who developed AGEP 3 weeks after receiving her first dose of a COVID-19 vaccine that resolved within 2 weeks by a short course of topical and systemic corticosteroid.[9]

In our study, it was hard to determine whether our patient had developed AGEP following COVID-19 infection or remdesivir as the treatment or the past history of two doses of COVID-19 vaccine. However, due to the long interval time between COVID-19 vaccination and AGEP development, it is less possible that the vaccine was the culprit for AGEP development. In our case, more probably, AGEP might be triggered by the COVID-19 infection or as a potential side-effect of remdesivir, or the synergic effect of both infection and the treatment. While previous reported cases of AGEP following COVID-19 infection mainly resolved with corticosteroids in shorter duration of time mostly less than 1 month, our case is unique in that she had a very prolonged course that took near 2 years to be completely resolved with multiple courses of systemic immunosuppressive treatments.

Our study highlights the importance of considering previous history of COVID-19 infection and remdesivir use as possible causative factors when visiting new-onset AGEP patients.

AUTHOR CONTRIBUTIONS

M. D. Yasamin Kalantari: Conceptualization; resources; validation; writing – original draft; writing – review and editing. **Alireza Ghanadan:** Conceptualization; data curation; investigation; validation; visualization. **Ifa Etesami:** Data curation; project administration; supervision; visualization; writing – original draft; writing – review and editing.

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CONFLICT OF INTEREST STATEMENT

The authors have no conflict of interest to declare.

DATA AVAILABILITY STATEMENT

The authors elect not to share data.

CONSENT

Written informed consent was obtained from the patient to publish this report in accordance with the journal's patient consent policy.

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