

Arthritis in leprosy without specific skin lesion

S Dewi, B Setiyohadi

Division of Rheumatology, Department of Internal Medicine, University of Indonesia School of Medicine/Cipto Mangunkusumo General Hospital, Jakarta

Leprosy patients could display a great variability of signs and symptoms. An overabundance of rheumatic manifestations, occurring alone or in varying combinations, are associated with leprosy, particularly with lepra reactions. A study involving seventy cases of leprosy found that rheumatic manifestations were seen in 61.42% of cases: arthritis in 54.28% and soft tissue rheumatism in 17.14%. Enthesitis was seen in 2.84% of cases. Rheumatic manifestations may be the primary complaint, thus delaying accurate diagnosis. Musculoskeletal involvement in leprosy is the third most frequent manifestation after dermatological and neurological involvements. It can occur at any time during the infection. Articular inflammation in leprosy, which closely mimics other rheumatic disorders, usually occurs in reactive states, particularly erythema nodosum leprosum (ENL).¹ About 1–5% of leprosy patients are reported of developing arthritis (synovial inflammation) at some stage of the disease but this rate increases to over 50% during lepra reactions.²

Here we report a case of arthritis in leprosy without any typical skin lesion thus causing a delay in diagnosis.

CASE REPORT

A 72-year-old woman was admitted at the immunology clinic complaining that her left hand had become smaller than her right hand within one year. The skin on her left hand was anesthetic with occasional tingling sensation. She reported no skin lesion on other parts of her body. There were not any significant constitutional symptoms and family history of arthritis or leprosy.



Figure 1 Muscle atrophy of the left hand with tight and shiny skin.

Physical examination showed normal vital signs, but her left hand was atrophic with tight, shiny anesthetic skin and pencil-like fingers. We did not find any arthritis or tremor. She had no leonine facies or any skin lesion on other parts of her body.

Laboratory examination revealed: hemoglobin 12.5 g/dL, hematocrit 37.5%, leukocyte count $7.9 \times 10^3/\text{mm}^3$, platelet count $287 \times 10^3/\text{mm}^3$, erythrocyte sedimentation rate 35 mm/hr, C-reactive protein 4.6 mg/dL, blood glucose 102 mg/dL, blood urea nitrogen 30 mg/dL, serum creatinine 0.5 mg/dL, aspartate aminotransferase 44 IU/L, alanine aminotransferase 31 IU/L, total protein 7.8 U/L, albumin 4.41 U/L, globulin 3.49 U/L, total cholesterol 161 mg/dL, low-density lipoprotein cholesterol 63 mg/dL, and high-density lipoprotein cholesterol 71 mg/dL. The urinalysis showed normal results. The latex rheumatoid factor test was negative. Antinuclear antibodies were negative and there were no antibodies toward extractable nuclear antigens. Radiography of the hands and wrists showed normal bones.

The patient was first diagnosed with vasculitis and carpal tunnel syndrome. However, we found no histopathologic feature of vasculitis on biopsy. The electromyography did show motoric neuropathy of the median nerve and sensoric neuropathy of the ulnar nerve, but we found no swelling of the lining of the flexor tendons (tenosynovitis) or evidence of joint dislocations, fractures, or arthritis that can narrow the carpal tunnel and put pressure on the nerve. She was then given steroid (prednisolone 32 mg/day) and calcium 1,500 mg/day.

One month after therapy, she complained of gradual pain, stiffness, swelling, and redness of fingers II and III of her left hand. There was no clear history of Raynaud's phenomenon. On physical



Figure 2 Arthritis of fingers II and III of the left hand. The size of both hands had become similar.

examination we found swelling of the fingers of her left hand, with arthritis of interphalangeal joints of fingers II and III (figure 2). Still there was no typical skin lesion on the fingers or on any other parts of her body.

She then underwent slit skin smear for acid-fast bacilli, which showed negative result. Skin biopsies were subsequently performed and histopathological examination revealed thickening of collagen and epitheloid granuloma in dermis, thus representing scleroderma, but borderline tuberculoid (BT) leprosy was also suspected. Fite-Faraco staining showed no acid-fast bacilli. She then underwent serological test with enzyme-linked immunosorbent assay (ELISA) for anti-phenolic glycolipid-I (anti-PGL-I). We found that IgM was normal (456 U/mL, cut off 605 U/mL) but there was slight rise of IgG (666 U/mL, cut off 630 U/mL). The diagnosis of BT leprosy was then made. The World Health Organization (WHO) multidrug therapy (MDT) 1982 regimens for paucibacillary (PB) leprosy, comprising of rifampicin 600 mg once a month and dapsone 100 mg q.d., was started immediately.

Five months after therapy, the size of both hands had become similar. Her arthritis symptoms had improved, although the complaint of recurrent numbness and tingling on her left hand persisted (figure 3). The dose of prednisolone was then tapered and MDT for PB was continued.



Figure 3 Five months after therapy: similar sizes of both hands, with swelling of fingers II and III of the left hand.

DISCUSSION

Leprosy, or Hansen's disease (HD), is a chronic granulomatous infection caused by *Mycobacterium leprae*. It has a global prevalence of 5.7 per 10,000 populations. At the end of 2005, the global prevalence of leprosy was estimated by the WHO to be around 1 per 10,000 population.³ It is estimated that 12–20 million people suffer from leprosy worldwide. Leprosy is endemic in Indonesia. Data from the Ministry of Health of the Republic of Indonesia showed that the prevalence of leprosy in Indonesia was 0.76/10,000 population in 2008.⁴

Leprosy exhibits a wide spectrum of presentation, varying from the tuberculoid to the lepromatous pole, with immunologically unstable borderline forms in between, depending upon the immunity status of the individual.

Traditionally, patients are classified according to the Ridley-Jopling scale, which includes indeterminate leprosy, tuberculoid leprosy, borderline tuberculoid leprosy, borderline leprosy, borderline lepromatous leprosy, and lepromatous leprosy. Tuberculoid leprosy represents a sufficient cell-mediated immune response. Patients may have one or two hypopigmented, erythematous, and anesthetic macules with a raised margin. Lepromatous leprosy may occur in the setting of immune dysfunction or if the patient is anergic to *M. leprae*. These patients may have widespread disease that involves the skin, upper respiratory tract, anterior chamber of the eye, testes, lymph nodes, periosteum, and superficial sensory and motor nerves.^{5,6} Cutaneous findings include diffuse, erythematous macules, papules, and nodules. The clinical system of classification for the purpose of treatment includes the number of skin lesions and nerves involved as the basis for classifying the patients into multibacillary (MB) or PB.^{7,8,9}

The presentation of leprosy can be variable. The skin lesions of leprosy have a great similarity to various other lesions, hence the term “the great imitator”. Sometimes, these skin lesions may be misdiagnosed because the physician does not consider leprosy. Although leprosy affects primarily the skin and the peripheral nervous system, it also secondarily involves the liver, spleen, testes, kidney, bone marrow, and eyes.^{5,6} Any peripheral or cutaneous nerve may be involved, but the ulnar nerve is the most commonly affected. In addition, leprosy patients may also suffer from reactions which are acute episodic inflammatory states unrelated to secondary infection and which occurs during the natural course of the disease.^{5,6,10}

The diagnosis of our patient was delayed because she had no symptom of arthritis or typical leprosy skin lesion before being treated with systemic corticosteroids. The diagnosis was confused clinically because she had developed neurological signs with atrophy of the left hand without the evidence of vasculitis or carpal tunnel syndrome. Although histopathological examination of skin biopsy revealed the presence of epitheloid granuloma, the diagnosis of BT leprosy was still doubted. The diagnosis of leprosy was finally made by serological test with ELISA, in which there was a slight rise of IgG anti-PGL-I. It fitted the theory that the rapid lateral flow test for anti-PGL-I antibody of *M. leprae* was highly positive at the beginning and moderately positive at the follow-up.¹¹

In BT leprosy, inflammation associated with active and reactive BT lesions may usually cause asymmetrical swelling of the hands and feet, particularly if the skin lesions are present at these sites.^{6,12} Our patient had asymmetrical oligoarthritis even though there was not any identifiable active leprosy skin lesion on the site of arthritis.

Pathogenesis of arthritis in leprosy remains unclear until now. Some experts stated that arthritis in leprosy is a reactive arthritis with immunological basis. Some others classified it as infective arthritis based on the presence of leprosy bacilli in synovial tissue or joint fluid. Arthritis could present either within a reactional state or without the reaction.¹³ The pathological effects of leprosy on the skeleton are primarily a consequence of neuropathy leading to denervation, direct

bony changes, secondary infection and the sequelae of trophic ulcers.¹⁴

In patient with leprosy, the following superficial peripheral nerve trunks may be palpably hypertrophied: facial, great auricular (neck), ulnar (elbow), median (wrist), radial cutaneous (wrist), lateral popliteal (neck of fibula), and posterior tibial (medial malleolus). The most commonly affected is the posterior tibial nerve followed by the ulnar nerve at the elbow, whose involvement results in clawing of the fourth and the fifth fingers, and loss of dorsal interosseous musculature and loss of feeling in the ulnar nerve distribution. Median nerve involvement impairs thumb opposition and grasp, while radial nerve dysfunction, though rare in leprosy, results in wristdrop. Three major nerve branches supply sensory and motor function to the hand and arm, listed in order of the frequency of their involvement in leprosy: the ulnar, the median and the radial nerve branches. Abnormality in any one of these peripheral nerve branches can result in a change from a normal sensory feedback and muscle function of the hand. Leprosy patients are somewhat unique in that they can also develop temperature-associated loss of sensory end-organs superficially in skin in areas not typical to a specific peripheral nerve area of innervation. On the palm in early stages of the disease, a loss of feeling has most often been related to specific nerve branches, thus an ulnar, median, or radial nerve loss. While leprosy can affect the peripheral nerve branches or superficial areas of the skin, other diseases and injuries can affect the same peripheral nerve branches. Information learned from patients with multiple nerve involvement has increased our understanding of the normal hand and of the role insensitivity and muscle loss plays in deformity and disability. An understanding of the mechanics of deformity from sensory and motor loss provides insight into prevention and correction.³

Specific bony lesions in leprosy are rare with an incidence of between 3 and 5% among hospitalized patients, and are mainly confined to the small bones of the face, hands and feet. These lesions are characterized by granulomatous tissue reactions, which are destructive and manifest radiographically as focal areas of increased rarefaction. The margins are thin, but may be sclerotic. Obliteration of the cavity may result from its collapse with flattening of the articular surface. In the hands and feet, the disease mainly involves the proximal and/or the middle phalanges. It may present as thinning of the endosteum with corresponding widening of the medullary canal localised to the area of the metaphysis. Fusiform swelling of the soft tissues overlying the corresponding part of the affected digit is more common. This is occasionally associated with enlarged nutrient foramina. Leprous osteitis in the hands commonly involves the distal ends of the proximal and middle phalanges, whereas it usually affects the metatarsal heads in the feet. If the disease progress and the trabeculae be destroyed, the radiographs reveal a "honeycomb and cystic" appearance. With healing, radiographic changes become sharply defined as cysts with sclerotic margins. The articular surface can also be involved and the intrinsic forces in the hand may result in fracture, subluxations and rigid clawing of the fingers.^{10,12-14}

In our patient there is no lesion on the hand radiograph.

It is vital to prevent the development of nerve palsies and ulcers. Primary prevention is by early detection and the use of antileprosy drugs. Secondary prevention is by health education and self-awareness of the patient; hygiene of the anaesthetic foot with attention to cracks and fissures, early detection of tenderness and adequate rest; awareness of potential injury mainly during work and cooking; appropriate foot wear.¹⁴

Multidrug therapy is the mainstay of treatment. The current multidrug therapy recommended by the WHO in adults with MB disease is rifampicin 600 mg orally once a month, dapsone 100 mg orally daily, and clofazimine 300 mg orally once monthly with additional 50 mg daily. The WHO recommends that it be continued for 12 months but patients with initial high bacterial loads may need longer treatment. For PB disease (bacteriological index 2+) the regimen is rifampicin 600 mg orally once monthly and dapsone 100 mg orally daily for six months.

Any patient who develops peripheral nerve damage during the last six months of treatment should receive a four- to six-month course of oral steroids.

There is usually stiffness of the fingers. Physiotherapy with active exercises, massage, passive stretching and wax baths and splinting should be undertaken before giving consideration to tendon transfer procedures.

Impairment of nerve function can occur before diagnosis and during or after multidrug therapy. Patients with multibacillary leprosy and pre-existing nerve damage are at the highest risk of impairment of nerve function during and after treatment. These patients should be under surveillance for two years from diagnosis. Regular clinical evaluation should include nerve palpation, motor testing of the small muscles of the hand. Steroids may also be given to reduce inflammation.^{3,6} After the treatment with MDT for PB disease and continued with low-dose steroid (4 mg/day), her joint disease had responded well but she had permanent neurological damage presented as recurrent numbness and tingling of her left hand, some of which might have been avoided if the diagnosis had been made earlier.

CONCLUSION

Symmetric polyarthritis involving the peripheral joints is the most common rheumatic manifestation in leprosy patients. This article reported the case of a patient affected with leprosy who developed asymmetrical oligoarthritis without any of the skin lesions characteristic of leprosy infection. There was a delay in diagnosis because of nonspecific feature that resulted in persistent nerve damage, which might have been prevented if the diagnosis had been made earlier.

REFERENCES

1. Vengadkrishnan K, Saraswat PK, Mathur PC. A study of rheumatological manifestations of leprosy. *Indian J Dermatol Venereol Leprol* 2004;70:76-8.
2. Ribeiro SLE, Pereira HLA, Silva NP, Neves RMS, Sato EI. Anti-cyclic citrullinated peptide antibodies and rheumatoid factor in leprosy patients with articular involvement. *Braz J Med Biol Res* 2008;41:1005-10.

3. Haroon N, Agarwal V, Agarwal A, Kumari N, Krishnani N, Mishra R. Arthritis as presenting manifestation of pure neuritic leprosy—a rheumatologist dilemma. *Rheumatol* 2007;46:653–6.
4. Gill AL, Bell DR, Gill GV, Wyatt GB, Beeching NJ. Leprosy in Britain: 50 years experience in Liverpool. *Q J Med* 2005;98:505–11.
5. Health Agency of East Java Province. The Nippon Foundation's visitation for leprosy in Indonesia and East Java [Kunjungan The Nippon Foundation seputar kusta di Indonesia dan Jawa Timur]. [Online]. 2009 Jun 13 [cited 2010 Jul 20]; Available from: URL:<http://www.surabaya-ehealth.org/dkksurabaya/berita/kunjungan-nippon-foundation-seputar-kusta-di-indonesia-dan-jawa-timur>.
6. Britton WJ, Lockwood DN. Leprosy. *Lancet* 2004;363:1209–19.
7. Pernambuco JC, Cossermelli-Messina W. Rheumatic manifestations of leprosy: clinical aspects. *J Rheumatol* 1993;20:897–9.
8. Armour KS, Scolyer RA, Barnetson RS. Borderline lepromatous leprosy presenting as a single cutaneous plaque. *Australas J Dermatol* 2005;46(3):181–3.
9. Jha PK, Talwar S, Suresh MS, Panvelkar V. Localized borderline lepromatous leprosy. *Lepr Rev* 1991;62(2):212–6.
10. Sapkota BR, Neupane KD, Maharjan RK. Single lesion multibacillary leprosy, a treatment enigma: a case report. *J Med Case Reports* 2009;3:8.
11. Cossermelli-Messina W, Festa-Neto C, Cossermelli W. Articular inflammatory manifestations in patients with different forms of leprosy. *J Rheumatol* 1998; 25:111–9.
12. Al-Raqum HA, Uppal SS, El Abdalghani RA, Lasheen I. First report of leprosy presenting as acute polyarthritis in the setting of type I downgrading lepra reaction. *Clin Rheumatol* 2006;25(1):101–5.
13. Holla VV, Kenetkar MV, Kolhatkar MK, Kulkarni CN. Leprous synovitis. A study of fifty cases. *Int J Lepr Other Mycobact Dis* 1983;51(1):29–32.
14. Moonot P, Ashwood N, Lockwood D. Orthopaedic complications of leprosy. *J Bone Joint Surg Br* 2005;87B:1328–32.