A rather difficult case of acute generalised exanthematous pustulosis: would colchicine be a treatment option?

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Case report

A 24-year-old lactating female patient presented with redness, burning, and rash on the face and body on the fifth day of hydroxychloroquine (HCQ) treatment, prescribed after diagnosis of coronavirus disease 2019 infection. Physical examination revealed numerous non-follicular pustular lesions on an erythematous background that started on the face and neck and extended to the whole body, especially in the folds and extremities, and in the palmoplantar regions (Fig 1a). Conjunctival involvement was also evident. Examination was otherwise unremarkable and the patient was afebrile.

Laboratory examinations were likewise unremarkable (Table). Histopathological examination of punch biopsy of the leg lesions, subcorneal pustule formation in the epidermis, oedema in the papillary dermis, and lymphocytic infiltration in the upper dermis was performed (Fig 2). There was no individual or family history of psoriasis, and the patient denied taking any medication except HCQ in the last 3 months. Based on these findings, the patient was diagnosed with HCQ-induced (acute generalised exanthematous pustulosis [AGEP]). Intravenous methylprednisolone 60 mg/day, etodolac, topical methylprednisolone, and moisturiser were prescribed. An initial partial response was achieved but on the 15th day of treatment, pustular lesions, itching, and complaints of burning recurred and the patient developed a fever of 38°C (Fig 1b). Blood cultures grew *Staphylococcus aureus*, sensitive to ciprofloxacin. Systemic ciprofloxacin 750 mg twice a day (1500 mg daily) was started with the addition of 0.5 mg colchicine thrice a day (1.5 mg daily). Her general condition improved and the skin lesions completely regressed with desquamation (Fig 1c). Systemic methylprednisolone treatment was tapered and stopped. Colchicine treatment was continued for 1 month and the dose then decreased to 0.5 mg twice a day for a further month before being stopped. The patient continues to attend for follow-up and remains well. A patch test for HCQ is planned when lactation stops.

FIG 1. (a) Numerous non-follicular pustules on an erythematous base on the leg. (b) Non-follicular pustules recurring in areas of desquamation. (c) Complete recovery after desquamation

TABLE. Laboratory blood test results

	Value	Normal range
Haemoglobin	13.3 g/dL	12.2-18.1 g/dL
Haematocrit	40.9%	37.7%-53.7%
WBC	26.500 mm^3	4.6-10.2 mm^3
Neutrophils	23.600 mm^3	2-6.9 mm^3
Eosinophils	116 mm^3	0-0.7 mm^3
Platelets	368 000 mm^3	142-424 mm^3
CRP	209 mg/L	0-5 mg/L
ESR	49 mm/h	
ALT	33 U/L	0-35 U/L
AST	25 U/L	0-35 U/L
Urea	33 mg/dL	17-43 g/dL
Creatinine	0.59 mg/dL	0.51-0.95 mg/dL

Abbreviations: ALT = alanine aminotransferase; AST = aspartate aminotransferase; CRP = C-reactive protein; ESR = erythrocyte sedimentation rate; WBC = white blood cell

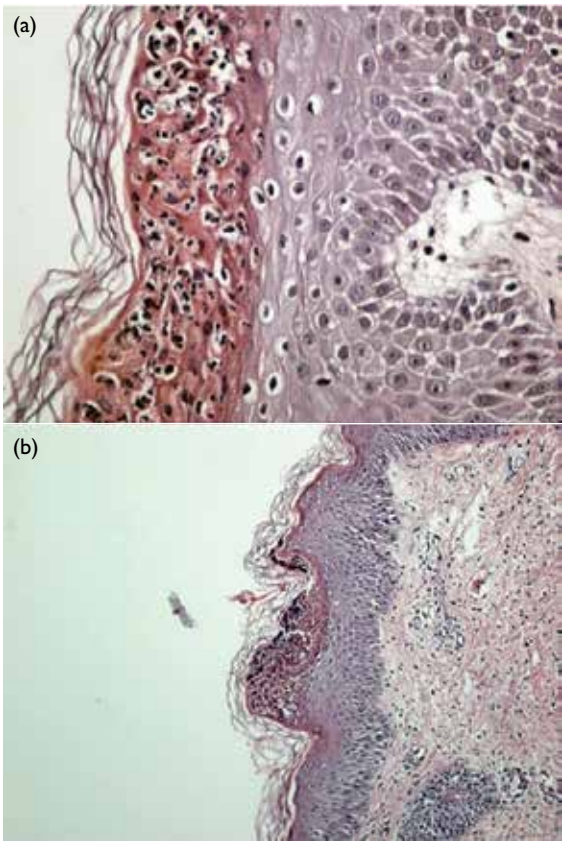

FIG 2. Subcorneal pustule formation in the epidermis, oedema in the papillary dermis, and perivascular inflammation accompanied by eosinophils and neutrophils in the upper dermis (a: ×10, b: ×40)

Discussion

Drugs constitute 90% of the aetiology of AGEP. The remaining 10% are due to infection. Although the pathogenesis of AGEP is not fully understood, the accumulation of cytokines released by helper T cells and drug-induced antigen-antibody complexes in the skin is blamed.[1]

The cutaneous side-effects of hydroxychloroquine include AGEP, urticaria, pruritus, xerosis, maculopapular rash, psoriasis, erythroderma, Stevens–Johnson syndrome, hair loss, and hair whitening.[2] Since hydroxychloroquine is a weak base with a long half-life, it passes into breast milk in minimal amounts.

In previously reported cases of HCQ-induced AGEP, the duration of exposure to HCQ was reported to be 2 to 30 days prior to symptom onset[3] and time to recovery after stopping HCQ has been reported to be 7 to 81 days.[4] The long persistence of symptoms can be explained by the long half-life of HCQ, approximately 40 to 50 days.[5]

Acute generalised exanthematous pustulosis cases due to HCQ have been reported during the pandemic. The typical features of these cases are a more prolonged course and a need for systemic steroid treatment. In this patient, colchicine was started because a complete response was not obtained with systemic corticosteroid treatment.

Colchicine suppresses inflammation at many stages. It has an antimitotic impact by binding to tubulin, preventing its polymerisation into new microtubules, inhibits neutrophil chemotaxis, and reduces free oxygen radical production by neutrophils. It is more useful in the treatment of neutrophilic dermatoses such as pustular conditions with predominant neutrophilic infiltrates, eg, pustular psoriasis. For this reason and the lack of response to systemic corticosteroid treatment, colchicine was added to our patient's treatment regimen.

We conclude that colchicine may be a treatment option for AGEP, a rare side-effect of HCQ, especially when it is resistant to systemic corticosteroid. It can also be used as an effective treatment during lactation due to its better safety profile.

Author contributions

Concept or design: All authors.
Acquisition of data: R Oztas Kara, H Tekmenler.
Analysis or interpretation of data: All authors.
Drafting of the manuscript: R Oztas Kara, H Tekmenler.
Critical revision of the manuscript for important intellectual content: All authors.

All authors had full access to the data, contributed to the study, approved the final version for publication, and take responsibility for its accuracy and integrity.

Conflicts of interest

The authors have no conflicts of interest to disclosure.

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Ethics approval

The patient was treated in accordance with the Declaration of Helsinki. The patient provided informed consent for the treatment/procedures and consent for publication.

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