

CASE REPORT

Livedoid vasculopathy. Is it a skin manifestation of autoimmune thyroiditis?

Yashpal Manchanda, MD, Arun Joshi, MD, Dhuha Al-Rqobah, MD

Department of Dermatology, Farwaniya Hospital, Kuwait

ABSTRACT

We report herein a case of a 24-year-old woman with recurrent ulcerations on the lower extremities. The clinical presentation, together with histopathological findings of vascular occlusion without overt vasculitis in the dermis, led to the diagnosis of livedoid vasculopathy. The laboratory investigations showed abnormal thyroid functions with positive anti-thyroid antibodies. The skin lesions improved dramatically after adding levothyroxine to the treatment regimen. This case suggests that livedoid vasculopathy may be one of the skin manifestations of autoimmune (Hashimoto's) thyroiditis.

INTRODUCTION

Livedoid vasculopathy (LV) is a chronic recurrent painful cutaneous disease that has often been confused with cutaneous small vessel vasculitis because of the semantic and classification problems.¹

Clinically, LV is usually manifested by foci of purpuric lesions that convert to shallow ulcerations that progress to atrophic scar-like plaques mixed with telangiectasia and hyperpigmentation.² The clinical challenge in the early stages of LV is the similarity with vasculitic lesions seen in diseases characterized by palpable and non-palpable purpura, shallow ulcers and livedo reticularis that constitute up to 75% of the cutaneous manifestations of cutaneous small vessel vasculitis.³

The disease can be associated with systemic autoimmune disorders, or may present in an "idiopathic" form which is considered as a non-inflammatory thrombotic disease that may occur in patients with coagulation abnormalities.⁴

CASE REPORT

A 24-year-old woman presented with bilaterally symmetrical skin lesions on the lower aspect of

both legs and medial aspect of the feet. The lesions started 2 years back as a purpuric eruption that gradually progressed to shallow ulcers and erosions with telangiectasia and edema. The lesions were largely asymptomatic. The lesions healed with hyperpigmentation and scarring.

Routine laboratory investigations (complete blood count, liver functions, kidney functions, blood sugar, lipid profile, serum electrolytes and urine analysis) showed no significant abnormalities. Immunological investigations showed negative ANA, dsDNA, antiScl-70, antiphospholipid antibodies, rheumatoid factor, hepatitis B & C virus antibodies. Doppler ultrasound of both lower limbs showed normal arterial flow but there was mildly elevated venous pressure.

At the beginning of the disease, a skin biopsy was taken from a purpuric lesion, but the pathological findings were non-specific and included extravasation of RBCs with mild lympho-histiocytic infiltrate and hemosiderin deposits. There was no evidence of vasculitis, but direct immunofluorescence (DIF) revealed precipitation of IgA and IgG in the walls of the blood vessels denoting the possibility of a late lesion of cutaneous vasculitis. Treatment

Correspondence: Dr. Yashpal Manchanda MD, Department of Dermatology, Farwaniya Hospital, Kuwait

was started with prednisolone (40mg daily) and dapsons (100mg daily) without satisfactory response even after 4 months of continuous therapy. Two months after the cessation of the treatment, she developed a severe attack with erythema, edema and ulceration of the lesions (Fig.1). Another biopsy was performed, which revealed vasculopathic reaction with hayalinization of the vessel wall, swelling of the endothelial cells, intravascular thrombosis, extravasation of RBCs, hemosiderin deposition and mixed lympho-histiocytic inflammatory infiltrate (Fig. 3,4). Direct immunofluorescence also revealed strong precipitation of

IgA and IgG in the walls of the blood vessels. The diagnosis was established as LV, and oral therapy was started with pentoxifylline (400mg daily), aspirin (75mg daily) and dipyridamole (75mg daily). However, the response was poor and the patient continued to have recurrent attacks of erythema and edema.

Further investigations were carried out to identify any underlying etiological factor. Surprisingly, abnormal thyroid functions were detected including elevated TSH(13mU/L), decreased FT4 (0.41ng/dl) and decreased FT3(1.6 pg/mL). Furthermore, there was marked elevation of anti-thyroid anti-



Fig. 1 The lesion before treatment shows multiple small erosions and ulcers with areas of pigmentations and atrophy associated with minimal edema.



Fig. 2 The lesion after treatment shows marked improvement with clearance of erosions and ulcers. The edema subsided with residual crust and pigmentation.

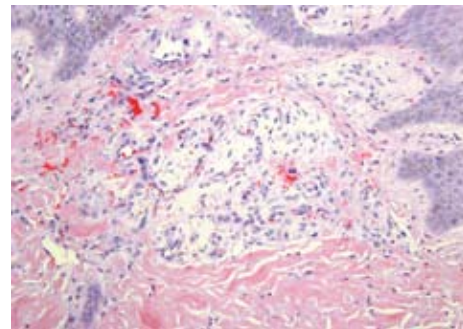


Fig. 3 The superficial dermal vasculature shows proliferation with mixed lympho-histiocytic inflammatory infiltrate, extravasation of RBCs and hyalinization of collagen.

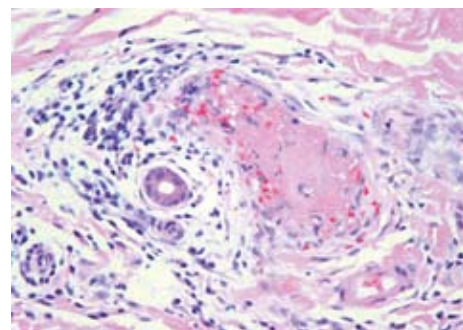


Fig. 4 A mid-dermal blood vessel shows vasculopathic reaction with hyalinization of the blood vessel wall, swelling of the endothelial cells, intravascular thrombosis and perivascular mixed infiltrate.

bodies (Antithyroglobulin antibody was 1700 UI/ml and thyroid peroxidase antibodies was 2600 UI/ml) denoting the diagnosis of autoimmune (Hashimoto's) thyroiditis.

After addition of levothyroxine (150 µg daily) to the conventional therapy, the patient showed marked improvement with satisfactory response (Fig. 2). Follow up of the patient revealed marked stability of the lesions without significant changes even at the end of 6 months.

DISCUSSION

Livedoid vasculopathy (LV) was suggested to be a process combining a clinical entity associated with ulceration and atrophie blanche with intraluminal thrombosis and a group of heterogeneous coagulation abnormalities.⁵

This disease usually affects the lower extremities but has also been reported to occur diffusely.⁶ The histopathologic features are usually not pathognomonic, but usually demonstrate a segmental hyalinizing vascular pattern involving the dermal blood vessels, with vessel wall thickening, endothelial proliferation, and focal thrombosis without leukocytoclasia or fibrinoid necrosis of the blood vessels.⁷

Direct immunofluorescence staining typically demonstrates immunoglobulin and complement components in the superficial, mid and deep dermal vasculature.⁸

There is a huge controversy about the underlying cause of LV. The association with coagulation disorders are common especially with factor V Leiden mutation,⁹ protein C deficiency,¹⁰ antiphospholipid antibody syndrome,¹¹ increased plasma homocysteine levels,¹² abnormalities in fibrinolysis,¹³ and increased platelet activation.¹⁴ To our knowledge, the association of LV with autoimmune thyroiditis (AIT) has not been reported

before. The association of AIT with other skin diseases was reported in many studies including a variety of immunological and non-immunological skin diseases.¹⁵

The association of LV with other autoimmune disorders was suggested and encountered with some diseases such as Sjögren's syndrome,¹⁶ and antiphospholipid syndrome.¹⁷ Furthermore, the disease was encountered also with some neurological disorders such as Mononeuritis multiplex,¹⁸ and peripheral neuropathy.¹⁹

The therapeutic modalities for LV are different and variable. An important therapeutic line includes those agents that used to control the coagulation disorders such as oral warfarin,²⁰ and tissue plasminogen activator.²¹

In addition, there are many trials that suggested other therapeutic modalities for the treatment of LV including danazol,²² hyperbaric oxygen,²³ PUVA,²⁴ and rituximab.²⁵

Our therapeutic trial in this patient revealed that the control of AIT enhanced the response of LV to the conventional therapy denoting that LV may be one of the cutaneous manifestations of AIT.

CONCLUSION

We alarm here to the possible association of LV with AIT, subsequently thyroid functions are recommended to be investigated in patients who not responding to routine therapy.

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