De novo histoid leprosy in a Colombian patient with multiple skin nodules on the ears and extremities


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Abstract
Histoid leprosy is an uncommon form of lepromatous leprosy with distinct clinical, histopathological, immunological, and bacteriological features. This variant usually occurs in multibacillary patients who have irregular or inadequate treatment. Herein, we report a case of de novo histoid leprosy diagnosed in a patient from Cali, Colombia. In endemic areas, histoid leprosy should be in the differential diagnosis of any patient presenting with skin nodules. Early diagnosis and appropriate treatment are recommended for mitigating the impact of histoid leprosy cases, which are important reservoirs of Mycobacterium leprae.

Keywords: Leprosy. Histoid leprosy. Mycobacterium leprae.

INTRODUCTION
Leprosy, also known as Hansen’s disease, is a chronic infectious disease caused by the non-cultivable, acid-fast, rod-shaped bacterium Mycobacterium leprae, which has affected humans since ancient times[1]. Leprosy mainly affects the skin and peripheral nerves in most cases, apart from some other structures, depending on the disease subtype[1]. Histoid leprosy is an uncommon variant of lepromatous leprosy that is generally reported in multibacillary patients who have irregular or inadequate treatment[2-4]. Herein, we describe a case of de novo histoid leprosy in a Colombian patient.

CASE REPORT
A 29-year-old unemployed man from Cali, Colombia presented to our hospital with a 1-year history of non-pruritic nodular skin lesions, which started on the anterior aspect of his right leg and progressed to involve his left leg, thighs, arms, neck, and ears. The patient’s medical history was otherwise unremarkable. He did not recall any contact with animals or sick people. He had not received any treatment for his lesions.

Physical examination revealed skin phototype VI, and multiple firm, keloid-like, skin-colored cutaneous nodules of various sizes localized on the ears (Figure 1), arms, thighs, and legs (Figure 2). The lesions were not tender, and there were no sensory deficits. Complete blood count and renal function tests were normal. Rapid plasma reagin and HIV serology results were non-reactive.

De novo histoid leprosy was highly suspected on the basis of clinical findings. Considerations in the differential diagnosis for this patient included spontaneous keloids, dermatofibroma, and lobomycosis. An slit-skin smear for acid-fast bacilli (AFB) taken from the earlobes and nodules revealed a bacteriological index of 1+. Examination of a skin biopsy specimen from one nodule demonstrated a dense inflammatory infiltrate within the dermis consisting primarily of histiocytes, admixed with occasional perivascular plasma cells. Histoid leprosy was confirmed by skin biopsy examination using the Fite-Faraco stain, which demonstrated the presence of abundant easily identifiable AFB predominantly arranged in clumps within histiocytes (Figure 3). The patient was started on multibacillary-multidrug therapy (MB-MDT) consisting of dapsone 100mg/d, clofazimine 50mg/d, and a monthly course of clofazimine 300mg and rifampin 600mg for 1 year. The patient had a good response to antimicrobials with no leprosy reactions or relapses. The Leprosy Control Program of the Secretaría de Salud Municipal of Cali performed monthly follow-up of the patient. Extensive education was provided by both the healthcare providers that
first evaluated the case and the medical staff from the local program following the patient.

There were no other leprosy cases among the patient’s family members and close contacts based on signs and symptoms; nevertheless, Bacillus Calmette-Guérin (BCG) vaccination was recommended.

**DISCUSSION**

Leprosy continues to be an important health problem in several countries of southeast Asia, Africa, and the Americas\(^1\)\(^5\). Cases in countries elsewhere are rare and usually linked to immigration from endemic areas. According to official reports from 143 countries and territories, the global registered prevalence of leprosy by the first quarter of 2017 was 0.23 cases per 10,000 population (171,948 cases)\(^5\).

The clinical-histopathological spectrum based on the Ridley-Jopling classification reflects the interplay between \(M. leprae\) and the host’s cell-mediated immunity, and includes the five presentations: polar tuberculoid (TT), borderline tuberculoid (BT), borderline-borderline (BB), borderline lepromatous (BL), and polar lepromatous (LL); indeterminate leprosy (I) and pure neuritic leprosy are not considered in this spectrum classification\(^6\). A simplified classification of leprosy based on the number of skin lesions and the bacillary load is used for the purpose of treatment. Multibacillary disease (BB, BL, and LL forms), which typically correlates with having more than five skin lesions, represents the most infectious form of the disease and needs to be treated with MB-MDT, which is a combination of dapsone, rifampin, and clofazimine, for at least 12 months. Conversely, paucibacillary disease (TT, BT, and I forms) requires treatment with dapsone and rifampin for 6 months\(^7\).

Histoid leprosy, first described by Dr. Herbert Windsor Wade in the 1960s\(^5\), is an uncommon variant of LL, affecting 1.1-3.6% of all patients with leprosy and occurring predominantly in men\(^2\)\(^-\)\(^4\). To date, there are no epidemiological data regarding histoid leprosy in Colombia, but a few cases have been described\(^8\). Histoid leprosy usually occurs in multibacillary patients who have irregular or inadequate treatment, particularly dapsone.
monotherapy, but relapsing cases after successful treatment as well as de novo cases have rarely been reported. Overall, treatment seems to influence the development of histoid leprosy in most cases. Histoid leprosy cases serve as an important infection reservoir and as a source of incident cases; therefore, it poses a threat to national leprosy eradication programs given the high bacillary load and the likely drug-resistant mutant strains harbored. The disease is characterized by distinct clinical, histopathological, immunological, and bacteriological features. Clinical findings include painless, firm, cutaneous and/or subcutaneous papules, nodules or plaques with well-defined edges and a smooth bright surface. The lesions are usually located on the posterior and lateral aspects of the arms, dorsum of the hands, back, buttocks, thighs, legs, and over bony prominences such as the elbows and knees, with a localized asymmetric pattern and arising from apparently normal-looking skin. In contrast, classical LL presents with generalized symmetric lesions that arise from infiltrated skin. Atypical skin lesions, such as tumor-like masses, molluscum contagiosum-like lesions, xanthoma-like, mucosal, and genital lesions, have been reported and may mislead the diagnosis of histoid leprosy. Nerve affection, leading to anesthetic lesions or sensory impairment to temperature, touch or pain, may be mild or absent. Earlobe infiltration could be present in some cases. The pathogenesis of histoid leprosy remains unclear but it is known that the cell-mediated and humoral immune responses against M. leprae in patients with histoid leprosy are enhanced compared with classical LL. This response includes increased cluster of differentiation 36 (CD36) expression by keratinocytes, CD4 T lymphocytes, B lymphocytes, and immunoglobulin levels. However, macrophages seem to lack functionality to kill M. leprae bacteria present in high numbers in histoid lesions.

The diagnosis of leprosy is initially clinical but must be supported by bacilloscopy and histopathology. Typical histopathological findings include epidermal atrophy with a subepidermal acellular band, known as the grenz zone. The lepra is contained within the dermis and is as a well-circumscribed area consisting of spindle-shaped histiocytes arranged in an intertwining, whorled, or storiform pattern, and surrounded by a pseudocapsule. An abundance of AFB, characteristically longer than ordinary lepra bacilli, can be seen within histiocytes, arranged singly, in clumps, or rarely as globi. The identification of AFB on skin biopsy specimens stained by the Fite-Faraco stain helps to confirm the diagnosis. On the other hand, skin smear examination under the microscope (bacilloscopy) by the Ziehl-Neelsen stain is useful to classify the disease; if the presence of M. leprae is detected (positive bacilloscopy), the case is classified as multibacillary leprosy. Histoid leprosy can clinically mimic dermatofibroma, neurofibromatosis, xanthoma, cutaneous lymphoma, keloids, molluscum contagiosum, sarcoidosis, lobomycosis, and leishmaniasis, among others. The standard treatment of histoid leprosy is MB-MDT. As with other leprosy cases, early detection and appropriate treatment are encouraged to prevent future disabilities and to stop disease transmission. Strict clinical follow-up must be ensured during and after treatment. Education is important to alert patients and household contacts about the clinical manifestations of the disease as well as to highlight the importance of follow-up and treatment.

To our knowledge, all of the present patient’s household contacts were asymptomatic and disease-free based on clinical examination. However, subclinical leprosy cases might be overlooked due to a lack of resources and access to testing modalities other than clinical examination. It has been reported that person-to-person transmission does not explain the patchy epidemiology of the disease because incident cases are often detected in persons with no known close contacts of leprosy. Periodic evaluation of household contacts for longer periods even after treatment of the index case and use of laboratory testing modalities (e.g., PCR or IgM anti-phenolic glycolipid [PGL-I]) may contribute to earlier detection of subclinical cases.

In conclusion, histoid leprosy is a rare presentation of LL that should be considered as a relevant differential diagnosis in endemic countries for patients presenting with skin nodules. Histopathological examination is needed for definitive diagnosis. Despite the low frequency of histoid leprosy among all leprosy cases, early diagnosis and appropriate treatment are crucial to mitigate the impact of these important reservoirs of resistant bacilli on the disease burden and spread worldwide.

Conflict of interest: The authors declare that there is no conflict of interest.

REFERENCES


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