

Profile of Rheumatological Manifestations in Leprosy in a Tertiary Care Hospital from Himachal Pradesh

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The rheumatological manifestations of leprosy occur singly or in varying combinations, particularly during lepra reactions. Despite being third most common, these remain under diagnosed and under reported. This study has been carried out to study the spectrum of rheumatological manifestations in leprosy patients. One hundred consecutive patients of leprosy presenting during January to December 2013 were studied for rheumatological manifestations. Complete hemogram, serum biochemistry, urinalysis, rheumatoid factor, ASO titer, C-reactive protein, ANA, and x-rays for hands, feet, chest and involved joints were performed. These 100 (M:F 66:34) patients aged between 16-80 years had indeterminate (2 patients), TT (4 patients), BT (26 patients), BB (2 patients), and LL leprosy (32 patients). 27 patients had rheumatological manifestations; arthritis involving large or small joints in 23 patients being the commonest. 7 of 24 patients in type-1 lepra reaction had enthesitis in 3 patients and oligoarthritis in 4 patients. Rheumatoid arthritis-like polyarthritis was noted in 19 patients with type-2 reaction. Tenosynovitis, dactylitis, bony changes were also noted. Except for one case, these features were present in patients having lepra reactions. Rheumatoid factor in 14, ANA in 15, C-reactive protein in 45 cases was positive. ASO was positive 34 cases. Symmetrical polyarthritis involving small joints of hands and feet, oligoarthritis, enthesitis and dactylitis are common in leprosy particularly with borderline leprosy, type-2 lepra reaction especially in the presence of positive RA factor.

Key words : Leprosy; Dactylitis; Enthesitis; Lepra reactions; Oligoarthritis; Osteopenia; Polyarthritis; Tenosynovitis

Introduction

Prevalence of rheumatological manifestations in leprosy varies from 1% to 70% depending upon the geographic regions and ethnicities studied

(Vengadkrishna et al 2004, Atkin et al 1989, Ribeiro et al 2008, Pereira et al 2009, Neder et al 2014). Charcot's arthropathy, acute symmetrical polyarthritis or swollen hands and feet syndrome

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during lepra reactions, insidious-onset chronically asymmetrical polyarthritis mimicking rheumatoid arthritis or as isolated tenosynovitis or tenosynovitis associated with arthritis or neuropathy are the usual manifestations of rheumatologic complications of leprosy. Additionally, leprosy dactylitis, enthesitis of the heel, sacroiliitis, cryoglobulinaemic vasculitis, painful hand edema associated with acute onset and severe restriction of movements, dermatomyositis, tenosynovitis and vasculitic rash may also occur (Haroon et al 2007). At times, articular involvement may be the sole presenting manifestation even without cutaneous lesions. Inflammatory arthritis, inflammatory swollen hands and/or feet, neuropathic arthritis or neuropathic destructive arthritis (Charcot's joints), septic arthritis, nonspecific arthralgias and myalgias, soft tissue rheumatism, or co-existing chronic forms of arthritis are common during lepra reactions. Enthesitis, sacroiliitis, cryoglobulinaemic vasculitis and dermatomyositis are also reported occasionally. However, musculoskeletal involvement in leprosy though third most common, remains mostly under diagnosed and under reported. We studied the spectrum of rheumatic manifestations in leprosy patients who attended the Dermatology OPD of our Hospital in 2013.

Material and Methods

One hundred (66 male and 34 females) patients of leprosy consecutively attending the dermatology outdoor clinic of Dr RP Medical College hospital during January to December 2013 were studied after obtaining their informed consent. They were diagnosed on basis of their clinical presentation and classification of leprosy was based on the clinical signs of disease, slit skin smears from lesion/earlobe and lesional/nerve biopsy whenever needed. The bacteriological and the

morphological indices of these patients recorded. A thorough clinical history and systemic examination was performed with special attention for rheumatological features such as history of presence of morning (joint) stiffness, painful/tender swelling of joints, joint movements, visible joint deformity with or without chronic pain, pain over insertion of tendons and ligaments, and pain and swelling of muscles. Laboratory workup included complete hemogram, blood sugar, hepatorenal function tests, urinalysis and serological markers such as rheumatoid (RA) factor, anti nuclear antibody (ANA), anti-streptolysin O titre (ASO) and C-reactive protein (CRP). Radio-imaging studies included x-rays for involved joints and chest radiogram.

Results

The majority, i.e. 87 patients were aged between 21-60 years while 12 patients were above 60 years of age and the youngest being a 16 years old girl (Table 1). The oldest patient was an 80 year old male. Clinically, 62 patients had borderline leprosy (BT-26, BB-2, BL-34); 32 patients were diagnosed as lepromatous leprosy; 4 patients with Tuberculoid leprosy and 2 patients had Indeterminate leprosy. Rheumatological manifestations were seen in 27 which included 21 males and 6 female patients (Table 1). Nineteen patients had symmetrical polyarthritis involving both large and small joints of hands and feet simulating rheumatoid arthritis and in 2 this was associated with tenosynovitis. Oligoarthritis involving large joints like wrists, ankles or knee joints was observed in 4 patients. Three patients had enthesitis, while dactylitis was seen in one patient only. No rheumatological manifestations were observed in Indeterminate and Tuberculoid patients. Among the total BT patients (n=26) 2 patients had oligoarthritis of the big joints, while one had enthesitis. One of the 2 BB patient had symptoms of polyarthritis. Of the total 34 BL

Table 1 : Distribution of patients according to age, classification and rheumatologic manifestations

Features	Clinical spectrum of leprosy					
	Ind	TT	BT	BB	BL	LL
Age groups (n=100)	(n=2)	(n=4)	(n=26)	(n=2)	(n=34)	(n=32)
<20 years	1	0	0	1	0	0
21-40 years	44	1	4	11	1	15
41-60 years	43	1	0	12	1	13
61-80 years	12	0	0	2	0	4
Rheumatologic manifestations (n=27)						
Rheumatoid arthritis-like Symmetrical Polyarthrititis and no Tenosynovitis	17	0	0	0	1	9
Symmetrical Polyarthrititis with Tenosynovitis	2	0	0	0	0	0
Oligoarthritis	4	0	0	2	0	0
Enthesitis	3	0	0	1	0	0
Dactylitis	1	0	0	0	0	1

Note: Ind - Indeterminate, TT - Tuberculoid leprosy, BT - Borderline Tuberculoid leprosy, BB - Midborderline leprosy, BL - Borderline lepromatous leprosy, LL - Lepromatous leprosy

patients 16 had rheumatological symptoms (47.1%) which included 9 with polyarthrititis (2 with tenosynovitis while the rest without tenosynovitis); 2 patients manifested with oligoarthritis while 2 with enthesitis. Among the 32 lepromatous leprosy patients 10 had rheumatic manifestations (31.3%); 9 presented with polyarthrititis without tenosynovitis while 1 presented with dactylitis.

Fifty two patients had lepra reactions (24 Type-1 and 28 with Type-2 reactions) during that one year of observation among the one hundred patients studied. In these 52 patients of both Type 1 and Type 2 reactions, rheumatic manifestations were observed in 27 patients (Table 2). In patients suffering from Type 1 reactions 7 patients had rheumatic manifestations while in patients with Type 2 reactions rheumatic manifestations were more common and were seen in 20 patients. The type of

manifestation observed is shown in Table 2. The most common manifestation observed was polyarthrititis with or without tenosynovitis.

Two or more radiological abnormalities were noted in 34 of 72 available x-rays of hands, feet and involved joints. Juxtra-articular osteopenia was commonest finding seen in 22 patients followed by distal resorption of phalanges in 12 patients. Other less common findings were soft tissue swelling in 8, subarticular bone erosion in 5 and arthropathy in 3 patients respectively.

None of the patients of Tuberculoid leprosy and Indeterminate leprosy were positive for any of the sero-markers studied for rheumatological manifestations. Thirty-two patients of lepromatous leprosy and 62 patients in borderline leprosy showed positivity for one or more seromarkers (Table 3). More than one seromarker was positive in some patients. More seropositivity was

Table 2 : Rheumatologic manifestations according to clinical classification of leprosy and Type of lepra reaction

Number of cases with lepra reaction	Type of lepra reaction (number of patients with lepra reactions)	Spectrum of leprosy (number of patients with lepra reactions)	Type of Rheumatic manifestations	Number of cases with Rheumatic manifestations (n=27)
52	Type-1 (24)	Tuberculoid (1)	0	0
		BT (13)	Oligoarthritis	4
		BL (10)	Enthesitis	3
	Type-2 (28)	BB (1)	Polyarthritis	8
		BL (12)	Polyarthritis with tenosynovitis	2
		Lepromatous (15)	Polyarthritis	9
No lepra reaction(1)		Lepromatous (1)	Dactylitis	1

Table 3 : Serological positivity for rheumatological markers in relation to leprosy spectrum and rheumatologic manifestations

Parameters		Number of patients with positive results for			
		RA factor	ANA	ASO	CRP
Spectrum of leprosy	Lepromatous (n=32)	9(28%)	9(28%)	15(46%)	18(56%)
	Borderline leprosy (n=62)	5(8%)	6 (9%)	19(31%)	27(44%)
	Tuberculoid leprosy (n=4)	0	0	0	0
	Indeterminate leprosy (n=2)	0	0	0	0
Presence of Rheumatologic manifestations	Patients with arthritis (n=23)	10(44 %)	5(22%)	12(52%)	15(65%)
	Patients with other rheumatic features (n=4)	1(25 %)	1(25%)	4(100 %)	2(50%)
	Patients without rheumatic features (n=73)	3(4%)	9 (12%)	18(25%)	28(38%)

Note: CRP = C - reactive protein; ASO = antistreptolysin O; RA factor = Rheumatoid factor; ANA = anti nuclear antibody

observed in patients of the lepromatous leprosy group as compared to borderline group. A higher proportion of patients with rheumatologic

manifestations were positive for the seromarkers as compared to patients without rheumatological manifestations.

Discussion

Primary articular involvement due to infiltration by *Mycobacterium leprae* as well as a part of lepra reaction is well recognized in leprosy. Rheumatoid arthritis-like acute and chronic symmetric polyarthritis may also occur in leprosy patients with or without lepra reactions. Sarkar et al (2001) observed rheumatological complications in 28% of leprosy patients studied. These included 47 patients of TT/BT type, 38 patients of BB/BL type and 10 patients with LL disease. Arthritis was the main manifestation in nearly 74% cases. This was symmetrical polyarthritis in 54%, oligoarthritis in 18% and monoarthritis in nearly 2% cases studied respectively. Similarly, Vengadkrishnan et al (2004) reported rheumatological manifestations in 61% of cases. These included polyarthritis in 44% and oligoarthritis in 10% cases. Twenty seven percent of our patients had rheumatological manifestations, 17 of them had borderline leprosy and 10 had lepromatous leprosy. None of the patients with tuberculoid or indeterminate leprosy had rheumatological manifestations.

Chronic symmetrical polyarthritis mimicking rheumatoid arthritis, isolated tenosynovitis and tenosynovitis associated with arthritis and neuropathy have been observed in leprosy patients by several investigators (Chauhan et al 2010, Cossermelli - Messina et al 1998). Arthritis was the most common presentation in our series with 85.2% with rheumatological symptoms presenting as acute onset rheumatoid arthritis-like symmetrical polyarthritis affecting small joints of the hands and feet (19 of 27 patients) and 4 patients with oligoarthritis, respectively. It has been reported that rheumatological manifestations can occur independently or with various reactions (Atkin et al 1989, Cossermelli -

Messina et al 1998). Specifically, type-2 lepra reaction/ENL (erythema nodosumleprosum) has been shown to be associated with different forms of arthritic symptoms (De Almeida et al 1993). All 19 patients, in the present study presenting with acute onset polyarthritis simulating rheumatoid arthritis had associated Type-2 lepra reaction while 4 patients with oligoarthritis were having Type-1 lepra reaction. However, none of our patients had Charcot's joints perhaps because of early diagnosis/treatment. Moreover, we did not follow up these patients to look for later complications. Rarely, leprosy has been diagnosed in a patient with isolated tenosynovitis (in the absence of arthritis) in a Primary Neuritic leprosy patient (Haroon et al 2007). It is reported that only 5-10% patients with Borderline Tuberculoid leprosy in reaction develop tenosynovitis while most patients with tenosynovitis have Lepromatous Leprosy (De Almeida et al 1993). Extensor tendons over dorsum of hands, feet, elbows and ankles are most commonly involved. Tenosynovitis involving extensor tendons over dorsum of hands in association with symmetrical polyarthritis was observed in our 2 of 27 (7.4%) BL patients with Type-2 lepra reaction. Other rheumatological manifestations rarely reported are sacroiliitis (Cossermelli - Messina et al 1998); enthesitis (Samant et al 1999) particularly during lepra reactions. Enthesitis was observed in 3 BT patients suffering from Type-1 lepra reaction. Juxtra-articular osteopenia (22 patients), distal digit resorption (12 patients), soft tissue swelling (8 patients), subarticular bone erosion (5 patients) and arthropathy (3 patients) seen in 34 patients of the present study, might have been due to chronic disease, nutritional deficiency, disuse of hands/feet, and long term systemic corticosteroids therapy.

Frequency of RA factor positivity varies between 3% and 35% irrespective of presence or absence of arthritis (Carpintero-Benitez et al 1996, Neder et al 2014, Pereira et al 2009, Prasad et al 2013, Ribeiro et al 2008, Salvi and Chopra 2013, Vegadakrishna et al 2004). The frequency of positive RA factor also varies considerably across spectrum of leprosy in the descending order lepromatous, BL, BB, BT, respectively (Neder et al 2014). In the present study RA factor positivity was observed in 9 LL patients (28%), 5BL patients and was negative in tuberculoid and indeterminate leprosy patients. Among 23 patients diagnosed having arthritis 44% cases had positive RA factor with or without lepra reactions as against 4% of 73 patients without rheumatological manifestations. Apparently, leprosy patient with positive RA factor are more likely to develop arthritis with or without lepra reaction. However, a longer follow-up of patients with positive and negative RA factor is required to observe the predisposition due to RA positivity. ANA positivity was observed in 28% patients of LL and 9% in BL patients with or without lepra reactions in the present study. Comparing the positivity in patients presenting with rheumatological manifestations, 6 of 27 (22%) patients with rheumatological manifestations and 9 of 73 (12%) patients without rheumatic manifestations were ANA positive. There may be some correlation between ANA positivity and lepromatous leprosy with or without rheumatologic manifestations, but, assessing these with longer follow-up is needed to come to any conclusion. ASO and CRP, the non-specific markers of inflammation, showed elevated levels in our 34 and 45 patients respectively with or without rheumatological manifestations. However, the exact significance of these markers remains difficult to establish as false positive

reactions in any inflammatory condition are common.

Symmetrical polyarthritis involving small joints of hands and feet, oligoarthritis, enthesitis and dactylitis are common in leprosy particularly with borderline leprosy, Type-2 lepra reaction more so in the presence of positive RA factor.

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