Leprosy in Britain: 50 years experience in Liverpool

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Received 21 December 2004 and in revised form 18 April 2005

Summary

Background: Leprosy is a chronic infection that presents with varying dermal and neurological symptoms, and which can lead to extensive disability and morbidity, often with accompanying social stigma.

Aim: To review the patients presenting to the Liverpool School of Tropical Medicine (LSTM) between 1946 and 2003, looking specifically at country of birth and of infection, details of clinical presentation, diagnosis, management and reactions.

Design: Retrospective record review.

Methods: We retrieved all available clinical records for patients seen between 1946 and 2003 (n = 50), consisting of letters, hospital and LSTM casenotes, and some radiographs and photographs. Any history of tuberculosis or diabetes was recorded.

Results: Most patients (64%) were born in the Indian subcontinent, and most were thought to have contracted the disease there (62%). Features at presentation included anaesthetic skin lesions in 19 (36%), hypopigmentation in 15 (30%), and peripheral nerve enlargement in 25 (50%). Diagnoses were made by a combination of clinical data and biopsy (60%), and slit skin smears were positive for acid-fast bacilli in 61% of multibacillary patients. Initial presentation was with a leprosy reaction in five cases (10%), and reactions were documented in 42% of all patients. Treatments were varied, progressing from traditional Eastern medicine to the WHO-approved multidrug therapy in use today, with prophylaxis for children and close contacts.

Discussion: Leprosy remains an important diagnosis to consider in patients with a history of work or travel in the tropics, and is a diagnosis with far-reaching medical, social and emotional consequences.

Introduction

Leprosy is a chronic and progressive granulomatous disease caused by Mycobacterium leprae, an acid-fast intracellular organism that has not yet been cultured in vitro. It is spread from person to person by droplet, and has a long incubation period, measured in years. It causes characteristic, often anaesthetic skin lesions, peripheral neuropathy and peripheral nerve thickening. The wide spectrum of clinical presentation is determined by the degree of host cell-mediated immunity (CMI) expressed against M. leprae. A high degree of CMI results in the tuberculoid presentation, with localized, asymmetric lesions and few viable bacilli; a lesser degree of CMI results in the more infectious lepromatous presentation, with widespread organisms and many lesions. Between these two extremes are a range of borderline presentations, with varying numbers of bacilli and type of lesions.

The introduction of combination multidrug therapy (MDT) with dapsone, rifampicin and clofazimine in 1982, has resulted in highly effective treatment with a low relapse rate. Most physical disability caused by the infection results from damage to inadequately protected anaesthetic limbs,

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or from acute nerve palsies during immunologically-mediated ‘reactions’ that occur as part of natural history of the infection, or following successful antimicrobial therapy. It is also important to note the high frequency of ‘silent’ progressive or recurrent neuritis among leprosy reactions, which can lead to significant morbidity. The most important aspects of successful prevention of disability are early diagnosis and treatment, early recognition and aggressive management of reactions, and continued education and motivation of the patient in the care of damaged skin, eyes and limbs. The disease still attracts significant social stigma, and patients may fail to recognize their own disease or deliberately conceal it to avoid potential ostracism.

Approximately 2.2 billion people worldwide live in areas with estimated prevalences of over one case of leprosy per 1000 population, and leprosy is still endemic in the Indian sub-continent, where approximately 70% of worldwide cases occur. The worldwide prevalence is difficult to quantify, due to variations in case definition and diagnosis, but in 2001 the World Health Organization (WHO) estimated that there were 0.7 million cases, a significant reduction from the 1980s, when cases were estimated to number 10–12 million. This reduction in prevalence is variously ascribed to improved and progressively shortened multidrug therapy, or to changes in coding and disease definition, such that certain patients are no longer classified as having active disease, especially once they have completed specific chemotherapy.

Leprosy is still an important diagnosis to consider in patients who have lived in the tropics, particularly the Indian subcontinent, with approximately 10 new cases notified each year in England and Wales. Diagnosis is frequently delayed, and patients typically see two or three specialists over a period averaging 18 months before the diagnosis is finally established. Most patients are referred to dermatologists, neurologists or orthopaedic surgeons, with a minority attending rheumatology clinics. Ultimately, all patients should be managed in conjunction with a named specialist in leprosy, as work-up and treatment requires specialist expertise and long-term follow-up for several years.

Patients with possible leprosy in the North of England are usually referred to the Liverpool School of Tropical Medicine (LSTM). We have reviewed our experience with 50 patients seen since 1946, looking particularly at modes of presentation and the geographical origins of patients. Where possible, we have compared our findings to a similar study performed in Birmingham in 1983, in order to draw conclusions about the role and importance of leprosy in British centres outside London.

**Methods**

The medical records of patients with leprosy are preserved for long periods in the LSTM clinic, as patients may be referred back after several years for advice or because of late disease complications. We retrieved all available clinical records for patients seen between 1946 and 2003, consisting of letters, hospital and LSTM casenotes, and some radiographs and photographs. All patients with leprosy should be notified to the public health authorities, and a central register of these notifications has been maintained since 1951, to which all our patients have been reported.

Clinical and demographic data were extracted from the records using a standardized proforma, followed by tabulation and simple descriptive analysis using Excel. Particular attention was given to the mode of presentation, including duration and type of symptoms and any reactions reported, and to patient history such as country of birth and disease acquisition. Past history of tuberculosis was noted, as this is thought to confer a limited degree of protection against other mycobacterial infection, including leprosy. As there is considerable crossover between the neurological presentations of leprosy and diabetic neuropathy, any history of diabetes was also recorded. Ethical permission was not required for this retrospective survey of our own patients, and data were anonymized and kept secure according to current recommendations.

**Results**

Clinical records were obtained for 50 patients, approximately 50% of whom first presented in the 1970s (Figure 1). The demographic and clinical features of the patients are summarized in Table 1.
Table 1  Demographic and clinical features of patients seen in Liverpool, compared to an earlier series of patients reviewed in Birmingham

<table>
<thead>
<tr>
<th>Liverpool</th>
<th>Birmingham</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of patients</td>
<td>50</td>
</tr>
<tr>
<td>Age (years)</td>
<td>Range 9–77</td>
</tr>
<tr>
<td></td>
<td>Mean (IQR) 39 (28–52)</td>
</tr>
<tr>
<td>Gender (M:F)</td>
<td>28:22</td>
</tr>
<tr>
<td>Years in UK before presentation</td>
<td>Range 0–38</td>
</tr>
<tr>
<td></td>
<td>Median (IQR) 4 (2–8)</td>
</tr>
<tr>
<td>Symptom duration (years)</td>
<td>Range 0–20</td>
</tr>
<tr>
<td></td>
<td>Median (IQR) 2 (0.4–3.0)</td>
</tr>
<tr>
<td>Patients (%) from Indian subcontinent</td>
<td>32 (64%)</td>
</tr>
<tr>
<td>Transmitted in Indian subcontinent (%)</td>
<td>31 (62%)</td>
</tr>
<tr>
<td>Classification</td>
<td>Tuberculoid (TT) 17 (34%) incl. 2 neuritic</td>
</tr>
<tr>
<td></td>
<td>Borderline tuberculoid (BT) 8 (16%)</td>
</tr>
<tr>
<td></td>
<td>Borderline (BB) 3 (6%)</td>
</tr>
<tr>
<td></td>
<td>Borderline lepromatous (BL) 5 (10%)</td>
</tr>
<tr>
<td></td>
<td>Lepromatous (LL) 15 (30%)</td>
</tr>
<tr>
<td></td>
<td>Unspecified 2 (4%)</td>
</tr>
<tr>
<td>Bacilli seen on skin smears</td>
<td>All recorded smears 14/33 (42%)</td>
</tr>
<tr>
<td></td>
<td>Multibacillary patients 14/23 (61%)</td>
</tr>
<tr>
<td>History of TB</td>
<td>10%</td>
</tr>
<tr>
<td>History of diabetes</td>
<td>6%</td>
</tr>
<tr>
<td>Known leprosy contact</td>
<td>10%</td>
</tr>
<tr>
<td>Reactions</td>
<td>32 reactions, 21 patients</td>
</tr>
</tbody>
</table>

IQR, interquartile range; N/A, not available.

Demographics

There was a broad range of ages, time spent in the UK before diagnosis, and duration of symptoms; the gender distribution was broadly equal. The distribution of age at presentation was positively skewed, so we performed a logarithmic conversion to bring this closer to a normal distribution, and calculated the median and IQR rather than mean and SD.

The majority of patients were born in Asia (64% from the Indian subcontinent), and lived in towns in the North-West of England with a long tradition of immigration from the Indian subcontinent. Most patients (25, 50%) presented to the LSTM within 5 years of arrival in the UK (usually within the first 2 years), and most had symptoms since before their arrival. Time spent in the UK prior to LSTM presentation ranged from zero (i.e. identified on immigration) to 25 years (Figure 2). The data were positively skewed, with a median of 4 years, IQR 2–8 years.

Similarly, the location of probable acquisition was the Indian subcontinent in 62% of cases, with the remainder being mainly from Africa and South America. There was one case of leprosy transmission within the UK. This 9-year-old girl was born in the UK, and acquired leprosy in the 1940s from her father, who had acquired lepromatous disease in Brazil.

Eighteen patients (36%) presented to the LSTM within one year of symptom onset. Only seven (14%) presented >5 years after symptom onset, and these were generally not new presentations of leprosy. Symptom duration was not known in 10 patients (20%). Again, the data were positively skewed, with a median of 21 months (IQR 5 to 36 months), and a bimodal distribution.

Only 22 (44%) of the patients presenting to the LSTM with leprosy were new diagnoses, and
complete data regarding the condition of the other patients before arrival in the UK were not always available. Sixteen (32%) had either been diagnosed previously (usually while overseas), or had presented with symptoms that, retrospectively, were prior manifestations of leprosy. Eight of these patients had been treated previously and were seen at the LSTM with relapsing symptoms.

Presenting features

For each symptom, data were not documented for 10–12% of patients. Eighteen patients (36%) had anaesthetic skin lesions at the time of presentation: of these, nine (18%) had multiple lesions, six (12%) had single lesions, and two (4%) described generally anaesthetic patches rather than discrete lesions. Fifteen patients (30%) had evidence of hypopigmentation at presentation. Thirty-one (62%) had peripheral neuropathy, and peripheral nerve enlargement was demonstrated in 25 (50%). Multiple presenting symptoms were reported in 30 patients (60%); only 12 patients (24%) had only one characteristic feature. Two patients, both from the Indian subcontinent, had all three characteristic signs at presentation. Two patients did not report any of the characteristic symptoms: one of these was noted on immigration from Kenya to have missing digits and the characteristic leonine facies of long-standing leprosy; the other, from Zambia, presented with an acute erythema nodosum leprosum (ENL) reaction, with no reports of previous symptoms.

Of the patients who presented with skin lesions, typical findings were nodular plaques and raised granulomatous depigmented lesions, but it was difficult to provide a useful classification of skin lesions from the notes available to us.

Data on the other relevant medical conditions were fully recorded in less than 20% of case-notes. There was a history of tuberculosis in five patients (10% of total sample); three from India, one from Kenya and one from Poland (via Brazil). Diabetes was present in three patients (6%) aged 55, 60 and 64, two of whom were from India. Only five patients (10%) were able to recall contact with other leprosy patients, including an expatriate who had worked for many years as a leprosy nurse throughout Asia.

Diagnosis and management

The majority of patients (30, 60%) were diagnosed by biopsy, and disease classification was generally based on a combination of clinical and histological features, according to the scheme of Ridley and Jopling. The classifications recorded by the attending clinicians at the time of presentation to the LSTM are summarized in Table 1.

Skin smear results were not documented in 17 (34%) of patients, although nine of these had a clinical diagnosis of tuberculoid (TT), neuritic or borderline tuberculoid (BT) disease in which skin smears are not expected to be positive. Leprosy bacilli were detected in slit skin smears at the time of presentation in 14/50 patients (28%) overall, and in 14 (61%) of the 23 with multibacillary (i.e. borderline, BB; borderline lepromatous, BL; lepromatous, LL) disease for whom results were recorded. In the multibacillary group, skin smears were positive in 8/16 of those who had received leprosy treatment for at least a year before presentation to the LSTM.

Reactions

A total of 32 reactions were documented in 21 patients (42%), with multiple reactions in nine patients. Reactions were the reason for initial presentation of five patients. The type of reaction was not clearly documented in some cases, but erythema nodosum leprosum (ENL) reactions were the most common (56%). These reactions are summarized in Table 2, with a breakdown of the type of reactions encountered in the various forms of leprosy. Ten of the 23 (43%) patients with multibacillary disease had ENL reactions and six (26%) had other types of reaction. Four of the 24 (16%) patients with paucibacillary disease had reactions, of which two reactions (in one patient) were classified at the time as ENL. On detailed review of the case notes of this patient, it was difficult to confirm or refute this unlikely classification in retrospect.

Treatment

The period of this review encompasses all the major advances in leprosy chemotherapy of the twentieth
century, and the early case notes included fascinating accounts of the use of treatments such as thiambutasine, promanide, and chaulmoogra oil. Chaulmoogra oil had been used in the East for centuries, and was integrated into Western medicine in the nineteenth century, but became redundant with the discovery of dapsone. Most patients in the 1960s and 1970s were treated with prolonged courses of dapsone, supplemented with clofazimine and rifampicin as they became available.4 As drug resistance became recognized, skin biopsy material from some patients was assessed for drug sensitivity after mouse footpad inoculation.4 Since 1982, patients have been treated using the MDT combinations recommended by the WHO.3–6 Multibacillary disease (LL, BL or BB) is treated with a combination of daily dapsone and clofazimine supplemented by monthly rifampicin and clofazimine. Paucibacillary disease (BT, TT, or indeterminate) is treated with daily dapsone and monthly rifampicin. After the WHO guidelines were published in 1982, several patients were recalled for ‘clean-up’ courses of MDT to prevent later relapses.21 The families of most lepromatous patients were offered BCG vaccination if they had not already received it,18 and young children in contact with newly-diagnosed lepromatous disease were given a 6-month course of chemoprophylaxis with monthly rifampicin.6

Discussion

Nearly half of the patients were first seen at the LSTM in the 1970s, the period predominantly covered by the case series reported from Birmingham17 (see Table 1 for a comparison). Nationally, notification of new cases peaked in the 1960s, but was still substantial in the following decade.13 Our sample is larger than that in the Birmingham report, with a more equal gender distribution. However, as males are usually affected twice as often as women, one would expect a truly representative sample to have a gender distribution somewhere between that of this sample and that of the Birmingham study.1,17 The gender ratio in leprosy is known to vary in different parts of the world, presumably due to differences in social mobility and hence exposure in women. The difference from Birmingham may be related to the lower proportion from the Indian subcontinent, and inclusion of patients from more recent years, with changes in social norms for women in many countries. In some parts of the South Asian sub-continent, a proportion of 45% women would not be uncommon in the present day.

Age distribution in our sample was similar to that in Birmingham, with young adults being over-represented in both cities. There was no clear reason for this, but a bimodal age distribution has been reported by other researchers, with a first peak among young adults, and a second peak in middle age, the reasons for which are unclear.22 The peak among young adults in our study may also be an artefact of the high levels of immigration among people of this age.

Time spent in the UK prior to presentation showed a bimodal distribution, with a peak in the first few years after arrival, and another at around 20 years after immigration. A similar bimodal distribution was seen in symptom duration, with a peak at 3 years, and another at over 10 years. This may reflect two broad groups of patients: those who seek healthcare when symptoms begin or become an inconvenience; and those who defer medical treatment, for financial, geographical or social reasons, until it becomes unavoidable.

The majority of patients in this study were from the Indian subcontinent. This was as expected, considering the high prevalence and endemicity of leprosy in this area, and was similar to the Birmingham review, where 26/30 patients included were from this region. Similarly, most leprosy transmission had occurred in the Indian sub-continent. There was however, one case of leprosy transmission in the UK, a phenomenon not reported since the early 1920s,23 although an immunological response to leprosy exposure was reported in two patients in a British nursing home in the late 1980s.24

Distribution of disease classification (Table 1) in this sample differed from that in Birmingham, where there were fewer cases of polar (pure tuberculoid or pure lepromatous) disease and a higher proportion of patients with borderline disease.17 This may be

Table 2  Details of 32 reactions as documented in the casenotes of 21 patients, according to leprosy classification (the columns add up to more than 100%, as some patients had more than one reaction or type of reaction)

<table>
<thead>
<tr>
<th>Reaction type</th>
<th>TT/BT/neuritic</th>
<th>Other</th>
<th>LL/BL</th>
<th>Total patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>None</td>
<td>19/24 (79.2%)</td>
<td>2/3</td>
<td>8/23</td>
<td>29/50 (58%)</td>
</tr>
<tr>
<td>ENL</td>
<td>2</td>
<td>0</td>
<td>16</td>
<td>18</td>
</tr>
<tr>
<td>Reversal</td>
<td>3</td>
<td>2</td>
<td>4</td>
<td>9</td>
</tr>
<tr>
<td>Downgrading</td>
<td>0</td>
<td>2</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td>Not specified</td>
<td>0</td>
<td>3</td>
<td>0</td>
<td>3</td>
</tr>
</tbody>
</table>

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due to variations in classification practices between the two centres.

The proportion of patients found to have leprosy bacilli on slit skin smears in this study was similar to the 33% reported in the Birmingham study. However, in over a third of our patients, slit skin smear results were not clearly documented.

Ten per cent of patients in this study had a history of tuberculosis. This is higher than would be expected in a normal population, but is likely to be due to high prevalence in the patients’ countries of origin, rather than a feature of leprosy. The prevalence of diabetes in this study was 6%, higher than the UK national average, though the numbers are small and the power low. The three patients in question were aged 55, 60 and 64, and as type 2 diabetes is common at such ages, this is also unlikely to be a feature of the leprosy itself. Diabetes prevalence is also known to be increased in Asian countries, with a prevalence of over 12% in Asians aged 60–69. These data make our high prevalence of diabetes less remarkable, although some reports suggest high rates of diabetes in patients with leprosy. Co-existing diabetes is particularly important to diagnose, as any peripheral neuropathy will exacerbate the dermal manifestations of leprosy and make disease control more difficult. Conversely, the diagnosis of leprosy may be overlooked in diabetic patients with neuropathy unless thickened nerves are palpated.

Only five patients (10%) could recall previous contact with leprosy, including one nurse who had worked for many years with leprosy patients in the tropics. Since transient contact with leprosy is usually not sufficient to allow transmission, more patients would be expected to recall such contact. However, as the majority of patients were from the Indian subcontinent, long-term contact with subclinical or unrecognized disease is quite possible.

One aspect that we have not been able to closely examine is treatment and outcome. This is partly due to ongoing treatments, but also a result of the variability of treatment over time. Also, we were unable to ascertain the proportion of patients who were initially misdiagnosed or inappropriately referred, which has been described as the cause of significant delay in diagnosis and treatment of 82% of leprosy patients in the UK.

The patients described here demonstrate the various features of leprosy, their temporal prevalence, and the high proportion of leprosy acquisition in the Indian subcontinent. An important point about the presentation of leprosy is that, whatever the presenting complaint, additional symptoms and signs were found on further questioning and examination of all but the two patients with pure neuritic leprosy.

In summary, leprosy, despite its low prevalence in the UK, is an important differential diagnosis, particularly in immigrants and expatriates from the Indian subcontinent who have dermatological or neurological complaints. It is an important cause of disability in these patients, and as a curable disease, rapid diagnosis and expert treatment are vital, and clinicians must be alert to avoid delay through inappropriate referrals to dermatologists or neurologists. This is particularly important in reactional states, which may be difficult for general clinicians to diagnose, and which may continue to occur and cause potentially severe disability long after curative chemotherapy has finished. Patients should be referred to a specialist with experience of managing leprosy (see Appendix). Notification to the appropriate health authority is also essential, but as this is a distressing diagnosis, discussion with the leprologist should precede this notification. Confidentiality and discretion is vital, with the use of the term ‘Hansen’s disease’ being preferable to ‘leprosy’. A multidisciplinary approach, including foot care, is crucial for optimal results. This study highlights the essential features of leprosy in the UK, and provides important epidemiological and clinical data for both general clinicians and leprologists.

Acknowledgements

We thank the clinicians who have referred patients to the clinic and shared in their care, and Mr Alistair Story from the Communicable Disease Surveillance Centre, Health Protection Agency, Colindale, for confirming the central notification status of our patients.

References


Appendix: Contact details for British leprosy experts

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