Livedo Vasculopathy

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CASE SUMMARY

History

A 40-year-old lady presented with a 6-month history of painful papules and ulceration at both ankles, which started in summer. She also complained of an asymptomatic pigmented rash on her legs for 8 years that became more prominent when exposed to cold. Constitutional symptoms were absent.

Her past health had been good. There was no history of vascular disease or dermatitis. There was no ankle oedema, Raynaud's phenomenon, photosensitivity or joint pain.

Physical examination

A reticulate hyperpigmented macular rash was seen on all four limbs and on the abdomen (Figure 1). At the ankles and the dorsal surfaces of the feet, there were ulcers covered in scab with adjacent erythema. Healed ulcers showed stellate atrophic white scars with pigmented margins and surrounding telangiectasia (Figure 2).

The peripheral pulses and the sensation were normal. Blood pressure was 100/70 mmHg.

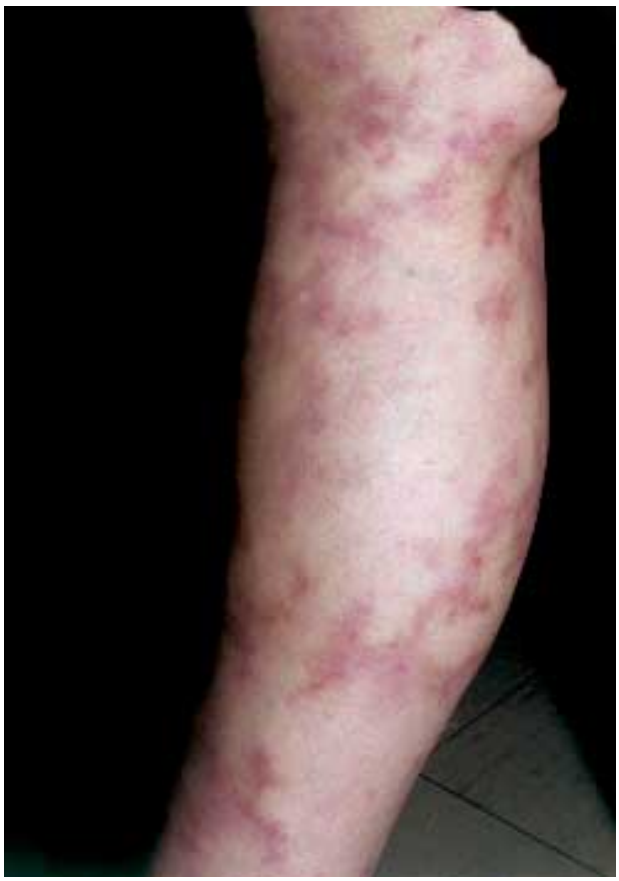

Figure 1: Reticulate hyperpigmented macular rash on leg

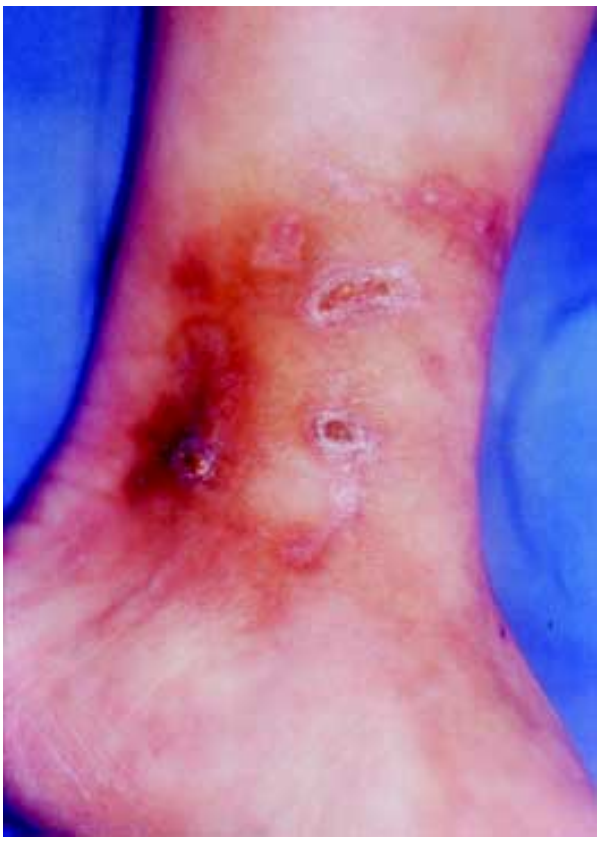

Figure 2: Healed ulcers with stellate atrophic white scars, pigmented margins and surrounding telangiectasia

Investigations

The complete blood picture, erythrocyte sedimentation rate, clotting profile, liver and renal function tests were normal. The autoimmune markers ANF, Anti-ENA and rheumatoid factor were negative. The patient was tested positive to c-ANCA, but negative for anti-PR3. Anti-cardiolipin IgG & IgM were normal and cryoglobulins were absent. The C3, C4 levels were normal. She was tested negative for hepatitis B surface antigen. Ulcer swab for bacteriological study did not reveal any persistent organisms.

Incisional skin biopsy of a papular lesion showed up fibrin thrombi within the venular lumen and fibrin deposit in the vessel wall. A mild perivascular mixed lymphocytic and neutrophilic infiltrate was present. The features were compatible with a diagnosis of livedo vasculopathy.

Diagnosis

The diagnosis of livedo vasculopathy was made.

Management

The patient responded only partially to oral pentoxyfylline and dipyridamole. Aspirin was not tolerated due to gastrointestinal symptoms. Her condition characteristically flared up in the summer with increased pain and ulceration. The disease usually became quiescent in winter with healing of ulcers. Oral corticosteroids were not effective in controlling the exacerbations. The pain was rather severe during these flare-ups, affecting daily activities and sleep, not helped by oral analgesics. Transcutaneous electrical nerve stimulation (TENS) was tried, however, this also did not give satisfactory pain relief.

Progress

The painful ulcers had undergone spontaneous resolution in November this year, about 4 months after the last relapse.

REVIEW ON LIVEDO VASCULOPATHY

There are many synonyms for this condition: livedoid vasculopathy, livedo or livedoid vasculitis, atrophie blanche, atrophie blanche vasculitis, livedo reticularis with summer/winter ulceration, segmental hyalinizing vasculitis, and PURPLE - painful purpuric ulcers with reticular patterning on the lower extremities.

Many of these terms reflected the prevailing belief of the pathogenesis of the disease. However, they often cause confusion, especially with the term "atrophie blanche", as some authors consider it to be an end-phenomenon arising from many other conditions as well, most commonly venous insufficiency.

Clinical features

Livedo vasculopathy is most commonly found in young and middle-aged females. It is a chronic disorder with persistent livedo reticularis and recurrent painful ulceration usually affecting the lower legs and ankles, but occasionally occurring on the hands, face and trunk. Exacerbation frequently occurs in the summer and/or winter season due to heat-induced vasodilation or cold-induced spasm with resulting vascular stasis.

Erythematous to violaceous macules and papules usually appear first which then ulcerate and may coalesce to form larger areas of breakdown. Ulcers heal with smooth, depressed, angulate, ivory-white scars with surrounding hyerpigmentation and telangiectasia (atrophie blanche).

Differential diagnosis

The differential diagnosis includes conditions that may produce livedo reticularis or ankle ulceration with atrophic scarring. These include chronic venous insufficiency, peripheral arterial occlusion, cryoglobinaemia, connective tissue diseases (e.g. example, systemic lupus eryethematosis, scleroderma, polyarteritis nodosa), hypercoagulative states, (e.g. antiphospholipid syndrome, protein C deficiency) and cholesterol embolism.

Histology

There may be a superficial and deep perivascular infiltrate of lymphocytes accompanied by some neutrophils in the upper part of the dermis. Heavy neutrophilic infiltration and neutrophilic nuclear dusts are typically absent. Immunoreactants can sometimes be demonstrated. Fibrin can be found in the walls of venules and thrombi within the lumen.

In late lesions, there is sclerosis in the upper part of the dermis, thinning of epidermis, and numerous telangiectases in the upper part of the dermis.

Pathogenesis

There are two schools of thought concerning the pathogenesis of this condition: immune-mediated vasculitis *vs*. occlusive vasculopathy. An immune-mediated mechanism was favoured in the past, because of the occasional presence of immunoreactants in biopsy material and the association with immune-mediated diseases. However, the condition is now considered by most authors to be an occlusive vasculopathy, due to the clinical evolution and the good response towards fibrinolytic and antithrombotic treatment. Studies also had shown that in these patients, there were increased platelet aggregation and elevated levels of serum fibrinopeptide A, a specific marker of thrombin generation.[1]

Treatment

Treatment of livedo vasculopathy had not been satisfactory. Avoidance of trauma to the affected area and limb elevation should be advised. Most of the drugs found useful in this condition belong to the antithrombotic or the fibrinolytic group.[2]

Antiplatelet agents such as low dose aspirin, dipyridamole and ticlopidine, in various combination, have been commonly used to treat livedo vasculopathy.[3] Heparin had also been shown to be useful.[4]

Fibrinolytic agents, phenformin and ethylestrenol, when used together produced very good results and was the most popular choice of treatment previously. However, phenformin had been withdrawn and ethylestrenol cannot provide satisfactory control on its own. Tissue plasminogen activator (t-PA) given together with warfarin was found to be useful in some cases, although haemorrhagic stroke could be a serious side effect.[5] Danazol was reported not only to result in clinical improvement, but also normalized the levels of antithrombin III, protein C, protein S and a_2-antiplasmin.[6]

Vasodilators reported useful in treating livedo vasculopathy included pentoxyfylline,[10] nifedipine, intravenous prostacyclin[7] or its oral analogue beraprost sodium,[8] and ketanserin,[9] a S2-serotonergic blocker.[7-10]

Other treatments used for livedo vasculopathy included sulfasalazine,[11] oral corticosteroid, nicotinic acid and systemic PUVA.[12] Excision of ulcers with skin grafting can be considered if medical therapy fails.

Learning points:

Livedo vasculopathy is now believed to be a thrombo-occlusive disease. Antithrombotic and fibrinolytic agents are the treatment of choice.

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