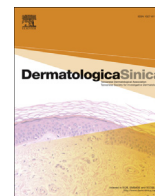


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## CASE REPORT

### Leprosy mimicking lupus erythematosus

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#### ABSTRACT

Leprosy, a contagious and chronic granulomatous disease caused by *Mycobacterium leprae*, is classically known to have cutaneous and neurologic sequelae. Leprosy usually has a long incubation period and may manifest with a variety of autoimmune phenomena reminiscent of autoimmune diseases, such as systemic lupus erythematosus (SLE) or rheumatoid arthritis. We describe a case of a 40-year-old man presenting with a long history of recurrent skin rashes and hand numbness, initially diagnosed as carpal tunnel syndrome and SLE, who was later proven to have borderline leprosy. This suggests that this underappreciated disease should still be considered in the differential diagnosis of granulomatous skin rashes with rheumatic manifestations, even in nonendemic regions.

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#### Introduction

Leprosy, also known as Hansen's disease, is a chronic granulomatous disease affecting mainly the skin and nerves caused by *Mycobacterium leprae*. The course and clinical manifestations of the disease are largely dependent on an individual's immune response to *M. leprae* and can be roughly classified into tuberculoid, borderline, and lepromatous forms. It has long been known that numerous clinical and serological similarities exist between patients with leprosy and connective tissue diseases. These varying clinical manifestations, as well as a tendency of the disease to have a protracted course, often lead to a delay in early recognition and diagnostic confusion. We report a patient with borderline leprosy who had initially been misdiagnosed for several years.

#### Case report

A 40-year-old Myanmar-born man, living in Taiwan for 25 years, presented to our hospital for acute appendicitis. During the admission period, an in-patient dermatology consultation was called to evaluate skin lesions and joint deformities. According to the patient, he had suffered from bilateral hand and wrist pain, swelling, and deformities for 4 years. Worsening fingertip tingling,

numbness, and pallor, especially during cold weather, were noticed around the same time. Decreased thermal sensation on the left palm and fingers ensued, which had resulted in burn injury several times. He had received open carpal tunnel release surgery twice 4 years earlier, once at the elbow and the other time at the wrist, but the symptoms still progressed. In addition, a malar rash was observed at that time, which had become even worse after sun exposure. Laboratory findings at that time showed positive antinuclear antibody [ANA; 1:1280 (+), speckled pattern] and positive antiribonucleoprotein antibody (9.9 U/mL; normal value <5.0 U/mL). He was previously diagnosed with systemic lupus erythematosus (SLE) at a regional hospital 3 years earlier based on four of the 11 American Rheumatologic Association criteria for the diagnosis of SLE (malar rash, photosensitivity, arthritis, positive ANA test). Treatment with prednisolone 20 mg daily and hydroxychloroquine 200 mg daily were initiated, followed shortly by the addition of cyclophosphamide 50 mg daily to control his disease. However, the therapy did not control the symptoms, and skin lesions spread to trunk and limbs in these 3 years. This patient had stopped using the immunosuppressive agents 1 year before presentation.

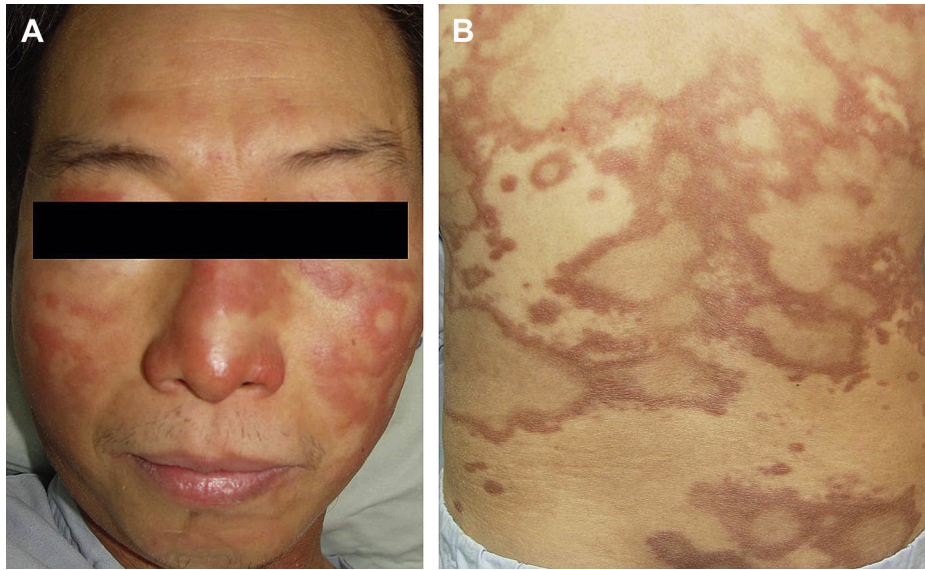
On examination, the patient had generalized erythematous annular patches and plaques with ill-defined borders on the face, trunk, and forelimbs (Figure 1). Hand swelling, muscle wasting, claw deformity of fingers, and drop hand were observed evidently in the left hand (Figure 2). Neurologic examination at these areas showed significant sensory loss (touch, pain, and temperature sensation) and muscle weakness.

Laboratory examination showed reduced hemoglobin (94 g/L) with increased reticulocyte production index (7.0%), a normal white

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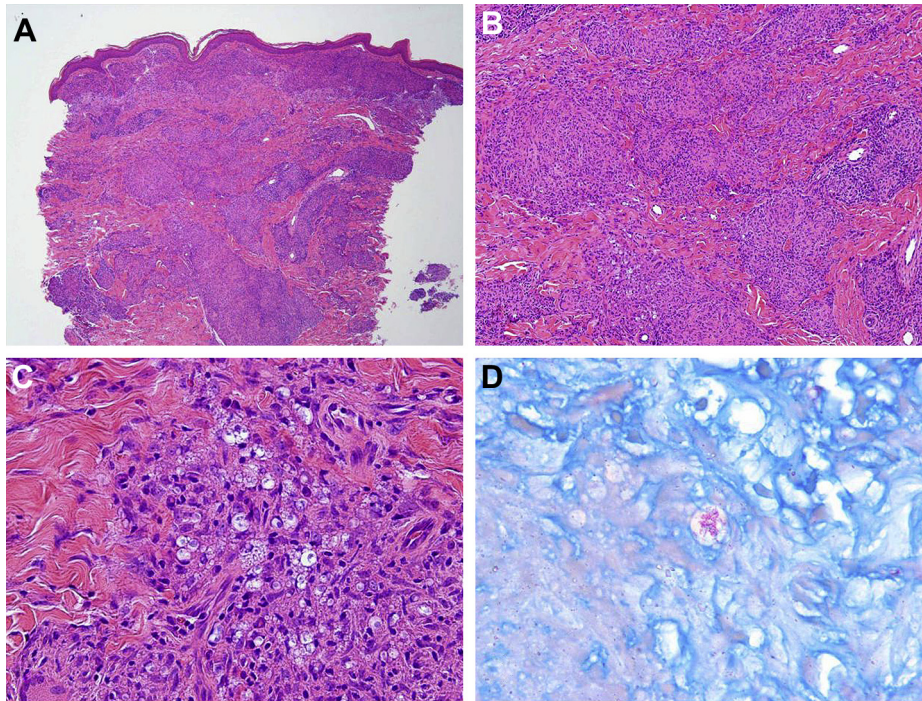
**Figure 1** Generalized erythematous annular patches and plaques with ill-defined borders on the (A) face and (B) back.

blood cell count, normal liver and kidney function tests, and elevated erythrocyte sedimentation rate (71 mm in the first hour; normal value <12 mm/hour). His autoimmune profile revealed seropositivity for ANA [1:160 (+), speckled pattern], but other data were within the normal limit, including complement fractions 3 and 4 (C3 and C4), antidouble strand DNA antibody, anticardiolipin antibody screen, extractable nuclear antigen autoantibodies screen, anti-Smith, antiribonucleoprotein, anti-Sjogren's syndrome A antibody (anti-SSA), and anti-Sjogren's syndrome B antibody (anti-SSB). This patient denied having other systemic disease, recent travel history, smoking, or substance abuse. The initial impression was subacute cutaneous lupus erythematosus with a sensorimotor polyneuropathy. A skin biopsy from the right forearm revealed

diffuse granulomatous infiltrate in the reticular dermis (Figure 3A,B) composed of histiocytes, plasma cells, a few lymphocytes, and multinucleated giant cells. Some globi were also noted in the granuloma. An acid fast stain showed an aggregate of bacilli within the globi in keeping with lepromatous leprosy (Figure 3C,D). The direct immunofluorescence study was all negative. Slit-skin smears from bilateral forehead and earlobes showed an average bacterial index of two. On nerve conduction studies, a decrease in motor and sensory conduction velocity combined with a prolonged motor distal latency and a decreased compound muscle action potential were noted in the left ulnar and radial nerve. These findings suggested sensorimotor polyneuropathy superimposed with multiple entrapment neuropathies.



**Figure 2** Bilateral hand lesions of our patient: (A,B) Muscle wasting and claw deformity on the left hand; (C) erythematous swelling on the right hand.



**Figure 3** (A) Diffuse granulomatous infiltrate in the reticular dermis [hematoxylin and eosin (H&E); original magnification,  $\times 40$ ]. (B) Granulomatous inflammation in the reticular dermis (H&E; original magnification,  $\times 100$ ). (C) Globi were noted in the granulomas (H&E; original magnification,  $\times 400$ ). (D) Aggregate of bacilli within the globi (acid fast stain; original magnification,  $\times 1000$ ).

Although the patient had clinical features of borderline tuberculoid leprosy including multiple asymmetrical annular infiltrated plaques and early neuritis, he had many bacillary globi found histopathologically, which pointed towards lepromatous leprosy. The average bacillary index from the skin smear of four sites was two, which represents a low to medium number of bacilli. Therefore, the final diagnosis was multibacillary borderline leprosy with dermatologic, neurologic, and rheumatic manifestations. Multidrug therapy (MDT) with rifampicin 600 mg once a month, dapson 100 mg daily, and clofazimine 300 mg once a month and 50 mg daily was initiated. Skin rashes, joint pain, and hand swelling improved greatly after the treatment. However, subjective left hand numbness and muscle weakness persisted at the 1-year follow up.

## Discussion

Our patient's presentation with peculiar skin rashes combined with sensorimotor polyneuropathy and rheumatic manifestations, all evolving over 3–4 years, led to the skin biopsy that confirmed the diagnosis of leprosy. Although the coexistence of SLE and leprosy has been reported,<sup>1–3</sup> SLE was not likely in this patient. First, immunosuppressive agents were ineffective, including on the skin and joint symptoms. Second, cutaneous manifestations gradually improved after using MDT alone. Third, the autoantibody profile, complement level, and direct immunofluorescence study result did not give good support to the diagnosis of lupus. Leprosy has a variable incubation period ranging from months to several years and may progress slowly. Although the Myanmar man had left the endemic area more than 25 years earlier, the disease may present long afterwards. It is not clear when our patient acquired his leprosy, but the most likely explanation is that his disease lay dormant for many years.

Rheumatic manifestations, observed in as many as 64–77% leprosy patients especially during reactional states,<sup>4,5</sup> form the

third most prevalent complication after dermatologic and neurologic abnormalities.<sup>6</sup> In our patient, swollen hands syndrome, arthritis, Raynaud's phenomenon, and indurated facial rashes on malar eminence were noted during the disease course. One possible explanation for our patient having facial rashes reminiscent of malar rashes in lupus is that *M. leprae* grows best in cooler areas of the human body. Hence, the skin lesions tend to be localized to the chin, forehead, earlobes, and malar eminences.

It has been estimated that 6–75% of leprosy patients develop arthritis at some stage of the disease.<sup>4,5,7–9</sup> In a retrospective review evaluating 1257 leprosy patients, Pereira et al found that the predominant type of leprosy in the patients with arthritis was lepromatous leprosy type (41.8%), followed by borderline tuberculoid type (23.6%), borderline (18.2%), and borderline lepromatous type (16.4%).<sup>9</sup> Also, the review showed that the most common type of joint involvement was polyarticular, followed by oligoarticular and monoarticular. The wrist, ankle, proximal interphalangeal joint, and metacarpophalangeal joint were most frequently affected.<sup>9</sup> Chauhan et al<sup>7</sup> classify the arthritis in leprosy into the following groups: (1) Charcot's arthropathy secondary to peripheral sensory neuropathy; (2) swollen hands and feet syndrome; (3) acute polyarthritis of lepra reaction; and (4) chronic arthritis from direct infiltration of the synovium by lepra bacilli. Since our patient had a chronic course without a lepra reaction during diagnosis and responded to MDT and nonsteroidal anti-inflammatory drugs, the joint involvement in our patient seemed to be due to Charcot's arthropathy or chronic arthritis. Two commonly involved nerves in Charcot's arthropathy are the ulnar and median nerves.<sup>10</sup> Early changes associated with ulnar neuropathy are flattening of the hypothenar muscles and ultimately result in claw-hand deformity, as observed in our patient.

Leprosy is invariably included in the list of diseases associated with positive ANA tests. The presence of ANA has been reported to vary from 3% to 34% usually in a low titer, and both speckled and

homogeneous patterns were identified.<sup>4,11–14</sup> The great variability probably reflects the heterogeneity of the sample, the duration, and the type of the disease. Patients with a longer duration of illness, an older age, multibacillary leprosy, and a history of repeated lepra reaction attacks have been reported to predispose to ANA production.<sup>13,15</sup> Also, many other chronic infections such as malaria, tuberculosis, and fungal infection often coexist with leprosy in developing countries and they could augment the humoral immune stimulation and increase the titer and range of autoantibodies produced.<sup>13</sup> It has been postulated that ANA presenting in leprosy patients results from weak cross-reactivity with complexed nucleic acids and nucleoproteins exposed after cell destruction in chronic inflammation. Newly exposed hidden antigens may provide antigenic determinants that stimulate adaptive immune response and polyclonal B cell activation.<sup>15</sup>

In addition to ANA, many other serologic similarities exist between leprosy and autoimmune disease. Rheumatoid factor,<sup>16,17</sup> antineutrophil cytoplasmic antibody,<sup>14,18,19</sup> anticyclic citrullinated peptide,<sup>16,17</sup> and antiphospholipid antibodies<sup>20,21</sup> have been reported with varying incidences in different forms of leprosy. These serology findings in conjunction with the rheumatic manifestations described above may lead to misdiagnosis as rheumatic disorders. Misdiagnosis often leads to years of corticosteroid or immunosuppressant administration, which probably modifies the clinical presentation of leprosy towards lepromatous forms.

Between 12% and 55% of new cases of leprosy have clinical signs and symptoms of neuropathy at diagnosis.<sup>22</sup> In the tuberculoid pole, isolated damage of nerve trunks or more superficial dermal nerves occurs, while in the lepromatous pole, glove and stocking sensory loss often take place. Granulomatous inflammation of peripheral nerves in leprosy causes nerve enlargement and impairs sensory, motor, and autonomic function. Among them, numbness and sensory loss occur earliest. As for sensory loss, temperature and pain sensations generally decreased earlier than position and vibration sense, and warmth perception is affected earlier than cold perception.<sup>22</sup> Motor function impairment, presenting later in the disease course, results in muscle weakness and atrophy in the distribution of involved peripheral nerves.<sup>23</sup> As in our patient, enlarged ulnar and median nerves are vulnerable to entrapment and irritation behind the olecranon process and flexor retinaculum, respectively. They are usually the first nerves to be compromised. Sensory nerve conduction parameters, in particular amplitude, and warm perception thresholds were by far the most sensitive measures for detecting neuropathy.<sup>22</sup>

Hansen's disease is a great mimicker, and the diagnosis is particularly challenging in patients in nonendemic regions and with many rheumatic manifestations clinically and serologically. Our case illustrates an unusual presentation of leprosy initially diagnosed as SLE based on the diagnostic criteria. It is important to recognize the potential association between rheumatic manifestations and leprosy, as delayed diagnosis and the use of immunosuppression in our patient probably led to a downgrading reaction,

which usually causes irreversible nerve damage. We need to keep a broad differential diagnosis in mind when assessing patients with an undiagnosed granulomatous rash, even in the absence of any history of recent prolonged stay in an endemic country until a particular disease is proven. Diagnosis and initiation of therapy as early as possible is necessary to prevent permanent nerve damage and to reduce the risk of secondary transmission.

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