Journal of General - Procedural Dermatology & Venereology Indonesia

Volume 5
Issue 1 *(December 2020 Edition)*

Article 5

12-31-2020

Lucio's phenomenon: A report on six patients in a tertiary referral hospital in Indonesia

Melani Marissa
Department of Dermatology and Venereology Faculty of Medicine Universitas Indonesia/ Dr. Cipto Mangunkusumo National Central General Hospital, Jakarta 10430, Indonesia

Rahadi Rihatmadja
Department of Dermatology and Venereology Faculty of Medicine Universitas Indonesia/ Dr. Cipto Mangunkusumo National Central General Hospital, Jakarta 10430, Indonesia

Denny Surya
Department of Dermatology and Venereology Faculty of Medicine Universitas Indonesia/ Dr. Cipto Mangunkusumo National Central General Hospital, Jakarta 10430, Indonesia

See next page for additional authors

Recommended Citation

Marissa, Melani; Rihatmadja, Rahadi; Surya, Denny; Lim, Henry W.; and Menaldi, Sri Linuwih (2020) "Lucio's phenomenon: A report on six patients in a tertiary referral hospital in Indonesia," *Journal of General - Procedural Dermatology & Venereology Indonesia*: Vol. 5: Iss. 1, Article 5.
DOI: 10.19100/jdvi.v5i1.225
Available at: https://scholarhub.ui.ac.id/jdvi/vol5/iss1/5

Lucio’s phenomenon: A report on six patients in a tertiary referral hospital in Indonesia

Authors

- Melani Marissa
  Department of Dermatology and Venereology Faculty of Medicine Universitas Indonesia/ Dr. Cipto Mangunkusumo National Central General Hospital, Jakarta 10430, Indonesia
- Rahadi Rihatmadja
  Department of Dermatology and Venereology Faculty of Medicine Universitas Indonesia/ Dr. Cipto Mangunkusumo National Central General Hospital, Jakarta 10430, Indonesia
- Denny Surya
  Department of Dermatology and Venereology Faculty of Medicine Universitas Indonesia/ Dr. Cipto Mangunkusumo National Central General Hospital, Jakarta 10430, Indonesia
- Henry W. Lim
  Department of Dermatology, Henry Ford Hospital, Detroit, Michigan 48202, USA
- Sri Linuwih Menaldi
  Department of Dermatology and Venereology Faculty of Medicine Universitas Indonesia/ Dr. Cipto Mangunkusumo National Central General Hospital, Jakarta 10430, Indonesia

Case Series

Lucio's phenomenon: A report on six patients in a tertiary referral hospital in Indonesia

Melani Marissa[1], Rahadi Rihatmadja[1], Danny Surya[1], Henry W Lim[2], Sri Linuwih Menaldi[1]

1. Department of Dermatology and Venereology Faculty of Medicine Universitas Indonesia/ Dr. Cipto Mangunkusumo National Central General Hospital, Jakarta 10430, Indonesia
2. Department of Dermatology, Henry Ford Hospital, Detroit, Michigan 48202, USA

Email: melani_marissa@yahoo.com

Abstract

Background: Lucio's phenomenon (LP) is a rare variant of leprosy reaction, with the clinical manifestation of "necrotizing erythema." LP was observed in patients with lepromatous leprosy who have not received or completed the treatment, and it is especially evident in patients with diffuse lepromatous leprosy (DLL), known as Lucio-Latapi's leprosy. LP occurs due to *M. leprae* invading the blood vessels, causing endothelial damage that leads to thrombosis, ischemia, infarction, and tissue necrosis. The clinical features of the disease are erythematous lesions that can be accompanied by vesicles or bullae, with ulcers forming scar tissues. Histopathological examination can help establish the diagnosis of LP. Until now, there is still controversy about LP management. Multidrug therapy for multibacillary leprosy (MDT-MB) is the preferred line of treatment. Lucio-Latapi's leprosy and LP are commonly found in Mexico and Central America, but rarely reported in Indonesia.
Case Illustration: We report here the clinical description and development of six patients with LP observed in the tertiary referral hospital in Indonesia over a five-year period from 2013 to 2017.
Discussion: All patients were diagnosed using clinical and histopathological examination, and all of them presented with ulceration and vasculitis. They were treated with MDT-MB WHO regimens and systemic corticosteroids. Five patients were alive, and one died due to extensive cutaneous lesions that lead to sepsis.
Conclusion: Early diagnosis and prompt institution of multidrug therapy with systemic corticosteroids may improve the prognosis and outcome of LP.

Keywords: *Indonesia, Lucio-Latapi's phenomenon, leprosy, reaction*

Background

Leprosy reaction is a collection of clinical manifestations in acute and subacute forms, which interrupt the course of the disease that is usually long and slow, with a polymorphic form. Lucio's phenomenon (LP) is a rare variant of leprosy reaction, with the clinical manifestation of "necrotizing erythema." LP was observed in patients with lepromatous leprosy who have not received or completed the treatment. It is especially evident in patients with diffuse lepromatous leprosy (DLL), known as Lucio–Latapi leprosy. LP is often said to be a variant of type 2 leprosy reaction because it is also caused by an immune complex.[1,2]

Lucio–Latapi leprosy and LP are commonly reported in Mexico and Central America but infrequent in Indonesia, though Indonesia is an endemic country. To the authors' knowledge, there are no data on the epidemiology of LP in Indonesia. However, several reports have indicated that the prevalence of LP is increasing in some parts of the world.

LP occurs due to *M. leprae* invading blood vessels, causing endothelial damage that leads to thrombosis, ischemia, infarction, and tissue necrosis. LP usually manifests three to four years after disease onset and is more often found in patients who were not treated or did not receive adequate treatment.[3,4] In patients with LP, secondary infections, which eventually cause sepsis and death, often occur.[5] The lesion initially begins with erythema patches on the legs and spreads to the lower limbs, thighs, hands, torso, and then face.[1,6] After 24 to 48 h, infiltration will start to appear. On the third or fourth day, the lesion becomes darker with purpuric features and central necrosis and appears as a small blister. Eventually, a dark reddish eschar will form and come off after a few days, leaving a white atrophic scar. The clinical diagnosis of LP must be confirmed by histopathology examination. Skin biopsy revealed five main characteristics, namely, acid fast bacilli (AFB) colonization of endothelial cells, endothelial proliferation and thickening of blood vessel walls, angiogenesis, vascular ectasia, and thrombosis.[1]

Until today, there are still many controversies regarding the management of LP.[1] A case study by Peixoto et al.[7] has shown that the management of LP using multidrug therapy (MDT) alone can provide good results. Corticosteroid use may pose a risk to severe infection.[7] In contrast, a case study by Misra et al.[8] has shown that management of LP with MDT, prednisolone, and thalidomide gave good results. We report here a clinical description and the development of six patients with LP observed in a tertiary referral hospital in Indonesia over a five-year period. A representative case is described in this paper in detail and the main clinical and laboratory findings of all patients are summarized in Tables 1 and 2.

Case 1

A 33-year-old female with lepromatous leprosy was referred with lesions on both hands and feet that occured 10 years ago and have not healed. Dermatologic examination of both arms and legs showed multiple nummular ulcers with erythematous infiltrative edge. Erosion and excoriation with black crust were visible. The initial diagnosis was suspected bacterial ulcer in borderline lepromatous leprosy. Gram-staining showed a large number of leukocytes and gram-positive bacilli and a moderate number of gram-positive cocci. Bacterial index (BI) was 2+; morphology index (MI) was 0%. The patient was given MDT-MB WHO regimen, methylprednisolone, and topical antibiotic fusidic acid cream and had normal saline dressings. She showed marked improvement, and no new ulcers were found. Later, she was diagnosed histopathologically with LP.

Case 2

A 25-year-old male presented with cyanosis on the tips of his fingers and toes that worsened three days before admission. Moreover, the patient had a numb hypopigmented patch on his right arm 10 years ago. On physical examination, madarosis and infiltrates on both ears and nose were observed. Multiple plaque-sized purpuras were present on both arms and legs, with ulceration and necrosis. The patient was diagnosed with lepromatous leprosy and suspected LP. BI was 2+ and MI was 0%. Skin biopsy was performed, and histopathology result was in accordance with granulomatous inflammation that can be found in lepromatous leprosy with LP. The patient was then given MDT-MB WHO regimen, ciprofloxacin, methylprednisolone, and mupirocin ointment and had normal saline dressings on the ulceration. He showed improvement.

Case 3

An elderly 64-year-old male presented with lesions on both legs two weeks before hospital admission. The patient complained of redness on both legs after taking piroxicam, demacolin (paracetamol, pseudoephedrine HCl, chlorpheniramine maleat, and caffeine), and amoxicillin 15 days before. There were also patches on both ears that turned into open wounds, blackened, and felt hot. Moreover, the patient felt numbness on his soles. On physical examination, diffuse infiltrates on both ears, madarosis and leonine facies were observed. There were also multiple shallow ulcers with irregular edges and black necrotic tissue on the base on both knees and lower legs. BI was 1+ and MI was 0.16%. Skin biopsy showed granulomatous inflammation that can be found in lepromatous leprosy with LP. The patient was given MDT-MB WHO regimen, methylprednisolone, levofloxacin, and salicylic acid 1% in petrolatum for ulcers and had normal saline dressings. The patient showed improvement at the follow-up examination.

Case 4

A 36-year-old male presented with painful blisters on both legs five days before admission. The patient had red patches on the lower extremities and constant pain especially when standing and

walking. On both lower legs, edema, infiltrate, diffuse erythema, vesicles, and flaccid bullae filled with red-yellow fluid were present. Erosion and shallow ulcers, with pus and necrotic tissue at the base, as well as black and yellowish crusts, were observed (Figure 1). On the facial region and both ears, infiltrates were palpable. The patient was diagnosed with lepromatous leprosy of a severe type II reaction (erythema nodosum leprosum) and secondary infection with LP as differential diagnosis. BI was 2+ and MI was 0.33%. Skin biopsy showed histology in accordance with borderline lepromatous leprosy with LP. The patient was given MDT-MB WHO regimen, methylprednisolone, ampicillin sulbactam, fusidic acid cream, and paracetamol 3x500 mg and had salicylic acid 1/1000 dressings for crusted lesion. The patient showed improvement at the follow-up examination.

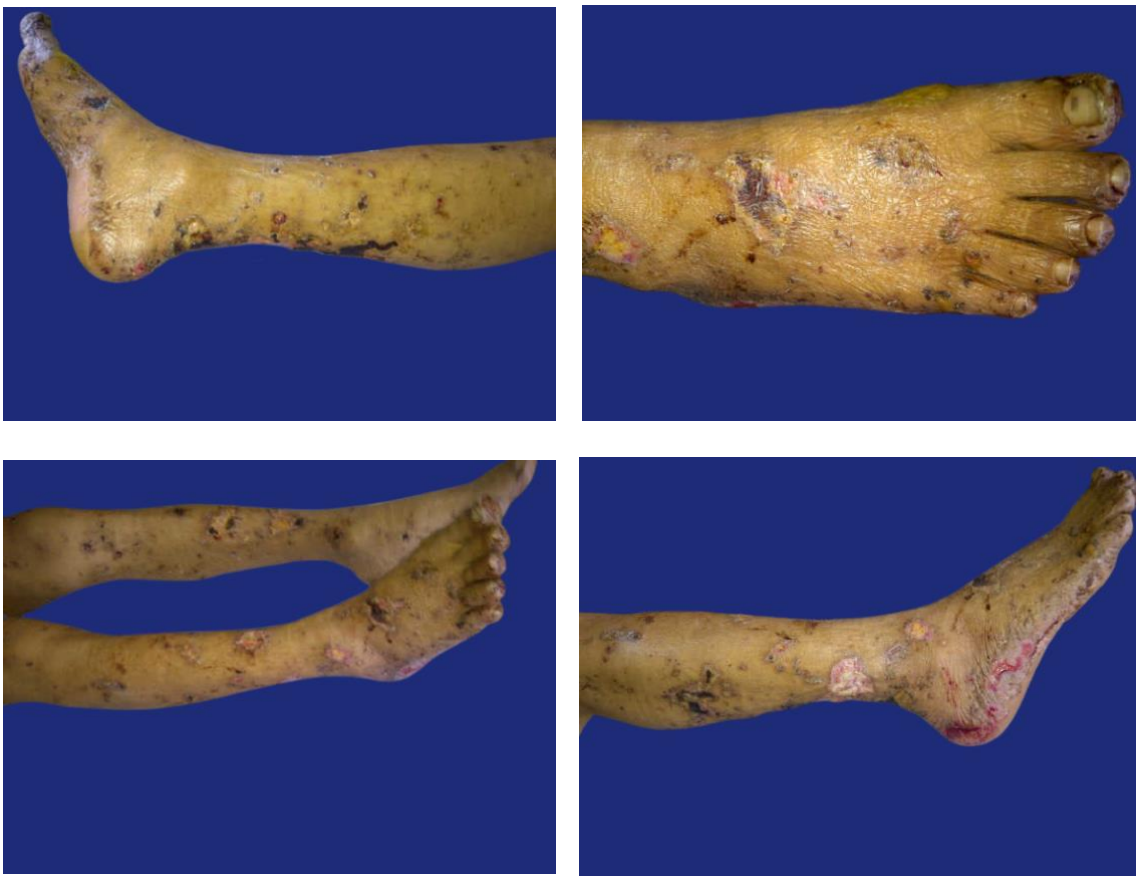

Figure 1. Clinical presentation of lower legs in patients with LP (patient number 4)

Case 5

A 30-year-old male presented with painful nodules on both arms and legs one week before admission. The patient was previously diagnosed with leprosy and took MDT-MB regimen for one year. The patient had been released from treatment. On both arms and legs, multiple discrete erythematous nodules and ulcer covered with black crust were present. BI was 2+ and MI was 0.14%. The histopathology showed findings that did not contradict with LP. The patient was diagnosed with relapsing borderline lepromatous leprosy with LP. He received leprosy retreatment with MDT-MB WHO regimen, prednisone, clindamycin, and natrium fusidate ointment and had normal saline dressings. He showed improvement.

Case 6

A 52-year-old male came to our emergency department (ED) with painful progressive purpuric lesions on his lower limbs one week before admission. The patient was initially assessed and treated as a case of acute limb ischemia. The pain was relieved, but purpuric lesions were still progressing and blisters were appearing. He was referred to the dermatology department for a possibility of allergic reactions due to the

administration of drugs in the ED. The skin examination revealed sharply marginated purpuric patches on both lower limbs. Both legs were swollen and shiny. Blisters and ulcers were present on the left leg (Figure 2). The patient's face was diffusely infiltrated, and he lost his eyelashes and had an anesthetic hypopigmented lesion on the abdomen. No nerve enlargement was found. He was never diagnosed with leprosy. His BI was +1 and MI was 0%. Histological findings showed obliterated and obstructed blood vessels mainly in the superficial and middermis. Fite-Faraco staining showed *M. leprae* in blood vessel walls (Figure 3). The patient was given MDT-MB WHO regimen, methylprednisolone, clindamycin, bullae aspiration, and salicylic acid 1% in petrolatum and had normal saline dressings on knee erosion. The patient succumbed to the extensive cutaneous infarcts and died due to consequent sepsis.

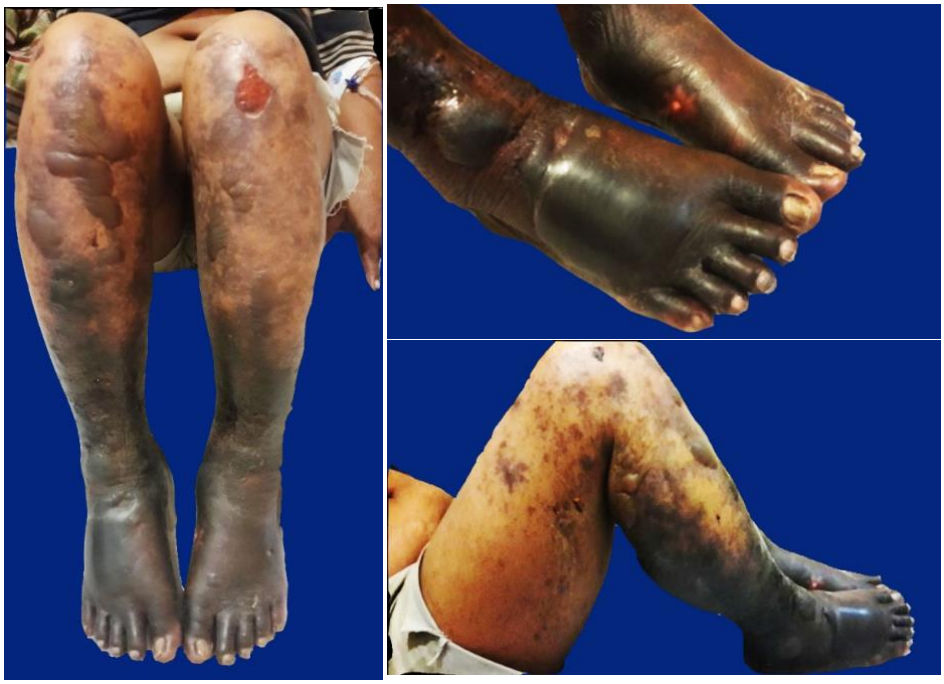

Figure 2. Clinical presentation of both lower legs and feet in a patient with LP (patient number 6)

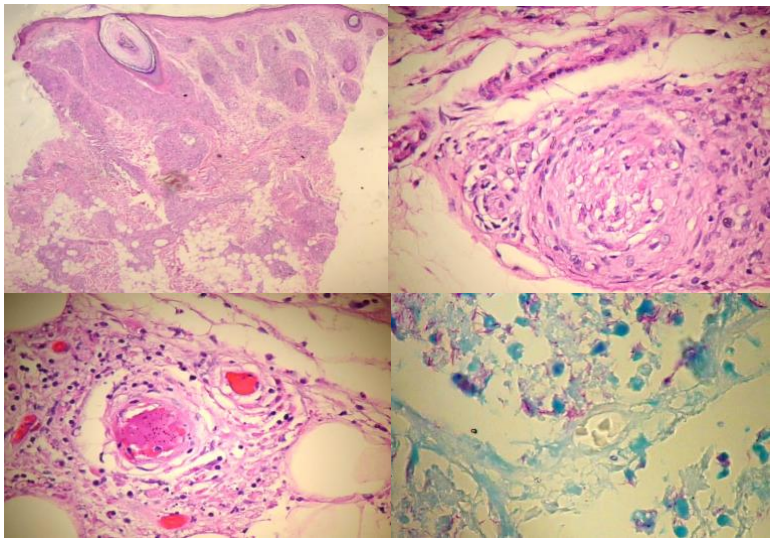

Figure 3. Histopathology result of a patient with LP (patient number 6)

Table 1. Patient demographics and clinical characteristics

Case	Sex	Age (years)	Type of leprosy	Clinical findings of leprosy	Clinical findings of LP	Treatment received
1	F[b]	33	LL	Both arms and legs: multiple ulcers with rising edge, hollow wall, subcutaneous tissue on the base. Some with erosions and excoriations covered with black crusts	Multiple nummular ulcers, some with erythematous infiltrative edge, multiple hyperpigmented plaques with scar and black crust on both arms and legs and back	MDT-MB regimen Methylprednisolone 32 mg/day NaCl 0,9% dressing Fusidic acid cream
2	M[a]	25	BL	Madarosis, infiltrate on ears and nose, multiple purpuras and plaques on both arms and legs, and multiple thin erythematous plaques on face with hypesthesia	Multiple purpuras with ulceration, some with necrosis, on both lower arms, base of manus and digiti manus, lower leg, dorsal pedis, and bilateral digiti pedis region	MDT-MB regimen Methylprednisolone 2x16 mg Ciprofloxacin 2x500 mg NaCl 0,9% dressing Mupirocin ointment
3	M[a]	64	LL	Madarosis, leonina facies, diffuse infltrates on face and both ears, multiple black crusts on both earlobes and arms, and multiple painless ulcers with an irregular shape filled with necrotic tissue and pus on both lower legs	Multiple shallow ulcers with black necrotic tissue on the base on both lower legs and knee	MDT-MB regimen Methylprednisolone 1x31,25 mg IV Levofloxacin 1x500 mg IV Salicylic acid 1% in vaseline album
4	M[a]	36	LL	Infiltrates on facial region and both ears, multiple hemorrhagic bullae and vesicles, pustules, and black crusts on both lower legs and soles, with palpable and nonpalpable purpuras	Infiltrates, multiple vesicles, loose-walled bullae filled with red-yellow fluid, erosions, and shallow ulcers with pus and necrotic tissue at the base on both lower legs and feet	MDT-MB regimen Methylprednisolone 3x16 mg Ampicillin sulbactam 4x1,5 gr Salicylic acid 1/1000 compress NaCl 0,9% dressing Fusidic acid cream
5	M[a]	30	BL	Multiple erythematous nodules and ulcers with pus on the base on both legs and arms	Multiple erythematous nodules and ulcers covered with black crust on both arms and legs	MDT-MB regimen Prednisone 40 mg/day Clindamycin 2x30 mg NaCl 0.9% compress Natrium fusidate ointment

6	M[a]	52	BL	Multiple thin hyperpigmented macules and plaques on both legs, feet, and arms, with hollow-walled bullae on top of several lesions	Multiple purpuras, hollow bullae filled with brown-yellow fluid, and erosions on both arms, legs, and feet	MDT-MB regimen Methylprednisolone 96 mg/day Clindamycin 4x300 mg Salicylic acid 1% in vaseline album NaCl 0,9% dressing

[a]M = male. [b]F = female.

Table 2. Laboratory and histopathologic results of patients with LP

Case	Bacterial index (BI)	Leukocytes x $10^3/mm^3$ N[d] 5–10	Histopathologic results
1	2.00	11.3	Granuloma macrophages Epidermal cleft and necrosis Leukocytoclastic vasculitis Thrombosis
2	2.00	25.1	Granuloma macrophages with positive solid AFB Leukocytoclastic vasculitis No thrombosis
3	1.00	10.1	Ulcer Granuloma macrophages (foamy granuloma/Virchow cells) through subcutis Lower dermis-subcutaneous necrosis Leukocytoclastic vasculitis Erythrocyte extravasation Blood vessel obliteration Thrombosis
4	2.00	15.2	Granuloma macrophages Leukocytoclastic vasculitis Cleft and blood vessel occlusion Epidermal necrosis Nerve damage Thrombosis
5	2.00	ND[c]	Granuloma macrophages Leukocytoclastic vasculitis
6	1.00	12.5	Granuloma macrophages with positive AFB Obliterated and obstructed blood vessels mainly in the superficial and middermis Leukocytoclastic vasculitis Fite-Faraco staining showing *M. leprae* in the blood vessel wall

[a]M = male. [b]F = female. [c]ND = not done. [d]N = normal.

Discussion

LP is a severe cutaneous necrosis reaction presenting as bullae and ulcers that usually occurs in patients with BL and LL. A rare condition, LP almost exclusively affects patients with leprosy from Mexico and Central America. LP generally occurs three to four years in the course of leprosy disease and is more commonly found in untreated or inadequately treated patients. This reaction is characterized by infiltrated erythematous macules that evolve with a central necrosis and turn into ulcerations. The most affected areas are the extremities. Dark flaccid blisters may also be observed. The pathophysiology of LP is still unknown, but it is believed to be a thrombo-occlusive process.[9]

Based on the clinical and histopathological data documented from the present case series, three patients were classified as having lepromatous leprosy, and the other three patients were classified as having borderline lepromatous leprosy. All cases were diagnosed histopathologically as having vasculitis of LP. We emphasized the rarity of LP, its progression if undiagnosed or left untreated, probable difficulty in the diagnosis, and treatment modality with corticosteroids.

All patients in this case series had ulcerations on the extremities. Besides the ulcerations, another form of lesions was found and it included vesicles, bullae, necrotic macules, and purpuras. This was in accordance with Ranugha et al.'s results[9], who found blisters and ulcers in patients with leprosy and LP. Nunzie et al.[10] also reported polymorphous necrotic and hemorrhagic macules in patients with leprosy and LP. LP itself was considered a necrotizing panvasculitis, so all of the aforementioned skin manifestations can be found in patients with LP. Lesions typically appeared on the lower extremities, before spreading to the trunk and upper extremities.[10]

There has been no consensus regarding the histopathological abnormalities in LP. However, histopathologically, LP can be seen as granulomatous and necrotizing panvasculitis.[10] As such, skin biopsy will show findings in accordance with this condition. All patients in this case series who underwent a skin biopsy were diagnosed with LP. We observed granulomatous inflammation, with a predominance of necrosis of the epidermis and dermis, vascular changes including thrombosis of small vessels, vessels with thickened walls, edema, and partial or total occlusion of the lumen. An inflammatory infiltrate consisting of mononuclear and polymorphonuclear leukocytes surrounding the vessels was also observed. Histopathology result will sometimes show signs of vasculitis involving medium and small-sized vessels.[11] We emphasized the presence of intact *M. leprae* on the vessel walls possibly triggering the vasculitic process in most cases.

Rea et al.[11] showed that, in LP, macrophages are the target cell of *M. leprae* involving also blood vessels. LP isma necrotizing panvasculitis that occurs due to an excess of antigen, not only as entire bacilli or its fragments, but as globi, which can be easily seen inside macrophages that infiltrate the vessel walls. The vessels are mostly muscular or medium-sized arteries (which explains the cutaneous infarcts), and they include arterioles, venules, and medium-sized veins. Smaller and more superficial vessels exhibit a leukocytoclastic vasculitis with immune complex deposition.[11] In all six patients, we observed granuloma macrophages (two of them had positive AFB inside the macrophage) and leukocytoclastic vasculitis. We also found thrombosis in four of the six patients.

Early and accurate diagnosis of LP in patients with leprosy was crucial in terms of initiating prompt treatment. The overall response to treatment in patients with LP was good and may happen rapidly, following the initiation of the usual multidrug regimen.[12] There is no consensus regarding the specific treatment of LP, which is mostly empirical, based on case reports of successful treatment. MDT-MB WHO regimen was reported effective in treating LP. The supporting theory behind the triggering factor of LP is the massive replication of *M. leprae*, which must be prevented and arrested to stop this unique reaction. MDT-MB WHO regimen is the treatment of choice for LP. When MDT for leprosy is introduced at the beginning of the LP outbreak, the prognosis is usually good. However, when patients present with extensive skin involvement, secondary infection, and anemia, as in the 6th case reported here, the prognosis is poor even with early treatment. The role of corticosteroids is controversial. We included systemic corticosteroids in all six cases described here. The dosage of steroids differs according to each case as it depends on the patients' body weight and the clinical judgment of each patients' conditions, including whether they have an infection or not. All patients were also given systemic antibiotics for the treatment of secondary

infections; the antibiotics were selected according to a microbiological culture and susceptibility testing. We administered an anti-inflammatory dose of corticosteroids (0.5–1 mg per kg body weight) in all aforementioned six cases. The prognosis varies and may result in death by sepsis or coagulation disorders. Severe prolonged morbidity and poor response to therapy were reported by Moschela et al.[13] and Donner et al.[14] LP is usually fatal and generally occurs as a result of secondary infections and sepsis.[15] One of our patients died for that reason.

Conclusion

Understanding the clinical manifestation and histopathological characteristics of LP is very important for clinicians to avoid misdiagnosis or underdiagnosis. Thus, clinicians must always be aware of LP, especially when encountering patients with multibacillary leprosy.
Cases of patients with LP manifestations diagnosed by clinical and histopathological examinations, which had an excellent response to MDT-MB WHO regimen and systemic corticosteroids, were discussed in this paper.

References

1. Jurado F, Rodriguez O, Novales J, Navarette G, Rodriguez M. Lucio's leprosy: A clinical and therapeutic challenge. Clin Dermatol. 2015;33:66-78.
2. Kamath S, Vaccaro SA, Rea TH, Ochoa MT. Recognizing and managing the immunologic reactions in leprosy. J Am Acad Dermatol. 2014;71:795-803.
3. Fogagnolo L, Souza EM, Cintra ML, Velho PENF. Vasculonecrotic reactions in leprosy. Braz J Infect Dis. 2007;11:378-82.
4. Kumari R, Thappa DM, Basu D. A fatal case of Lucio phenomenon from India. Dermatol Online J. 2008;14:10.
5. Curi PF, Villaroel JS, Migliore N, et al. Lucio's phenomenon: Report of five cases. Clin Rheumatol. 2016;35:1397-401.
6. Monteiro R, Abreu MAMM, Tiezzi MG, Roncada EVM, Oliveira CCM, Ortigosa, LCM. Lucio phenomenon: Another case reported in Brazil. An Bras Dermatol. 2012;87:296-300.
7. Peixoto AB, Portela PS, Leal FRPC, Brotas AM, Rodrigues NCS. Lucio's phenomenon. Case study of an exceptional response to treatment exclusively with multibacillary multidrug therapy. An Bras Dermatol. 2013;88:S93-6.
8. Misra DP, Parida JR, Chowdhury AC, et al. Lepra reaction with Lucio phenomenon mimicking cutaneous vasculitis. Case Rep Immunol. 2014;2014:1-4.
9. Ranugha P, Chandrashekar L, Kumari R, Thappa DM, Badhe B. Is it lucio phenomenon or necrotic erythema nodosum leprosum? Indian J Dermatol. 2013;58:160.
10. Nunzie E, Ortega Cabrera LV, Macanchi Moncayo FM, et al. Lucio leprosy with Lucio's phenomenon, digital gangrene and anticardiolipin antibodies. Lepr Rev2014;85:194-200.
11. Rea TH, Levan NE. Lucio's phenomenon and diffuse nonnodular lepromatous leprosy. Arch Dermatol. 1978;114:1023-28.
12. Herath S, Navinan MR, Liyanage I, et al. Lucio's phenomenon, an uncommon occurrence among leprosy patients in Sri Lanka. BMC Res Notes. 2015;8:672.
13. Moschella SL. The lepra reaction with necrotizing skin lesions: A report of six cases. Arch Dermatol. 1967;95:565-75.
14. Donner R, Shively J. The "Lucio phenomenon" in diffuse leprosy. Ann Intern Med. 1967;67:831-6.
15. Gelber R. Hansen's disease. In: Mandell G, Bennett J, Dolin R, editors. Principles and practice of infectous diseases. 4th ed. New York: Churchill-Livingston; 1995.p.2243–50.