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.

P hotosensitivity is a well-recognized complication of the tetracycline group of antibiotics.1-3 Nail involvement is characterized by photoonycholysis and may occur in association with a generalized phototoxic reaction or, less commonly, as an isolated event.4,6 This has rarely been reported in pediatric patients.7 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 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;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.6-8 It may also occur with other tetracyclines and with psoralens and fluoroquinolones.1 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.4,8 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.8

It is suggested that patients with skin types 1 and 2 may be more susceptible to doxycycline photosensitivity than patients with darker skin pigmentation.9 Both ultraviolet A and ultraviolet B radiation have been implicated.10 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.11 Antioxidant status may affect the degree of vulnerability to photosensitivity.12,13 It is generally believed that cystic fibrosis patients may have low antioxidant status and, therefore, may be more vulnerable to damage by this mechanism.14 It has been observed that cystic fibrosis patients have a high incidence of ciprofloxacin (quinolone)-induced photosensitivity.15 A
vitamin E level measured in our patient was 11.8 μmol/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. 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 clinical presentation of subungal 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 subungal 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.
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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

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