

LETTER  
DERMATOLOGY

# Generalized exanthema due to hydroxychloroquine during COVID-19 prophylaxis

Hydroxychloroquine (HCQ) is a drug that is used for both chemoprophylaxis and treatment of COVID-19. At the moment, HCQ maintains its popularity and tens of thousands of people across the world are still receiving the current drug.<sup>1</sup> After the COVID-19 pandemic, several cutaneous side effects of HCQ are reported.<sup>2-7</sup> Herein, we reported generalized exanthema after a single dose of using HCQ. A 58-year-old male patient presented with resistant rashes on his upper extremities and neck region. Rashes appeared all over the body along with severe pruritus just a day after receiving a single 200 mg dose of oral hydroxychloroquine for COVID-19 prophylaxis. The patient had started hydroxychloroquine without any recommendation. He was also receiving pramipexole for restless legs syndrome for 3 years. He presented to our dermatology outpatient clinic 10 days after the beginning of the rashes. When he presented to our clinic, the rashes have begun to disappear except on the neck and arms. Also, there was still mild pruritus in his body. There was no other new drug, over-the-counter drug, nutrient, food supplement, past or active infection history to explain the rash. With these clinical findings, a diagnosis of hydroxychloroquine associated generalized exanthema was made. Because of its characteristic features, we did not perform a histopathologic examination. We searched published articles in PubMed about cutaneous side effects of HCQ during the COVID-19 pandemic between January 1, and July 1, 2020. These side effects can be listed as acute generalized exanthematous pustulosis, urticaria, palmoplantar itching, erythema multiforme, drug reaction with eosinophilia and systemic symptoms, and exacerbation of psoriasis (Table 1).<sup>2-7</sup>

As we know, there is a dilemma for cutaneous reactions in patients with COVID-19. It is difficult to differentiate whether they appear because of the infection itself or because of the drugs used in the treatment. In this regard, we divided articles which were mentioned above into three categories according to the indications in order to analyze HCQ reactions in the COVID-19 pandemic as follows: "HCQ use for COVID-19 infection," "HCQ use for COVID-19 prophylaxis" and "HCQ use for diseases unrelated to the COVID-19."

The duration of treatment and doses of HCQ is different according to the indications. These differences may give some clues for the dilemmas of cutaneous reactions although the onset of cutaneous manifestations of COVID-19 is not known exactly. In this context, acute generalized exanthematous pustulosis as in cases 7 and 9 approximately appeared at the same time which may suggest that case 9 was more compatible with a drug reaction rather than a manifestation of COVID-19 (Table 1).<sup>5,7</sup> The group of "HCQ use for diseases

unrelated to the COVID-19" may show that cutaneous reactions such as AGEP, DRESS, and erythema multiforme may appear with long term HCQ use. Moreover, "HCQ use for COVID-19 prophylaxis" group shows that even low and single doses of HCQ may lead to cutaneous side effects such as urticaria and pruritus. In this report, we first describe a generalized exanthema after using a single low-dose of HCQ during the COVID-19 pandemic. Although the patient had no risk factors for COVID-19, he started 200 mg HCQ per week for 3 weeks on his own. This situation shows the possible effects of unnecessary drug use during the COVID-19 pandemic.

Given the anticipated widespread use of HCQ, we believe that reviewing cutaneous side effects of the HCQ during the COVID-19 pandemic is important especially for the consultations of COVID-19 patients.

## DISCLOSURE

The authors declare that there are no conflicts of interest regarding the publication of this paper.

## DATA AVAILABILITY STATEMENT

The data of this case are available on request from the corresponding author. The data are not publicly available because of privacy or ethical restrictions.

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**TABLE 1** Cutaneous side effects of Hydroxychloroquine during the COVID-19 pandemic

No/type of drug reaction	Age/gender	HCQ treatment doses	Indications	Duration of lesions occurrence	Additional drugs/duration of treatment	References
1/Exacerbation of Psoriasis	71/W	800 mg on the first day followed by 400 mg daily for the next days	COVID-19	4 day	Oseltamivir/4 days	Kutlu et al <sup>2</sup>
2/Urticaria with maculopapular rash and palmoplantar itching	26/W	800 mg on the first day followed by 400mg weekly for the next weeks	COVID-19 prophylaxis	2 day after starting the loading dose	None	Sardana et al <sup>3</sup>
3/Urticaria	37/W			7 days after starting the loading dose		
4/Palmoplantar itching	22/W			7 days after starting the loading dose		
5/Urticaria	26/W			One week after 3rd weekly dose		
6/Drug reaction with eosinophilia and systemic symptoms	69/W	400 mg daily	Lichen planopilaris	20 days	PPI/3 years ACE inhibitors/10 years Levothyroxine/15 years	Grandolfo et al <sup>4</sup>
7/Acute generalized exanthematous pustulosis	76/M	400 mg daily	Calcium pyrophosphate dihydrate crystal deposition disease	18 days	None	Munshi et al <sup>5</sup>
8/Erythema multiforme	60/W	400 mg daily	Arthritis	19 days	N/A	Koumaki et al <sup>6</sup>
9/Acute generalized exanthematous pustulosis	39/W	600 mg daily	COVID-19	18 days	Enoxaparin 18 day	Litaïem et al <sup>7</sup>
10/Generalized exanthema	58/M	200 mg single dose	COVID-19 prophylaxis	1 day	Pramipexole/3 years	Current article

Abbreviations: ACE inhibitors, angiotensin-converting enzyme inhibitors; HCQ, hydroxychloroquine; M, man; N/A, not applicable; PPI, proton pump inhibitor; W, woman.

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**REFERENCES**

- Alia E, Grant-Kels JM. Does hydroxychloroquine combat COVID-19? A timeline of evidence. *J Am Acad Dermatol*. 2020;83:e33-e34
- Kutlu Ö, Metin A. A case of exacerbation of psoriasis after oseltamivir and hydroxychloroquine in a patient with COVID-19: Will cases of psoriasis increase after COVID-19 pandemic? *Dermatol Ther*. 2020;33(4):e13383
- Sardana K, Mathachan SR, Deepak D, Khurana A, Sinha S. Cutaneous side effects of hydroxychloroquine in health care workers in a COVID referral hospital—implications for clinical practice. *J Dermatol Treat*. 2020;1:3.
- Grandolfo M, Romita P, Bonamonte D, et al. Drug reaction with eosinophilia and systemic symptoms syndrome to hydroxychloroquine, an old drug in the spotlight in the COVID-19 era. *Dermatol Ther*. 2020.
- Munshi M, Junge A, Gadaldi K, Yawalkar N, Heidemeyer K. Ixekizumab for treatment of refractory acute generalized exanthematous pustulosis caused by hydroxychloroquine. *JAAD Case Rep*. 2020;6:634.
- Koumaki D, Koumaki V, Bertias G, et al. Hydroxychloroquine-induced erythema multiforme. *Clin Case Rep*. 2020;8:578-579.
- Litaïem N, Hajlaoui K, Karray M, Slouma M, Zeglouï F. Acute generalized exanthematous pustulosis after COVID-19 treatment with hydroxychloroquine. *Dermatol Ther*. 2020.