

# *Systemic manifestations and ulcerative skin lesions in leprosy: differential diagnosis with rheumatic diseases*

Sandra Lúcia Euzébio Ribeiro<sup>1</sup>, Eriane Leite Guedes<sup>2</sup>, Helena Lucia Alves Pereira<sup>3</sup>, Lucilene Sales de Souza<sup>4</sup>

---

## ABSTRACT

Leprosy is a systemic disease with predominant involvement of skin and nerves; articular manifestations are common and, in some cases, represent the initial complaint. We describe the case of a female patient with borderline leprosy, which manifested, initially, with symmetric polyarthritis, cutaneous ulcerative lesions on the lower limbs, and systemic manifestations mimicking rheumatic disease. The authors emphasize the importance of the differential diagnosis of the systemic, joint and, cutaneous involvement of leprosy with rheumatic diseases.

**Keywords:** leprosy, polyarthritis, cutaneous ulcerative lesions.

---

## INTRODUCTION

Leprosy is a chronic infectious disease caused by *Mycobacterium leprae*, an acid-alcohol resistant bacillus with affinity for skin and peripheral nerve cells.<sup>1</sup>

This disease can present a wide range of clinical manifestations, including those secondary to systemic involvement, which is seen especially in multibacillary patients (borderline and lepromatous). Those manifestations are uncommon; however, they are important due to the similarity of the clinical presentation to rheumatic diseases.<sup>2,3</sup>

We present a case of leprosy in which the patient presented, initially, asthenia and weight loss followed by symmetrical polyarthritis, involving small and large joints, associated with ulcerative skin lesions on the lower limbs suggestive of vasculitis, mimicking a connective tissue disease.

---

## CASE REPORT

This is a 58-year old patient who, in January of 2009, developed asthenia, progressive muscle weakness, and skin ulcers on the lower limbs associated with symmetrical polyarthritis of the hands, wrists, knees, ankles, and feet. After three months her symptoms worsened, with a 10 kg weight loss, secondary infection of the skin lesions, and difficulty walking. She went to the dermatology outpatient clinic and, at that time, presented with generalized xeroderma, predominantly of the legs, feet, and hands; cyanosis of the 5<sup>th</sup> right finger and of the 2<sup>nd</sup>, 3<sup>rd</sup>, and 4<sup>th</sup> left toes (Figures 1A and 1B), edema and ulcerative lesions on both legs (feet, ankles, and the area of insertion of the Achilles tendon) of different sizes, with elevated and hyperemic borders surrounding a center with purulent secretion (Figures 2A and 2B) were observed. The

---

Received on 7/07/2009. Approved on 08/10/2009. We declare no conflict of interest.

1. Professor of Rheumatology Internal Medicine Department of Universidade Federal do Amazonas (UFAM).

2. Internal Medicine.

3. Assistant Rheumatologist of the University Hospital Getúlio Vargas, Universidade Federal do Amazonas (UFAM).

4. Dermatologist of the Fundação Alfredo da Matta (FUAM).

Correspondence to: Sandra Lúcia Euzébio Ribeiro, MD. Avenida Apuriná 04, Bairro Praça 14. Manaus – Amazonas, Brasil. CEP: 69020-170. Tel: 55 92 3633-4977. E-mail: sandraeuzebio@vivax.com.br



**Figure 1.** Cyanosis of the extremities. **A)** Edema of the proximal interphalangeal joints and cyanosis of the right 5<sup>th</sup> finger; **B)** Edema and cyanosis of the extremities of the toes associated with ulcerated lesions on the left 4<sup>th</sup> toe and lateral aspect of the left foot.



**Figure 2.** Ulcerated lesions with elevated borders, hyperemia, and signs of necrosis of the left ankle (**A**), which are deeper and more extensive in the lower third and dorsal aspect of the right foot (**B**).

skin lesions were biopsied and antibiotics were instituted. Laboratorial tests revealed hypochromic microcytic anemia (hemoglobin = 9.5 g/dL, hematocrit = 24.7%), eosinophilia = 11%, erythrocyte sedimentation rate (ESR) = 64 mm, C-reactive protein = 6 mg/dL, rheumatoid factor (latex) = 64 IU/mL, antinuclear factor (ANF) HEp 2 1:160 fine speckled pattern, aspartate aminotransferase (AST) = 115 U/L, and alanine aminotransferase (ALT) = 83 U/L. Imaging exams: X-ray of the lower limbs, knee and ankles, and lumbar spine without changes; total abdominal ultrasound (US) with signs of hepatosplenomegaly and periportal lymph nodes. Due to the polyarthrititis and severe pain in the cervical spine, the patient went to the rheumatology clinic where non-

steroidal anti-inflammatories were prescribed. On follow-up appointment, the patient referred subtle improvement of the skin lesions, but systemic symptoms (severe asthenia, anorexia, and fever) and polyarthrititis of large and small joints persisted. The histopathological report was consistent with mycobacteriosis (epidermal hyperplasia, severe dermal fibroplasia, inflammatory infiltrate with macrophages, lymphocytes, and plasma cells in the cutaneous adnexa), and countless fragmented acid-alcohol resistant bacilli. Fite-Faraco-Wade staining showed several fragmented acid-alcohol bacilli. In May, after the biopsy results, the patient was referred for bacilloscopy, and the presence of a positive bacilloscopy index (BI – 2.25) confirmed the diagnosis of borderline

borderline (BB) leprosy, and polychemotherapy (PCT) with 60 mg of prednisone a day was instituted. After the second cycle of PCT and on 10 mg of prednisone a day, the patient has had improvement of the systemic manifestations, skin lesions, and polyarthritis. On 07/07/09, prednisone, 40 mg a day, for ten days, was instituted, which was subsequently reduced to 10 mg/day. It has been planned to maintain her on specific therapy for 12 months.

## DISCUSSION

The different clinical complaints related to leprosy that often resemble other disorders with insidious clinical evolution, make this chronic disease a diagnostic challenge in the first months to years. Fever, fatigue, paresthesia, and musculoskeletal complaints, associated with skin lesions and visceral involvement, contribute for the similarities between leprosy and other disorders.<sup>1</sup>

Active *M. leprae* infection is characterized by a wide diversification in clinical course, ranging from pauci- to multibacillary types, according to the bacillary load of the lesions<sup>1</sup>. The similarities between the clinical and laboratorial manifestations of leprosy and connective diseases have been known for a long time.<sup>2</sup>

The literature describes leprosy patients who were initially diagnosed with and treated for systemic lupus erythematosus (SLE), rheumatoid arthritis (RA), dermatopolymyositis, and systemic vasculitis.<sup>3-8</sup> Those systemic manifestations are seen mainly in multibacillary leprosy, especially during reactional states, and are secondary to the direct infiltration and proliferation of the bacillus in the affected organ.<sup>2-9</sup>

Systemic manifestations include malar erythema, subcutaneous nodules, ulcerations, purpuras, ischemic necrosis, Raynaud's phenomenon, polyneuropathy, multiple mononeuritis, muscle weakness, generalized lymphadenopathy, hepatosplenomegaly, and glomerulonephritis.<sup>2,8-10</sup> The presence of rheumatoid factor, anti-cyclic citrullinated antibodies, ANF, anticardiolipin antibodies, antineutrophil cytoplasmic antibodies, and others are among the serologic changes observed.<sup>2-11</sup>

Joint involvement is seen especially in reactional types and erythema nodosum leprosum is the most common manifestation. Other types of joint involvement include Charcot's arthropathy, post-traumatic non-specific septic arthritis, and specific arthritis due to the direct infiltration of *M. leprae*.<sup>12,13</sup> In the present case, although synovial biopsy was

not performed, we believe that the polyarthritis was caused by the presence of bacilli in the joints and, therefore, a specific polyarthritis caused by *M. leprae*. Although rare, polyarthritis may be explained by the elevated bacillary load and the fact that specific treatment was not instituted. The insidious and progressive development of polyarthritis is similar to the clinical presentation of rheumatoid arthritis.<sup>7</sup>

In the present case, clinical manifestations, such as exuberant polyarthritis and necrotic skin lesions, and laboratorial findings were suggestive of a connective tissue disease, but the identification of Hansen's bacillus in the biopsy specimen was diagnostic of multibacillary leprosy. The multisystem involvement most likely was secondary to bacillary infiltration and consequent focal granulomatous reaction. The presence of bacillemia has been described, especially in non-treated LL patients, and histopathological exam shows the presence of bacilli in macrophages, endothelial cells, lumen of end-circulatory blood vessels, and marginal sinus of lymph nodes, phagocytosed by macrophage or free inside the sinus. Bacilli can, therefore, reach multiple sites, proliferating and stimulating granulomatous reaction. Involved organs include lymph nodes, liver, spleen and bone marrow, synovial membranes, mucous membranes of the upper respiratory tract, and testicles.<sup>14</sup>

Skin necrosis in leprosy are attributed to vascular thrombosis induced by the direct invasion of the wall of the blood vessels and endothelium by Hansen's bacilli.<sup>15</sup> In the present case, the presence of several cyanotic, ulcerated, and necrotic skin lesions on the extremities, similar to Lucio phenomenon, which is characterized by necrosis of erythema nodosum lesions during the evolution of a leprosy reaction in non-treated multibacillary leprosy, was most striking. However, our patient did not complain of lesions similar to erythema nodosum, which were also not observed on the physical exam. The histopathology of Lucio phenomenon shows endothelial proliferation, thrombosis, ischemic necrosis, discrete mononuclear infiltrate, and countless bacilli around and in the walls of blood vessels, which was not described in the biopsy of this patient.<sup>15</sup>

With the advent of PCT and programs for the early detection of the disease, cases of multisystem involvement, as the one reported here, are becoming increasingly uncommon; however, the rheumatologist must be attentive for its development, since those are the ones that resemble the clinical and laboratorial manifestations of rheumatic disorders.

## REFERÊNCIAS

### REFERENCES

1. Britton WJ, Lockwood DN. Leprosy. *Lancet* 2004; 363:1209-19.
2. Mathews LJ, Trautman JR. Clinical and serological profiles in leprosy. *Lancet* 1965; 7469:915-18.
3. Freire M, Carneiro HE, Teodoro RB, Cecin HA. Manifestações Reumáticas na hanseníase: dificuldades no diagnóstico precoce. *Rev Bras Reumatol* 1998; 38: 210-14.
4. Ferro RC, Fernandes SRM, Costallat LTL, Adilmuhib S. Lúpus Eritematoso Sistêmico associado à moléstia de Hansen. Relato de três casos. *Rev Bras Reumatol* 1991; 31:31-5.
5. Iveson JMI, Mc Dougall AC, Leatherm AJ. Lepromatous leprosy presenting with polyarthritis, myositis and immune complexes glomerulonephritis. *Br Med J* 1975; 3:619-21.
6. Ribeiro SLE, Erilane, Pereira HLA, Sales LS. Vasculite na hanseníase mimetizando doenças reumáticas. *Rev Bras Reumatol* 2007; 47:140-44.
7. Haroon N, Agarwal V, Aggarwal N, Kumari N, Misra R. Arthritis as presenting manifestation of pure neuritic leprosy a rheumatologists dilemma. *Rheumatology* 2007; 46:653-56.
8. Flower C, Gaskin D, Marquez S. A case of recurrent rash and leg numbness mimicking systemic rheumatic disease: the occurrence of leprosy in a nonendemic area. *J Clin Rheumatol* 2007; 13: 143-145.
9. Karat ABA, Karat S, Job CK, Furness MA. Acute Exudative Arthritis leprosy- rheumatoid-arthritis like in Association with Erythema Nodosum Leprosum *Br Med J* 1967; 3:770-72.
10. Lane JE, Balagon MV, Dela Cruz EC *et al.* Mycobacterium leprae in untreated lepromatous leprosy: more than skin deep. *Clin Exp Dermatol* 2006; 31(3):469-70.
11. Ribeiro SL, Pereira HL, Silva NP, Neves RM, Sato EI Anti-cyclic citrullinated peptide antibodies and rheumatoid factor in leprosy patients with articular involvement. *Braz J Med Biol Res* 2008; 41(11):1005-10.
12. Holla VV, Kenetker MV, Kolhatkar MK, Kulkarni CN. Leprous synovitis: a study of fifty cases. *Int J Lepr* 1983; 51:29-32.
13. Pereira HLA, Ribeiro SLE, Sato EI. Manifestações reumáticas da hanseníase. *Acta Reumatol Port* 2008; 33:407-14.
14. Drutz DJ, Chen TS, Lu WH. The continuous bacteremia of lepromatous leprosy. *N Engl J Med* 1972; 287:159-64.
15. Azulay-Abulafia L, Spinelli L. Revendo a Hanseníase de Lúcio e o Fenômeno de Lúcio. *Med Cutan Iber Lat Am* 2005; 33(3):125-33.