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The diagnosis of leprosy is delayed in the United Kingdom

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Summary

Diagnostic delay in leprosy can have serious neurological consequences for the patient. We studied the presentation of leprosy patients, focusing on delays in diagnosis, in a retrospective case-note review of 28 patients referred to The Hospital for Tropical Diseases during 1995–1998. The median ages at onset of symptoms and at diagnosis were 25.1 years (range 9–77.7) and 30.1 years (range 9–78.3), respectively. The median time from symptom onset to diagnosis was 1.8 years (0.2–15.2). Prior to referral to a leprologist, patients had seen a dermatologist (20), neurologist (9), orthopaedic surgeon (5) and rheumatologist (2). Delay in diagnosis occurred in 82% of cases. Misdiagnoses as dermatological and neurological conditions were important causes of delay, and 68% of patients had nerve damage resulting in disability. Leprosy can be difficult to diagnose outside endemic areas. Increased awareness amongst general practitioners and hospital specialists would lead to more rapid diagnosis, thus minimizing damage and disability.

Introduction

Leprosy may be a difficult disease to diagnose outside its endemic areas. The disease has a long incubation period (2–11 years),[1,2] and patients may have long left the endemic area when they first present to a doctor with symptoms and signs of leprosy. A combination of skin lesions and neuropathy that would have been quickly recognized as leprosy in an endemic country may not be recognized in another country where leprosy is rare. Leprosy may also present with a variety of skin lesions and nerve damage that is only apparent on careful testing. For patients it is important that the diagnosis of leprosy should be made as early as possible so that effective antibacterial treatment can be started and steps taken to prevent nerve damage.

In the UK, the usual sequence of consultation for the patient is from the general practitioner to a dermatologist (most commonly), a neurologist or a rheumatologist, and thence to The Hospital for Tropical Diseases, London for a specialist opinion.

We reviewed the presentation of patients with leprosy seen at the Hospital for Tropical Diseases over the last four years, with respect to the clinical presentation of disease, patient characteristics, the type of medical practitioners they presented to, and when they presented. We wanted to determine if there was a delay in diagnosis, to quantify and identify reasons for any delay and to describe the consequences of delay in terms of disability.

Methods

The case notes of 28 patients with leprosy referred to one of us (DL) at the Hospital for Tropical Diseases between May 1995 and December 1998 were reviewed retrospectively using a proforma. Data were collected on age, sex, ethnicity, and geographical origin. All patients had been asked about their first symptoms and their timing, and the medical services they had consulted both abroad and in England.

Routine clinical evaluation includes detailed body charting with descriptions of skin lesions,

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testing for anaesthesia in skin lesions, and neurological evaluation. All peripheral nerves are palpated for enlargement and tenderness; peripheral nerve function is assessed by testing muscle function of the small muscles of the hands and feet and orbicularis oculi. Sensation in the hands and feet is tested using graded Semmes Weinstein monofilaments (calibrated nylon threads that deliver a known weight when applied to the skin).[3] All cases had either a skin biopsy from a suspect lesion or a peripheral nerve biopsy taken and reviewed by Professor Sebastian Lucas (King's, Guys and St Thomas's Hospitals, London).

Nerve damage was defined as failure to feel a 4 g monofilament in the hands or a 10 g monofilament in the feet, or power 4 or less on the MRC scale, and evidence of muscle wasting. Disability was graded according to the WHO grading system.[4] For hands and feet: Grade 0 (G0), no anaesthesia, no visible deformity or damage; Grade 1 (G1), anaesthesia as defined above, without visible deformity or damage; and Grade 2 (G2), visible deformity or damage. We modified the WHO criteria G1 into G1a and G1b. G1a was retained as the original G1 definition and G1b was taken as weakness (MRC 4 or less) but no visible deformity or damage. For eye disability: G0, no eye problems due to leprosy, no evidence of visual loss; G1, eye problems due to leprosy but with vision not severely affected (vision 6/60 or better); G2, severe visual impairment (vision worse than 6/60). The grade recorded was that of the eye most severely affected.

A delay in diagnosis was defined as being a point of consultation along the referral pathway where no diagnosis or a misdiagnosis was made.

Results

Twenty-eight new patients were seen between 1995 and 1998; 19 were male and nine female. Seven patients were seen in 1995, 12 in 1996, four in 1997, and five in 1998. All the cases in the UK were resident in England; there were no cases referred from Wales, Scotland or Northern Ireland. Table 1 shows the ethnicity of the patients. The largest single group of patients (43%) came from the Indian subcontinent, with 25% from Bangladesh. Patients came from a wide-range of leprosy-endemic areas. Three patients were Caucasian-British, and had acquired their leprosy in India, Nepal and Bangladesh, having lived there 24 years, 8 years, and 48 years, respectively. One of these three was an orthopaedic surgeon (not a leprosy specialist), another a missionary, and the third had been born in India. For all other patients, ethnicity and geographical site of leprosy acquisition were concordant. Table 2 summarizes age at entry to the UK, age of onset of symptoms, age at time of diagnosis, time interval from onset of symptoms to diagnosis (lag time) and time interval from entry to UK and diagnosis (latency). Three patients were diagnosed before arriving in the UK, and their data were not included in the calculation of latency. Only one patient in our series was a child when first seen at the Hospital for Tropical Diseases. There was a long lag time, mean 3.1 years (range 0.2–15.2 years) between symptom onset and diagnosis. In 15 (54%) patients, symptoms started after leaving the endemic area. The nine lepromatous (7LL, 2BL) patients were potentially infectious to others before diagnosis and treatment; in this subgroup the latent time to diagnosis was 5.3 years (1–27) with a mean lag time of 2.6 years (0.3–13.1).

Table 1 Geographical origin of 28 patients presenting with leprosy between 1995 and 1998 to The Hospital for Tropical Diseases

Region	*n*	%
Indian subcontinent *(Bangladesh 7; India 3; Nepal 1; Sri Lanka 1)*	12	43
Africa *(Nigeria 3; Sierra Leone 2; Congo 1; Egypt 1)*	7	25
Americas *(Brazil 1; Ecuador 1; Guyana 1)*	3	11
Caucasian-British	3	11
Caribbean *(Jamaica 1; St Lucia 1)*	2	7
China	1	3
Total	28	100

Table 2 Timing of leprosy symptoms and diagnosis

	Mean (years)	Median (years)	Range (years)
Age of entry to UK	32.6	29.5	12.0–76.0
Age onset symptoms	33.4	25.1	9–77.0
Age of diagnosis	35.7	30.1	9–78.3
Time from symptom onset to diagnosis (lag)	3.1	1.8	0.2–15.2
Time from UK entry to diagnosis (latency)	7.7	2.6	0.2–47.8

Nine patients presented with tuberculoid leprosy, nine with borderline-tuberculoid, one with mid-borderline, two with borderline-lepromatous, and seven with lepromatous leprosy. With these small numbers it is not possible to comment on any association between type of disease and endemic region. Four patients (14%) had pure neuritic leprosy (i.e no detectable skin lesions). Of the 28 patients, 21 had typical leprosy skin lesions (Figure 1), 22 had thickened nerves, and 17 had nerve damage, at their first consultation at the Hospital for Tropical Diseases. The clinical course of leprosy is frequently complicated by 'reactions', which are episodes of immunologically-mediated inflammation. Nine patients were in reaction at the time of presentation: eight of these were Type I (reversal) reactions requiring treatment with steroids and one had erythema nodosum leprosum. One female patient presented with a type 1 reaction 20 weeks after delivering a baby.

Table 3 documents the peripheral nerves that were affected and the number of patients with involvement of particular nerves. The posterior tibial nerve was the most commonly affected nerve trunk, and a third of patients had a generalized glove and stocking neuropathy. Table 4 documents the severity of nerve involvement, 19 (68%) patients had evidence of disability from nerve damage involving their hands or feet, with 36% having Grade 2 disability of hands or feet. Six (21%) patients had ocular disability due to leprosy, one a Grade 2 disability.

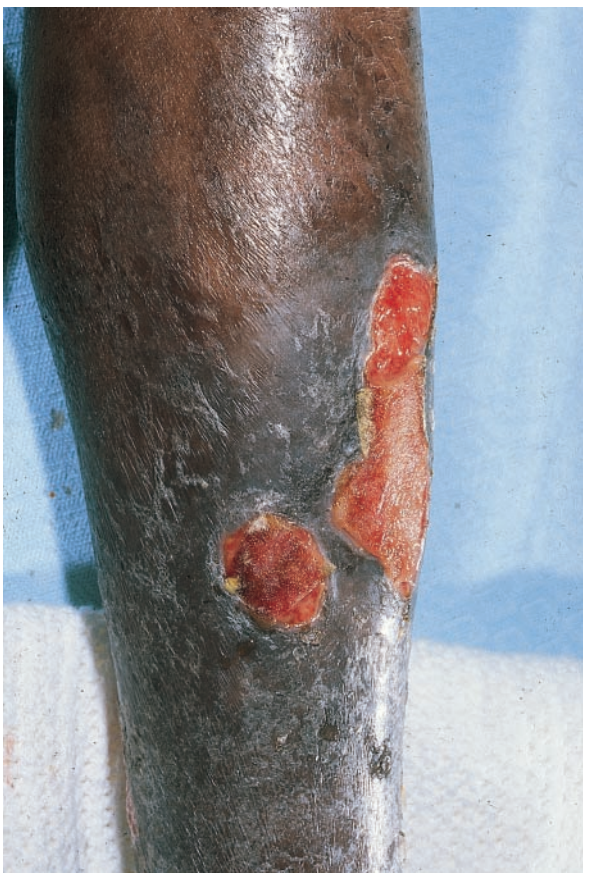

Figure 1. A typical lepromatous skin lesion. The skin is dry, infiltrated and anaesthetic with secondary injury.

The diagnosis of leprosy was made in the UK for 26 patients. The commonest referral pathway was from a general practitioner to a dermatologist to the leprologist ($n = 11$). Twenty-five patients had seen a general practitioner for their first consultation. The specialists seen before the leprologist were dermatologists (20), neurologist (9), orthopaedic surgeon (5), and rheumatologist (2). Seven patients were seen by two specialists and four by three specialists. In 23 cases, the diagnosis of leprosy had been unreasonably delayed. Points of delay identified along the referral pathway in the UK were general practitioner (10), orthopaedic surgeon (5), neurologist (4), dermatologist (3), the Hospital for Tropical Diseases (2), rheumatologist (2), ENT surgeon (1), and unknown (2). Three patients were misdiagnosed overseas. Table 5 documents the misdiagnoses. The main reason for delay was misdiagnosis as commoner conditions. In 23 patients a misdiagnosis was made: 7 were dermatological, and 8 neurological. Both neurologists and orthopaedic surgeons failed to consider leprosy as a possible cause of ulnar neuropathy (four cases). Six patients had an unusual presentation, two patients withheld the previous diagnosis of leprosy and two patients languished on waiting lists (Table 6). Cultural factors can cause delay: one patient declined nerve biopsy during Ramadan and was lost from the waiting list. Diagnosis by biopsy was important, as in 7/17 cases diagnosed by

Table 3 Peripheral nerve involvement in patients

Nerve	*n* (of 28 total) (%)
Ulnar	12 (43%)
Median	6 (21%)
Common peroneal	10 (36%)
Posterior tibial	13 (46%)
Trigeminal	1 (3.5%)
Glove or stocking neuropathy	11 (39%)

Table 4 Disability grades present in patients at diagnosis

	G0	G1a	G1b	G1a&b	G2
Hands and feet	9 (32%)	4 (14%)	3 (11%)	2 (7%)	10 (36%)
Eyes	8	5	–	–	1

Table 5 Misdiagnoses in patients presenting with leprosy between 1995 and 1998

Dermatological condition *(fungal 3; cellulitis 2; psoriasis 1; vasculitis 1; ulcer unspecified 3)*	10
Neurological condition *(unexplained neuropathy 4; ulnar nerve entrapment 2)*	6
Orthopaedic condition *(soft tissue infection 3; ulnar nerve entrapment 2)*	5
Rheumatological condition *(arthritis 2; gout 1)*	3
Tropical condition (filariasis)	1
Total	25

Table 6 Causes of delay in diagnosing leprosy in patients presenting with leprosy between 1995 and 1998

Unusual presentation *(pure neuritic leprosy 4; trigeminal nerve involvement 1; anaesthetic thigh ulcer 1)*	6
Patient-related factors *(patient withheld previous diagnosis 2; patient unaware of previous diagnosis of leprosy 1; cultural 1)*	4
Administrative factors *(out-patient waiting list 1; waiting for nerve biopsy 1)*	2
Total	12

dermatologists it appeared that leprosy was not the principal diagnosis at the time of biopsy.

Discussion

This analysis of new leprosy patients over four years shows a steady flow of patients from all leprosy endemic regions to the UK. Each year about 12 new cases of leprosy are diagnosed in the UK. Our study does not include all new leprosy patients in the UK, since not all new patients are referred to the Hospital for Tropical Diseases. Nevertheless this cohort is typical of leprosy in the UK.[6] We did not include in this study previously diagnosed patients who were referred to the Hospital for Tropical Diseases with complications secondary to their treated leprosy. Two major factors determine the profile of leprosy patients presenting outside endemic areas: firstly, the migration patterns from endemic areas to non-endemic countries and secondly, the incidence of leprosy in patients' home countries. There are many immigrants from Indian subcontinent to the UK, but few from South America. India has the highest case detection rate in the world at 44 per 100 000 population, Bangladesh 9.4/100 000, Pakistan 1.0/100 000 and Sri Lanka 8.4/100 000.[7] Therefore it is not surprising that over half of our patients come from the Indian subcontinent. However an important lesson is that patients also come from areas of low endemicity such as St Lucia (no cases reported in 1998) and Ecuador (1.0/100 000). Studies from Birmingham[8] and Kuwait[9] have reported on the diagnosis of leprosy in immigrants. The Birmingham series reported on 30 people in the West Midlands diagnosed and treated for leprosy between 1970–83. The Kuwaiti series comprised 121 newly diagnosed leprosy patients over the six years 1983–8. In both series, the majority of patients came from the Indian sub-continent: 86% and 61% of patients in Birmingham and Kuwait, respectively. Latency (the time from entry to the UK to diagnosis) is important because disease transmission could occur then. In our series the mean latent period was 7.7 years (median 2.6 years, range (0.2–47.8). This compares with <1 year to 18 years in the Birmingham series and a mean of 3.7 years in the series from Kuwait. Our series is skewed by a possible latency of 47.8 years in one patient. The incubation period of leprosy has been documented to be as long as 40 years. We have not seen any secondary cases, i.e. cases infected from index cases in the UK, the last published case being in 1925.[10] A recent case of lepromatous leprosy in an old people's home in SE England prompted examination of contacts within the home.[11] None of the 23 staff contacts had evidence of clinical leprosy but five had positive skin test responses to lepromin, and two contacts had raised antibody levels to *M. leprae*-specific phenolic glycolipid, suggesting that subclinical infection had occured. It is curious that secondary cases are so rare in the UK,[12] given that untreated lepromatous patients have a high mycobacterial load, shed *M. leprae* in nasal secretions, and in our series take 5.3 years to be diagnosed. The three Caucasian-British patients in this series had all spent >8 years in a leprosy-endemic country. This means that one can reassure people who have had a short exposure in a leprosy-endemic country that they are highly unlikely to have acquired leprosy.

The lag time (onset of symptoms to diagnosis) is important because the longer it is, the greater the potential for nerve damage and disability. In our series, the mean lag time was 3.1 years (median 1.8 years, range 0.2–15.2). This compares with a mean lag time of 9.4 months in Kuwait, suggesting that Kuwaiti physicians are more alert to the diagnosis of leprosy. Some 68% of our patients had clinical evidence of disability of hands or feet at G1 or G2 levels. A study from Thailand[13] has shown a

highly significant correlation between the proportion of new cases with disability and the delay in diagnosis. An Ethiopian study found an odds ratio of 2.1 for grade 2 disability when registration was delayed by more than 2 years.[14] Although leprosy is rare in the UK, and its clinical presentation is similar to common conditions such as diabetic neuropathy, there are often features unique to leprosy that should alert the physician: anaesthetic skin lesions, nerve enlargement, and nerve tenderness. In our series, leprosy was confused with fungal infection, cellulitis, psoariasis, and arthritis (Table 5). Confusion in diagnosis with dermatological, neurological and rheumatological conditions[5,15,16] is not a new phenomenon and has been reported previously. If doctors think about the possibility of leprosy when a patient from a leprosy-endemic area presents with a skin rash, joint symptoms, or neurological symptoms, then misdiagnosis can be reduced. No other condition causes anaesthetic skin lesions. Sensation of skin lesions in someone who has lived in an endemic region should always be tested. Leprosy is the commonest cause of nerve thickening in the world (rare causes include Dejerine-Sottas disease and amyloid), and 22/28 of our patients presented with thickened nerves. However nerve thickening can be a difficult sign to elicit reliably and reproducibly.

Identifying points of delay in diagnosis should help to identify groups of doctors in whom to raise leprosy awareness. General practitioners with high numbers of patients from endemic areas on their lists should be alert to the possibility of leprosy. The distribution of leprosy in England and Wales reflects immigrant patterns: the Thames region accounts for half the cases, and the former Northwestern, Yorkshire, Trent, Mersey, and West Midland regions for one third of cases.[17]

The Department of Health has produced a Memorandum on Leprosy to aid doctors in diagnosing leprosy. Patients with suspected leprosy can be referred to a doctor on the Panel of Leprosy Opinion.

Twenty-one of our 28 patients were seen by a dermatologist, and their disease was then diagnosed promptly. Only three of these patients experienced a diagnostic delay. Biopsy of unusual skin lesions is an important factor in minimizing diagnostic delay with dermatologists; if the diagnosis cannot be made clinically it is often made on histological examination. However, dermatologists can have long waiting lists and one patient whose general practitioner did not suspect leprosy was on a waiting list for 18 months. It is also important that the histopathologist reviewing the biopsy should know the geographical origin of the patient, and consider leprosy as a cause of granulomatous skin lesions. Neurologists were the second group of specialists to whom leprosy patients were referred (9/28); three of these patients were then referred on to a dermatologist. Pure neuritic leprosy can be difficult to diagnose, and the diagnosis may only be reached after excluding other peripheral neuropathies. Four (14%) of our patients had pure neuritic leprosy. The condition is well recognized in India, where 5–18% of all cases present this way.[18,19] Nerve biopsy is necessary to confirm the diagnosis.[15]

Table 7. Key messages to avoid missing leprosy

Leprosy patients may present long after leaving the leprosy-endemic area
Undiagnosed skin patches should be tested for anaesthesia
Consider leprosy as a cause of unexplained neuropathy
Consider leprosy as a cause of unexplained foot ulcers
Leprosy may present with joint symptoms
50% of UK leprosy patients come from the Indian subcontinent

Two patients in our series were seen by a rheumatologist. Rheumatologists should retain clinical suspicion for leprosy, as it can present with arthritis and other immune-mediated phenomena.[16] Undiagnosed leprosy patients present to orthopaedic surgeons with neuropathic ulcers, soft tissue infections, osteomyelitis, deformities of hands and feet, and nerve damage that can be wrongly interpreted as nerve compression or entrapments. Among our patients, four presented to orthopaedic surgeons with soft tissue infection (2) and nerve entrapment (2). Misdiagnosis could be reduced if neuropathic ulcers in Asians without diabetes and ulnar nerve entrapments in people from leprosy-endemic areas are regarded as leprosy until proved otherwise.

Leprosy remains a stigmatizing disease, and patients may not volunteer their past history of leprosy, especially if it was a long time ago.

In summary, although leprosy can be a difficult disease to diagnose outside leprosy-endemic areas, for patients it is important the diagnosis be made as early as possible so that effective treatment can be started and steps taken to prevent nerve damage. Clinical markers that should raise the level of suspicion of leprosy include a history of travel to an endemic region, a skin rash and/or neurological symptoms, and possibly a history of joint symptoms. Table 7 summarizes the key points.

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Note

The *Memorandum on Leprosy* contains contact details of the experts who constitute the Panel of Leprosy Opinion who are available to advise and consult on the diagnosis and management of individual patients. Copies can be obtained from Department of Health Stores, PO Box 777, London SE1 6XH. The Hospital for Tropical Diseases, Mortimer Market, Capper Street, London WC1E 6AU, Tel. 020 7387 9300 ext 5970; fax 020 7380 9761, is the national referral centre for cases of leprosy and suspected leprosy.

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