

# Sporotrichoid *Mycobacterium marinum* skin infection treated with minocycline hydrochloride

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*Mycobacterium marinum* is the most commonly reported cause of atypical mycobacterial skin infections. The infections usually resolve spontaneously within 3 years, but have occasionally persisted for more than 40 years.<sup>1-3</sup> The chemotherapeutic approach to treatment of the infections by internists and specialists in infectious diseases has been with various combinations of ethambutol, isoniazid, and rifampin.<sup>4-6</sup> Several recent reports by dermatologists have documented the effectiveness of treatment with tetracycline hydrochloride and minocycline hydrochloride.<sup>6-9</sup> Our patient had the sporotrichoid variety of *M. marinum* infection and responded rapidly to treatment with minocycline hydrochloride.

## Case report

A small lump developed on the right dorsal fourth finger of a 54-year-old black woman in February 1977. The lesion did not heal and 2 weeks later similar lesions appeared on the right dorsal hand and forearm. Most of the lesions gradually became larger but were not painful. The patient felt well and had no fever or chills. Several of the lumps decreased in size spontaneously during a 4-week period leaving small residual lumps in the skin.

A dermatologist was consulted in April 1977, and skin biopsy specimens from the right wrist showed "acute and chronic granulomatous inflammation." Cultures and

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special histochemical stains were negative for deep fungus and acid-fast organisms.

Treatment with liquid nitrogen, iodo-chlorhydroxyquin-hydrocortisone cream, gentamicin sulfate 0.1% cream, and erythromycin given orally had no effect.

The patient was a homemaker and also did custodial work in a hospital. She did not recall receiving any traumatic injuries to the right hand or fingers. However, her husband fished regularly in Lake Erie and she usually cleaned the fish.

The patient was referred to the Cleveland Clinic in April 1978. She had undergone a simple mastectomy for carcinoma of the left breast in 1964. Latent syphilis had been treated with penicillin intramuscularly in 1949 and again in 1977. Examination revealed multiple nontender, erythematous nodules, 1 to 2.5 cm in diameter, extending in a linear fashion from the right dorsal fourth finger to the mid-right extensor forearm (*Fig. 1*).

### Laboratory studies

Results of laboratory studies revealed a hemoglobin of 13.9 g/dl; white blood cell count (WBC), 9200 mm<sup>3</sup>; and red blood cell (RBC) indices were normochromic. The serum cholesterol value was mildly elevated at 325 mg/dl. Examination of a random urine specimen revealed occasional red blood cells. The RPR was reactive at 1:4 dilutions and the FTA was positive. A chest x-ray film revealed clear fields with increased tortuosity and prominence of the aortic arch. The electrocardiogram was normal.

### Histopathology

Skin biopsy specimens from the right forearm, right wrist, and right dorsal fourth finger showed subcutaneous nodules with concentric zones of inflammation. The outermost zone was composed of epithelioid and multinucleated giant cells and the central zone showed abscess formation. The periodic acid-



**Fig. 1.** Multiple erythematous nodules extending in linear fashion from dorsal right hand onto forearm.

Schiff (PAS) and acid-fast stains were negative for organisms.

### Cultures and susceptibility studies

Portions of the skin biopsy specimens were processed for acid-fast culture. Luxuriant growth of a smooth, buff-colored colony at 32 C was noted at 22 days. Light growth of similar-looking colonies was noted at 37 C. The colonies produced a yellow pigment after exposure to light. Results of niacin and nitrate tests were negative. Tween hydrolysis was positive at 48 hours. These features identified the organism as *M. marinum*. In vitro susceptibility studies re-

vealed the organism to be susceptible to minocycline hydrochloride at 12  $\mu\text{g}/\text{ml}$  and also to tetracycline hydrochloride at 25  $\mu\text{g}/\text{ml}$ .

### Clinical course

The patient was started on a regimen of minocycline hydrochloride, 200 mg/day. The nodules were much smaller after 4 weeks of treatment and had resolved completely by 8 weeks (Fig. 2). Treatment was continued for an additional 6 weeks. Routine follow-up in June 1979 revealed no recurrence of the infection.



Fig. 2. Skin lesions have nearly resolved after 8 weeks treatment with minocycline hydrochloride, 200 mg/day.

### Discussion

*M. marinum* infections have been reported from both fresh and salt water regions of the world. The patient in this report most probably incurred an inapparent injury while cleaning fish caught in Lake Erie. This injury to the skin provided the portal of entry for the organism. The skin nodules occurred in a sporotrichoid distribution, which is not uncommonly seen with *M. marinum* infections.<sup>6,10</sup>

In the past 5 years several reports have been published advocating treatment of *M. marinum* infections with tetracyclines.<sup>7-9</sup> The initial report cited six cases, all of which responded to tetracycline hydrochloride at a dose of 1 to 1.5 g/day.<sup>7</sup> The healing time was 8 to 16 weeks. Drug susceptibility studies were reported on only two of the six cultured organisms and these showed resistance to tetracycline hydrochloride at 100  $\mu\text{g}/\text{ml}$ . This apparent resistance of *M. marinum* to tetracycline hydrochloride in vitro coupled with the excellent clinical response in the patients suggested that the drug did not have a direct antibacterial effect on the organism. The author postulated that the anti-inflammatory qualities of tetracycline might better explain its effect on *M. marinum*.

Izumi et al<sup>8</sup> subsequently reported clearing of *M. marinum* infections with tetracycline hydrochloride at a dose of 2 g/day. In vitro susceptibility studies showed all five cultured organisms to be susceptible to tetracycline hydrochloride at 25 to 50  $\mu\text{g}/\text{ml}$ . The authors believed the clinical response of the five patients was due to a direct antimicrobial effect of tetracycline hydrochloride on *M. marinum*. Pien<sup>11</sup> later noted that the in vitro antimicrobial studies reported by Izumi et al<sup>8</sup> did not correlate well with serum levels of tetracycline hy-

drochloride that would be produced by a dose of 2 g/day. They implied that a direct antimicrobial effect did not completely explain the clinical response of *M. marinum* infections to tetracycline hydrochloride.

Loria<sup>9</sup> reported resolution of three *M. marinum* infections following treatment with minocycline hydrochloride, 200 mg/day. Unfortunately, in vitro drug susceptibility studies were not done in this series.

We believe that the case reported here is the first to show minocycline hydrochloride activity against *M. marinum* clinically and also in vitro. The organism was susceptible to minocycline hydrochloride in vitro at a concentration of 12 µg/ml. The patient received oral doses of 200 mg/day, which would be expected to give serum levels of 2 to 4 µg/ml.<sup>12</sup> These serum levels do not approach the 12 µg/ml required for in vitro inhibition of the organism from our patient. It is not known whether *M. marinum* granulomas can concentrate tetracycline or minocycline. The fact that the organisms are surrounded by an area of granulomatous inflammation may make the organisms more susceptible to tetracycline or minocycline.

Our patient responded to minocycline hydrochloride at a dose of 200 mg/day. The skin lesions resolved in 8 weeks and treatment was continued for an additional 6 weeks in an attempt to avoid relapse.

Further reports on *M. marinum* infections responding to minocycline hydrochloride may confirm the value of minocycline hydrochloride in the treatment of *M. marinum* infections.

## Summary

A patient with the sporotrichoid variety of *M. marinum* infection was treated with minocycline hydrochloride, 200 mg/day. In vitro susceptibility studies had shown the organism to be susceptible to minocycline hydrochloride at a level of 12 µg/ml. The skin lesions resolved completely by 8 weeks and there was no recurrence after a 15-month follow-up.

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