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CONTACT POINT

Drug-induced ultraviolet B photosensitivity due to hydroxychloroquine: The unexpected side effect

David Pesqué¹ | Juliette Pérez-Manich² | Irene García-Díez¹ |
Sonia Segura¹ | Marta Ferran¹ | Mònica Gonzàlez-Farré³ | Ramon M. Pujol¹ |
Ana M. Giménez-Arnau¹

¹Department of Dermatology, Hospital del Mar- Institut Mar d'Investigacions Mèdiques, Universitat Autònoma de Barcelona (UAB) and Universitat Pompeu Fabra (UPF), Barcelona, Spain

²Department of Dermatology, Hospital Universitari Arnau de Vilanova, Universitat de Lleida (UdL), Lleida, Spain

³Department of Pathology, Hospital del Mar- Institut Mar d'Investigacions Mèdiques, Universitat Autònoma de Barcelona (UAB), Barcelona, Spain

Correspondence

Ramon M. Pujol and Ana M. Giménez-Arnau, Department of Dermatology, Hospital del Mar- Institut Mar d'Investigacions Mèdiques, Universitat Autònoma de Barcelona (UAB) and Universitat Pompeu Fabra (UPF), Passeig Marítim, 25-29, 08003 Barcelona, Spain.

Email: rpujol@psmar.cat and anamariagimenezarnau@gmail.com

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Despite hydroxychloroquine (HC) having well-known photoprotective properties, photo-induced dermatoses may occasionally be triggered by this drug.¹⁻⁴

With the suspicion of a drug-induced reaction, and HC being the only imputable drug, patch testing (extended European baseline series and in-house prepared HC 5% pet.⁵) and photopatch testing (including HC 5% pet.) were performed in accordance to European guidelines.^{6,7} Patch and photopatch test readings were performed on Days 2, 4 and 7. All tests were applied on the back with Finn Chambers (Smart Practice, Phoenix, Arizona) on Scanpor tape (Norgesplaster, Vennessla, Norway). Patch tests were negative. Minimal erythema dose (MED) was normal for her phototype II (37 mJ/cm²). Despite the intake of oral corticosteroids until 48 h before testing, photopatch testing with ultraviolet B (UVB) 12 mJ/cm² was positive (+) for HC at 48 h following irradiation (i.e., Day 4 following the start of the test procedure) (Figure 1D), and negative on Day 7, whereas photopatch testing with UVA 5 J/cm² remained negative. In accordance with these results, HC was stopped and the flare-ups of the skin rash resolved within weeks. Three months later, the skin tests were repeated. All patch tests were again negative. MED was normal for her phototype. Photopatch testing with UVB again showed positive results for HC on Day 4 (++) and this time persisting on Day 7 (+). UVA testing was again negative. A biopsy of the positive photopatch reaction was taken and it showed features similar to the previous skin biopsy. During a 1-year follow-up, while avoiding HC, no further flare-ups of the skin rash occurred.

CASE REPORT

A 73-year-old woman, with a past history of oral lichen planus and frontal fibrosing alopecia, consulted our department due to a skin rash located in photo-distributed areas (neck, arms, dorsum of the hands, and face) which developed in the previous 4 weeks (Figure 1A,B). The rash was characterized by erythema, mild desquamation, and pruritus. No other skin or systemic symptoms were associated. Eight weeks prior to the onset of the eruption, HC had been prescribed for lichen planus. The patient had already taken HC in the past but it had been discontinued due to significant clinical improvement. A differential diagnosis between a drug-induced photodermatitis and an autoimmune disease was made. Initially, comprehensive autoimmune, serologic, and metabolic blood tests were obtained and a skin biopsy was performed. The former studies showed no relevant findings, whereas the latter disclosed an interface dermatitis with apoptotic keratinocytes (Figure 1C). There was no mucin deposition nor CD123 reactivity, and direct immunofluorescence was negative. Therefore, no findings favouring the possibility of a connective tissue disease were found.

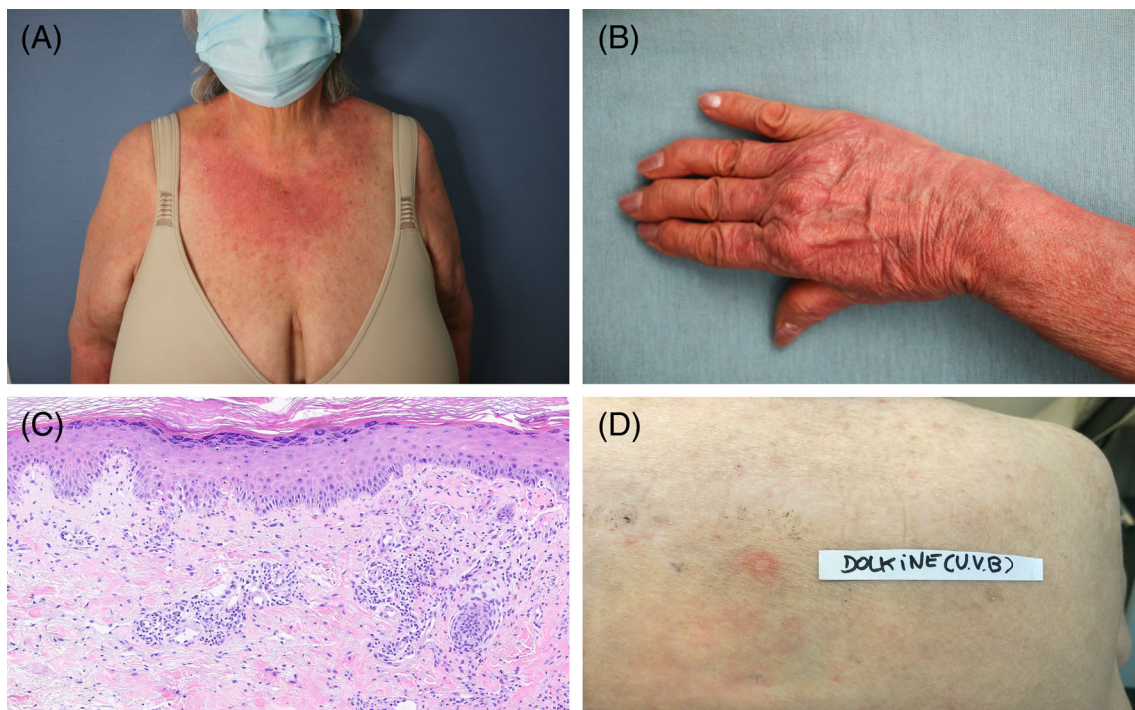


FIGURE 1 (A) Erythema and desquamation in the photo-exposed areas of neck and chest. (B) Erythema of the dorsum of the hand. (C) Histopathologic features: apoptotic keratinocytes at the dermal-epidermal junction and a discrete perivascular lymphocytic infiltrate in the upper dermis (H-E 200 \times). (D) Phototest positivity (+) for hydroxychloroquine (HC) 48 h following irradiation (first test session, Dolquine being the commercial name for the drug in Spain).

DISCUSSION

It has been hypothesized that photoallergic and phototoxic reactions in relation to HC are due to the expression of intracellular cell adhesion molecule-1 (ICAM-1) triggered by UV-induced cytokines.⁴ Previous studies have described a very heterogeneous nature of photopatch results in patients with photoallergy to chloroquine and HC, with occasional positivity to tests with UVA in the former, or, more commonly, with positive UVB testing in the latter.¹⁻⁴ In some cases, a reduced MED has also been detected.¹ We describe a case of HC-induced photosensitivity in which, despite a normal MED, photopatch testing evidenced positive results restricted to UVB wavelengths.

Systemic drugs are more frequently associated with phototoxicity.⁸ This case, however, presents an overlap between findings of phototoxicity (histology and some clinical features such as sharp delimitation of the lesions) and photoallergy (positive result to a low concentration of HC, presence of flare-ups, and previous exposure to the drug). One limitation of this study is that no controls for HC photopatch testing were performed; nevertheless, the test results are clear-cut positive, and rapid and complete resolution of the skin eruption occurred after withdrawal of the drug.

The aim of this report is to highlight that HC is a well-established possible cause of photo-induced reactions in clinical practice. Moreover, although most photosensitive reactions occur in the UVA range, the current reaction was only evidenced in the UVB range. An

increased awareness regarding this rare, but not exceptional side effect, seems necessary to perform the adequate confirmatory tests and avoid unnecessary diagnostic delays.

AUTHOR CONTRIBUTIONS

David Pesqué: Conceptualization; writing – original draft; formal analysis. **Juliette Pérez-Manich:** Conceptualization; formal analysis; writing – original draft. **Irene García-Díez:** Conceptualization; visualization. **Sonia Segura:** Visualization; formal analysis. **Marta Ferran:** Visualization; formal analysis. **Mònica González-Farré:** Methodology; formal analysis. **Ramon Pujol M:** Supervision; formal analysis; methodology. **Ana Giménez-Arnau M:** Supervision; methodology; visualization; conceptualization; formal analysis.




CONFLICT OF INTEREST

Ana M. Giménez-Arnau has been a medical advisor for Uriach Pharma/Neucor, Genentech, Novartis, FAES, GSK, Sanofi-Regeneron, Amgen, Thermo Fisher Scientific, Almirall, Celldex and Leo-Pharma. She has received research grants from Uriach Pharma, Novartis, and Instituto Carlos III- FEDER. She has participated in educational activities for Uriach Pharma, Novartis, Genentech, Menarini, Leo-Pharma, GSK, MSD, Almirall, Sanofi, Avène. All other authors declare that they have no relevant conflicts of interest.

CONSENT STATEMENT

The patient has given written consent to publish her case details.

1 ORCID

- 2 David Pesqué  <https://orcid.org/0000-0002-5821-9780>
- 3 Juliette Pérez-Manich  <https://orcid.org/0000-0003-2900-1173>
- 4 Ana M. Giménez-Arnau  <https://orcid.org/0000-0001-5434-7753>

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