

Generalized Pustular Drug Rash Induced by Hydroxychloroquine

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A 69-year-old man developed a generalized pustular drug rash 2 weeks after starting on hydroxychloroquine sulfate (HCQ) medication. This form of drug eruption had not previously been attributed to HCQ, although a diagnosis of pustular psoriasis cannot be ruled out. Key words: Generalized pustulosis; Drug eruption.

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Hydroxychloroquine sulfate (HCQ) is an acceptable agent for a variety of skin diseases, in addition to its antimalarial properties. Like the parent molecule, chloroquine, cutaneous side effects include generalized pruritus, pigmentary changes of skin, mucosae, hair and nails, lichenoid and morbilliform eruptions and uncommonly fixed drug eruption and erythema annulare centrifugum.

We describe here a patient treated with HCQ for pemphigus erythematosus who developed a generalized subcorneal pustular rash 3 weeks after initiation of therapy.

CASE PRESENTATION

A 69-year-old man had been suffering from pemphigus erythematosus for 5 years. This diagnosis was based on typical skin lesions associated with the histology and immunofluorescence of superficial pemphigus. Since it was impossible to reduce his maintenance dose of prednisone to less than 15 mg per day, HCQ (Plaquenil)[®] 200 mg/day was added as an adjuvant therapy. Other medications which the patient was taking included quinidine bisulfate 500 mg/day and isosorbide dinitrate 10 mg/day for ischemic heart disease.

Two weeks after initiation of HCQ, erythematous patches developed with predilection to the trunk and flexures which were soon covered with multiple small pustules, partly in a circular arrangement. The eruption was accompanied by a systemic fever, mild leukocytosis and negative cultures of pustule contents. A skin biopsy revealed subcorneal accumulations of neutrophils with mild perivascular lymphocytic infiltration around blood vessels in the dermis. There was no evidence of acantholysis.

On admission, HCQ was stopped and prednisone was raised to 80 mg/day without improvement and then to 120

mg/day. It took 4 weeks for clearing of the skin to become evident. The prednisone dose was then reduced gradually to 10 mg/day. During this whole period, the preceding skin lesions of pemphigus erythematosus were completely unaffected by the newly developed eruption. During the year following this episode, no further skin lesions appeared. For obvious reasons, HCQ has not been prescribed again.

DISCUSSION

Although the histological picture of our patient's skin lesions was suggestive of subcorneal pustular dermatosis, subcorneal pustulosis is no synonym for 'subcorneal pustular dermatosis' in the absence of the typical clinical features and course. Similarly, there is no basis for a diagnosis of pemphigus foliaceus in the absence of acantholysis.

There are well established observations that psoriasis is worsened by antimalarials in general (1) and by HCQ in particular (2). It takes the form of a generalized erythroderma or extension of plaques. There was one report of a generalized pustular psoriasis during HCQ medication in a man assumed to have had psoriasis previously (3). In our patient, generalized pustular psoriasis cannot be ruled out, although the lack of history or future development of psoriasis and the unyielding nature of eruption to administration of corticosteroids do not favour this diagnosis.

Generalized pustulosis as a form of drug eruption is a rare yet a known entity (Table I, refs. 5–9). Searching the literature, we found a previous description of a generalized pustular rash during anti-

Table I. *Drugs associated with a generalized pustular rash*

	Ref.		Ref.
Ampicillin	(4)	Chloramphenicol	(8)
Cefazolin	(5)	Diltiazem	(9)
Cefalexin	(6)	Fusid	(8)
Cephadrine	(7)	Pyrimethamine	(8)

malarial therapy, although not regarded as such (8). We suggest that this etiology could account for our patient's eruption. The combination of HCQ with another quinine (quinidine bisulfate) that the patient was taking could have had an auxiliary effect for inducing this adverse reaction.

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