Concise Report

Arthritis as presenting manifestation of pure neuritic leprosy—a rheumatologist’s dilemma

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Objectives. Leprosy classically presents with cutaneous and neurological manifestations. In diagnosed cases of leprosy, rheumatological involvement varies from 1% to 70%. A primary articular presentation without cutaneous manifestations is not yet known. Herein, we present our experience of five cases of leprosy that presented with predominant articular involvement in the absence of cutaneous manifestations.

Methods. The study was conducted in the Department of Clinical Immunology, Sanjay Gandhi Postgraduate Institute of Medical Sciences located in the state of Uttar Pradesh, one of the nine endemic states in India. Case records of patients with a definite diagnosis of leprosy were screened for the presenting manifestations, pattern of articular involvement, tenosynovitis, neurological signs and symptoms. Reports of nerve conduction study (NCS), nerve and synovial biopsy and other diagnostic tests were retrieved from laboratory records. Available radiographs were examined for evidence of juxta-articular osteopenia and erosions.

Results. Case records of 11 740 patients were screened, of which 28 had a diagnosis of leprosy. Twenty patients had presented with rheumatological complaints primarily. Five of the patients who presented with inflammatory arthritis with/without tenosynovitis (n = 4) and tenosynovitis alone (n = 1) had pure neuritic leprosy. All of these patients had thickened peripheral nerves and abnormal NCS. Sural nerve biopsy confirmed the diagnosis of leprosy in all these cases.

Conclusion. A combination of tenosynovitis and thickened nerves in association with symmetric polyarthritis should raise a suspicion of leprosy even in the absence of cutaneous features.

Key words: Hansen’s disease, Arthritis, Neuropathy, Lepra bacilli, Tenosynovitis.

Introduction

Leprosy is a chronic granulomatous infectious disease caused by Mycobacterium leprae with predominant involvement of skin, nerves and eyes [1]. The introduction of multi-drug therapy in 1988 has reduced the burden of disease considerably except in a few countries [2]. As of June 2006, the prevalence in India is 0.84 per 10,000, but nine states/union territories of the country still have not achieved the elimination target of the World Health Assembly [3]. India is considered to be the epicentre of the problem, where 260,000 of the 408,000 people diagnosed across the world in 2004 reside [4].

The classical presentation of leprosy is in the form of hypesthetic/anaesthetic, anhidrotic macules, patches, plaques or papulo-nodular lesions. Neural involvement can manifest as paresthesias or as sensori-motor mononeuropathy, mononeuritis multiplex or polineuropathy. Articular involvement in leprosy has been recognized since 600 B.C. in Chinese literature [5]. The two most common and well-recognized forms of articular involvement, neuropathic joints and post-traumatic septic arthritis occur as a consequence of neuropathy [6, 7].

In recent times, primary articular involvement in leprosy, due to infiltration by M. leprae or as part of lepra reaction, has been recognized. The reported prevalence varies from 1% to 70% [8–10]. Acute and chronic symmetric polyarthritis involving hand joints, mimicking rheumatoid arthritis (RA), has been described with or without lepra reaction [11]. Acute onset painful oedema of hands with marked restriction of movements and nodules along the extensor tendons was described in 1980 [10]. Pure enthesitis of the heel [12], sacroilitis [13], cryoglobulinaemic vasculitis [14], dermatomyositis [10], tenosynovitis and vasculitic rash [10] are included in the spectrum of rheumatological manifestations of leprosy. However, almost all of these major reports are in patients with characteristic features of leprosy.

Our centre is a major tertiary care hospital of northern India and is located in Lucknow (latitude: 26° 50’ North, longitude: 80° 54’ East) in the state of Uttar Pradesh, one of the nine states where leprosy is endemic. Patients come from four more nearby states where leprosy is endemic—Bihar, Chattisgarh, Jharkhand and Orissa. In our rheumatology clinic we have observed a unique, predominantly articular presentation in the absence of skin lesions of leprosy. To the best of our knowledge, this presentation is not described in literature.

Methods

The study was conducted in the Department of Clinical Immunology, Sanjay Gandhi Postgraduate Institute of Medical Sciences in north India. Patients with a definite diagnosis of...
leprosy (demonstration of *M. leprae*) made at our centre during the period January 2000–December 2005 were included. Case records were screened for the diagnosis of leprosy manually and with the help of a computer-based hospital information system using the key words ‘leprosy’ and ‘Hansen’s disease’. Presenting manifestations, provisional diagnosis, pattern of articular involvement, tenosynovitis, myositis, neurological signs and symptoms were noted. Reports of nerve conduction study (NCS), nerve and synovial biopsy and other diagnostic tests were retrieved from laboratory records. Anti-nuclear antibody (ANA) and anti-neutrophil cytoplasmic antibody (ANCA) tests were carried out by indirect immunofluorescence, and rheumatoid factor (RF) test was done by nephelometry. Available radiographs were examined for evidence of juxta-articular osteopenia and erosions. Two illustrative cases have been described.

**Case 1**

A 51-yr-old male, a teetotaler and non-diabetic, presented with acral paresthesias of 2 yrs duration and swelling with marked limitation of movement of hands and feet since 2 weeks. There were no constitutional symptoms and no family history of neuropathy. He had extensor tenosynovitis of hands, arthritis of wrists, metacarpophalangeal (MCP) and proximal interphalangeal (PIP) joints (Fig. 1A) and tender swollen feet (Fig. 1B). There were no skin lesions. Bilateral ulnar and common peroneal nerves were thickened. There was 50% loss of fine touch over the lateral aspect of the right foot. Rest of the nervous and systemic examination was unremarkable. Investigations revealed raised inflammatory parameters (erythrocyte sedimentation rate 88 mm in the first hour, C-reactive protein 10.5 mg/dl; normal <0.6 mg/dl) and mild transaminitis (aspartate and alanine transaminase 48 and 54 U/l, respectively). Complete haemogram, renal function tests and urinalysis were normal. RF, ANA, ANCA, serum and urine electrophoresis were negative. NCS showed symmetric polyneuropathy in the lower limbs and absence of conduction in the right sural nerve. Right sural nerve biopsy revealed abundant, Wade-Fite positive lepra bacilli and granulomas (Fig. 2). Synovial biopsy of the left extensor tenosynovial sheath showed extensive mononuclear inflammatory infiltrate but no lepra bacilli were seen. A diagnosis of pure neuritic (PN) leprosy with symmetric arthritis and tenosynovitis was made. Multi-drug therapy (dapsone, rifampicin, clofazimine) with prednisolone (1 mg/kg/day) was started. He had mild improvement in his symptoms at 8 weeks, but after addition of thalidomide 100 mg/day he had dramatic relief in arthritis and tenosynovitis. He discontinued thalidomide after 3 months when he had complete remission of arthritis and tenosynovitis. Prednisolone was discontinued at 6 months. At last follow-up, 14 months later, he is in complete remission and is continuing on multi-drug therapy.

**Case 2**

A 42-yr-old man, a teetotaler and non-diabetic, presented with persistent bilateral wrist swelling and acral paresthesias of 6 months duration. Elsewhere, he was diagnosed to have RA based on symmetric polyarthritis involving hands, elbows, knees and feet, 1 yr back. He was receiving methotrexate (12.5 mg/week), folate supplementation (10 mg/week) and prednisolone (7.5 mg/day) at the time of presentation to us. He denied any history of skin rash, dry eyes or mouth, macroglossia, red eye, chest pain, cough or dyspnoea, oliguria, haematuria and facial puffiness. There was no family history of neuropathy. Examination showed extensor tenosynovitis of both hands and tenderness of MCP joints bilaterally. Nervous system examination did not reveal any sensory or motor deficit. Rest of the general and systemic examination was unremarkable except for mild hepatomegaly. Complete haemogram, renal and liver function tests and urinalysis were normal. Erythrocyte sedimentation rate was 56 mm in the first hour. RF, ANA, ANCA and serum and urine electrophoresis were negative. The hand radiograph showed juxta-articular osteopenia at the wrists and MCP joints. NCS showed demyelination of bilateral common peroneal (CPN), sural and ulnar nerves. Biopsy of the left sural nerve showed abundant...
lepra bacilli. A diagnosis of PN leprosy with chronic symmetric polyarthritis was made. Immunosuppressive drugs were discontinued, and he was treated with multi-drug anti-leprosy therapy (dapsone, rifampicin, clofazimine) for 2 yrs. By the end of the first year of therapy, his articular symptoms remitted completely and he remained in remission till the last visit.

Results

Case records of 11 740 patients were screened, of which 28 had a diagnosis of leprosy. Twenty patients had presented with rheumatological complaints primarily and were diagnosed at our centre by demonstration of M. leprae. Five among these patients, including the two illustrative cases, had PN leprosy with rheumatic complaints. The demographic and clinical features are given in the Table 1.

Four patients had arthritis with or without tenosynovitis and one had only tenosynovitis. All four patients with arthritis had symmetric inflammatory polyarthritis of small joints of hands, wrists, elbows and knees. Two among these patients had additional involvement of small joints of the feet. Tenosynovitis was present in four patients; extensors of both hands and feet (n = 2), extensors of hands alone (n = 1) and both extensors and flexors of hands (n = 1). Two patients were on disease-modifying drugs and steroids, one on steroids alone and two on analgesics alone from elsewhere for the rheumatic complaints.

Slit skin smear, ANA and RF were negative in all patients. ANCA, done in three patients, was negative. Urinalysis was normal in all patients except one who had mild proteinuria that remitted on treatment. All patients underwent NCS and sural nerve biopsy. NCS revealed both demyelinating and axonal type of neuropathy with polyneuropathy of upper and lower limbs in two patients and mononeuritis multiplex with predominant involvement of sural, ulnar and CPN nerves in three. Nerve biopsy showed lepra bacilli in four patients and epithelioid granulomas in two. Synovial biopsy was available in only one case (illustrative case 1).

Discussion

In endemic areas, predominant or sole rheumatic presentation can make the diagnosis of leprosy difficult in the absence of classical skin manifestations. The illustrative cases clearly bring out the atypical presentation of this subset of patients. Four patients were erroneously diagnosed to have RA, Sjögren’s syndrome or unclassifiable arthritis initially, even at our specialty clinic. Only the fifth patient was diagnosed to have leprosy on the first visit. Short duration of symptoms and experience from the previous four cases facilitated an early diagnosis. All the patients were managed in consultation with a dermatologist, experienced in treating leprosy, for closer evaluation of skin lesions soon after confirmation of the diagnosis and subsequently during the course of therapy for leprosy. However, none of the patients developed any skin lesions during the course of treatment.

There is paucity of world literature on PN leprosy. PN leprosy is characterized by neuropathic symptoms and thickened nerves with or without motor and sensory loss, in the absence of any cutaneous manifestation of leprosy [15]. In India, PN leprosy is well recognized and its prevalence varies from 4.6% in northern to 17.7% in southern India [15, 16]. It is a diagnostic challenge and therefore under-reported. Arthritis in PN leprosy has been reported only in two patients previously [17]. However, no detailed clinical or laboratory information was provided on these patients.

Acute arthritis in leprosy usually occurs as part of lepra reactions (both types I and II), whereas chronic arthritis may result from direct infiltration of the synovium by lepra bacilli [5, 10]. Arthritis in our first patient appeared to be a manifestation of type II lepra reaction, as arthritis and tenosynovitis appeared acutely on a background illness of acral paresthesias of 2 yrs duration. In addition, synovial histology did not reveal infiltration by the lepra bacilli, and arthritis and tenosynovitis had poor response to prednisolone and multi-drug therapy and responded dramatically to thalidomide. In the second patient, articular manifestations appeared to be a manifestation of type II, downgrading reaction as the patient was receiving methotrexate and prednisolone with a diagnosis of RA. Discontinuation of immunosuppressive therapy and treatment with multi-drug therapy led to resolution of symptoms within 1 yr without any recurrence further. In rest of the patients, musculoskeletal manifestations appeared either acutely or were associated with constitutional symptoms, suggesting lepra reaction. However, in the absence of synovial histology in these patients, a definitive conclusion is not possible. In view of neurological involvement,

Table 1. Demographic, clinical and laboratory features of patients

<table>
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<tr>
<th>Patients</th>
<th>1</th>
<th>2</th>
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<td>JAO</td>
<td>JAO</td>
<td>Soft tissue swelling</td>
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<td>MDT + P</td>
</tr>
</tbody>
</table>

The diagnosis was established by nerve biopsy in all patients.

Poly, polyneuropathy; MM, mononeuritis multiplex; NCS, nerve conduction study; A, axonal; D, demyelinating; ESR, erythrocyte sedimentation rate; JAO, juxta-articular osteopenia; SNV, systemic necrotizing vasculitis; RA, rheumatoid arthritis; MDT, multi-drug therapy for leprosy; P, prednisolone; Thal, thalidomide.

*aAll were non-tender.
*bParotid enlargement suggested primary Sjögren’s syndrome.
all these patients were treated with a combination of prednisolone and multi-drug therapy, to which all these patients responded.

Is symmetric arthritis in leprosy due to co-occurrence of RA? No doubt RA is a common disease, but male predominance, seronegative status for RF, absence of extra-articular manifestations of RA and response to anti-leprosy treatment argue against that. Another clue to differentiate leprosy from RA is the presence of nerve involvement early in the disease. Rheumatoid vasculitis leads to neuropathic symptoms usually in patients with long-term, severe, seropositive and erosive RA [18]. Further, presence of epithelioid cell granulomas, occasional lepra bacilli and neutrophilic predominance reported in synovial biopsies suggest that arthritis is indeed related to leprosy [17, 19, 20].

Conclusion

Recognition of the infective agent as an aetiopathological factor in rheumatic manifestations is important in the management of patients more so in the endemic regions. A combination of tenosynovitis and thickened nerves in association with/without symmetric polyarthritis should raise a suspicion of leprosy even in the absence of cutaneous features.

<table>
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| A combination of tenosynovitis and thickened nerves in association with/ without symmetric polyarthritis should raise a suspicion of leprosy even in the absence of cutaneous features.

The authors have declared no conflicts of interest.

References