

Leprotic Arthritis

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Received: August 14, 2015; Accepted: January 25, 2016; Published: February 04, 2016

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Abstract

Leprosy is a chronic mycobacterial disease primarily affecting the peripheral nervous system and secondarily involving skin and other tissue. The radiological changes may be either Early radiological change as; Soft tissue, swelling, Osteoporosis, Acroosteolysis or Late radiological changes as joint space, narrowing, Acroosteolysis, Arthritis multilans, Deformities and ankylosis. Leprosy patients should be treated with patience, perseverance and understanding. Beside medical treatment, they need moral support and reassurance so that they regain self-confidence and self respect.

Leprotic Arthritis

The clinical features of leprotic arthritis

Leprosy is a chronic mycobacterial disease primarily affecting the peripheral nervous system and secondarily involving skin and other tissues [1]. In the past, Leprotic Polyarthritits was considered a unusual manifestation [2], but today arthritis is one of the most important features of leprosy as it occurs either as a complication [Charcot's joint] or as a manifestation of the disease itself Hanafi, M.I, Hesham, SH, 1997.

An early description of acute polyarthritits was provided following a group of Indian leprosy patients [3]: Stiff joints as a complication of leprosy are reported also in ancient Chinese literature [4]. Arthralgia is a recognized as a clinical manifestation in leprosy [5]. Rheumatic manifestations of leprosy have been reported [6] and they are an important cause of continuous morbidity in leprosy.

Karat, et al. [3] Stated that a true arthritis may occur in patients with erythema nodosum and reported a rheumatoid arthritis like syndrome in ten patient with erythema nodosum leprosum, where the hands, knees and ankles joints were mainly affected.

Mc Dougall and Archibald, [7] reported a male Pakistani living in England, who was admitted to the rheumatology unit with acute widespread polyarthritits associated with fever and night sweats. Preliminary examination suggested Reiter's disease, but further investigation showed acute glomerulonephritis with uremia (blood urea, 246 mg/ 100 ml) and proteinuria leading to diagnosis of polyarteritits nodosa but muscle tenderness prompted a biopsy of gastrocnemius and skin which identified leprosy bacilli and typical lepromatous leprosy which were found also on renal biopsy.

Albert, et al. [6] found in fifteen out of twenty one leprotic patients rheumatic manifestations. The largest single group was fourteen patient with erythema nodosum leprosum of whom five had objective evidences of arthritis, and seven had painful swelling of one hand and wrist. The remaining two patients, one was a male of Mexican origin who was admitted to hospital with symmetrical polyarthritits of large and small joints, fever, and a widespread purpuric rash. Because of his history of pulmonary tuberculosis and finding of acid-fast bacilli in sections of bone marrow he was unsuccessfully treated with antitubercular. Several weeks later, large areas of dermal infarction developed on his legs and feet.

The last patient, a male Filipino, was at first thought to have dermatomyositis because of fever, muscle and joint pain and scaly Erythematosus rash, but a finding of sensory changes in his extremities and palpably enlarged ulnar nerves, led to correct diagnosis of lepromatous leprosy. Morley, et al. [8] state that the possibility of leprosy should be considered in any patient who has lived in an endemic area and develops a persistent rash, unusual arthritis or unusual peripheral neuropathy. The clinician should test skin lesions for sensibility, especially light touch and pinprick and feel for peripheral nerves particularly superficial radial, ulnar and lateral popliteal. In addition, biopsy of active skin lesions should be performed.

Another form of arthritis occurs secondary to bone involvement. Direct bone infection occurs most commonly in the distal parts of the phalanges and subchondral bone may collapse and cause destruction of the adjacent joint [3].

Jobling, [2] stated that, reactive arthritis presents as follows:

1. Acute arthritis of one or more of the large joints, typically knees or ankles, with or without effusion.
2. Acute polyarthritis of small joints of the hands, especially metacarpophalangeal joints, with small joints in the feet sometimes also involved.
3. A combination of 1 and 2.
4. Involvement of the first interphalangeal joint of one finger or toe giving an acutely tender spindle-shaped digit, which is a less common presentation. Although similarity to rheumatoid arthritis is close, there are distinguishing features about arthritis in leprosy [1]: Firstly, It is much more common in males, secondly the affected joints resolve when the lepra reaction subsides without residual damage, and thirdly the biopsy of synovial membrane shows leucocyte infiltration.

Hanafi, M.I, Hesham, S, H, 1997 observed that in the upper limbs wrists, Distal Interphalangeals (DIP) and Metacarpophalangeals (MCP) joints were significantly more affected in leprotic cases than both household contacts and control groups ($p < 0.001$). In the lower limbs, knees and Metatarsophalangeal (MTPs) joints were more affected ($p < 0.001$). In leprosy, "Mycobacterium leprae specific antigens" have been given high priority in attempts to develop new diagnostic reagents and techniques. A specific phenolic glycolipid (Phenolic Glycolipid-I or PGL-I) which is a member of 'mycoside A' group of glycolipids has been identified in *M. leprae*. Although almost all features of the dicyle phenolic phthiocerol portion of PGL-1 have been recognized in other mycobacterial species, the trisaccharide which contains immunodominant segment is novel and unique to *M. leprae*. PGL-I therefore appears is a highly valuable chemical marker for *M. leprae*. It is readily demonstrated in biopsy material and body fluids of lepromatous patients and in type 2 lepra reactions [9] (Table 1).

The mean serum level of APGLI (A IgM) antibodies was more among cases than contacts and control groups with a very high significant difference ($p < 0.0001$). Also, it was significantly more frequent among contacts than in control groups ($p < 0.0001$). Also, the mean serum level of APGLI (A IgG) antibodies was significantly higher among cases than contacts and control groups ($p < 0.0001$), and was more frequent among contacts than in controls ($p < 0.0001$). Hanafi, M.I, Hesham, S, H, 1997.

The pattern of leprotic arthropathy is represented by arthralgia and / or arthritis similar to RA, or sometime it may be monoarticular.

Imaging of leprotic arthritis

The radiological changes may be either Early radiological change as; Soft tissue, swelling, Osteoporosis, Acroosteolysis

or Late radiological changes as joint space, narrowing, Acroosteolysis, Arthritis mutilans, Deformities and ankylosis. Hesham, S, H, EULAR, 2006.

Pathology of leprotic arthritis

Hanafi, et al [10] found the following characteristics: hyperplasia of the synovial cells which form several layers of cubical flattened epithelium, villous hypertrophy.

1. Inflammatory cells in the synovial tissue, mainly lymphocytes, few plasma cells and histocytes.
2. Proliferation of the endothelial lining of blood vessels, with narrowing of lumen that contains exudates consisting of fibrin network, thickening of vessel wall (end arteritis obliterans). No lepra bacilli were detected in the synovium. Muscle biopsy (jenu reticularis) revealed lymphocytic infiltration within the muscle bundles and loss of muscle striation in area of lymphocytic infiltration.

Four patients were found with mild rheumatoid-like synovitis [3]. While, erythema nodosum showed inflammatory changes with no acid fast bacilli. Andreoli, [11] observed a well-marked infiltration of the synovial membrane and increase in vascularity with polymorphonuclear leucocytes which is profoundly different from the lymphocytic and plasma cell infiltration of the synovium found in RA.

Mc Carthy, [12] reported an acute synovial Inflammatory reaction and suggested that synovitis was due to infection rather than to immune complexes. The synovial fluid aspirated from one knee joint of leprotic patient with arthritis was found to contain degenerating polymorphs and some fragmented (dead) leprosy bacilli [13].

Berman, [14] and Albert, et al. [6] found an exudative inflammatory joint fluid in fifteen patients with leprosy who had rheumatoid manifestations. Riordan, [15] summarized the changes seen in the bones and joints of patients with Leprotic arthritis as follow:

1. Leprous osteitis may be a true leproma caused by *M. leprae*.
2. Periostitis is due to the presence of *M. leprae*, without secondary infection.
3. Bone absorption of in the upper and lower extremities; occur in both major types of leprosy is due to nerve involvement.
4. Osteomyelitis is frequently superimposed on pre-existing bone changes when ulcerations penetrate to underlying bone.
5. Destructive joint changes of leprosy (Charcot joint), is secondary to nerve changes.

Differential diagnosis between rheumatoid and leprotic arthritis (Bassiouni and Hanafi, et al. [10])

Differential diagnosis of bone erosion & absorption of extremities

(Acro-osteolysis)-O'Reilly and Show, et al. [16].

A. Resorption of phalangeal tufts

| Table 1: | | |
|--------------------------------|---|---|
| Clinical finding | Rheumatoid Arthritis | Leprotic Arthritis |
| Age of onset | Childhood and adult, peak incidence in 50 years | Age of case reported range from 10 to 60 yr |
| Early Symptoms | Morning stiffness | Morning stiffness recorded in 40 patients out of 50 |
| Joint Involved | Metacarpophalangeal joint, wrist, proximal interphalangeal joints most common, distal interphalangeal joints almost never, elbow T.M.J., Sternoclavicular, knee, ankle and foot joints mainly lateral compartment | M.C.P., P.I.P. And D.I.P joints, most often, elbow, wrist, knee, ankle, foot, T.M.J., elbow were most common involved joints. All of which were tender |
| Joint Swelling | Synovial thickening and effusion often moderate to large | Synovial thickening and effusion often small to moderate |
| Skin Manifestations | | |
| A) E.N.L. and reaction. | Not present but there is palmer erythema. | Often present 30-40 % |
| B) Hypoesthetic macules | Not present | Often present |
| C) Subcutaneous nodules | Mostly on proximal interphalangeal joints and extensor surface of the elbow | On proximal and distal interphalangeal joints |
| | In 20-35 % of rheumatoid patients | In 60 % of the examined patients. |
| Pathology of Nodule | Central area of necrosis rimmed by a corona of palisading fibroblast which in turn is surrounded by a collagenous capsule, with perivascular collection of chronic inflammatory cells | Lepromatous granulomata with fragment of lepra bacilli. |
| Neurologically | Muscle wasting and peripheral neuritis may occur, but not common | -Hypoesthetic macules |
| | | -Glove and stocking hypoesthesia |
| | | -Paralysis |
| | | -Marked muscle wasting of hand and foot |
| | | -Thickening and tenderness of peripheral nerves |
| Deformities | Swan neck, boutonniere, flexion deformity of elbow and knee | Claw hand, foot and wrist drop, loss of fingers and toes, but swan neck deformity is also detected |
| Radiologically | Periarticular osteoporosis, marginal erosion, proximal interphalangeal joints most often while D.I.P almost never | Osteoporosis, erosion and bone absorption |
| | Carpal bones most commonly affected | New bone formation. Involvement of P.I.P. and D.I.P |
| | | Carpal bones are less common & there is discrepancy between metacarpal, phalangeal bone lesion and carpal bones. Proximal & distal interphalangeal joints are nearly equally effected |
| Laboratory | High E.S.R, Latex test positive in 85%% | High E.S.R, Latex test negative in all the fifty patients |
| | Negative for Leprae Bacilli | Positive for Leprae Bacilli |
| Histopathology | -Villous hypertrophy | -Villous hypertrophy |
| | -Proliferation of synovial cells | -Proliferation of synovial cells |
| | -Lymphocytic & plasma cells infiltration and synovial proliferation are more in RA than in Leprotic arthropathy | -Lymphocytic & plasma cells infiltration |
| | | -no lepra bacilli were detected in synovial membrane |

Progressive Systemic Sclerosis (PSS)

-Reynard's-Sarcoidosis

-Psoriatic arthritis-Neuropathic arthritis

-Thromboangitis obliterans-Thermal injuries

-Trauma-Hyperparathyroidism

-Epidermolysis-bullosa Porphyria

-Progeria-Pachydermo periostosis

B. Resorption of mid-portion of phalanges

-Polyvinyl chloride-tank cleaners

-Hyperparathyroidism

-Hajdu-cheney syndrome

C. Periarticular resorption

-Psoriatic arthritis-Hyperparathyroidism

-Scleroderma-Erosive O.A

-Multicentric reticulocytosis

Treatment of leprotic arthritis

General considerations: leprosy patients should be treated with patience, perseverance and understanding. Beside medical

treatment, they need moral support and reassurance so that they regain self-confidence and self respect. Proper attention should be paid to the diet and general health. It should be explained to the patient with established deformity that the chemotherapy will not change this aspect of the disease. At the first visit, the patient should be given a realistic view of what combined treatment with anti-leprosy drugs can achieve and roughly how long he will need to be treated without seeing an improvement. The patient should be informed that tablets are more effective than injections in curing leprosy. It is essential to explain to him the importance of compliance and in particular that he needs to follow the treatment completely and regularly. Every effort should be made to encourage out patient care and keep treatment in leprosy hospitals to a minimum. If the patient is treated while living at home, he will remain integrated in texture of the society also keeping his work Thangaraj and Yawalkar, [17]. All the drugs used except rifampicin are bacteriostatic [18].

Anti-leprosy drugs

Dapsone: This is the most important and cheapest drug in the treatment of leprosy. It was first used for the treatment of leprosy (intramuscular oily suspension) by Cochrane in India. In 1947 Lowe tried dapsone orally in Nigeria [19].

It is a bacteriostatic (weakly bactericidal) and the mechanism of action is thought to be interference of the folic acid synthesis through competition with para-aminobenzoic acid. The morphological index of the skin in LL patients falls to zero after 5-8 months of treatment compared to about 5 weeks in patients treated with rifampicin [20].

Clinical improvement is not usually seen within 3 -6 months of treatment, if clinical improvement is not evident after 6 months for regular intake of dapsone in standard dosages (50-100 mg/day, 1-2 mg/ kg), the possibility of dapsone resistance should be considered. Irregular intake of dapsone in small doses leads to development of dapsone resistant strains of leprosy bacilli. A daily dose of less than 100 mg dapsone must not be given to adult patient weighting more than 50 kg. The full dosages should therefore, be given from the start and should not be reduced during lepra reaction [21]. Side effects in patients with leprosy are rare. It may occasionally lead to malaise, weakness, hemolytic anemia, leucopenia, drug fever, nephritis, acute peripheral neuritis, fixed drug eruptions, exopholiative dermatitis, hepatitis and acute psychosis.

Rifampicin: It is a semi synthetic derivative of a fermentation product of *Streptomyces mediterranei*, with an estimated minimal inhibitory concentration (MIC) of 0.3 µg/ml rifampicin. It inhibits the bacterial RNA synthesis. It is the most potent bactericidal anti-leprosy drug available today. A single dose as low as 600 mg/month will kill the great majority (about 99.9%) of *M. leprae* within a few days, so rendering multi bacillary multi bacillary patients non-infectious.

Although the bacteria are killed rapidly, the rate of fall of BI, the speed of clinical improvement and the incidence of type II lepra reaction in LL patients are the same as with dapsone [22].

The most common side effect is red colourful of urine due to drug excretion. It may also cause skin rashes, gastrointestinal symptoms, dizziness, drowsiness and weakness. Rarely does it result in hepatitis, thrombocytopenia, psychosis, porphyria cutenea tarda and Stevens-Jonson syndrome [23]. The recommended dosage was 450-600 mg/ month.

Languillon, et al. [24] were the first to report the efficacy and good tolerability of a single oral rifampicin dosage 1200 mg/month schedule as a combination regimen for the treatment of LL patient. Later Yawalkar, et al. [25] confirmed these findings.

Clofazimine (Lamprene): It is a substituted aminophenazine bright-red dye. Its overall ant leprosy effect is similar to dapsone [26]. However; it has a slower onset of action than dapsone. The drug is mainly bacteriostatic and weakly bactericidal [27].

Hypothetically, lamprene interacts with mycobacterial DNA. It gives no sign of cross-resistance with dapsone or rifampicin. Although this drug has been on the market since 1969, the first case of Clofazimine resistant *M. leprae* has so far reported in 1982 [28].

Lamprene is the only ant leprosy drug possessing an anti-inflammatory effect [29], which is clinically valuable in controlling type II leprae reactions occurring in patients with MB leprosy. It may also be useful in controlling reversal reaction in borderline leprosy. Clofazimine-mediated anti-inflammatory and immunosuppressive active may be due to its stimulating effect on the synthesis of prostaglandin E2 by human polymorphonuclear leukocytes, and macrophages. It is advisable to administer 50 mg lamprene daily to adult patients with leprosy. It should be taken with meals or with glass of milk. For MB cases the WHO Study Group on leprosy recommends supervised dose of 300 mg lamprene per month in addition to daily dose of 50 mg lamprene [21].

Multidrug Therapy (MDT): It is known that simultaneous administration of several different antibacterial agents may prevent the emergence of drug-resistant mutants. The only way to prevent the spread of drug-resistant bacteria is to use different anti-leprosy drugs simultaneously in full dosage for an adequate period and without interruption [28].

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