Generalized Annular Borderline Tuberculoid Leprosy and Update in Management of Hansen's Disease

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GOAL

To review the identification and treatment of leprosy.

OBJECTIVES

1. To discuss the epidemiology and bacteriology of leprosy.
2. To outline the clinical presentations and classifications of leprosy.
3. To describe the recommended therapy for leprosy.

CME Test on page 210

We describe a patient with widespread borderline tuberculoid leprosy and significant peripheral nerve involvement. Despite the presence of widespread lesions, Fite stains and polymerase chain reaction studies were initially negative. We discuss the diagnosis and treatment of leprosy including recent changes in treatment regimens and duration.

Most patients with widespread lesions of leprosy have many organisms easily demonstrated in tissue sections (multibacillary disease). We describe a patient with negative stains and polymerase chain reaction studies despite widespread cutaneous lesions.

Case Report

A 73-year-old white male presented with a two-year history of chronic, erythematous, indurated, annular, and polycyclic plaques without associated epidermal change (Figure 1). The lesions ranged from 3 to 10 cm in diameter and were distributed over the abdomen, back, and lower extremities (Figures 2 and 3). Examination was also remarkable for a claw hand, which the patient had attributed to a surgical procedure involving the ulnar nerve several years before his cutaneous disease manifestations. Laboratory tests including complete blood cell count, blood chemistries, hepatic panel, and chest x-ray were normal. Examination of a biopsy of a representative plaque revealed granulomatous dermatitis with many naked granulomas, some in association with small nerves (Figure 4). Acid-fast bacilli and fungal stains were negative, as were cultures for *Mycobacterium* and fungus. PCR (polymerase chain reaction) results for atypical mycobacteria (including *Mycobacterium leprae*) were negative. Upon questioning for other organ involvement, the patient noted decreased sensation in his left arm and he was referred to a neurologist, who confirmed neurologic deficits "compatible with sarcoidosis." A trial of prednisone was instituted. His cutaneous lesions resolved completely but recurred several months later once the dose was tapered to 20 mg. Based on our clinical suspicion of Hansen's disease, he had four additional punch biopsies taken from lesions on his trunk, abdomen, and leg. Histologic analysis was confirmatory for Hansen's disease with a Fite stain showing rare acid-

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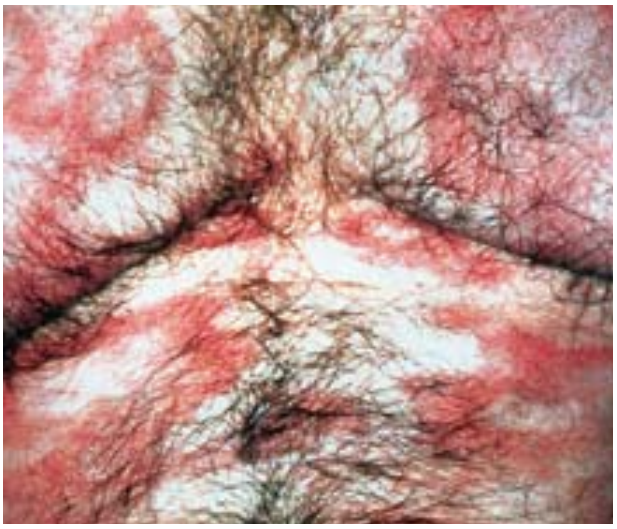

FIGURE 1. Anterior trunk, generalized, polycyclic erythematous plaques.

fast bacilli (Figure 5). He was started on dapsone 100 mg daily, rifampin 600 mg monthly, and clofazamine 50 mg daily. The monthly dose of rifampin was selected over the usual daily regimen to minimize interaction with the coumadin he was also given. Rifampin given as a monthly 600-mg dose is highly bacteriocidal and almost as effective as daily rifampin.[1]

Discussion

Epidemiology and Bacteriology–Leprosy affects over 1.15 million people worldwide[1] and over 7,000 in the United States.[2]The widespread implementation of multi-drug therapy has reduced the numbers from the 10 to 12 million cases in the mid-1980s.[1] Leprosy is endemic in sub-Saharan Africa, India, Southeast Asia, and Brazil.[3] Although most new cases in the United States have occurred among immigrants from leprosy-endemic countries,[2] the disease is also endemic to the southern states (including Texas, Louisiana, Florida, and California) and Hawaii. A high index of suspicion must be maintained in patients who present with skin disease in conjunction with focal anesthesia or motor neuropathy. New multi-drug treatment regimens have reduced the length of therapy considerably for this treatable and curable disease. In addition, multi-drug therapy offers not only a cure but also the chance for global elimination of leprosy [currently the goal of the World Health Organization (WHO)].

The causative organism, *M. leprae*, is a slow-growing, acid-fast bacillus that cannot be cultured *in vitro*. However, it can be slowly cultured within mouse footpads, an advance that first allowed drug sensitivity testing. The organism has a predilection for peripheral nerves and the skin of the cooler parts of the body. Hansen's disease has a long incubation period

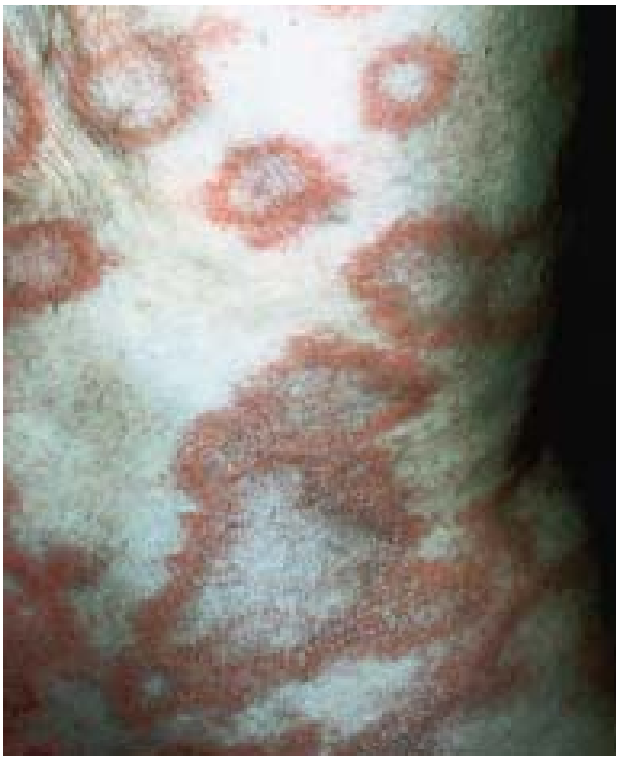

FIGURE 2. Close-up of truncal plaque.

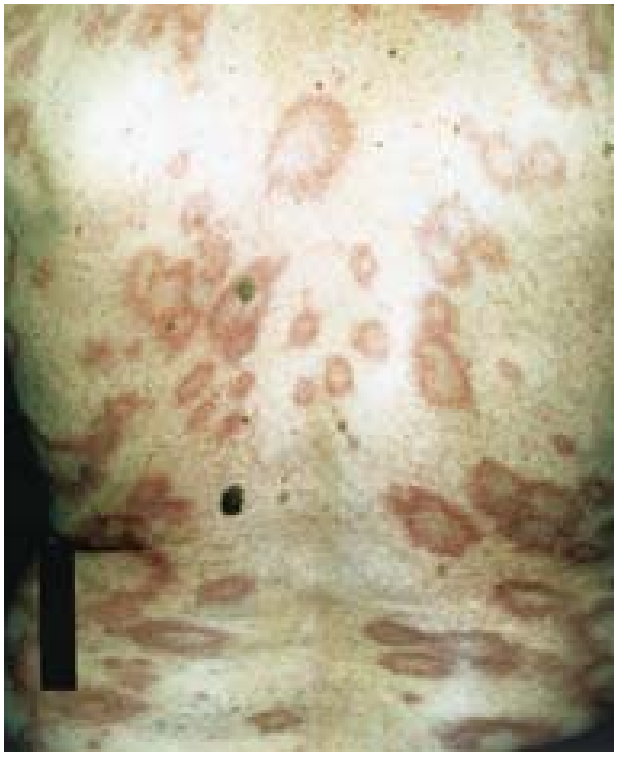

FIGURE 3. Lesions ranging in size from 3 to 10 cm on the back.

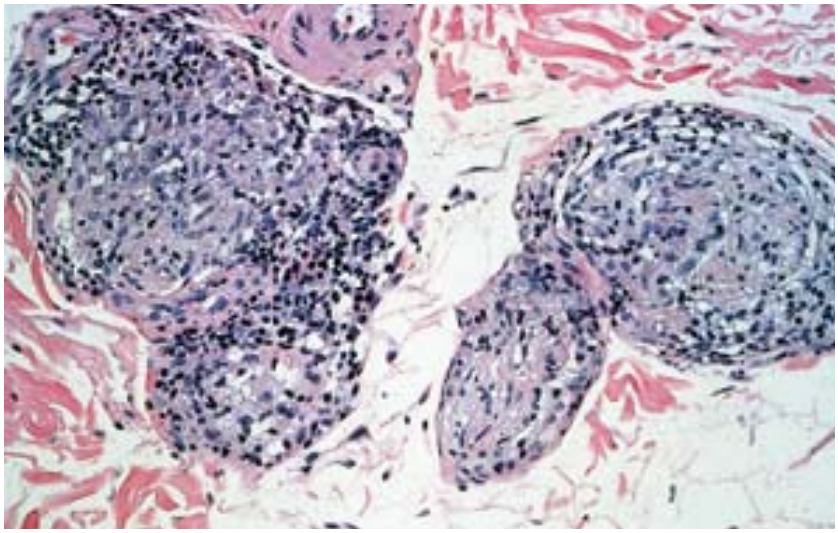

FIGURE 4. Skin biopsy shows granulomatous dermatitis, some in association with small nerves (H&E).

ranging from 6 months to several decades, with an average of 2 to 5 years.[4]

Leprosy is believed to be spread by airborne droplets from the nasal mucosa or upper respiratory tract. The nine-banded armadillo also serves as an animal reservoir of the disease. Our patient related a history of hunting and eating armadillo as a 10- to 11-year-old child and had killed an armadillo at his home in 1983. Studies have shown the prevalence of *M. leprae* infection in armadillos in Lousiana and Texas to be 2 to 12%.[5] Transmission from armadillos is supported by reports of leprosy in patients who have a history of hunting, trapping, curing, skinning, eating, or wrestling armadillos.[5]

Clinical Presentations and Classifications–The standard nomenclature divides cases into five groups based on the clinical types of lesions and the histopathologic findings: 1) tuberculoid; 2) borderline tuberculoid; 3) borderline; 4) borderline lepromatous; and 5) lepromatous.[5]

The WHO recently instituted a new simplified classification.[1] The three categories are based simply on the number of clinical lesions: paucibacillary "single-lesion" leprosy (one lesion), paucibacillary (two to five lesions), and multibacillary (more than five skin lesions) leprosy.

Borderline forms of leprosy are unstable. They change as a patient's immune response changes, drawing closer to either the tuberculoid spectrum or the lepromatous form. Our patient's disease is best classified as borderline tuberculoid leprosy.

To confirm the diagnosis, either an incisional or large punch biopsy (such as a 6 mm) should be taken from the edge of an active lesion and should include the deep fat. A Fite stain should be requested to confirm the presence of acid-fast bacilli, and all slides must be examined thoroughly and diligently. Skin slit smears, which may be taken from the center of any lesion, are also usually obtained from the following standard peripheral sites: both ears, elbows, and knees. It is important to realize that despite numerous and widespread cutaneous lesions, borderline tuberculoid leprosy may show few if any acid-fast organisms. PCR for Hansen's bacilli is now available. Specimens may be transported in alcohol. Specimens placed in formalin must be processed and embedded in paraffin within 24 hours. Despite prompt processing, PCR may be negative, especially in paucibacillary forms of leprosy.

Updated Treatment Regimens from Carville and WHO–Multi-drug regimens for the treatment of leprosy are now standard. WHO recommended regimens[1] reflect difficulties in follow-up and cost considerations in nations with limited financial resources. A single-dose combination consisting of 600 mg of rifampin, 400 mg of ofloxacin, and 100 mg of minocycline (known commonly as "ROM") has been used as a regimen to treat "single-lesion" paucibacillary leprosy. The regimen for most paucibacillary disease consists of multidrug therapy (MDT) with rifampin (600 mg once a month, supervised) and dapsone (100 mg daily, self-administered) for 6 months. Multibacillary disease is treated with three drugs: rifampin (600 mg once a month, supervised), clofazimine (300 mg once a month, supervised, and 50 mg once daily, self-administered), and dapsone (100 mg daily, self-administered) for 24 months. Worldwide, the WHO reports a relapse rate below 1 per 1000 patients per year with MDT. Drug resistance following MDT has not been reported (WHO). Within 3 months of starting treatment with dapsone or within 1 to 2 weeks after starting rifampin, patients are no longer contagious.[5,6]

The Gillis W. Long Hansen's Disease Center in Carville, Louisiana, proposed these updated regimens

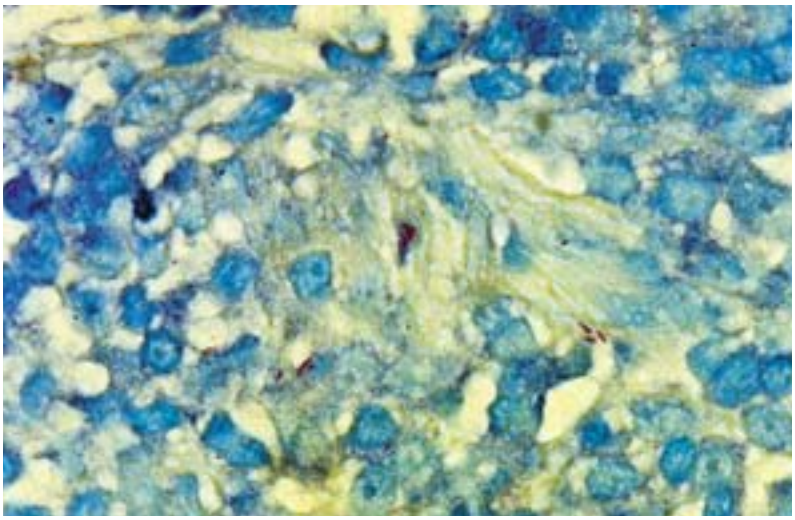

FIGURE 5. Fite stain showing few rare acid-fast bacilli.

in June 1997 for all newly diagnosed Hansen's disease patients in the United States: 1) for paucibacillary disease, dapsone 100 mg daily, plus rifampin 600 mg daily, for 1 year; 2) for multibacillary disease, dapsone 100 mg daily, rifampin 600 mg daily, and clofazamine 50 mg daily, for 2 years. The patients should have follow- up every 6 months for 2 years after the treatment is completed, and then annually for 3 more years for paucibacillary cases and for 8 more years for multibacillary cases.

In the event of intolerance or toxicity to the aforementioned regimens, the Hansen's Disease Center may be contacted for recommendations on alternative regimens. Medications used as alternatives include ofloxacin, clarithromycin, and minocycline.

Further Information

The National Ambulatory Hansen's Disease Center can be reached by telephone at 1-800-642-2477 (fax: 504 642-4774). Although they do plan to move from Carville, Louisiana, in the future, they will continue to provide consultative services, medications, histologic interpretations, patient evaluations, and rehabilitative services, and are quite generous in their assistance.

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Dr. Elston reports no conflict of interest.