European Journal of Molecular & Clinical Medicine

ISSN 2515-8260 Volume 10, Issue 01, 2023

"RHEUMATOLOGICAL MANIFESTATIONS IN LEPROSY"

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Abstract

Leprosy (Hansen's disease) is caused by Mycobacterium leprae,through respiratory root and affects skin and nerves predominantly. This nerve injury can induce a lack of pain sensitivity, motor dysfunction and can ultimately lead to limb loss. Neuropathy causes post-traumatic septic arthritis and neuropathic joints. Acute and chronic joint involvement as symmetric polyarthritis mimicking rheumatoid arthritis (RA) with or without lepra reaction has been reported. Leprosy appears in rheumatology as primary arthritis, a concomitant infection, or a treatment outcome. Joint pain and arthritis occur during reactive inflammation. Hansen's disease may also cause rheumatoid-like erosive deforming arthritis in large and small joints.

A descriptive cross-sectional study was undertaken in the Department of Dermatology and Venereology. The study included all leprosy cases but excluded patients with other types of arthritis. Patients with coagulopathy, connective tissue disorders, and collagen vascular disorders were excluded.

The mean age of 100 study participants was 41.30 years (SD - 19.23 years), 76% were male, 24% female. Most study participants had ulcers on their feet. 24 had left foot ulcers and 17 on the right. Lesions were also present on medial malleolus, hand, lower limbs, etc. 56% had no leprosy reaction, 24% type 2, and 20% type 1. Polyarthritis was the most prevalent rheumatological manifestation (34%), followed by tenosynovitis (32%). Some patients had enthesitis (16%), oligoarthritis (15%), dactylitis (12%), etc. Most lepromatous and tuberculoid leprosy patients had increased ESR and CRP.

Borderline and lepromatous leprosy often causes symmetrical polyarthritis, oligoarthritis, enthesitis, and dactylitis. Leprosy is rare in outpatient rheumatology, but rheumatologists must know this crucial differential diagnosis. Dermatologists should be involved when anti lepromatous medications to prevent unnecessary antirheumatic therapy.

Keywords: Leprosy, Arthritis, Enthesitis, Tenosynovitis

Introduction:

The bacteria Mycobacterium leprae or Mycobacterium lepromatosis causes leprosy, commonly known as Hansen's disease (HD). It mainly affects skin and nerves. This nerve injury may cause a loss of pain perception, and motor dysfunction which can lead to the loss of sections of a person's limbs due to repeated traumas or infection from undiscovered wounds. [1] Except in a few countries, the advent of multi-drug treatment in 1988 has significantly lowered illness burden. [2] Of the 669 districts in India, 551 (82.36 percent) had a prevalence of 1/10,000 persons at the end of March 2016, which is the target for eliminating it as a public health danger.[3]

Leprosy often manifests as hypoesthetic/anaesthetic, anhidrotic macules, patches, plaques, or papulo-nodular lesions. Paresthesias, sensorimotor mononeuropathy, mononeuritis multiplex, and polyneuropathy are all symptoms of neural involvement. Articular involvement in leprosy has been documented in Chinese literature from 600 B.C. [4]

The two most common and well-known kinds of articular involvement, neuropathic joints and post-traumatic septic arthritis, are caused by neuropathy.[5,6] Primary articular involvement in leprosy has recently been identified as a result of M. leprae infiltration or as part of the lepra

reaction, with reported prevalence ranging from 1% to 70%. [7-9] According to two Indian studies, the prevalence of arthritis is 61.4 percent and 10%, respectively. [10.11] Pereira et al. found a prevalence rate of 6.3 percent in a population of 1257 leprosy patients. [12]

Acute and chronic symmetric polyarthritis affecting joints of hands and feet, simulating rheumatoid arthritis (RA), with or without lepra reaction, has been documented. [13] A instance of severe acute hand oedema with nodules along the extensor tendons and significant movement restriction was documented in 1980. 9 Pure heel enthesitis 14, sacroiliitis 15, cryoglobulinaemic vasculitis 16, dermatomyositis, tenosynovitis, and vasculitic rash are among the list of rheumatological symptoms of leprosy.[9]

Practitioners have seen leprosy as a primary cause of arthritis, a concurrent infection, or a side effect of treatment. Since joint involvement is thought to occur in 70% of leprosy patients and might occasionally be the only observable symptom, rheumatologists should be aware of this condition. [17]

During the reactive inflammatory phase, joint discomfort and arthritis are common. Additionally, Hansen's illness can cause rheumatoid-like persistent erosive deforming arthritis that affects both large and small joints.[18] Also, it has been connected to clinical and laboratory findings that resemble vasculitis and autoimmune connective tissue disorders.[19]

One of the nine states where leprosy is endemic in Maharashtra, where our centre is a significant tertiary care hospital. This research was conducted to study rheumatological manifestation among patients suffering from leprosy in our population.

Material & methods:

A descriptive cross sectional study conducted in the Department of Dermatology and Venereology at Padmashree Dr. D. Y. Patil Medical College, Hospital & Research, Pimpri Pune after taking permission from the Ethical committee of the institute. All diagnosed cases of leprosy were included in study while patients having known arthritis due to other causes were excluded from study.Patients with established connective tissue problems, such as collagen vascular abnormalities and coagulopathy, were excluded from the study. Patients who were going to the OPD were evaluated for eligibility based on the selection criteria. The 100 patients who met the inclusion criteria at the Skin & V. D. OPD and wards, as well as the Leprosy clinic, were all eligible to participate in the study based on the selection criteria. Patients were informed of the study's goal. Prior to the patients actually participating in the

trial, their informed written consent was obtained. They were all clinically assessed, looked into, and classified. Ziehl-Neelson staining was used to acquire skin smears and check them for the presence of AFB. Calculations were made for the morphological and bacteriological indices. Leprosy-like lesions were biopsied, and histological results were recorded.Each patient had a comprehensive hemogram, standard urine testing, serum bilirubin, renal profile, blood sugar, and radiography of the affected areas done. Serological markers such rheumatoid factor, ASO titer, and C-reactive protein were also measured in each case. Data was done in Microsoft Excel and analysed using SPSS software 16 version.

Results:

Mean age of 100 study samples was 41.30 years (standard deviation - 19.23 years), with the highest 85 years and lowest 14 years. There were 76% male and 24% female in the study while 22% samples were from 21-30 & 31-40 years age group each. Foot was the most common site of ulcer among study subjects. 24 subjects had ulcers over their left foot while 17 on their right foot. Some subjects were having lesions over medial malleolus, hand, lower limbs etc. Ulnar nerve (67%) was most commonly affected among leprosy subjects followed by common peroneal nerve (35%). Radial cutaneous (12%), radial nerve (6%), greater auricular (4%) etc. nerves were also involved. Some subjects were having bilateral nerve involvement or more than one nerve involved. Lepromatous leprosy (40%) was the most common leprosy among study subjects followed by borderline lepromatous (30%) and borderline tuberculoid (18%). 56% of subjects were not having any leprosy reaction while 24% with type 2 reaction and 20% with type 1 reaction.

Rheumatological complications	Frequency
Tenosynovitis	32
Enthesitis	16
Rash	4
Monoarthritis	6
Oligoarthritis	15
Dactylitis	12
Polyarthritis	34

Table 1: Rheumatological complications among study subjects

Above table shows that polyarthritis was the most common rheumatological complication and it was present in 34% of subjects having leprosy followed by tenosynovitis in 32% of subjects. Enthesitis (16%), Oligoarthritis (15%), Dactilytis (12%) etc. were also present in some subjects; some subjects had more than one rheumatological complication.

8 out of 40 subjects have lepromatous leprosy where belongs to 31 to 40 years age group and 41 to 50 years age group each while 6 out of 18 subjects having borderline tuberculoid leprosy belongs to 11 to 20 years age group and 21 to 30 years age group each. 4 out of 6 subjects having pure neuritic leprosy belong to the 31 to 40 years of age group. 14 out of 56 not having any reaction due to leprosy belong to 21 to 30 years of age group, while 10 out 20 leprosy subjects having type 1 reaction belong to 31 to 40 years of age group.

Arthritis	**Type of leprosy**				
	BL	**BT**	**LL**	**TT**	**Pure Neuritic**
Tenosynovitis	10	9	10	0	3
Enthesitis	4	5	7	0	0
Monoarthritis	0	2	3	0	1
Oligoarthritis	4	2	6	0	3
Dactylitis	6	2	4	0	0
Polyarthritis	11	2	21	0	0
Rash	3	1	0	0	0

Table 2: Rheumatological manifestations according to type of leprosy

Above table shows that 21 subjects with lepromatous leprosy were having polyarthritis followed by tenosynovitis in 10 subjects, similarly tenosynovitis and enthesitis were common rheumatic manifestations in subjects with borderline lepromatous leprosy (10 and 4 respectively). Details of rheumatological manifestation according to type of leprosy among study subjects as per above table.

Arthritis	Type of lepra reaction			Total
	None	Type 1	Type 2	
Tenosynovitis	9	15	8	32
Enthesitis	2	7	7	16
Monoarthritis	3	3	0	6
Oligoarthritis	10	1	4	15
Dactylitis	2	4	6	12
Polyarthritis	16	3	15	34
Rash	1	0	3	4

Table 3: Rheumatological manifestations according to lepra reaction

Above table shows that 15 subjects with type 2 lepra reaction having polyarthritis followed by tenosynovitis in 8 subjects, similarly tenosynovitis and enthesitis were common rheumatic manifestations in subjects with type 1 lepra reaction (15 and 7 respectively). Details of rheumatological manifestation according to type of lepra reaction among study subjects as per above table.

Type of leprosy	Blood investigations				
	ANA Positive	RF positive	Raised ESR	Raised CRP	ASO Positive
BL	2	4	16	14	10
BT	0	0	10	10	10
LL	16	6	28	22	6
Pure neuritic	2	0	4	4	0
TT	0	0	2	0	6
Total	20	10	60	50	32

Table 4: Details of blood investigations according to type of leprosy

Above table shows that most of lepromatous leprosy subjects were ANA positive and having raised ESR & CRP while tuberculoid leprosy subjects were having raised ESR. Details of blood investigations according to type of leprosy among study subjects as per above table.

Discussion:

Leprosy incidence in endemic countries like India have dropped from 260063 in 2004 to 127295 in 2011. [20] Although the conventional manifestations that affect the skin and nerves are widely known, its "atypical" appearance, in which the musculoskeletal system is affected first, with dermatological and neurological manifestations occurring later or not at all, has drawn attention recently. This "atypical" presentation has raised awareness of this illness. The "atypical" musculoskeletal illness excludes Charcot's disease's characteristic neuropathic joints, which medical students learn about but rarely see.

The mean age of the 100 study participants was 41.30 years (SD -19.23 years), ranging from 14 to 85. Wakhlu et al. [21] studied 29 participants, 19 of them were male, with a mean age of 38 $\pm$ 17.2 years. Singh R et al. had 87 patients aged ranged from 21 to 60, 12 patients were beyond 60 years, and youngest was 16-year-old girl.[22]

40% of research participants had lepromatous leprosy followed by Borderline lepromatous leprosy (30%). In the study by Singh R et al., 62 patients were diagnosed with borderline leprosy (BT-26, BB-2, and BL-34), 32 with lepromatous, 4 with tuberculoid, and 2 with polyneuritic. [22]

34 of the participants in our study have trophic ulcers on one or both foot. 22 individuals with clinical peripheral neuropathy and 13 patients with pure sensory loss were found to have glove- and stock-type sensory loss, according to Salvi S et al.[23] Additionally, the feet of five patients, three of whom had leprosy, exhibited digital trophic ulcers. Nerve conduction velocity (NCV) testing confirmed that four people had axonal neuropathy (two tuberculoid, one lepromatous, and one neuritic leprosy). In our study 24% had a type 2 leprosy reaction, 20% had a type 1, and 56% had no reaction. Salvi S et al. observed 15 reactional cases (type I and type II). Thirteen people took Hansen's disease medicine. 60% of reactions were type II, which is typical in lepromatous leprosy patients. [23]

In our study 34% of leprosy patients experienced polyarthritis, the most common rheumatological consequence. 32% had tenosynovitis, the second most prevalent issue. Some patients experienced enthesitis (16%), oligoarthritis (15%), dactylitis (12%), and other rheumatological issues. In the Singh R et al. study, 19 patients had symmetrical polyarthritis that affected both small and big joints of the hands and feet, suggesting rheumatoid arthritis.[22] Sarkar et al. discovered 28% of leprosy patients had rheumatological issues. Arthritis was the

most prevalent symptom (74%), 54% of cases had symmetrical polyarthritis, 18% had oligoarthritis, and 2% had monoarthritis. [24] Vengadakrishnan et al. (2004) showed 61% of cases had rheumatological symptoms in a similar research. Polyarthritis was 44% and oligoarthritis 10%, 27% of our patients showed rheumatological symptoms.[25]

Manifestation	Present study	Wakhlu et al [21]	Prasad et al [26]	Sarkar et al [24]	Salvi S et al [23]
Polyarthritis	34 (42%)	12 (41.3%)	14 (31.8%)	49 (48%)	28 (84.8%)
Oligoarthritis	15 (18%)	2 (6.8%)	7 (15.9%)	4 (4.7%)	-
Tenosynovitis	32 (39%)	5 (17.2%)	9 (20.4%)	16 (15.6%)	-
lepra reaction / ENL	44 (44%) /24 (24%)	15 (51.7%) / 13 (44.8%)	-	43 (42.1%) /13 (12.7%)	-
RF	10 (10%)	7 (24.1%)	2 (4.5%)	72 (70%)	9 (26.6%)
ANA	20 (20%)	3 (10.3%)	1 (2.2%)	22 (21.5%)	12 (37.5%)

Table 5: Comparison of current study findings with another studies

15 out of 38 type 2 lepra reaction patients in our study experienced polyarthritis. Type 1 lepra response patients also developed tenosynovitis and enthesitis (15 and 7 respectively). Singh R et al found 27 rheumatic patients among 52 Type 1 and Type 2 patients. 7 Type 1 and 20 Type 2 individuals exhibited rheumatic symptoms, Type 2 reactions caused greater rheumatic symptoms. [22]

Other rheumatology tests 20% of our study participants had a positive antinuclear antibody (ANA) test, and 10% had a positive rheumatoid factor test (RF). According to Salvi S et al, 26.6% of patients with inflammatory arthritis and leprosy tested positive for RF antibodies, and 37.5% tested positive for ANA antibodies. [23] Leprosy may give false positive results for RF and ANA, which are routinely tested in rheumatological illnesses. [27] Their investigation shows a similar erroneous seropositivity. None of the patients in this series obtained a positive serology result for anti-CCP, a more sensitive RA marker. [28] Leprosy patients have ANA due to weak cross-reactivity with complex nucleic acids and nucleoproteins exposed after cell death in chronic inflammation. [29]

Conclusion:

In borderline and lepromatous leprosy, symmetrical polyarthritis, oligoarthritis, enthesitis, and dactylitis are common symptoms. Leprosy mimics rheumatoid arthritis, seronegative spondyloarthritis, and systemic necrotizing vasculitis. Neurocutaneous lesions in rheumatological patients may indicate leprosy. Unexplained articular signs may be the only symptom of leprosy, so they should be thoroughly checked. Even though leprosy is rare in outpatient rheumatology, rheumatologists and dermatologists must be aware of this important differential diagnosis. When anti lepromatous drugs save patients from unnecessary antirheumatic therapy.

Acknowledgement

The authors thank all the Department of Dermatology and Venereology staff for their cooperation. All the authors read and approved the paper.

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