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Diagnosis of leprosy in a Nigerian migrant: implementation of surveillance measures in the current migration context

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Parole chiave: Lebbra, Salute degli immigrati, Inchiesta epidemiologica, Sorveglianza delle malattie neglette

Abstract

Background. *In Italy, leprosy diagnosis is reported in immigrants from endemic countries or Italians who have stayed in endemic areas. We report the first leprosy case to be observed in a migrant from Nigeria in the Rimini district (Emilia-Romagna, Northern Italy).*

Methods. *After describing the tasks of the various health Institutions in the Italian integrated system for diagnosis, treatment, and surveillance of leprosy, we describe the management and outcomes of the leprosy case and of the patient's contacts.*

Results. *In April 2017, Multibacillary Lepromatose Leprosy was diagnosed in a 29-year-old Nigerian man who arrived in Rimini in July 2014 after a 2-year stay in Libya. The local Public Health Service implemented the epidemiological investigation and identified the patient's close contacts. The management of the case and the surveillance of the 13 identified contacts, 7 Italians and 6 migrants, highlighted some critical issues. The late diagnosis of the case, due to the lack of knowledge of exotic diseases by general practitioners and other health and social professionals, and the loss at follow up of the close contacts (5 out of 6 migrants), represented important obstacles to the full success of surveillance measures.*

Conclusions. *Although in Italy there is a well codified system of notification and surveillance of leprosy, the recognising of cases and the tracing and follow up of contacts are made difficult by the particular conditions of the involved people. This represents a new challenge for the Italian Public Health Authorities which, in the current context of immigration, often uncontrolled, must know how to respond to the new needs, in close collaboration with the State Institutions responsible for registering migrants and those health and social professionals who could facilitate the access of foreign people to health services.*

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Introduction

Hansen's disease, commonly called leprosy, is a chronic infectious disease caused by *Mycobacterium leprae*. The implementation of the multidrug therapy (MDT) in the 1980s produced a reduction of cases worldwide; however, leprosy is far from being eradicated and more than 200,000 new cases per year have been detected in the last decade, with a prevalence of around 192,000 cases at the end of 2017 (1-3). Untreated leprosy is a globally important cause of permanent disabilities from communicable diseases (4, 5).

Host immune response to *M. leprae* is responsible for the clinical type of leprosy: 95% of infections are subclinical and resolve spontaneously (6, 7). Clinical manifestations are heterogeneous and mainly involve the skin and peripheral nerves. The broad spectrum of clinical pictures ranges between two extremes: Tuberculoid Leprosy (TT), characterized by a very high immune response and a low bacteriological index (BI: 1), and Lepromatous Leprosy (LL) characterized by a strong inability of the immunologic reaction and a high bacteriological index (BI: 6). The disease is clinically classified into a multibacillary form, including cases with more than 5 skin lesions, and a paucibacillary form, characterized by 5 or fewer skin lesions (8). The multibacillary form is the most contagious form of leprosy. It is necessary to perform a nasal swab searching for mycobacteria by microscopy to determine if a patient is contagious and requires isolation.

According to the World Health Organization (WHO) Global Leprosy Update, a total of 210,671 cases were reported from 150 countries during 2017, corresponding to an overall new-case detection rate of 2.77 per 100,000 people. Around 95% of cases occurred in 22 high burden countries of tropical Africa, Asia and Southern America. The number of new cases detected over the 10-year period 2008-2017 showed a slow decline. The registered global prevalence was instead increasing, with 192,713 cases at the end of 2017. The WHO received reports from European countries only in 2015 (18 cases), 2016 (32 cases) and 2017 (33 cases) (3, 9). In Europe leprosy is mainly diagnosed in foreign-born patients coming from endemic countries (6, 10-14).

In Italy autochthonous leprosy cases progressively decreased from the 1990s, and in 2003 the last case was reported (15). Today in Italy, as in most of Europe, leprosy is diagnosed in immigrants or Italians who have stayed or lived in endemic areas (16-18). Of the 65 cases reported from Europe in the 2-year period 2016-2017, 20 were from Italy (3, 9). In the 10-year period 2008-2017, the number of new cases ranged from 5 to 19 per year, about 80% of which were extra EU immigrants (17).

The cases of imported leprosy in Italy have been described from a clinical and therapeutic point of view (16, 17) and in terms of the general epidemiological trend (15), but not of the implications related to the management of cases and contacts by the Public Health Service of Local Health Authorities (LHAs) that have a specific role in the surveillance of infectious diseases. This paper describes the epidemiological investigation on the first case of imported leprosy in the Province of Rimini, an important tourist area on the Adriatic Sea, with a population of around 340,000 resident inhabitants (Emilia-Romagna Region, Northern Italy). The case has already been presented with the modalities of a letter (19) in which we have highlighted the critical issues of the surveillance measures in a low incidence country. Here we described in detail the epidemiological investigation and the management of the case and contacts in cooperation with the national and regional regulations and guidelines.

Control strategies for Hansen's disease in Italy

Leprosy has been a notifiable disease in Italy since 1934. Its notification is mandatory and currently regulated by the Health Ministry Circular n. 4, 13 March 1998 (20). To ensure greater effectiveness in the prevention and treatment of leprosy, the Italian Conference for the relations between the State and Regions, in 1999, defined the guidelines on diagnostic/therapeutic protocols and active surveillance of Hansen's disease (21). Subsequently, the government issued the Decree 31 May 2001 for the Regions (22), which updated the previous Presidential Decree of 21 September 1994 and established the tasks of the different institutions for the management of leprosy cases. Figure 1 summarizes the institutions involved in the integrated system for diagnosis, treatment, notification, information flow, and surveillance of leprosy.

The Regional Health Authorities must identify the dermatological operative units in their territory that act as Territorial Leprosy Centers (TLCs) for the monitoring of patients with suspected diagnosis and send them to one of the National Leprosy Centres (NLCs) for the confirmation of the case and the definition of the therapeutic protocol. Four NLCs have been established, one in Northern Italy (Genoa), one in Southern Italy (Gioia del Colle, Bari), and two in the major islands (Sicily and Sardinia). This surveillance system assures that patients are referred to centres experienced in the diagnosis and treatment of leprosy, which, being a sporadic disease in Italy, is little known by general clinicians. After the reporting of the suspected case from TLC and the confirmation from NLC, the LHA Public Health Service has to notify the case to the Regional Health Authority, implementing the epidemiological investigation to reconstruct the case history and to trace the patient's contacts. All the identified close contacts, in particular the household contacts, must be addressed to the TLC for the necessary clinical checks.

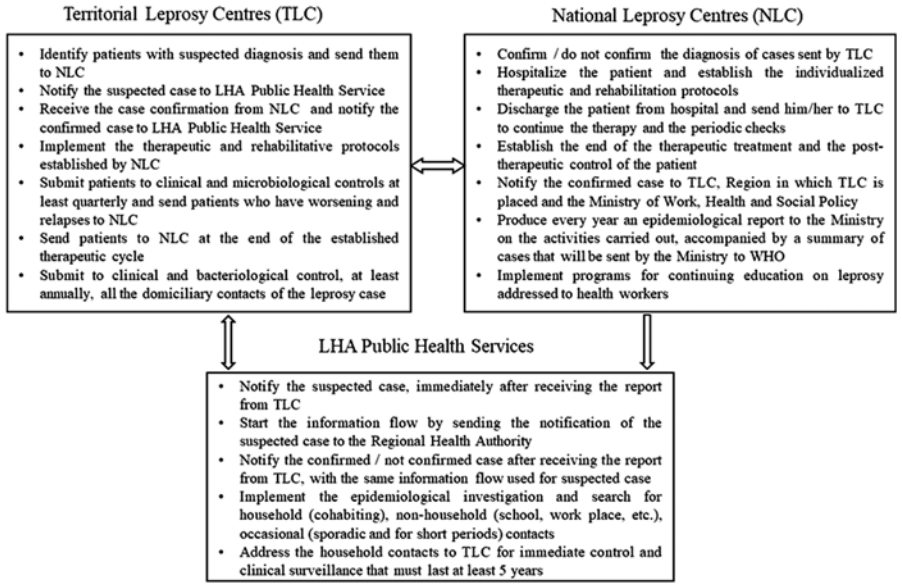

Figure 1 - Different tasks in the integrated system for diagnosis, treatment, notification, information flow and surveillance of leprosy in Italy

Due to the long incubation period of leprosy (3-5 years for the paucibacillary form, 9-15 years for the multibacillary form) follow up of the contacts must be carried out for at least 5 years with periodic visits at intervals of not less than 12 months (20).

Case Presentation

On 5 April 2017, a 29-year-old man from Nigeria referred to the dermatological unit of the public hospital of Rimini, because of non-itchy papulose lesions located on his head and hands. A first biopsy of the skin lesions of the head was made; the histological examination of the biopsy material revealed a chronic superficial and profound dermal inflammation of granulomatous epithelioid cells, without necrosis. The granulomas were well-formed and preferentially arranged in the periannexial and perineural sites, with a modest lymph-plasma cell component. The Ziehl-Neelsen staining revealed numerous alcohol-acid-resistant bacilli (ARB) while PCR analysis for *Mycobacterium tuberculosis* complex-DNA was negative. The patient was admitted to the infectious disease isolation ward, where a second biopsy from a lesion of the left helix was made. In the biopsy material *M., leprae* was identified by 16SrRNA gene sequence analysis. Neurological symptoms such as plantar anesthesia were also compatible with leprosy.

On 29 April 2017, the case was reported to the Public Health Service of Rimini, which started the information flow, notifying the suspected case to the Regional Health Authority. At the same time, the patient was addressed to the National Reference Centre for Hansen's disease (S. Martino Hospital, Genoa, Italy) where he was transferred on 3 May 2017. Based on microbiological examination of slit-skin smears, on 5 May 2017, the case was confirmed as Multibacillary Lepromatose Leprosy (BI = 4.67) and a nasal swab was found positive for ARB. The patient started specific therapy with the WHO schedule. After about 40 days the patient was discharged after three consecutive nasal swabs were negative for ARB.

Epidemiological investigation

Following the reporting of the suspected case by the dermatological unit of the city's public hospital, the LHA Public Health Service immediately started the epidemiological investigation to identify the contacts and adopt the necessary surveillance and control measures, according to the regional and national regulations (20-22). The case was interviewed. As well as general information and date of onset of symptoms, details were collected also on contacts. The patient was native of Nigeria and came to Rimini in July 2014. Before arriving in Italy he lived in Libya from May 2012 to June 2014. According to the interview, the first signs of the disease appeared in April 2014, when he was still in Libya. In Rimini, he participated in training programs promoted by local institutions and associations and worked first as an agricultural worker, then as a storekeeper in a company for agricultural products.

Considering the highly contagious form of leprosy (presence of numerous ARB in the nasal swab), the possible contacts in the years of permanence in the district of Rimini were sought, with the collaboration of the Prefecture of Rimini, where the data and the movements of non-Italian nationality immigrants are recorded. Figure 2 shows the data of the identified close contacts and the outcomes to follow up. In the first 6 months of stay in Italy, the patient lived at a hostel run by a cooperative that housed about 20 immigrants. For another period, in 2015, he was hosted in the homes of two Italian families, on a voluntary basis according to a

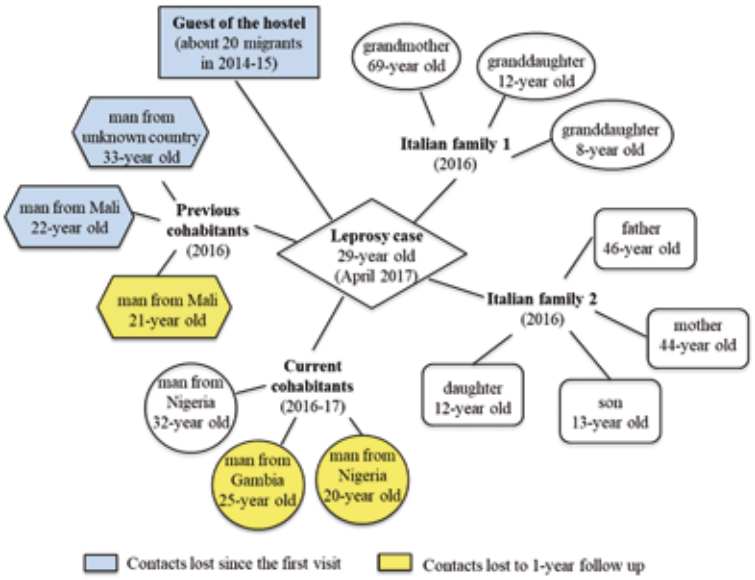

Figure 2 - Close contacts of the leprosy case

project of integration of foreign people, and had close contact with the family members: an elderly woman and two of her young grandchildren (family 1 contacts in Figure 2) and another family consisting of mother, father and two children (family 2 contacts in Figure 2). In the last year, the patient lived in an apartment together with other immigrants, three still living together at the time of diagnosis (current cohabitants in Figure 2) and three who had lived in the same apartment previously (previous cohabitants in Figure 2). The contacts in the hostel could not be traced, due to the long-time spent. A total of 13 close contacts were therefore identified, corresponding to the cohabitants of the case, defined by the Italian guidelines as "household contacts". Among these 13 close contacts, one was no longer traceable since the first visit and another refused to undergo the interview and medical examination. The others were interviewed and underwent a dermatological examination which gave a negative result for leprosy in all subjects.

Surveillance of case and contacts

The case underwent follow-up checks every month at the local infectious disease unit and every six months at the National Reference Center for Hansen's disease in Genoa, where he was hospitalized for more detailed clinical and laboratory controls. The checks carried out so far (the last in January 2019) evidenced no signs of evolving disease.

The patient's close contacts underwent surveillance with annual visits to the health center dedicated to the pathologies of migrants of the Rimini area. The surveillance did not include any chemoprophylaxis treatment, while they were recommended to undergo a visit at the local dermatology department in case of signs and symptoms onset. Up to now, one follow up check-up has been carried out. Only 8 of the 13 contacts attended the first visit after one year, all the 7 Italians and only 1 of the foreigners (Figure 2). No signs or symptoms of leprosy were reported and dermatological reports were negative.

Discussion

The Italian guidelines and the national and regional regulations establish the tasks of the different health institutions for the management of leprosy cases and contacts, in an integrated system for diagnosis, treatment, notification, and surveillance of leprosy in Italy (21, 22). Despite the low prevalence of leprosy (15), Italy is the European country that has reported the most cases to the WHO (20 out of 65 in the two years period 2016-17). This may be due to an actual higher number of cases of imported leprosy in Italy compared to other European countries, but also to the well-regulated and structured national surveillance system which allows for good management and notifications of cases.

Surveillance data are important for monitoring the leprosy burden and epidemiology, especially in the context of the migration flow, such as that occurring in Italy. In the province of Rimini, the registered foreign residents, updated to 2015, were about 37,000 (11% of the resident population) of which 15.3% incoming from Africa (6.2% Morocco, 4.4% Senegal, 3.1% Tunisia, 0.6% Nigeria). Asylum seekers are constantly increasing: from 189 in 2013 to more than 700 in 2016, coming from Nigeria, Bangladesh, Somalia, Eritrea and Pakistan (data provided by the Prefecture of Rimini).

This first case of leprosy observed in the Rimini area highlighted how the Italian system ensured efficient clinical management of the case, which was addressed and assisted in a center of reference that could guarantee the necessary expertise. The national reference center also managed the clinical follow-up of the case.

However, some critical issues can be highlighted. The first concerns the delay in recognizing the case that arrived in Italy with signs and symptoms of leprosy already present. In the 3 years of stay in Italy, after arriving from Libya, no health care providers suspected the disease and proceeded with the necessary clinical tests. The delay in diagnosis made surveillance impossible for the close contacts living with the case in the first period of stay in Rimini (guests of the hostel). It is therefore fundamental to promote expertise among general clinicians and other health and social professionals on leprosy and other neglected diseases (18, 23). Leprosy should be always considered among the differential diagnosis in migrants with cutaneous and neurological suspect signs and symptoms, as recommended by many experts (1, 6, 15, 17).

A second critical issue regards the management of contacts due to the particular characteristics of the involved people, who are above all migrants for whom it is difficult to trace the movements. To provide information on migrant movements and to reduce the loss at follow-up, the involvement of State institutions responsible for registering migrants (in Italy the Prefectures) is fundamental. Besides, also non-health institutions and professionals in the social context (non-profit organizations, charities, voluntary associations, etc.) should be involved to improve the access of foreign people to health services, in particular, the irregular migrants who stay in temporary reception centers or other facilities where they participate in integration programs. The case and contact management are equally important, following the WHO Global Leprosy Strategy 2016-2020, that recommends the development of national plans to ensure screening of all close contacts, especially household contacts (5).

The experience gained from this event highlights that, although in Italy there is a codified system of notification and surveillance of leprosy, it is not always possible to comply with the surveillance measures established by the guidelines and regulations, due to the particular conditions

of the involved people. Probably this is one of the main causes of the underestimation of imported leprosy cases in Italy which, as assessed by Massone et al. (15), are 90% lower than expected. In the current context of immigration, often uncontrolled, the management of exotic neglected diseases represents a new challenge for the Italian Public Health Authorities, which must know how to respond to the new needs.

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Riassunto

Diagnosi di lebbra in un migrante nigeriano: implementazione di misure di sorveglianza nel contesto migratorio attuale

Background. In Italia la lebbra si presenta con casi di importazione in migranti provenienti dai paesi endemici o in italiani che hanno soggiornato nelle stesse aree di endemia. Qui riportiamo il primo caso di lebbra osservato nel territorio di Rimini (Emilia Romagna) in un migrante originario della Nigeria.

Metodi. Dopo la descrizione dei compiti delle varie Istituzioni sanitarie coinvolte nel sistema integrato per la diagnosi, il trattamento e la sorveglianza della lebbra in Italia, sono descritte le modalità di gestione e di sorveglianza del caso di lebbra e dei suoi contatti stretti.

Risultati. Un caso di lebbra lepromatosa multibacillare è stato diagnosticato nell'aprile del 2017 in un uomo nigeriano di 29 anni che era arrivato a Rimini nel luglio del 2014, dopo un soggiorno in Libia di 2 anni. Il Servizio di Sanità Pubblica locale ha condotto l'inchiesta epidemiologica e identificato i contatti stretti del paziente. La gestione del caso e la sorveglianza dei 13 contatti domiciliari identificati, 7 italiani e 6 migranti, hanno messo in evidenza alcune criticità. La diagnosi tardiva del caso, dovuta alla carenza di conoscenza sulla malattia dei medici di medicina generale e di altri professionisti socio-sanitari, e la perdita al follow up dei contatti stretti (5 dei 6 migranti) hanno rappresentato importanti ostacoli al pieno successo delle misure di sorveglianza.

Conclusioni. Benché in Italia ci sia un sistema ben codificato di notifica e sorveglianza della lebbra, il riconoscimento del caso e l'identificazione e il follow up dei contatti sono resi difficili dalle particolari condizioni delle persone coinvolte. Questo rappresenta una sfida per i Servizi di Sanità Pubblica che, nell'attuale contesto di immigrazione, spesso incontrollata, devono saper rispondere alle nuove esigenze, in stretta collaborazione con le Istituzioni statali responsabili della registrazione dei migranti e di quei professionisti socio-sanitari che potrebbero facilitare l'accesso degli stranieri ai servizi sanitari.

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