



A Case of New Manifestation of Leprosy Six Months after Immigration to Germany

Sogkas Georgios¹, Pott Carl-Christoph¹, Schacht Vivien², Sedlacek Ludwig³, Schmidt Reinhold Ernst¹ and Stoll Matthias^{1*}

¹Department of Immunology and Rheumatology, Hannover Medical University, Germany

²Department of Dermatology, Hannover Medical University, Germany

³Department of Medical Microbiology, Hannover Medical University, Germany

Abstract

Leprosy is a chronic infectious disease mainly prevalent in subtropical and tropical areas, caused by *Mycobacterium leprae*. It typically affects the skin and the peripheral nervous system. Leprosy presents in distinct clinical forms, depending on the immune response, elicited to combat *Mycobacterium leprae*. We report the case of a previously asymptomatic 28-year-old male from Sudan, who was admitted with since five months appearing progressive bilateral leg and hand edemas. Skin biopsy revealed a multibacillary mycobacterial granulomatous inflammation and molecular analysis for *Mycobacterium leprae* was positive, confirming the diagnosis of leprosy. This case emphasizes that leprosy can also appear in people from endemic areas immigrating asymptomatic to Europe, several months after immigration.

Keywords: Leprosy; Mycobacteria; *Mycobacterium leprae*; Refugee; Migrants; Europe; Germany

Introduction

Leprosy (or Hansen's disease) is a chronic infectious disease mainly of the skin and nerves, caused by *Mycobacterium leprae* [1]. *Mycobacterium leprae* is an obligatory intracellular pathogen, whose exact mode of transmission remains unclear. However, a recent study by Araujo "et al." [2] strongly supports an aerosol route of transmission and infection [2].

Leprosy is an important public health problem in the subtropics and tropics. In Germany and the rest of Europe, leprosy is an extremely rare infection, mainly imported by immigrants from endemic areas [3]. Growing migration flows from endemic regions to Europe and other countries, where leprosy is considered eradicated, is expected to increase its incidence. Further, due to the rarity of leprosy in Europe, it can be difficult for physicians to consider leprosy as a differential diagnosis, which may delay diagnosis. Delayed diagnosis may have debilitating consequences, including blindness and permanent nerve damage [4].

We report the case of a previously asymptomatic 28-year-old male from Sudan with progressive peripheral edema, which was diagnosed with leprosy.

Case Presentation

A 28-year-old male-a refugee from south Sudan – who had been living in Germany for 9 months was referred to our clinic by his general practitioner with bilateral leg and hand edema of unclear etiology.

On admission the patient complained of progressive edema in his both legs and hands as well as of his eyelids. Moreover, he had numbness in the affected areas of legs and hands. He reported repeated burn injuries in his hands, which according to him happened all recently, due to the absence of thermal sensitivity in his peripheral extremities. He also complained of progressive weakness in his legs. The aforementioned problems started gradually during the last three months. Since a couple of months he had fever; a maximum auricular temperature of 38.6 °C was reported. Weight loss and night sweat were denied. The clinical examination revealed symmetric extremely dense edemas of lower legs with diffuse hyperkeratosis, a few palpable nodular changes, some of which were also viewable and a few hypo pigmented macules (Figure 1). Similar - though less pronounced - edemas were observed in the dorsum of both hands and in the fingers. A few nodular changes were palpable in the lateral sides of both elbows of the patient. In the face there was bilateral periorbital edema of

OPEN ACCESS

*Correspondence:

Matthias Stoll, Department of Immunology and Rheumatology, Clinic for Immunology and Rheumatology, Hannover Medical University, Carl-Neuberg-Strasse 1, 30625, Hannover, Germany, Tel: 49-511-532-9672; Fax: 49-511-532-5648; E-mail: stoll.matthias@mh-hannover.de

Received Date: 11 Apr 2017

Accepted Date: 09 May 2017

Published Date: 12 May 2017

Citation:

Georgios S, Carl-Christoph P, Vivien S, Ludwig S, Ernst SR, Matthias S. A Case of New Manifestation of Leprosy Six Months after Immigration to Germany. *Ann Clin Case Rep.* 2017; 2: 1358.

ISSN: 2474-1655

Copyright © 2017 Stoll Matthias. This is an open access article distributed under the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.



Figure 1: Symmetrical edema of lower legs on presentation (left) and a month after introduction of therapy (right).



Figure 2: Bilateral periorbital edema with loss of eyelashes and eyebrows (middle photo), compared to the ID-photo, which was taken 9 months ago (left) and the follow-up photo, which was taken 1 month after therapy-introduction (right).

soft consistency with loss of eyelashes and eyebrows (Figure 2). The neurological examination revealed loss of touch and pin sensation in the affected edematous areas.

On admission the C-Reactive Protein (CRP) was elevated (41.9 mg/l, normal range < 5 mg/l). The full blood count revealed a slight hypochromic anemia. Other routine laboratory tests were normal, except for a slight elevation of gamma-glutamyl-transferase (gGT, 126 U/l, normal range < 55 U/l) and Alkaline Phosphatase (ALP, 190, normal range 40-129 U/l). An HIV-test was negative. We also performed an interferon-gamma release assay (IGRA), which was positive. However, all specimens submitted for microbiological testing remained culturally and PCR negative for *Mycobacterium tuberculosis*. In addition, serum analysis for leishmaniasis and syphilis as well as blood analysis for microfilariasis were negative. A conventional chest X-ray and an abdominal sonography revealed no pathological findings. An electroneurography revealed substantially reduced motor and sensory potentials in the lower legs (nervus peroneus, nervus tibialis, nervus suralis) as well as the forearm and the hands (nervus medianus), indicating severe axonal polyneuropathy.

The histological examination of a skin-biopsy from the left leg revealed the formation of multiple granulomata and areas with lymphocytic infiltration (Figure 3). The acid-fast stain revealed lots of mycobacteria diffuse in the dermis (Figure 4). Polymerase Chain Reactions (PCR) were employed to specify the mycobacterial species. A PCR analysis of the bacterial 16S rRNA gene, followed by sequencing identified *Mycobacterium leprae*, whereas the molecular analysis for *Mycobacterium tuberculosis* was negative. Evaluation of the mycobacterial load in skin-biopsy stained with Ziehl-Neelsen stain, revealed approximately 80 bacilli per high powered field,

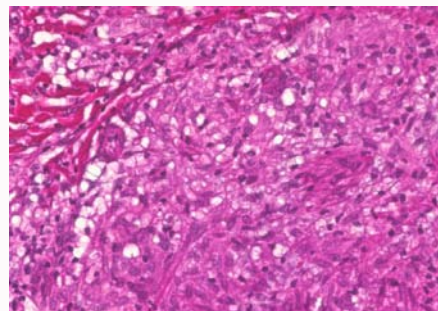


Figure 3: Skin-biopsy: hematoxylin and eosin stain. Dermis with formation of a granuloma with macrophages surrounded by lymphocytes (evident at the barrier between granuloma and connective tissue at the lower left corner of this figure) (40x magnification).

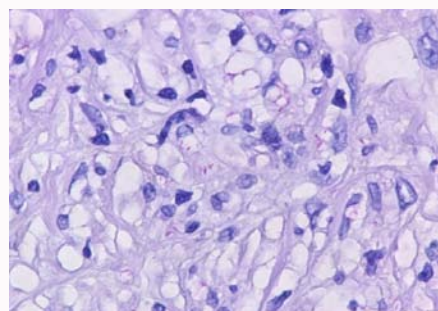


Figure 4: Skin-biopsy: Ziehl-Neelsen stain. Mycobacterial infiltration of dermis (100x magnification).

matching a bacterial index of 4+ [5]. A Fite-Faraco-stain, which is more sensitive at identifying *Mycobacterium leprae*, was not performed, as it is unavailable in our Pathology lab.

Taken the above described clinical findings (numerous macular and nodal skin lesions with partially symmetric distribution, pronounced symmetrical edema of lower legs, severe polyneuropathy) and the results of the histological examination we made the diagnosis of multibacillary form of leprosy.

Based on our diagnosis, we started a multidrug therapy with daily administration of 100 mg dapsone, 50 mg clofazimine as well as a supervised monthly administration of 600 mg rifampicin and 300 mg clofazimine. Due to the progressive weakness of the lower legs, which started gradually in the last month, and the findings of the electroneurography, we set the diagnosis of a lepra reaction-mediated neuronal injury, so that we started an anti-inflammatory therapy with 50 mg prednisolone, whose dose was slowly tapered. This led to an alleviation of the numbness and could reverse the weakness of the lower legs, strongly suggesting the coexistence of an inflammatory lepra reaction. In the follow-up, two months later, the edemas of the lower legs (Figure 1), hands and face (Figure 2) had substantially regressed. The macular and nodular changes of skin disappeared and CRP was normal. However, loss of sensitivity could not be reversed. The above mentioned therapy with dapsone, clofazimine and rifampicin should be continued for ten more months (1-year regimen).

Discussion

Leprosy (or Hansen's disease) is a chronic infection endemic in the subtropics and tropics, causing a broad range of clinical

manifestations [1]. The causative agent is *Mycobacterium leprae*. Leprosy typically presents with cutaneous manifestations. Involvement of the peripheral nerves with sensory loss is also common. Apart from direct pathogenicity of the chronic infectious process, leprosy may be complicated with immunologic reactions, which drive the mounting of acute inflammatory manifestations. These can appear before, during or after starting an antimycobacterial treatment (reverse reaction) and may lead to permanent damage if not treated with immunomodulatory and anti-inflammatory agents.

The therapy of leprosy depends on its form [1]. Classification of leprosy is based on clinical, immunological and histopathological criteria [6]. The phenotype of borderline leprosy, sharing features of both the two classical extreme clinical phenotypes of tuberculoid and lepromatous leprosy, was sub-classified in the classification of Ridley and Jopling, which is based on clinical and histopathological criteria (Tuberculoid Tuberculoid-TT, Borderline Tuberculoid-BT, Borderline Borderline-BB, Borderline Lepromatous-BL, Lepromatous Lepromatous-LL) [7]. In case of our patient, despite the clinical presentation with a bilateral symmetrical involvement pattern, including symmetrical edema of the lower legs and feet, which is a typical feature of LL leprosy, the histological findings matched BL leprosy. This discrepancy between the histological and clinical phenotype, suggests the existence of overlapping phenotypes of leprosy, including features of neighboring forms. In 1982 the World Health Organization (WHO) proposed a primarily bacteriological classification, based on the number of acid-fast bacilli in the dermis [6]. Bacilli-counts are expressed as bacteriologic index on a logarithmic scale. This classification distinguishes between a paucibacillary form, matching TT- and BT-form, and a multibacillary form, matching the BB-, BL- and LL-form of the Ridley-Jopling classification. Because of the absence of required infrastructure in areas with the highest disease prevalence for a classification dependent on bacilli-counts, the WHO suggested in 1988 a clinical classification based on counting of skin lesions; patients with 5 or less lesion should be treated as paucibacillary leprosy, whereas patients with more than 5 lesion should be treated as multibacillary leprosy. Despite the conflict with respect to the duration of multidrug therapy, a 6-month regimen with dapsone and rifampicin is recommended in case of paucibacillary leprosy, whereas for the multibacillary forms a 12-month regimen with dapsone, rifampicin and clofazimine is required, as had been started in our patient [8].

The highest prevalence of leprosy is observed in Southeast Asia (especially in India and Indonesia), in Latin America and Africa [9]. Its transmission is only partially understood. Sustained exposure appears to be a prerequisite for clinically manifest disease, whose development is genetically controlled, as suggested by genome-wide association studies [10]. Since the introduction of the multidrug therapy in the mid-1980s the prevalence of leprosy is substantially and constantly decreasing. In 2015, a total number of 210.758 new leprosy-patients were globally registered, of which only 18 were registered in Europe (8 of them in Spain). In Europe most cases are imported from countries of high prevalence [3,11]. Due to its long incubation time (between 3 and 4 years for paucibacillary and longer-up to 15 years for multibacillary form), leprosy may develop in people emigrating asymptomatic many years after their emigration [11].

With respect to the positivity of IGRA and in particular of the Quantiferon-Gold tuberculosis test, several reports have demonstrated a cross-reactivity of constituent peptides of this test (ESAT6 and CFP10) between *Mycobacterium leprae* and *Mycobacterium tuberculosis* [12].

Conclusion

Early diagnosis and treatment of leprosy can prevent incapacitating disease, which may also appear early in disease course mainly through the irreversible peripheral neuronal injury. Biggest obstacle towards diagnosing of leprosy in Europe and western countries is its rarity and the consequent low level of clinical suspicion. Especially nowadays, due to the increasing immigration from countries with high disease prevalence, a high index of suspicion is required for early diagnosis of leprosy. To this end the long incubation time of leprosy and thus, the possibility of appearance of the first disease manifestations several months, even years after settlement in a low prevalence country have to be considered.

Compliance with Ethical Standards

This is a report on a single patient. This case report complies with the Declaration of Helsinki. Approval is also obtained from the Ethics committee of the Medical University of Hannover. A written consent form has been obtained from the patient for this case report.

References

1. Britton WJ, Lockwood DN. Leprosy. Lancet. 2004;363:1209-19.
2. Araujo S, Freitas LO, Goulart LR, Goulart IM. Molecular Evidence for the Aerial Route of Infection of *Mycobacterium leprae* and the Role of Asymptomatic Carriers in the Persistence of Leprosy. Clin Infect Dis. 2016;63(11):1412-1420.
3. Ramos JM, Romero D, Belinchón I. Epidemiology of Leprosy in Spain: The Role of the International Migration. PloS Negl Trop Dis. 2016;10:e0004321.
4. Aftab H, Nielsen SD, Bygbjerg IC. Leprosy in Denmark 1980-2010: a review of 15 cases. BMC Res Notes. 2016;9:10.
5. Massone C, Belachew WA, Schettini A. Histopathology of the lepromatous skin biopsy. Clin Dermatol. 2015;33(1):38-45.
6. Pardillo FE, Fajardo TT, Abalos RM, Scollard D, Gelber RH. Methods for the classification of leprosy for treatment purposes. Clin Infect Dis. 2007;44:1096-9.
7. Ridley DS, Jopling WH. Classification of leprosy according to immunity. A five-group system. Int J Lepr Other Mycobact Dis. 1966;34:255-73.
8. Reibel F, Cambau E, Aubry A. Update on the epidemiology, diagnosis, and treatment of leprosy. Med Mal Infect. 2015;45:383-93.
9. Global leprosy update, 2015: time for action, accountability and inclusion. Wkly Epidemiol Rec. 2015;91:405-20.
10. Alter A, Grant A, Abel L, Alcaïs A, Schurr E. Leprosy as a genetic disease. Mamm Genome. 2011;22:19-31.
11. Massone C, Brunasso AM, Noto S, Campbell TM, Clapasson A, Nunzi E. Imported leprosy in Italy. J Eur Acad Dermatol Venereol. 2012;26:999-1006.
12. Rendini T, Levis W. Quantiferon-Gold Tuberculosis Test Cannot Detect Latent Tuberculosis in Patients With Leprosy. Clin Infect Dis. 2015;61:1439-40.