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Imported and autochthonous leprosy presenting in Madrid (1989–2015): A case series and review of the literature

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Summary *Background:* Leprosy remains infrequent in non-endemic areas. The objective of this study was to describe the cases of leprosy reviewed at a referral unit for imported diseases in Europe and to compare these findings with published data on imported leprosy.
Methods: Cases of leprosy evaluated at a referral centre are described and salient features of autochthonous and imported cases are compared. A review of the literature on imported leprosy was performed.
Results: During the study period, 25 patients with leprosy were followed-up (10 were autochthonous cases and 15 were considered to be imported). Regarding imported cases, the majority were diagnosed in Latin American immigrants (10/15, 67%), mean age was 42 years, there were no differences in gender distribution, estimated average time from arrival in Spain to first visit at the unit was 3 years and from symptom onset to diagnosis was 2 years. Over 80% of imported cases had multibacillary disease and over one third of patients had been previously diagnosed with leprosy. One third had received alternate incorrect diagnoses initially, <50% of patients with imported leprosy completed standard therapy and were considered cured and over one third were lost to follow-up.
Conclusions: Leprosy remains a complex disease for healthcare professionals unfamiliar with this infection. Manifestations are polymorphic so misdiagnoses and consequent delays in diagnosis are not infrequent and may lead to resulting disabilities. Early diagnosis and management are essential to prevent sequelae and possible transmission. Improving access to health care, especially for vulnerable groups, would be necessary to advance in the control of this disease.
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1. Introduction

Leprosy is the result of a slowly progressive infection with *Mycobacterium leprae* which mainly affects the skin, peripheral nerves, and upper respiratory tract as well as other organs [1]. Since 1985 the reported prevalence of the disease worldwide has decreased by over 90% [1], and at the beginning of 2014, around 215, 000 new cases of leprosy were detected with a registered prevalence of 180.000 cases [2]. Prevalence of leprosy varies according to geographical region and according to WHO data the majority of new cases in 2013 were registered in India, Brazil, Indonesia, Ethiopia, D. R. Congo, Nigeria, Nepal, Bangladesh, Myanmar and Tanzania [3]. However, leprosy may be diagnosed in any country due to recent increases in travel and migration.

In Spain, specific geographical areas were previously considered endemic for leprosy but official epidemiological surveillance data for communicable diseases in Spain have revealed a steady decrease in the incidence of leprosy with less than 15 new cases registered in total in the country in 2013, 75% of which occurred in immigrants [4].

Leprosy remains a stigmatizing disease with physical, social and psychological consequences.

The objective of this study was to describe the cases of leprosy reviewed at a national referral centre for imported diseases in a European country and to compare these findings with published data on imported leprosy.

2. Methods

Patients diagnosed with leprosy at a Tropical Medicine Referral Unit (TMRU) in Madrid, Spain during the period 1989—2015 were identified from a database and the main epidemiological data and clinical features were reviewed.

A mini-review of the literature was performed in PubMed for published articles until January 2016 using the terms "leprosy" or "*M. leprae*" or "Hansen's disease" AND "travel" or "immigrant(s)" or "imported". Articles reporting $\geq$5 imported cases were considered.

A secondary search of the references for the main articles identified additional cases. Articles in English were considered as well as abstracts in English from non-English language articles when available.

3. Results

The main epidemiological and clinical features for the patients in the study are summarized in Tables 1 and 2 (cases are numbered according to year of diagnosis) [5,6]. During the study period 12, 363 new patients were seen at the TMRU and 2, 076 of these (16.8%) presented with dermatologic conditions. During this period, 25 patients with leprosy were followed-up at the TMRU. Of these, 10 were autochthonous cases (6 males, 4 females) and 15 were considered to be imported (8 males, 7 females). The main characteristics of autochthonous and imported cases are summarized in Table 3. Most of the patients with imported leprosy were immigrants (14/15, >90%) who were considered to have acquired the infection in their country of origin. Three of these patients were from Paraguay, 2 from Brazil, 2 from Colombia, 2 from the Dominican Republic, 2 from Equatorial Guinea, and one each from the Philippines, Mali and Venezuela, respectively. The other patient with imported leprosy (patient #9) was a 72-year old expatriate who had been living in Cuba for over 70 years and symptoms had initiated before his return to Spain. Among the Spanish nationals with autochthonous leprosy, patient #12 had lived in Germany between 1961 and 1966 but was diagnosed in 2004 after 1 year of symptoms; patient #20 was initially diagnosed in Belgium in 1965 and #24 was a frequent short-term traveller. For these patients the most likely place of exposure was considered to be Spain. The average age at presentation was 48 years (56 years for autochthonous patients and 42 years for patients with imported leprosy). Of note, 13 patients (7 with autochthonous leprosy and 6 with imported leprosy) had been previously diagnosed with leprosy at another hospital (some had received prior treatment) and were referred to the TMRU for review and further follow-up. The estimated average time from symptom onset to diagnosis was 6.8 years for non-imported cases (data available for 7/10 patients) and 2.1 years for imported cases (data available for 11/15 patients). In total, 20 patients were diagnosed with multibacillary (MB) leprosy (7 autochthonous cases, 13 imported cases) according to the WHO classification and 5 patients had paucibacillary (PB) leprosy (3 autochthonous cases, 2 imported cases).

3.1. Treatment and outcome

Regarding treatment, 12/25 patients (48%) received a minimum of standard therapy for either multibacillary or paucibacillary leprosy (rifampicin 600 mg once a month, dapsone 100 mg daily and clofazimine 300 mg once a month and 50 mg daily for at least 12 months for multibacillary disease and rifampicin 600 mg once a month and dapsone 100 mg daily for at least six months for paucibacillary leprosy. Single skin lesion paucibacillary treatment includes a single dose of rifampicin 600 mg, ofloxacin 400 mg and minocycline 100 mg). In 12 cases either treatment was initiated and/or completed at other hospitals and/or doses and duration were not clearly documented, non-standard regimens were used, there was loss of follow-up or non-standard regimens were used due to intolerance/side-effects. One patient (1/25, 4%) was receiving treatment at the time of writing.

In total, 17 patients were considered to be cured. Of these, 9/10 of the autochthonous patients were cured (1/10 lost to follow-up) and 8/15 of the imported cases (6 lost to follow-up and 1/10 receiving treatment at the time of writing) were cured.

3.2. Drug adverse effects and reactions

Documented side-effects with therapy included a flu-like illness with rifampicin (leading to discontinuation) and anaemia due to dapsone in #5, anaemia and leucopenia due to dapsone in #6, haemolytic anaemia and a severe cutaneous reaction due to dapsone in #9 (requiring change in

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