

CASE REPORTS

Lucio's phenomenon: A report of two cases and review of the literature

Gustavo Alexis Lemus-Barrios¹, Julian Andrés Hoyos-Pulgarín¹, Carlos Eduardo Jimenez-Canizales², Diana Melisa Hidalgo-Zambrano², Fredy Escobar-Montealegre², Alvaro Mondragon-Cardona², Diego Alejandro Medina-Morales¹

¹Internal Medicine Research Group, Technological University of Pereira, Pereira, Colombia

²Department of Internal Medicine, Surcolombiana University, Neiva, Colombia

Received: December 6, 2018

Accepted: March 21, 2019

Online Published: April 23, 2019

DOI: 10.5430/crim.v6n2p15

URL: <https://doi.org/10.5430/crim.v6n2p15>

ABSTRACT

Introduction: Leprosy is a chronic, multisystemic granulomatous infection caused by *Mycobacterium leprae*. Lucio's phenomenon is an uncommon reaction consisting of a severe chronic necrotizing vasculitis. The purpose of this article is to present two cases of Lucio's phenomenon and a review of the literature on its clinical presentation and management.

Case Presentation: Two middle-aged men presented with ulcers and ecchymosis in lower extremities, with simultaneous peripheral nerve damage and leonine facies. Both were treated according to World Health Organization recommendations, with a favorable clinical response.

Discussion: The clinical characteristics presented in this article make part of the classical description. A proper history and physical examination allowed for a correct diagnostic approach and prompt confirmation of diagnosis, despite the unspecific nature of these signs and symptoms.

Conclusions: Leprosy and Lucio's phenomenon are infrequent conditions that are difficult to diagnose. We suspect this condition to be under-registered. Awareness and a high clinical suspicion are necessary in endemic regions.

Key Words: *Mycobacterium leprae*, Lepromatous Leprosy, Lucio's phenomenon, Lepra reaction, Colombia

1. INTRODUCTION

Leprosy is a chronic multisystemic granulomatous infection caused by *Mycobacterium leprae*, a rod-shaped, acid-fast, obligate intracellular bacterium discovered by Gerhard Armauer Hansen in 1873.^[1,2] Infection occurs mainly through close contact with those who are infected. Leprosy may also be transmitted to humans by armadillos.^[3] In most cases the infection may be asymptomatic. When overt disease is present, it mainly affects the skin and peripheral nerves and may lead to permanent sequelae if left untreated.^[3] Clinical manifestations depend on the immune response to infec-

tion, ranging in a spectrum of Tuberculoid (TT), Borderline Tuberculoid (BT), Mid-borderline (BB), Borderline Lepromatous (BL) and Lepromatous (LL) Leprosy according to the Ridley-Jopling classification scheme. In 1998 the World Health Organization (WHO) proposed a more practical classification: paucibacillary (≤ 5 lesions) and multibacillary (≥ 6 lesions).^[1]

Up to 30% of people with Leprosy may develop leprosy reactions, manifesting as acute flares of disease activity overlapping the clinical picture due to an imbalanced host immune response in which neurologic, dermal, ocular and even

*Correspondence: Gustavo Alexis Lemus-Barrios; Email: cardiogus@gmail.com; Address: Internal Medicine Research Group, Technological University of Pereira, Pereira, Colombia.

visceral (liver, spleen) compromise has been reported, with potential necessity for aggressive immunosuppressive therapy as well as generating disability.^[4] There are 3 known types of Leprosy reactions:^[5] Type I reactions occur as a result of increased cell-mediated immune response among patients with borderline leprosy (BT, BB, and BL); Type II reactions result from immune complex deposition and is frequent in patients with BL and LL. Type III reactions or Lucio’s phenomenon is an uncommon reaction presenting exclusively in patients with LL and a clinical variety known as the diffuse leprosy of Lucio and Latapí or “Lepra bonita”.

Lucio’s phenomenon was first described by Ladislao de la Pascua (1844) and was originally described under the name of “Greek Elephantiasis”, as a severe necrotizing vasculitic reaction characterized by the appearance of ulcerative lesions that affect the extremities of patients with LL or BL typically 1 to 3 years after disease onset without adequate treatment.^[2,5-9]

In this article we present 2 cases of Lucio’s phenomenon, a complex and uncommon condition which is difficult to diagnose and must be identified promptly in order to prevent the adverse outcomes associated with it.



Figure 1. A, B, C & D. Deep, painful, necrotizing skin ulcers that compromise the mid-distal third of lower extremities

2. CASE PRESENTATIONS

2.1 Case 1

A 49-year-old male presented with a history of 8 years of ulcerative lesions in lower limbs associated with progressive pain, arthralgias, purulent discharge and abnormal gait. On examination ulcerative lesions were found in mid-distal third of both legs (see Figure 1), he was also reported to have generalized hyporeflexia, thenar and hypothenar neural atrophy, painless nodules on forehead, cheekbones and brows, as well as a deformed and hypertrophic auricle with partial loss of skin continuity, madarosis, nasal bridge lowering and thickened alae nasi (see Figure 2).



Figure 2. A & B. Leonine facies: loss of eye brows (madarosis), destruction of the nasal septum and nodular dermal lesions that alter facial configuration. C & D. Thickened and deformed pinna

Table 1. Laboratory studies of case 1

Blood count		
White blood cell count	8,500 cells/mm ³	
Hemoglobin	8.6 g/dl	
Platelets	345,000/mm ³	
Bacilloscopy and Ziehl/Neelsen staining		
Earlobe and nasal secretion specimens	Positive; 2.0 Bacterial Index	

Due to clinical suspicion of Lepromatous Leprosy with superimposed bacterial infection blood tests as well as other laboratory studies were drawn (see Table 1) and a skin biopsy revealed epidermal atrophy, subepithelial collagen bands, thickened anterior tibial nerves and severe dermal infiltrates

comprised mainly of foamy macrophages, lymphocytes and plasma cells. Ziehl-Neelsen stain identified a large amount of acid-fast bacilli compatible with Hansen bacilli (see Figure 3).

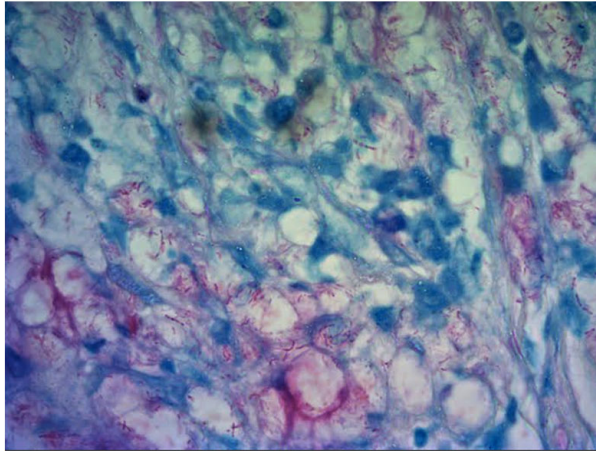


Figure 3. Ziehl-Neelsen stain: Large amount of acid-fast bacilli. The clumps of bacilli are arranged in a parallel fashion resembling cigarettes-in-pack

Table 2. Laboratory studies of case 2

Blood count	
White blood cell count	15,400 cells/mm ³
Neutrophils	13,860 cells/mm ³ , 90%
Hemoglobin	14.1 g/dl
Platelets	336,000/mm ³
Acute phase reactants	
C-reactive protein (CRP)	12.7 mg/dl
Erythrocyte sedimentation rate (ESR)	80 mm/seg
Bacilloscopy and Ziehl/Neelsen staining	
Elbow, earlobe and nasal swab specimens	Negative

2.2 Case 2

40-year-old male with past medical history of Lepromatous Leprosy, presented at the emergency department with 2 weeks of painful ulcers in lower extremities associated with paresthesia, fever, arthralgias, chills and malaise. The patient worked as a farmer and armadillo hunter, was a smoker and had received a complete supervised 6-month course of treatment 5 years prior with rifampin, clofazimine and dapson. On admission patient was found to have madarosis, ecchymosis on both lower extremities as well as an ulcerative lesion with signs of recent hemorrhage on his right thigh (see Figure 4). Patient was also found to have hypoesthesia below the knees. The rest of the physical examination was normal. Laboratory tests (see Table 2) and a skin biopsy

were taken, reporting a thinned epidermis, a recent focal dermal hemorrhage and inflammatory damage to nerve fibers as well as perivascular thickening. Ziehl-Neelsen staining was positive, compatible by *Mycobacterium leprae*.

Written informed consent and authorization to publish and reproduce confidential information was previously obtained from each patient.



Figure 4. A, B & C. Lower extremities with ecchymoses following a net-like pattern B. Bleeding skin sore is also visible on right knee. C. A pale atrophic scar is also present on right thigh

3. DISCUSSION

Leprosy is a disease of major public health interest, it's global incidence has been notably reduced following the introduction of multidrug therapy (MDT) as a treatment approach. Early detection, transmission interruption and prevention of disability are key elements for reducing the burden of disease. In Colombia, 587 cases were reported in 2015, most of which were multibacillary causing higher disability scores.^[10,11]

We presented two cases with a similar clinical course and characteristics. Both patients presented with a chronic clinical picture of ulcerative lesions and peripheral nerve compro-

mise. Case 2 had received treatment for Lepromatous Leprosy 5 years prior to admission.^[8] Both patients developed a necrotizing vasculitis reported as Lucio's phenomenon, one of the clinical and pathological forms of Lepromatous Leprosy, which has been reported to occur in patients with chronic untreated LL 1 to 3 years after disease onset and is endemic to Central America and Mexico.^[4,9]

Clinical manifestations of Lucio's phenomenon consist of a variety of skin lesions from painful ecchymosis or macular purpura to blisters that rupture and develop ulcers.^[2,12,13] These lesions are generally located in lower extremities, and progress in a distal to proximal manner. Upper extremities, torso and face can also be affected.^[5] As described in the literature, lesions presented in our cases were well delimited, of variable size and depth, with the appearance of red sores that leave a pearly white atrophic scar^[2,5] (see Figure 2). In more advanced lesions, diffuse infiltration of the skin confers a thickened ichthyosis-like aspect to it. Systemic manifestations such as fever, chills, malaise, myalgia and arthralgia tend to appear after skin lesions.^[2] Other manifestations include splenomegaly, hepatomegaly and glomerulonephritis, which were not present in the cases we have reported.^[2,14] In terms of neurological compromise, peripheral nerve hypertrophy is a pathological hallmark of Leprosy. Infection is usually centripetal and ascending, starting with sensory nerve fibers and further progressing to compromise motor fibers as well, thus explaining how sensory symptoms precede motor symptoms. Case 1 featured abnormal gait as well as hyporeflexia, similar to the findings of Pandya SS et al.^[15] The most frequent abnormalities found in laboratory tests include anemia, hypocalcemia, hypoalbuminemia, leukocytosis, neutrophilia and an elevated erythrocyte sedimentation rate.^[16,17,23]

Lucio's phenomenon's pathophysiology is unclear. Immunoglobulin G and C3 deposits have been described on blood vessels as well as circulating immune complexes, supporting an autoimmune mechanism as a likely etiology. Direct damage and invasion by the bacillus has also been proposed. The diagnosis of Lucio's phenomenon is based on the clinical picture and medical history.^[1,12,13,17] Microbiologic diagnosis can be established through a positive bacilloscopy in body secretion or skin specimens, nerve biopsies with Ziehl-Neelsen stain or PCR assays.^[1]

Histological findings vary depending on disease stage, but is generally characterized by bacilli infiltrated endothelial cells, vascular wall proliferation and thickening and epidermal necrosis. In our cases, the presence of chronic inflammatory changes in neural tissue, vascular necrosis and positive ZN stains are compatible with the diagnosis. There is no

current consensus on pathological findings in Lucio's phenomenon. Some authors consider it to be a leukocytoclastic vasculitides, but there is stronger evidence towards it being a pseudovasculitides.^[6,18-20]

The main differential diagnosis to consider is erythema nodosum, a type II leprosy reaction that is considered one of the classic LL clinical presentations.^[5] The difference between these conditions can be established based on clinical aspects alone, but it is important to keep in mind that both leprosy reactions can present simultaneously. Other differential diagnoses include systemic vasculitides, arterial or venous ulcers, pyoderma gangrenosum, generalized impetigo, fungal infections, atypical mycobacterial infections and squamous cell lung cancer

Even though species identification was not possible, it is important to highlight that since *Mycobacterium lepromatosis* was discovered in 2008, it has been proposed as the causal agent of Diffuse Lepromatous Leprosy or Lucio's Leprosy, as well as other forms of multibacillary Leprosy. Some authors report fatal combined *Mycobacterium leprae* infections.^[21,22]

Treatment options are controversial because no consensus has been established yet. The use of Thalidomide or Steroids along with MDT has shown successful results.^[2,5,12,23] Treatment for Lepromatous Leprosy recommended by The World Health Organization includes Rifampin, Dapsone and Clofazimine. Initial doses of Thalidomide range from 200 to 600 mg qd depending on severity, if clinical improvement is achieved the dose may reduced to 50 to 100 mg qd for 10 days. Prednisolone may be initiated at 0.5 mg/kg/day and should be tapered down to 5 mg per week according to patient response to therapy.^[12]

We presented two cases of Lucio's phenomenon in patients with Lepromatous Leprosy, presenting with ulcers and ecchymosis in lower extremities, with simultaneous peripheral nerve damage and leonine facies. A proper history and physical examination allowed for a correct diagnostic approach and prompt confirmation of diagnosis. Both patients received treatment according to WHO recommendations as well as systemic steroids, achieving a proper clinical response. These two case reports are of special importance, due to the fact that Leprosy and Lucio's phenomenon are infrequent conditions that are difficult to diagnose. The clinical characteristics presented in this article make part of the classic description, but due to the unspecific nature of these signs and symptoms, it is common for clinicians to be misled into suspecting other entities. We suspect this condition to be under-registered, we therefore consider it a priority that the occurrence of this condition as well its clinical presentation and response to treatment should be communicated to the

scientific and academic community.

ACKNOWLEDGEMENTS

We thank Dr. Maria Helena Bohórquez-Lozano for the help provided with the interpretation of histopathological samples. We would also like to express great appreciation to the staff of pathologists at Patólogos Asociados Tolima SAS for their

kind assistance. This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

CONFLICTS OF INTEREST DISCLOSURE

The authors declare no conflicts of interest.

REFERENCES

- [1] Eichelmann K, González SG, Salas-Alanis J, et al. An update: definition, pathogenesis, classification, diagnosis, and treatment. *Actas Dermo-Sifiliográficas (English Edition)*. 2013; 104(7): 554-63. <https://doi.org/10.1016/j.adengl.2012.03.028>
- [2] Jurado F, Rodríguez O, Novales J, et al. Lucio's leprosy: A clinical and therapeutic challenge. *Clinics in Dermatology*. 2015; 33(1): 66-78. <https://doi.org/10.1016/j.clinidermatol.2014.07.004>
- [3] Rodrigues LC, Lockwood DN. Leprosy now: epidemiology, progress, challenges, and research gaps. *The Lancet Infectious Diseases*. 2011; 11(6): 464-70. [https://doi.org/10.1016/S1473-3099\(11\)70006-8](https://doi.org/10.1016/S1473-3099(11)70006-8)
- [4] White C, Franco-Paredes C. Leprosy in the 21st century. *Clinical Microbiology Reviews*. 2015; 28(1): 80-94. <https://doi.org/10.1128/CMR.00079-13>
- [5] Costa IMC, Kawano LB, Pereira CP, et al. Lucio's phenomenon: a case report and review of the literature. *International Journal of Dermatology*. 2005; 44(7): 566-71. <https://doi.org/10.1111/j.1365-4632.2005.02566.x>
- [6] Vargas-Ocampo F. Diffuse leprosy of Lucio and Latapí: a histologic study. *Lepr Rev*. 2007; 78: 248-60. PMID:18035776.
- [7] Lezcano L, Di Martino B, Galeano G, et al. Reacciones vasculonecroticas en la lepra. Descripción de dos casos de fenómeno de Lucio. *Med Cutan Iber Lat Am*. 2010; 38(4): 161-3.
- [8] Ranugha P, Chandrashekar L, Kumari R, et al. Is it Lucio Phenomenon or Necrotic Erythema Nodosum Leprosum? *Indian J Dermatol*. 2013; 58(2): 160. <https://doi.org/10.4103/0019-5154.108087>
- [9] Magana M, Fernández-Díez J, Magana ML. Lucio's phenomenon is a necrotizing panvasculitis: mostly a medium-sized granulomatous arteritis. *The American Journal of Dermatopathology*. 2008; 30(6): 555-60. <https://doi.org/10.1097/DAD.0b013e318181270a>
- [10] Instituto Nacional de Salud (INS). Protocolo de vigilancia en salud publica lepra. 2016.
- [11] World Health Organization (WHO). Guidelines for the diagnosis, treatment and prevention of leprosy. 2018.
- [12] Berrío J, Jaramillo F. Lepra lepromatosa, fenómeno de Lucio, paniculitis mixta más vasculitis y da-o renal. *Acta Méd Colomb*. 1999; 24(3): 112-5.
- [13] Sehgal VN. Lucio's phenomenon/erythema necroticans. *International Journal of Dermatology*. 2005; 44(7): 602-5. <https://doi.org/10.1111/j.1365-4632.2005.02567.x>
- [14] Ang P, Tay YK, Ng SK, et al. Fatal Lucio's phenomenon in 2 patients with previously undiagnosed leprosy. *Journal of the American Academy of Dermatology*. 2003; 48(6): 958-61. <https://doi.org/10.1067/mjd.2003.326>
- [15] Pandya SS, Bhatki WS. Severe pan-sensory neuropathy in leprosy. *International Journal of Leprosy and Other Mycobacterial Diseases*. 1994; 62: 24-31. PMID:8189085.
- [16] Rivas AM, Gómez LM. Lepra. *Rev Asoc Colomb Dermatol Cir Dermatol*. 2008; 16(3).
- [17] Pursley TV, Jacobson RR. Lucio's phenomenon. *Arch Dermatol*. 1980; 116(2): 201-4. PMID:7356353. <https://doi.org/10.1001/archderm.1980.01640260077020>
- [18] Bielsa MI. Pseudovasculitis: concepto, mecanismos de lesión vascular y diagnóstico diferencial. *Piel*. 2014; 29(6): 350-8. <https://doi.org/10.1016/j.piel.2013.12.008>
- [19] Gower RG, Sams WM, Thorne EG, et al. Leukocytoclastic Vasculitis; Sequential Appearance of Immunoreactants and Cellular Changes in Serial Biopsies. *Journal of Investigative Dermatology*. 1977; 69(5): 477-84. PMID:908847. <https://doi.org/10.1111/1523-1747.ep12511631>
- [20] Misra DP, Parida JR, Chowdhury AC, et al. Lepra Reaction with Lucio Phenomenon Mimicking Cutaneous Vasculitis. *Case Reports in Immunology*. 2014; 2014. <https://doi.org/10.1155/2014/641989>
- [21] Kowalska M, Kowalik A. Mycobacterium leprae: pathogenic agent in leprosy. Discovery of new species Mycobacterium lepromatosis. Perspectives in research and diagnosis of leprosy. *Int Marit Health*. 2012; 63(4): 213-8. PMID:24595978.
- [22] Han XY, Seo YH, Sizer KC, et al. A new Mycobacterium species causing diffuse lepromatous leprosy. *American Journal of Clinical Pathology*. 2008; 130(6): 856-64. <https://doi.org/10.1309/AJCPP72FJZZRRVMM>
- [23] Kamath S, Vaccaro SA, Rea TH, et al. Recognizing and managing the immunologic reactions in leprosy. *Journal of the American Academy of Dermatology*. 2014; 71(4): 795-803. <https://doi.org/10.1016/j.jaad.2014.03.034>