

# An Unusual Presentation of Doxycycline-Induced Photosensitivity

Collin K. K. Yong, BSc, MB, ChB, FRCP(C)\*; Julie Prendiville, MB, MRCPI, FRCP(C)‡;  
Don L. Peacock, MB, ChB, FRCP(C)\*; Lawrence T. K. Wong, MBBS, FRCP(C)\*; and  
A. George F. Davidson, BSc, MD, FRCP(C)\*

**ABSTRACT.** Photoonycholysis in association with a generalized phototoxic reaction or as an isolated event is a well-recognized complication of the tetracycline group of antibiotics. We describe a 14-year-old white girl with cystic fibrosis who developed photoonycholysis of all 20 nails while receiving treatment with doxycycline. Pediatricians who prescribe tetracyclines should be aware of this potential complication. *Pediatrics* 2000;106(1). URL: <http://www.pediatrics.org/cgi/content/full/106/1/e13>; doxycycline, cystic fibrosis, photosensitivity, onycholysis, vitamin E, antioxidants.

Photosensitivity is a well-recognized complication of the tetracycline group of antibiotics.<sup>1-3</sup> Nail involvement is characterized by photoonycholysis and may occur in association with a generalized phototoxic reaction or, less commonly, as an isolated event.<sup>4,6</sup> This has rarely been reported in pediatric patients.<sup>7</sup> We report a teenage girl with cystic fibrosis who developed painful subungual hemorrhage while being treated with doxycycline.

## CASE REPORT

A 14-year-old white girl with cystic fibrosis was seen for evaluation of painful, discolored fingernails and toenails. Two weeks earlier, she was hospitalized with an acute deterioration in respiratory function. Sputum cultures were positive for *Pseudomonas aeruginosa*, *Stenotrophomonas maltophilia*, and *Burkholderia cepacia*, and she was treated with intravenous tobramycin and penicillin. *S maltophilia* and *B cepacia* were sensitive to doxycycline. She was discharged from the hospital on doxycycline (100 mg twice daily). The patient and mother were aware of tetracycline-induced photosensitivity and a chemical sunscreen with sun protection factor 45 was applied to all exposed areas of skin. Four days later, after spending time sunbathing, she complained of discomfort on the tips of her toes. This progressed to a throbbing pain that was unrelieved by 500 mg of acetaminophen. Within 3 days, the discomfort had spread to involve her fingernails. Nine days after the onset of symptoms a pinkish purple discoloration developed on the toenails. This darkened to a purple-black color and the fingernails became involved as well. The throbbing pain subsided as the discoloration progressed.

On physical examination, there was a purplish black subungual discoloration of the thumbnails and several toenails. There was violaceous erythema of the remaining nail beds (Fig 1). The nail plates showed no evidence of trauma or onycholysis. There was minimal residual tenderness. Mild clubbing was observed. The

remainder of the cutaneous examination revealed only slight facial erythema.

Doxycycline was discontinued after 17 days of treatment. The nail changes resolved spontaneously within the following 4 weeks. Onycholysis was not observed during this period. However, 4 months later, distal onycholysis was observed on the thumbnails and great toenails (Fig 2). Beau's lines were observed on all nails.

## DISCUSSION

The incidence of phototoxic cutaneous reactions to doxycycline is reported to be <5%. A study of 106 acne patients found a much higher incidence (35.8%) and suggested that the phenomenon is dose-related<sup>5</sup>; 20% of patients taking 150 mg/day of doxycycline developed a light-sensitive rash, whereas 42% of those taking 200 mg/day were affected. One of these patients had painful photoonycholysis.

Photoonycholysis refers to separation of the nail plate from the nail bed after exposure to ultraviolet light. Drug-induced photoonycholysis is seen most commonly with the second-generation tetracyclines, doxycycline and demeclocycline.<sup>6-8</sup> It may also occur with other tetracyclines and with psoralens and fluoroquinolones.<sup>1</sup> Pain in the nail bed or tips of the fingers and toes is often the first symptom with subsequent progression to subungual erythema, subungual hemorrhage, and onycholysis.<sup>4,8</sup> Pain and subungual erythema are infrequently the only manifestations at the time of presentation. Onycholysis develops after a variable period. Pain and tenderness seem to decrease as the nail changes become clinically evident. Three separate patterns of onycholysis have been described.<sup>8</sup>

It is suggested that patients with skin types 1 and 2 may be more susceptible to doxycycline photosensitivity than patients with darker skin pigmentation.<sup>9</sup> Both ultraviolet A and ultraviolet B radiation have been implicated.<sup>10</sup> The mechanism of the phototoxic reaction has not been fully elucidated. It is believed to be mediated by excited-state singlet oxygen and free radicals after irradiation with ultraviolet A radiation, thereby causing selective injury to mitochondria, within which doxycycline and other tetracyclines are localized.<sup>11</sup>

Antioxidant status may affect the degree of vulnerability to phototoxicity.<sup>12,13</sup> It is generally believed that cystic fibrosis patients may have low antioxidant status and, therefore, may be more vulnerable to damage by this mechanism.<sup>14</sup> It has been observed that cystic fibrosis patients have a high incidence of ciprofloxacin (quinolone)-induced phototoxicity.<sup>15</sup> A

From the Divisions of \*Biochemical Diseases and †Dermatology, Department of Pediatrics, British Columbia's Children's Hospital, University of British Columbia, Vancouver, British Columbia, Canada.

Received for publication Aug 19, 1999; accepted Feb 2, 2000.

Reprint requests to (A.G.F.D.) Room 2C66, Division of Biochemical Diseases, British Columbia's Children's Hospital, 4480 Oak St, British Columbia, Vancouver, Canada, V6H 3V4. E-mail: [gdaavidson@cw.bc.ca](mailto:gdaavidson@cw.bc.ca)

PEDIATRICS (ISSN 0031 4005). Copyright © 2000 by the American Academy of Pediatrics.

**Fig 1.** Purplish black discoloration of the thumbnails and erythema of the fingernail beds.



**Fig 2.** Distal onycholysis and hemorrhage of the great toenails 4 months later. Transverse Beau's lines are seen on all nails.

vitamin E level measured in our patient was 11.8  $\mu\text{mol/L}$  (13.0–24). She was prescribed a vitamin E supplement.

A number of possible explanations for why the nails should be a site of predilection for phototoxic damage in some patients have been proposed. Irradiation with 313- to 500-nm wavelengths (3%–20%) can penetrate a .7-mm fingernail plate.<sup>8</sup> The nail acts as a convex lens, which may enhance and concentrate ultraviolet penetration. There is less melanin and, therefore, less ultraviolet protection in the nail beds than in other sites. It is also possible that application of chemical sunscreen may afford sufficient photoprotection for exposed areas of skin while leaving the nail bed unprotected. The cause of the intense pain during the early stages of the process is unclear but may be related to vasodilation of the nail bed capillaries.

As a differential diagnosis, trauma was excluded because this could not occur symmetrically on all 20 nail beds without evidence of nail damage. The clin-

ical presentation of subungual hemorrhage on all 20 nail beds would not be consistent with a fixed drug eruption, which occurs as circumscribed round to oval patches with erythema in localized areas. Hemorrhagic lesions secondary to raised intravascular pressure from coughing usually lead to petechiae and not subungual erythema and hemorrhage.

With renewed interest in the use of tetracyclines and their second-generation derivatives for the treatment and prophylaxis of specific infectious diseases, it is important for physicians and pediatricians to be aware of potential photosensitivity. This may be more common in cystic fibrosis patients or others with compromised antioxidant status. Rarely, as in our patient, pain and discoloration of the nail beds may be the sole manifestation of phototoxicity. Fair-skinned patients who are prescribed doxycycline during the summer months should be advised to avoid sun exposure. Reassurance may be given that the complication is not dangerous but potentially painful.

## REFERENCES

1. Kapusnik-Uner JE, Sande MA, Chambers HF. Tetracyclines, chloramphenicol, erythromycin and miscellaneous antibacterial agents. In: *The Pharmacological Basis of Therapeutics*. 9th ed. New York, NY: McGraw-Hill Companies, Inc; 1996:1123–1153
2. Joshi N, Miller DQ. Doxycycline revisited. *Arch Intern Med*. 1997;157:1421–1428
3. Edwards R. Doxycycline and photosensitivity. *N Z Med J*. 1987;100:640
4. Segal BM. Photosensitivity, nail discoloration and onycholysis. *Arch Intern Med*. 1963;112:63–65
5. Layton AM, Cunliffe WJ. Phototoxic eruptions due to doxycycline—a dose related phenomenon. *Clin Exp Dermatol*. 1993;18:425–427
6. Maibach H. Second generation tetracyclines: a dermatologic overview. *Cutis*. 1991;48:411–417
7. Coffin SE, Puck J. Painful discoloration of the fingernails in a 15-year-old boy. *Pediatr Infect Dis J*. 1993;12:702–706
8. Baran R, Juhlin L. Drug induced photo-onycholysis. *J Am Acad Dermatol*. 1987;17:1013–1016
9. Smith EL, al Raddadi A, al Ghamdi F, Kutbi S. Tetracycline phototoxicity. *Br J Dermatol*. 1995;132:316–317. Letter
10. Bjellerup M, Ljunggren B. Differences in phototoxic potency should be considered when tetracyclines are prescribed during summertime: a study on doxycycline and lymecycline in human volunteers, using an objective method for recording erythema. *Br J Dermatol*. 1994;130:356–360
11. Shea CR, Olack GA, Morrison H, Chen N, Hasan T. Phototoxicity of lumidoxycycline. *J Invest Dermatol*. 1993;101:329–333
12. Darr D, Dunston S, Faust H, Pinnell S. Effectiveness of antioxidants (vitamin C and E) with and without sunscreens as photoprotectants. *Acta Derm Venereol*. 1996;76:264–268
13. Lopez-Torres M, Thiele JJ, Shindo Y, Han D, Packer L. Topical application of alpha-tocopherol modulates the antioxidant network and diminishes ultraviolet-induced oxidative damage in murine skin. *Br J Dermatol*. 1998;138:207–215
14. Dominquez C, Gartner S, Linan S, Cobos N, Moreno A. Enhanced oxidative damage in cystic fibrosis patients. *Biofactors*. 1998;8:149–153
15. Peacock D, Wong LTK, Davidson AGF. Photosensitivity due to ciprofloxacin in children with cystic fibrosis. *Israel J Med Sci*. 1996;32:S170

**An Unusual Presentation of Doxycycline-Induced Photosensitivity**  
Collin K. K. Yong, Julie Prendiville, Don L. Peacock, Lawrence T. K. Wong and A.  
George F. Davidson  
*Pediatrics* 2000;106:e13  
DOI: 10.1542/peds.106.1.e13

**Updated Information & Services**

including high resolution figures, can be found at:  
<http://pediatrics.aappublications.org/content/106/1/e13>

**References**

This article cites 14 articles, 0 of which you can access for free at:  
<http://pediatrics.aappublications.org/content/106/1/e13#BIBL>

**Subspecialty Collections**

This article, along with others on similar topics, appears in the following collection(s):

**CME**  
<http://www.aappublications.org/cgi/collection/cme>

**Permissions & Licensing**

Information about reproducing this article in parts (figures, tables) or in its entirety can be found online at:  
<http://www.aappublications.org/site/misc/Permissions.xhtml>

**Reprints**

Information about ordering reprints can be found online:  
<http://www.aappublications.org/site/misc/reprints.xhtml>

American Academy of Pediatrics

DEDICATED TO THE HEALTH OF ALL CHILDREN®



# PEDIATRICS®

OFFICIAL JOURNAL OF THE AMERICAN ACADEMY OF PEDIATRICS

## **An Unusual Presentation of Doxycycline-Induced Photosensitivity**

Collin K. K. Yong, Julie Prendiville, Don L. Peacock, Lawrence T. K. Wong and A.

George F. Davidson

*Pediatrics* 2000;106:e13

DOI: 10.1542/peds.106.1.e13

The online version of this article, along with updated information and services, is located on the World Wide Web at:

<http://pediatrics.aappublications.org/content/106/1/e13>

Pediatrics is the official journal of the American Academy of Pediatrics. A monthly publication, it has been published continuously since 1948. Pediatrics is owned, published, and trademarked by the American Academy of Pediatrics, 345 Park Avenue, Itasca, Illinois, 60143. Copyright © 2000 by the American Academy of Pediatrics. All rights reserved. Print ISSN: 1073-0397.

American Academy of Pediatrics

DEDICATED TO THE HEALTH OF ALL CHILDREN®

