An interesting case of Lucio phenomenon triggered by activation of hepatitis C infection

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ABSTRACT

Lucio phenomenon (LP) or erythema necroticans is a rare type of reaction pattern found in untreated patients with diffuse non-nodular leprosy. It is important to distinguish this from vasculonecrotic erythema nodosum because thalidomide with high-dose steroids is the mainstay of treatment for the latter, whereas LP shows no response to thalidomide. We report a case of a 60-year-old man who presented with purpuric patches, hemorrhagic blisters, and ulcers over extremities of 15 days duration. On cutaneous examination, there were multiple stellate purpuric patches, hemorrhagic bullae, and deep necrotic ulcers, mainly over extremities. Slit-skin smear examination from six sites revealed bacteriological index 6+ with globi, and morphological index 5%. Histopathology revealed diffuse infiltration of bacilli in epidermis, dermis, and endothelial cells along with neutrophilic and lymphocytic infiltrate. Fibrinoid necrosis and thrombosis of blood vessels was also noted. The above clinicohistopathological features helped in making the diagnosis of LP. Concomitantly he was found to be infected with hepatitis C virus. Many triggering factors have been described in literature; however, activation of hepatitis C as a trigger for Lucio phenomenon has not been reported. In addition, IgM and IgG anticardiolipin antibodies were found to be positive. The patient was started on high-dose steroids along with multibacillary antileprosy therapy and improved within 2 weeks.

Key words: Diffuse lepromatous leprosy, erythema necroticans, Lucio phenomenon, stellate purpura

INTRODUCTION

Lucio phenomenon (LP) or erythema necroticans was initially described by Lucio and Alvarado in 1852. It was later confirmed by Latapi and Zamoraas, as a necrotizing panvasculitis occurring in patients with diffuse non-nodular form of leprosy (DLL), who have not received any treatment. Also known as Type III reaction, LP is endemic in Mexico, but has also been reported in the USA, Spain, and South and Central America. So far, there are only about 10 case reports of LP from India after searching available databases. We hereby report a case of a 60-year-old man who presented with necrotic ulcers and purpuric patches typical of LP, triggered by activation of hepatitis C infection.

CASE REPORT

A 60-year-old man presented with a history of nasal stuffiness, multiple episodes of epistaxis, and persistent pedal edema since 2 years. He also complained of painful purpuric patches, which developed hemorrhagic blisters within 1–2 days, and later broke down to form painful ulcers with purulent discharge, following which he developed low-grade fever and joint pains since 15 days. The patient was poorly built and nourished, pallor and bilateral pitting pedal edema was seen. Systemic examination was within normal limits. On cutaneous examination, multiple stellate purpuric patches, angular infarcts, and gangrene, few with overlying hemorrhagic bullae and deep jagged necrotic ulcers were present mainly over extremities, with few purpuric patches noted over abdomen, back, and ears [Figures 1–3]. All peripheral pulses were felt normally. There was diffuse infiltration of face and ears, ciliary and supraciliary madarosis, and perforation involving nasal septum. No

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lesions suggestive of lepromatous nodules or patches were noted. Bilateral glove and stocking anesthesia was present, with symmetrically thickened peripheral nerves, that is, ulnar, radial cutaneous, ulnar cutaneous, lateral popliteal, posterior tibial, and sural nerves. Motor examination and cranial nerve examination results were within normal limits. Ophthalmological examination did not reveal any contributory findings. With the above findings of stellate purpuric patches and gangrene of extremities with absence of constitutional symptoms, a provisional diagnosis of diffuse lepromatous leprosy with Lucio phenomenon and grade I disability was considered, keeping necrotic erythema nodosum (EN), medium vessel vasculitis, purpura fulminans, and cryoglobulinemic vasculitis as the other differential diagnosis. Investigations revealed neutrophilic leukocytosis, deranged liver function test (AST 63, normal <37), (ALP 154, (normal <116), (GGT 132, normal <55), which was later on, attributed to hepatitis C infection. HCV RNA levels were noted to be 1,00,000 copies/mL (Normal <100 copies/mL). ELISA for hepatitis B antigen and HIV antibodies was negative. Ultrasound scanning of abdomen revealed splenomegaly and cholelithiasis with normal liver span and echotexture. GI endoscopy was normal. Arterial doppler of both lower limbs was within normal limits. IgM (100 IU/mL, normal <20 IU/mL) and IgG (22 IU/mL, normal <20 IU/mL) anticardiolipin antibodies were significantly elevated. Antilupus anticoagulant, anti-beta2 GPI were negative. ANA, ANCA, cryoglobulin, protein C, and protein S antibodies were negative. Slit-skin smear using Ziehl Neelson stain showed a bacteriological index of 6+ with morphological index of 5% [Figure 4]. Histopathological examination using Hematoxylin and Eosin stain revealed diffuse infiltration of solid staining and granular bacilli in epidermis and dermis, including endothelial cells. Dense neutrophilic and lymphocytic infiltrate was present throughout dermis. Fibrinoid necrosis of small- and medium-sized blood vessels, with karrorhexis, extravasation of RBCs and thrombosis were also seen [Figure 5]. Modified Fite Faraco stain revealed numerous acid fast bacilli with globi. In view of diffuse infiltration of skin, absence of nodules, classical angular infarcts, hemorrhagic blisters and jagged necrotic ulcers, with mild constitutional symptoms, and histopathological correlation, a final diagnosis of Lucio phenomenon was made.

The patient was started on WHO recommended multibacillary antileprosy therapy with rifampicin, clofazimine, and dapsone along with 60 mg of prednisolone and oral antibiotics. However, continued therapy with rifampicin was not possible in view of deranged liver function tests and hepatitis C after consultation with the gastroenterologist. Substantial improvement in skin lesions was seen within 1 week. Oral steroids was tapered over the following 2 weeks and the patient was asked to follow up with gastroenterology department after 3 weeks. Most of the ulcers healed slowly within this time, leaving depigmented atrophic scars.
DISCUSSION

Vasculonecrotic reactions in leprosy may be of two types, Lucio phenomenon and vasculonecrotic EN. LP usually manifests three to four years after onset of the disease, mostly in untreated patients with diffuse lepromatous leprosy. They begin as erythematous painful patches over extremities, which later evolve into purpuric lesions and become necrotic jagged ulcers of 0.5–1 cm size, which heal in about 2–4 weeks with superficial, atrophic scars. Occasionally, hemorrhagic blisters are seen.[1] Typically, there are minimal or absent constitutional symptoms. This phenomenon tends to disappear 6–8 weeks after initiation of treatment, and may develop reaction, mainly of EN-type while on treatment.[2] All the above features were seen in our patient. Many triggering factors have been described, such as certain intercurrent infections (streptococcal, cryptococcal, respiratory), drugs (iodide), and pregnancy.[3]

Vasculonecrotic EN on the other hand, usually occurs in lepromatous leprosy and borderline lepromatous leprosy cases after starting multidrug therapy. These patients in contrast, develop deep painful ulcers associated with constitutional symptoms and neuritis.[4] The clinicopathological differences between the above two reactions have been summarized in Table 1.

Histopathology of LP reveals infiltration of acid fast bacilli (both solid and fragmented), singly or as globi within macrophages and endothelial cells found in vessel walls, mostly of muscular/medium-sized arteries, less commonly

### Table 1: Differences between Lucio phenomenon and vasculonecrotic erythema nodosum

| Features                  | Lucio phenomenon                          | Vasculonecrotic EN                      |
|---------------------------|--------------------------------------------|-----------------------------------------|
| Type of leprosy           | Diffuse leprosy with no nodules            | BL, LL mostly                          |
| Treatment situation       | Untreated                                   | First few months of treatment           |
| Constitutional symptoms   | Absent/mild                                 | Present                                 |
| Neuritis                  | Absent                                     | Present                                 |
| Site                      | Lower limbs, ear, nose, then spreads to remaining body | Upper limbs, then spreads to trunk and lower limbs |
| Cutaneous lesions         | Superficial, irregular ulcers              | Deep, round ulcers                      |
| Scarring                  | Small, hypochromic scars with hyperchromic border | Large scars, mostly hypertrophic         |
| Symptoms                  | Burning sensation                           | Ischemic pain                           |
| Medina test               | Positive                                   | Negative                                |
| Histopathology            | Solid and/or granular bacilli in endothelial cells, macrophages | Granular, fragmented bacilli in macrophages |
|                           | Leukocytoclastic vasculitis                | Leukocytoclastic vasculitis, lobular panniculitis |
|                           | Endothelial cell proliferation, mild mononuclear cell infiltrate | Neutrophilic infiltrate                 |
|                           | Thrombosis+necrosis of small vessels       | Necrosis of small- and medium-sized vessels |
| Resolution                | 15 days                                    | Slow                                    |
| Treatment                 | No response to thalidomide                 | Responds to thalidomide                 |

EN: Erythema nodosum, BL: Borderline lepromatous leprosy, LL: Lepromatous leprosy
in arterioles, venules, and medium-sized veins. Smaller vessels can exhibit leukocytoclastic vasculitis.\[5\] Endothelial cell proliferation, thrombosis, ischemic necrosis are among the other features commonly seen.\[1\] All the above histopathological characteristics were seen in our patient. Medina reaction using lepromin test could not be elicited due to nonavailability.

In view of IgM and IgG anticardiolipin antibodies being positive, but absence of clinical features of antiphospholipid antibody syndrome (APS) in our patient, it is important to follow up such patients carefully, as they can develop full-blown APS later, with life-threatening thromboembolic complications. Antibodies 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 multi-bacillary patients) in literature, predominantly of IgM subtype. The frequency of aCL in LL leprosy patients is around 70%–89%. Coexistence of LP and APS has been described in few case reports. Azulay-Abulafia et al. reported a 53-year-old Brazilian man with clinical features of both LP and APS, along with positive aCL and lupus anticoagulant (LA). In addition, Ang et al. reported the coexistence of fatal LP and APS in two patients from Singapore, with typical clinical features of both; however, aCL antibodies could not be tested in either. These observations may indicate that aCL and LA should be tested in patients with LP as this may have different therapeutic implications.\[6\]

In addition, our patient was found to be hepatitis C positive, with no reports so far of coexistence of hepatitis C and LP.

**CONCLUSION**

This case is being reported because of the rarity of Lucio phenomenon in India and also to emphasize the importance of keeping a high index of clinical suspicion to identify such cases early. It is also important to identify the potential trigger, which in itself can be life threatening. This case also highlights the clinicopathological differences between LP and necrotic EN and suggests a possible association between APS and LP, although this needs further validation.

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**Conflicts of interest**

There are no conflicts of interest.

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