

Livedo reticularis associated with dapson therapy in a patient with chronic urticaria

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Abstract

Dapsone is a drug commonly used in the treatment of various dermatological diseases. Here, we report the case of a 45-year-old female prescribed dapson for chronic urticaria after which she developed extensive livedo reticularis in the limbs, abdomen, and trunk. The use of dapson may be associated with a plethora of adverse effects including rash but livedo reticularis has been very rarely reported. Emphasis should be laid on the possible drug etiology in any patient who develops new signs and symptoms while on medications, even if it may not be supported by enough literature.

KEY WORDS: Chronic urticaria, Dapsone, livedo reticularis, rash

Introduction

Dapsone, 4-4-diaminodiphenyl-sulfone (DDS), was synthesized over a century ago and still continues to be used as a treatment option in many skin diseases including leprosy, dermatitis herpetiformis, acne, bullous pemphigoid, pyoderma gangrenosum, recurrent erythema multiforme, and urticaria.[1] Hemolysis and methemoglobinemia are the frequently reported adverse effects of dapson. Agranulocytosis, rash, dapson syndrome, and peripheral neuropathy have also been observed. Other adverse effects occurring infrequently include vomiting, anorexia, headache, hepatitis, insomnia, psychosis, tachycardia, and hypoalbuminuria.[1]

Livedo reticularis is a complex clinical syndrome caused by changes in the blood flow of skin vasculature. This condition demands a detailed and meticulous etiological investigation since it can result from a wide variety of conditions including certain drugs. However, livedo reticularis after treatment with dapson is extremely rare. We report a case of a female patient who developed livedo reticularis during her therapy with dapson for chronic urticaria.

Case Report

A 45-year-old normotensive and non-diabetic female presented with chronic urticaria of seven months duration. She was prescribed a fixed dose combination of montelukast 10 mg and levocetirizine 5 mg on a daily basis, and IV hydrocortisone 100 mg and IM pheniramine maleate 45 mg on an as and when required basis. One week later, the patient was given first dose of Autologous Serum Therapy (AST). She received weekly injections for 10 weeks. The day patient received third dose of AST, she was also prescribed tablet dapson 100 mg once a day as three days earlier she had an episode of urticaria. Two weeks after starting dapson, she developed a lace-like reddish rash all over her body particularly on the inner surface of upper and lower limbs, abdomen, and trunk [Figure 1]. The patient did not give any history of recent surgery,

abortions or similar cases in family or complain of any joint symptoms, fever, and thrombotic episodes. Other skin changes like nodules and ulcerations were not found. The rash was not cold induced. Cardiac and pulmonary auscultation was normal. Relevant laboratory investigations were advised, and dapsone was stopped. Complete blood count (CBC), coagulogram, erythrocyte sedimentation rate (ESR), thyroid function tests (TFT), kidney function test (KFT), serum calcium, serum C₃, C₄, cryoglobulin, antinuclear antibodies, rheumatoid factor, serologies for hepatitis B and C, and urine analysis were reported to be normal. A diagnosis of livedo reticularis was made, and skin biopsy from left thigh region was sent for histopathological examination, which revealed hyperkeratosis of epidermis and mild perivascular collections of chronic inflammatory cell infiltrate along with a few eosinophils in subjacent dermis without thrombi [Figure 2].

Patient was asked to come for follow up every week. The rash persisted for first month and then resolved gradually over the period of next three months.

Discussion

Livedo reticularis is a reticular red-violaceous mottling of the skin that appears usually on legs but may be generalized. It occurs due to reduction or interruption of the blood flowing through dermal vessels of skin. Blood is supplied to skin in cones with 1-4-cm base located on the skin surface. Each cone is fed by an arteriole, and it is this arteriole that is affected in the livedo, causing a mottled reticular pattern. Livedo reticularis may be physiological (due to cold), idiopathic, or secondary to many causes, for example, intravascular obstruction, drugs, arteritis, and infections.[2] The evaluation of a case of livedo reticularis involves detailed history, physical examination, and laboratory tests along with histopathological examination, which may aid in identifying the underlying cause. In patients with secondary livedo reticularis or livedo racemosa, addressing the approximate cause is important for improvement.

Amantadine as a causal agent for livedo reticularis is well known with other drugs like bismuth, pentazocine, non-steroidal anti-inflammatory drugs, and minocycline also implicated.[2] Amantadine-induced livedo reticularis was first described by Shealy *et al.* in 1970[3], occurring in 2-28% of patients, with most of them being females. Skin biopsy specimens from these patients were normal without signs of vasculitis. Livedo reticularis following amantadine usually appears weeks after initiation of therapy; its etiology is not entirely understood, but it is believed to be due to the depletion of catecholamines at the peripheral nerve terminals.[4]

Dapsone, one of the oldest antibacterial agents, continues to treat a range of dermatologic disorders characterized by abnormal neutrophil and eosinophil accumulation.[5] DDS acts by inhibiting bacterial synthesis of dihydrofolic acid. It has been reported to affect other cellular processes that occur in eukaryotic cells, such as inflammation, migration, and apoptosis.[6] In our patient, the condition appeared two weeks after dapsone therapy was started suggesting a temporal relationship. During this time, changes leading to development of livedo reticularis might have been in progress; for instance, depletion of neurotransmitters or development of antibodies. Punch biopsy of the lesion was inconclusive; livedo reticularis is an occlusive condition rather than inflammatory one. Skin biopsies often do not yield diagnostic arterial lesions in these patients. All other causes of livedo reticularis were investigated for and excluded. There was no evidence of systemic involvement and the discoloration of skin disappeared gradually. After stopping dapsone ingestion, re-challenge was not attempted.

Indeed, this form of iatrogenic reticular discoloration of skin needs more understanding. Livedoid rash with dapsone is extremely rare. We could not find any case of livedo reticularis with dapsone in PubMed or Vigiflow database, while eight such cases have been reported to Ehealthme.com till our last search. This reaction was reported by Sher-i-Kashmir Institute of Medical Sciences (SKIMS), Srinagar via Indian Pharmacopoeia Commission-National Coordinating Centre (IPC-NCC), Pharmacovigilance Programme of India (PvPI) on Vigiflow. A causality category of “probable” using the Naranjo scale was assigned to this adverse event.

In view of the widespread use of dapsone, it was important to draw the attention of clinicians and dermatologists to this possible and rare adverse cutaneous reaction of dapsone.

Footnotes

Source of Support: Nil

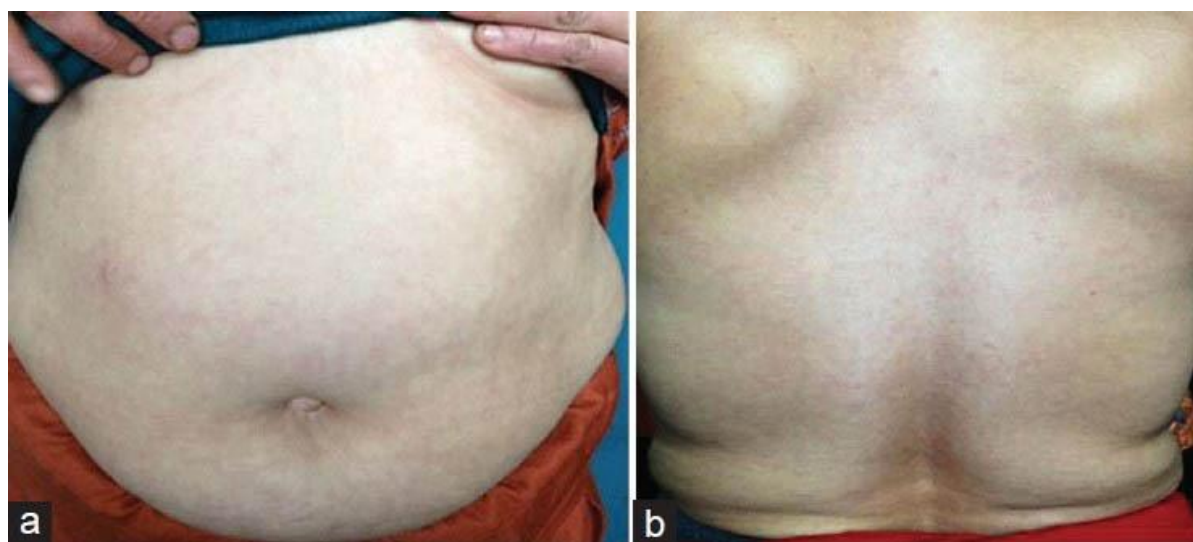
Conflict of Interest: No

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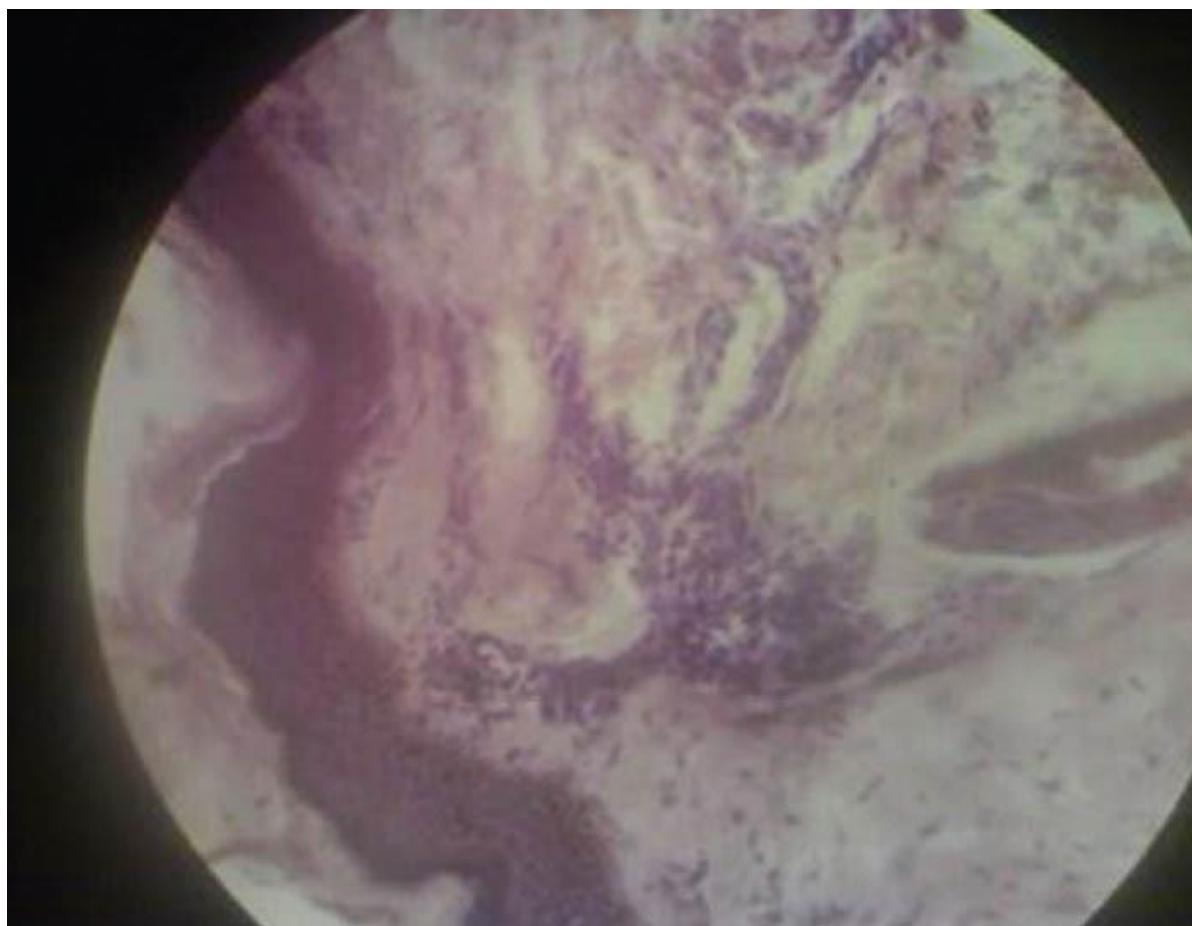
Figures and Tables

Figure 1



(a) Reticular reddish mottling of the skin of abdomen of the patient (b) Reddish mottling of the skin of trunk of the patient

Figure 2



Histopathological examination showing hyperkeratosis of epidermis and mild perivascular collections of chronic inflammatory cell infiltrate along with a few eosinophils in subjacent dermis

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