Molecular Origin of Endemic Leprosy in New York City

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We report an indigenous case of leprosy in New York City in an immunocompetent patient who was infected with a Mycobacterium leprae genotype that is consistent with an exogenous origin. Physicians in the eastern United States should be alerted that, although most patients who develop leprosy in the United States are foreign born, native-born Americans are also susceptible to the infection.

Leprosy is a chronic granulomatous infection of the skin and peripheral nerves that is caused by the intracellular bacterium Mycobacterium leprae. Although the burden of leprosy is greatest in developing countries, patients may present with disease long after leaving a region of endemicity [1]. In the United States, these cases of imported leprosy comprise 90% of diagnosed cases [2]. Until the past decade, patients with leprosy in the eastern United States were sent to the US leprosarium, which closed in 2000. The advent of effective multidrug therapy and the introduction of the Regional Hansen’s Disease Program in the 1980s led to a shift in management of patient care from leprosaria to ambulatory care programs [3]. We report a case of indigenous leprosy in an immunocompetent adult with molecular evidence of an exogenous origin.

Case report. The patient was a 43-year-old African-American man born in the Bronx, New York, with no history of travel outside of the United States. In 2002, he presented to his primary care physician with a single erythematous lesion on his left biceps but was told that it was inconsequential. Four years later, the patient presented to the New York University School of Medicine Dermatology Clinic (New York, NY) with complaints of multiple erythematous plaques, nasal congestion, and intense right elbow pain. On examination, there was a total of 5 infiltrated, erythematous, well-demarcated, nontender plaques with surrounding hypopigmentation on his upper arms, right buttck, and posterior thigh. The plaques were hypoaesthetic. The patient had evidence of motor neuropathy in the median and ulnar nerve distribution of his hands. Biopsy specimens from 2 skin lesions revealed granulomatous inflammatory infiltrate, and positive Fite stain findings were diagnostic of borderline tuberculoid leprosy. The patient was otherwise healthy, with a medical history remarkable for injury to the fifth and sixth vertebrae while in the military. At 18 years of age, the patient was stationed in North Carolina for 3 years while completing his service in the US Marine Corps. He denied history of exposure to armadillos or a history of sarcoidosis. Results of serological studies for leprosy that were performed at the time of diagnosis were negative for HIV and hepatitis B antibodies. The patient’s electrolyte levels, WBC count, and urea level were within normal limits.

The patient started receiving therapy with oral dapsone (50 mg/day) and minocycline (100 mg/day) for leprosy. Minocycline is an alternate for clofazimine, which now requires informed consent in the United States. Although the standard dosage for initiating dapsone is 100 mg/day and the patient demonstrated glucose–6-phosphate dehydrogenase activity within normal limits, he was monitored for evidence of hemolytic anemia at the lower dosage of dapsone prior to advancing his dosage to 100 mg/day. Approximately 2 weeks later, the patient developed symptoms of a reversal reaction (type I), characterized by bilateral tenderness of the ulnar nerve and swelling of the ulnar and median nerves. Minocycline therapy was discontinued, and prednisone was added to the patient’s regimen at an initial dosage of 60 mg/day. His neuritis and skin lesions responded to therapy, and the prednisone dosage was subsequently titrated down over 6 months. The patient’s current treatment includes prednisone (20 mg/day) and dapsone (50 mg/day), and minocycline therapy (100 mg/day) was restarted. Because rifampin also upregulates the hepatic pathway, rifampin will be added after prednisone is completely withdrawn [3].

In this study, skin biopsy specimens were genotyped for single-nucleotide polymorphisms (SNPs) for 3 loci in M. leprae, as described by Monot et al. [4]. In brief, genomic DNA was extracted from skin biopsy specimens and was subjected to nested PCR, with conditions described elsewhere [5], and subsequent sequencing of PCR amplicons. Genomic DNA from
M. leprae strain Br4923 and Mycobacterium tuberculosis H37rv was used as positive and negative controls, respectively.

**Results.** DNA extracted from the patient’s skin biopsy specimens was identified as M. leprae SNP type 2 (figure 1), whereas genomic DNA from strain Br4923 was identified as SNP type 4 (data not shown) [4].

**Discussion.** An early epidemiologic survey of leprosy in New York revealed that 99 of 100 leprosy cases occurred in foreign-born patients [1]. In 1998, ~85% of leprosy cases reported in the United States occurred in immigrants [6], with changes in leprosy incidence largely accounted for by immigration from regions where leprosy was endemic [1, 2]. The incidence of indigenous cases of leprosy may be underestimated, because foreign-born patients from countries where leprosy is endemic were assumed to have been exposed to leprosy in their country of origin; however, this classification does not account for those immigrants who may have contracted leprosy in the United States. We have described a native-born American who contracted leprosy despite an absence of travel to areas of endemcity or known exposure to infected animals or individuals.

The major risk factor for contracting leprosy is exposure to infected individuals [7]. We performed a laboratory investigation for a patient with leprosy who had no known risk factors to establish the geographic origin of the M. leprae strain. Our study provides molecular evidence of secondary transmission of imported leprosy in the eastern United States and raises important questions regarding the surveillance of leprosy and the likelihood of secondary transmission in the United States.

At least 4 distinct SNP genotypes of M. leprae have been reported [4]. Minimal geographic overlap is observed between SNP types, with heterogeneity in SNP genotypes observed in locations where multiple human ethnic migrations have occurred [4]. Wild armadillos from Louisiana are infected with M. leprae that are predominantly SNP type 3 [4], making it less likely that our patient contracted leprosy from an animal source. In contrast, the M. leprae strain recovered from our patient was identified as SNP type 2, which corresponds to an east African/south Asian origin [4]. Additional genotyping studies are warranted to confirm the global distribution of M. leprae SNP genotypes. In the initial analysis by Monot et al. [4], SNP type 2 was found in 14 of 175 samples, with a limited number of samples from selected countries in Africa and Asia; additional sampling in additional geographic locations would minimize sample-size bias.

The mechanism by which M. leprae is disseminated to new hosts remains unclear; however, genetic predisposition, proximity to infected contacts, and nutritional status may each play a role in susceptibility [7]. Copious acid-fast bacilli were recovered from the nasal secretions of patients with lepromatous leprosy, demonstrating that it is likely that transmission can be airborne [3]. It is difficult to establish the period when our patient was exposed to M. leprae, because the incubation period between infection and symptomatic illness may last for years [3].

The chronic course of leprosy may be complicated by 2 categories of acute inflammatory reactions: type I (reversal reaction) and type II (erythema nodosum leprosum) [8]. Reversal reactions are a consequence of an upregulated Th1 response to M. leprae and are characterized by edema, neuritis, and outlining of skin lesions by erythema [3]. Type II reactions involve an immune complex–mediated vasculitis that results in formation of subcutaneous tender nodules of the skin [3]. Type I reactions are treated with oral prednisone, and thalidomide is used to treat type II reactions [3].

Because of the current case from the Bronx, New York, along with another recent endemic case in Georgia, it is especially important for physicians in the eastern United States to be alerted so that they are aware that endemic cases of leprosy have recently been detected in the United States. Although the patient in Georgia was reported to have had exposure to an armadillo [9], no direct exposure was reported in the article, and no armadillo with leprosy has been identified east of Mississippi [10]. Because of the development of SNP and variable-number tandem repeat loci analyses for strain typing of M. leprae [4, 11], it is possible to examine these cases with mo-

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Figure 1. Single nucleotide polymorphism (SNP) analysis of Mycobacterium leprae from patient skin biopsy specimens. The results of DNA sequencing of 3 loci (positions 14676, 1642875, and 2935685) in M. leprae, after PCR amplification of skin biopsy specimens from the patient, are shown for determination of the SNP genotype.
molecular methods to determine reservoir and mode of transmission.

Because of our molecularly proven endemic case of leprosy, it is important to alert physicians in the eastern United States that leprosy is known to occur in native-born Americans. Although the majority of cases occur in immigrants from the Caribbean, South America, Asia, and Africa (including HIV-infected patients) [12], native-born Americans are also susceptible. The recent recognition of HIV infection and leprosy in patients treated with infliximab [13] makes it especially important for physicians to be aware that leprosy is not disappearing [14].

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References