A case of livedo vasculopathy

Commentary by
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Livedo vasculopathy is a relatively easy condition to diagnose but a challenging one to manage.

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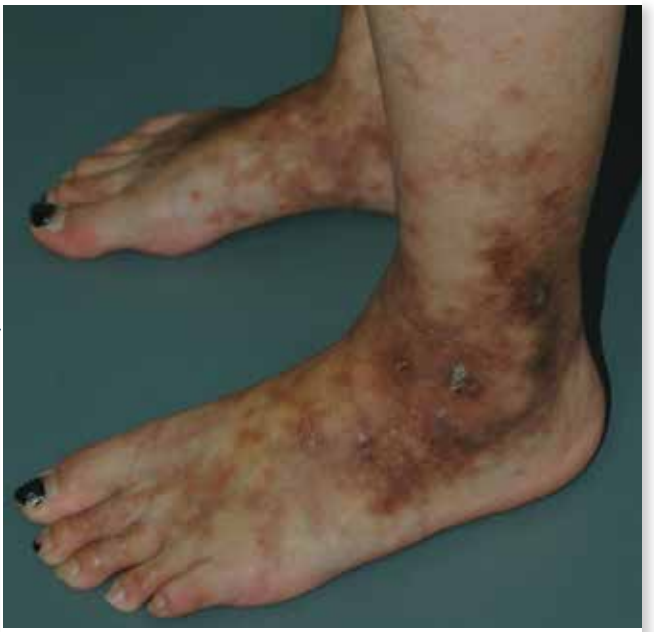

Figure 1. Reticulate pigmentation and atrophie blanche affecting both feet and ankle areas in a patient with livedo vasculopathy. Note livedo racemosa (branched erythema) on the lateral calf and dorsum of the foot.

CASE SCENARIO

Clare, aged 62 years and a new patient at the practice, came to request a narcotic script to deal with the pain from her long-term problem of 'livedo vasculopathy'. She said that this had started during a pregnancy when she was 25 years old and that despite taking prophylactic medication, she has had recurrent attacks a few times a year ever since.

The pattern was that first she would develop intense pain in both lower legs, and then areas of skin on her legs would break down and form shallow and painful ulcers, which eventually healed leaving scars.

She appeared to have adequate peripheral circulation and was slim, active and a nonsmoker. She regularly took as prophylaxis aspirin, colchicine and indomethacin. No screening tests or other investigations had been performed.

What is the aetiology of this condition? Has Clare been treated appropriately?

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COMMENTARY

Livedo vasculopathy (LV) is a rare dermatological condition characterised by recurrent painful ulcerations that generally heal to leave porcelain-white, atrophic, stellate scars (atrophie blanche). The ulcers may recur cyclically in a seasonal fashion. LV is classified as a 'reticulate eruption', given the netlike pattern of pigmentation seen on the lower limbs.

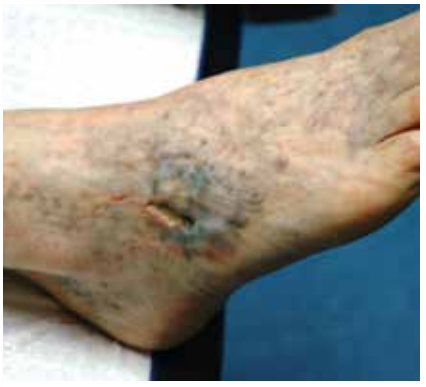
First described in 1967 by Bard and Winkelmann, the condition is known by a host of names, including:

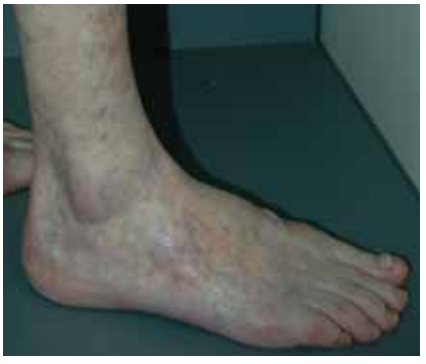
- livedo reticularis with summer or winter ulcerations
- PURPLE (painful purpuric ulcers with reticular pattern of the lower extremities)
- segmental hyalinising vasculitis
- livedoid vasculitis.

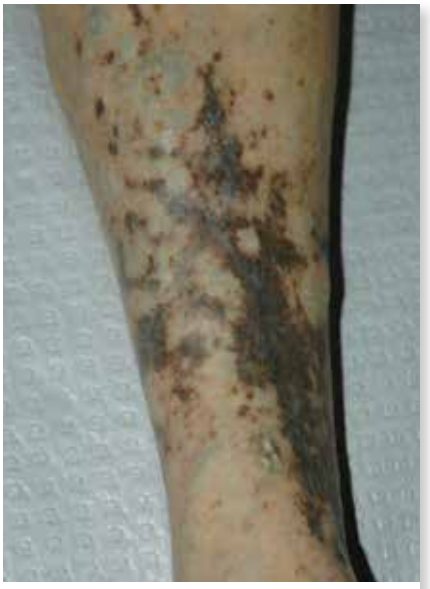
Given the lack of a true histological vasculitis, LV should be more accurately categorised as a cutaneous vasculopathy rather than a vasculitis.

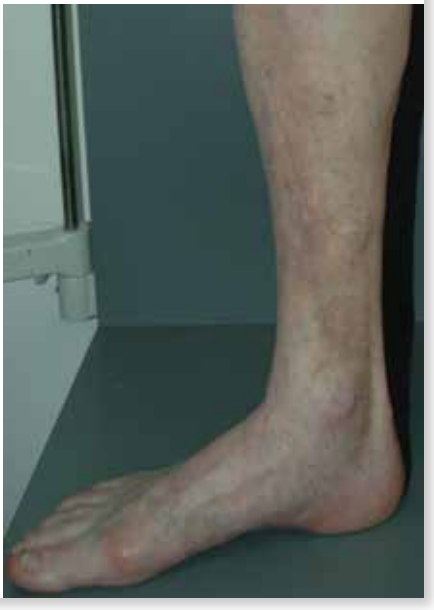
The aetiology of LV is unknown, although the disease is widely believed to have a procoagulant pathogenesis. Investigations and treatment strategies have largely focused on identifying and managing an underlying hypercoagulable state. Abnormalities of coagulation are well documented to be associated with LV, including but not limited to factor V Leiden mutation, protein C deficiency, antiphospholipid syndrome (APS), increased plasma homocysteine levels, abnormalities in fibrinolysis, increased platelet activation and autoimmune disorders such as systemic lupus erythematosus (SLE) and Sjögren syndrome.

Clare seems to have been appropriately diagnosed as her









Figures 2a to d. Livedo vasculopathy. This patient was taking colchicine with no improvement when referred to the author. Note the stellate punched out ulceration of the right lateral foot (a, upper left) and reticulate pigmentation of the anterior shin (b, upper right). Following treatment of the associated chronic venous disease with endovenous laser ablation and foam sclerotherapy, the ulcers healed (c, lower left) and pigmentation cleared (d, lower right) over the next four years.

history and presentation are consistent with LV. The diagnosis needs to be confirmed by a skin biopsy.

History

History-taking should focus on the following features:

- the cyclical or seasonal nature of ulceration with winter or summer exacerbations
- symptoms and, in particular, the associated pain
- past or concurrent history of connective tissue disorders, APS, Sneddon's syndrome (livedo reticularis or livedo racemosa in association with severe transient neurological symptoms or stroke) and other thrombophilias
- a family history of venous or arterial thrombotic events.

Results of any previous investigations, particularly skin biopsies and blood tests, should be obtained.

Examination

Patients with LV present with a reticulate pattern of pigmentation, typically affecting the lower limbs and in particular the ankles and the feet (Figure 1). Small ulcers develop a stellate (star-like) pattern of necrosis, and heal to leave the porcelain-white scars of atrophie blanche.[1,2] Livedo racemosa or livedo reticularis (see below) may be seen in the proximal calves and thighs. Cutaneous signs of connective tissue disease, particularly SLE, should be sought.

The reticulate pigmentation of LV should be differentiated from the blanchable, symmetrical and diffuse pattern of livedo reticularis. Livedo reticularis is much more common and although it may represent an underlying pathology, it is usually due to a physiological response to cold in young women.

Occasionally livedo reticularis, but more commonly livedo racemosa, is seen in patients with APS. Livedo racemosa is a branched, partially blanchable, non-symmetrical eruption. It always represents an underlying pathology. It is seen in conditions such as polyarteritis nodosa (PAN), LV and APS. These reticulate eruptions should be assessed with the patient standing. More detailed information on the differentiation of these eruptions is provided in the references.[1,2]

Investigation

The key investigation to confirm the clinical diagnosis and exclude other causes is a skin biopsy. One or multiple samples should be obtained from the affected intact skin (not ulcers). Typical histological features include segmental hyalinisation, endothelial cell proliferation and intravascular fibrin deposition but no neutrophilic vasculitis. A perivascular lymphocytic infiltrate may be present.

The key association of LV is thrombophilia and hence screening should include the following:

- activated protein C resistance
- factor V Leiden and prothrombin gene mutations

- protein C, protein S and antithrombin levels
- fasting serum homocysteine level
- antiphospholipid antibodies, including anticardiolipin, lupus anticoagulant and anti-beta-2 glycoprotein.

Platelet function studies, conventional clotting times and baseline D-dimer levels will be useful for future monitoring. Connective tissue screening should include measurement of antinuclear antibodies (ANA) and antibodies to extractable nuclear antigen (ENA) and double stranded DNA (ds-DNA).

Other cold-precipitated conditions presenting with a reticulate pattern and possibly ulceration should be excluded. Screening for these should include tests for cryoglobulins, cryofibrinogen and cold agglutinins. Cryofibrinogenaemia has been associated with LV.

General baseline tests include a full blood count with peripheral smears, erythrocyte sedimentation rate and renal and liver function tests.

Vascular imaging should be performed. This should include a detailed venous incompetence study, ankle–brachial indices and peripheral arterial studies. Patients with LV will benefit from compression stockings; before applying compression, an understanding of their arterial supply and venous drainage will be essential.

Other investigations need to be arranged based on the underlying conditions and other findings.

Management

Treatment of LV is challenging and may require treatment of the associated coagulopathy and venous hypertension.

General measures include avoiding temperature variations that trigger the ulceration. Some patients report the onset of ulceration in winter whereas others report that it happens in summer. All patients need to be vigilant to avoid the extremes of ambient temperature that lead to ulceration.

Improved outcomes have been reported with compression therapy. The best grade of compression is class II (20 to 30 mmHg). Venous flow abnormalities, endothelial dysfunction and microthrombi in dermal vessels have been associated with LV. Treatment of associated venous hypertension will expedite the healing of the ulcers (unpublished personal data).

Many of the documented treatments for LV have focused on anticoagulant therapy with warfarin, heparin or low molecular weight heparin and rivaroxaban (all off-label uses). The evidence is mostly anecdotal and based on small case series. Similarly, antiplatelet agents including aspirin, clopidogrel, ticlopidine, pentoxifylline and dipyridamole have all been tried with varying success (all off-label uses).

Oral anti-inflammatory measures such as oral corticosteroids and NSAIDs and antineutrophilic agents such as colchicine have a role in the management of patients with an underlying inflammatory disease.

Other proposed treatments based on anecdotal experience include nicotinic acid, hyperbaric oxygen, calcium channel blockers, L-arginine, intravenous immunoglobulin and danazol (all off-label uses). More severe cases have responded to infusions of tissue plasminogen activator and to intravenous immunoglobulin (off-label uses).

Chronic venous insufficiency results in stagnation of blood flow in the superficial venous network and a predisposition to thrombosis. Figures 2a to d show a patient with LV who was taking colchicine with no improvement. Following treatment for venous disease using a combination of endovenous laser ablation and foam sclerotherapy, the patient's ulcers healed and the pigmentation cleared. Chronic venous insufficiency should be carefully treated in patients with LV.

CONCLUSION

LV is a relatively easy condition to diagnose but a challenging one to manage. Its aetiology remains unknown. The emphasis of treatment should be on reducing the thrombotic load in the dermal microvasculature. Cyclical ulceration, reticulate pigmentation, livedo racemosa and atrophie blanche are the hallmarks of LV. Affected patients should be referred to an appropriate specialist such as a vascular physician or a vascular dermatologist with experience in managing this condition. MT

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COMPETING INTERESTS: None.