CASE REPORT

Lucio Leprosy with Lucio’s phenomenon, digital gangrene and anticardiolipin antibodies

ENRICO NUNZIE*, ORTEGA CABRERA LV*, MACANCHI MONCAYO FM**, ORTEGA ESPINOSA PF***, CLAPASSON A**** & MASSONE C*****

*Institute of Dermatology, Hospital UTPL - Universidad Técnica Particular de Loja, Loja, Ecuador
**Hospital Isidro Ayora, Loja, Ecuador
***Hospital Manuel Ygnacio Monteros IESS, Loja, Ecuador
****Unit of Social Dermatology, National Reference Center for Hansen’s Disease, Azienda Ospedaliera Universitaria “San Martino”, Genoa, Italy
*****Department of Dermatology, Medical University of Graz, Graz, Austria

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Summary Lucio’s phenomenon (LPh) is considered a necrotizing panvasculitis and a variant of leprosy Type 2 reaction, clinically characterised by necrotic-haemorrhagic lesions on the extremities and trunk. LPh is observed in diffuse lepromatous leprosy (DLL or Lucio–Latapi leprosy). This is a distinct form of lepromatous leprosy (LL) reported mainly in Mexico. Anti-phospholipid antibody syndrome (APS) has been rarely described in LPh. We report a case of Lucio–Latapi leprosy with LPh observed in a patient from the province of El Oro in Ecuador, who presented clinical manifestations of long standing DLL (non-nodular infiltration of the skin, collapse of the nasal pyramid, maderosis, atrophy of the earlobes), of LPh (necrotic-haemorrhagic macules with irregular shapes) and of APS (necrosis of the right big and second toe). Histopathology showed perineural and periadnexal foamy macrophages with numerous bacilli (diagnostic of LL) in the subcutis, a mild lobular panniculitis with a large subcutaneous vessel infiltrated by macrophages in the wall (typical of LPh) and vessels of the superficial and mid dermis occluded by thrombi but without signs of vasculitis (typical of occlusive vasculopathy as in APS).
Our observations suggest that some cases of LPh may be associated with APS. Anti-cardiolipin antibodies (aCL) and lupus anticoagulant (LA) should be tested in patients with LPh because this may have therapeutic implications.

Introduction

Lucio’s phenomenon (LPh) is considered a necrotizing panvasculitis and a variant of leprosy Type 2 reaction, clinically characterised by necrotic-haemorrhagic lesions on the extremities and trunk. LPh is observed in diffuse lepromatous leprosy (DLL or Lucio–Latapí leprosy). This is a distinct form of lepromatous leprosy (LL) reported mainly in Mexico, but also in other areas of Central and South America and exceptionally it has been diagnosed in other continents.1–5 Anti-phospholipid antibody syndrome (APS) has been rarely described in LPh.6

We report a case of Lucio–Latapí leprosy with LPh observed in a patient from the province of El Oro in Ecuador, who presented also anti-cardiolipin antibodies (aCL) and skin necrosis typical of APS.

Case report

A 76 year old women originally from El Oro (Ecuador) presented with haemorrhagic lesions on her trunk and extremities, which had appeared one week previously. She complained of arthralgia, myalgia, fever and asthenia.

Physical examination revealed polymorphous necrotic-haemorrhagic macules with irregular shapes, angulated or ‘stellar’ on the lower extremities, buttocks and trunk (Figure 1), the collapse of the nasal pyramid, madarosis, atrophy of both auricular lobes, diffuse infiltration of the skin of the trunk, atrophy of both thenar and hypothenar eminences of both hands, with flexion of the proximal interphalangeal joints and claw fingers of both hands.

On neurological examination, the superficial peripheral nerves did not appear enlarged or painful on palpation; upper and lower extremities showed glove-and-stocking anesthesia.

Interestingly, she presented a blue discoloration of the right big and second toe with distal gangrene and onychodistrophy (Figure 2a); the foot was not cold or painful and all the peripheral arteries were well felt; there was no radio-femoral delay.

She was not taking any drugs and was not a smoker; she did not report symptoms of claudication, nor did she suffer from arterial hypertension or diabetes. One week later all toes on the right foot presented with dry gangrene (Figure 2b).

Two skin biopsies taken from purpuric lesions on her back and right lower leg were performed and both showed similar features. The epidermis was necrotic (Figure 3a); in the superficial and mid-dermis oedema and haemorrhages were seen, the vessels were occluded by thrombi and surrounded by a very mild lymphocytic infiltrate without signs of vasculitis (Fig. 3b).

A mainly perineural and periadnexal infiltrate with foamy macrophages was seen (Figure 3c).

In the subcutis a large subcutaneous vessel showed a macrophagic infiltrate in the wall (Figure 3d).
The Fite-Faraco stain disclosed numerous solid bacilli, both singly and in ‘globi’ in the macrophages (bacteriological index: 6+), but also in the vessel walls and inside the vessels. The Polymerase Chain Reaction (PCR) identified *Mycobacterium leprae*.

The clinical diagnosis of DLL and LPh with Grade 2 disability were confirmed. Leprosy had not previously diagnosed in the patient. According to WHO guidelines, skin smear with bacteriological index was not performed.

Routine laboratory investigations including red and white blood cell count, liver and renal function, blood sugar, serology for HIV and hepatitis B and C, prothrombin time and lipid profile were within normal limits. Anti-cardiolipin antibodies (aCL, measured by a β2-GPI-dependent enzyme-linked immuno-sorbent assay [ELISA]) were positive for IgM (196,8 U/GL, n.v. up to 14) and negative for IgG and IgA. Antinuclear antibodies (ANA), anti-neutrophil cytoplasmic antibody (ANCA) and lupus anticoagulant (LA) were negative. The patient denied abortions and previous thrombosis. DOPPLER of the lower limb arteries did not reveal any abnormality.

**Figure 1.** Polymorphous necrotic-haemorrhagic macules with irregular shapes, angulated or ‘stellar’, on lower extremities, buttocks and trunk.
According to WHO guidelines, multidrug therapy (MDT) for multibacillary (MB) leprosy with rifampicin 600mg/month, dapsone 100mg/day, clofazimine 50mg/day and 300mg/month was given for 12 months; the patient was started on prednisolone 60mg/day for 2 weeks with progressive tapering over 6 weeks. Acetylsalicylic acid 100mg/day was also started.

At a 2-month follow-up the patient was still under MDT without side effects. The hemorrhagic macules and general symptoms improved and prednisolone was stopped. The right big toe spontaneously amputated, and the other toes were still necrotic. The patient and the family declined further investigations or follow-up visits at our Institute (the patient lives 140km from Loja). She is therefore being followed up by the peripheral rural medical service. No other family cases of leprosy have been reported.

Discussion

Lucio leprosy is a diffuse type of DLL that corresponds to the polar form of lepromatous leprosy (LLp) according to Ridley and Jopling. Lucio leprosy is characterised by diffuse non-nodular infiltration of the skin (similar to myxoedema), and the face looks healthy (lepra bonita); the earlobes are thick, hands are swollen and legs are oedematous. In time, the skin becomes flaccid and atrophic. Clinical changes may be so subtle that often Lucio leprosy is diagnosed only because of the sudden development of LPh (as it was in our patient). In 2008, Han et al. identified a new strain of mycobacterium (Mycobacterium lepromatosis) in two Mexican patients who presented with DLL, purpuric and ulcerative skin lesions due probably to LPh, and who subsequently died. Subsequently, M. lepromatosis was identified in 55/120 Mexican patients with various clinical forms of leprosy; 14 had also a co-infection with M. leprae. According to Han et al., M. lepromatosis is another cause of leprosy and is probably more prevalent than M. leprae in Mexico. However, M. lepromatosis and DLL have also been identified outside Mexico. In our patient the causative organism was M. leprae.
LPh is characterised by the occurrence of painful, red or purpuric macules, of irregular shape, angulated or 'stellar', in a patient with DLL (Lucio–Latapı´ leprosy). Lesions appear on the lower extremities and then spread to the trunk and upper extremities. Patients may present with fever, myalgia or arthralgia. Histopathologically, LPh is a distinctive type of granulomatous and necrotizing panvasculitis; the involved vessels are mostly medium-sized arteries, located deeply in the dermis, and within the hypodermis, whose walls are widely infiltrated by macrophages and many bacilli. In smaller vessels in the dermis, such as venules, a leukocytoclastic vasculitis may be seen. Moreover, histopathological changes typical of APS with endothelial cell proliferation, thrombosis, a mild mononuclear cell infiltrate and ischemic necrosis have been reported in LPh.

APS is characterised by typical clinical manifestations [livedo reticularis, livedo racemosa, livedo vasculitis, thromboembolic phenomena with necrosis and ulceration of the extremities, digital gangrene, purpura, and purpura fulminans] and persistent aPL positivity (at least 12 weeks apart). The positivity for aPL can be defined as at least one positive test among the lupus anticoagulant (LA), aCL and anti-β2-glycoprotein-I antibodies. Histopathology of a skin biopsy shows dermal haemorrhages with thrombi in arteries and veins without vasculitis.

aPLs against cardiolipin (aCL), beta(2)-glycoprotein I (anti-beta(2)GPI), and prothrombin (anti-PT) have been found to be increased in leprosy, (mainly in MB patients) in different studies and without differences between leprosy patients not under therapy,
taking MDT or those who have completed MDT. The predominant isotype has been frequently found to be IgM. The frequency of aCL in LL leprosy patients has been described as between 70% and 89%,18–23 and aCL in MB leprosy patients is mainly of the GPI-dependent type.24,25 However, leprosy do not usually present with APS.18–21

Interestingly, our patient presented features of both Lucio leprosy with LPh and APS. In fact, she presented clinical manifestations of long standing DLL (non-nodular infiltration of the skin, collapse of the nasal pyramid, madarosis, atrophy of the earlobes), of LPh (necrotic-haemorrhagic macules with irregular shapes) and of APS (necrosis of the right big and second toes). Histopathology showed perineural and periadnexal foamy macrophages with numerous bacilli (diagnostic of LL), in the subcutis, a mild lobular panniculitis with a large subcutaneous vessel infiltrated by macrophages in the wall (typical of LPh) and vessels of the superficial and mid dermis occluded by thrombi but without signs of vasculitis (typical of occlusive vasculopathy as in APS).

Our patient satisfied the clinical criteria for APS (gangrene) and had one positive serological result for aCL.19 Unfortunately, it was not possible to confirm positivity of aCL 3 months later, because the patient and the family declined further investigations and follow-up at our Department. Anyhow, our patient was highly likely to have had APS; diabetes, peripheral neuropathy, arterial insufficiency, cholesterol emboli could be excluded. Moreover, digital skin necrosis is not a typical manifestation of LPh.1–4

Gangrene of the extremities in leprosy has been reported to be caused also by intimal thickening and medial infiltration, embolization and resultant grafting of Virchow cells, and arterial entrapment due to nerve trunk hypertrophy in the osteoligamentous canal.25,26 Different angiographic alterations have been reported in 75-94% of leprosy patients.25,27 Only rare cases of thrombo-embolism occurring in leprosy patients have been described, and the pathophysiology of this condition remains unclear. Akerar and Bichile reported a patient with borderline tuberculoid leprosy, positive aCL (IgM) confirmed two times and gangrene of bilateral toes.25

Interestingly, APS and aCL have never been investigated in Lucio leprosy nor in LPh but there are observations that may lead one to think that in some cases an association is possible. In 2006, Azulay-Abulafia et al. reported a 53 year old Brazilian man presenting features of LPh and APS with positive aCL and LA.6 Ang et al. reported two patients from Singapore with DLL and fatal LPh,5 M. lepromatosis was subsequently identified.14 Clinically, both patients manifested features of purpura fulminans, as occurs in catastrophic APS, and presented at autopsy with signs of disseminated intravascular coagulation, but aCL or LA were not tested.5,14

Our observation confirms that of Azulay-Abulafia suggesting that some cases of LPh may be associated with APS. aCL and LA should be tested in patients with LPh because this may have therapeutic implications. Of course, this finding needs to be verified on a larger series of cases.

Authors contribution

Nunzi E (Corresponding author & guarantor): looked after the patient, wrote and edit the manuscript.
Ortega Cabrera LV: looked after the patient and provided the images.
Macanchi Moncayo FM: looked after the patient and provided the literature.
Ortega Espinosa PF: looked after the patient and provided the literature.
Clapasson A: performed the PCR studies.
Massone C: wrote the paper, reported histology, prepared figures.

References