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Dermatologica Sinica

CORRESPONDENCE

# Leukocytoclastic vasculitis due to thalidomide

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Dear Editor,

Thalidomide is an anti-inflammatory, immunomodulatory, and antiangiogenic agent used since the 1950s. It is used in the treatment of multiple myeloma, myelodysplastic syndrome (MDS), Behcet's disease, systemic lupus erythematosus, rheumatoid arthritis, and graft-versus-host disease. The most common adverse effects of thalidomide are sedation, constipation, nausea, pruritus, neuropathy, tremor, rash, and edema.[1—3] Among the cutaneous adverse effects, maculopapular rash has been reported as being common with a frequency of 14% to 16% in the diverse studies.[3—5] To our knowledge, leukocytoclastic vasculitis due to thalidomide therapy has been reported twice previously.[2,4] Herein, we report a case of leukocytoclastic vasculitis due to thalidomide therapy used for MDS.

A 49-year-old female was referred from the hematology department of Mugla Sitki Kocman University Training and Research Hospital, Turkey with an erythematous rash on the legs that had been present for 3 days. On physical examination, erythematous-purpuric macules and papules that did not fade when pressed, with diameters ranging from 5 mm to 10 mm, were observed on the legs (Figure 1A and 1B). The patient had been diagnosed with MDS 4 months previously and thus, was taking 100 mg/d thalidomide for approximately 3 months. The medical history showed no other drug use. Laboratory tests were as follows: hemoglobin, 9.75 g/dL; hematocrit, 29.2%; white blood cells, 53,000/mm^3; platelets, 286,000/mm^3; blood urea, 26 mg/dL; creatinine, 0.62 mg/dL; and C-reactive protein, 7.28 mg/dL. Urine analysis was normal. A punch biopsy was taken from the skin lesions. The histopathological examination showed intradermal vasculitic reaction with neutrophils, scattered eosinophils, and fibrinoid necrosis compatible with vasculitic drug eruption (Figure 2A and 2B). Thalidomide therapy was stopped and oral antihistamine was started. The eruption cleared within 10 days. When we reintroduced thalidomide therapy 2 weeks later, the eruption recurred within 3 days. Consequently, thalidomide therapy was withdrawn permanently.
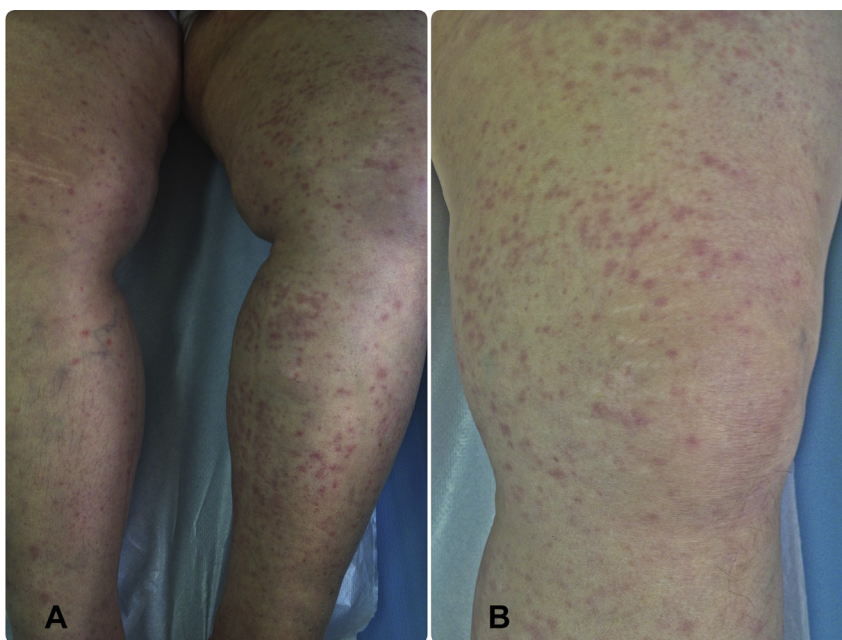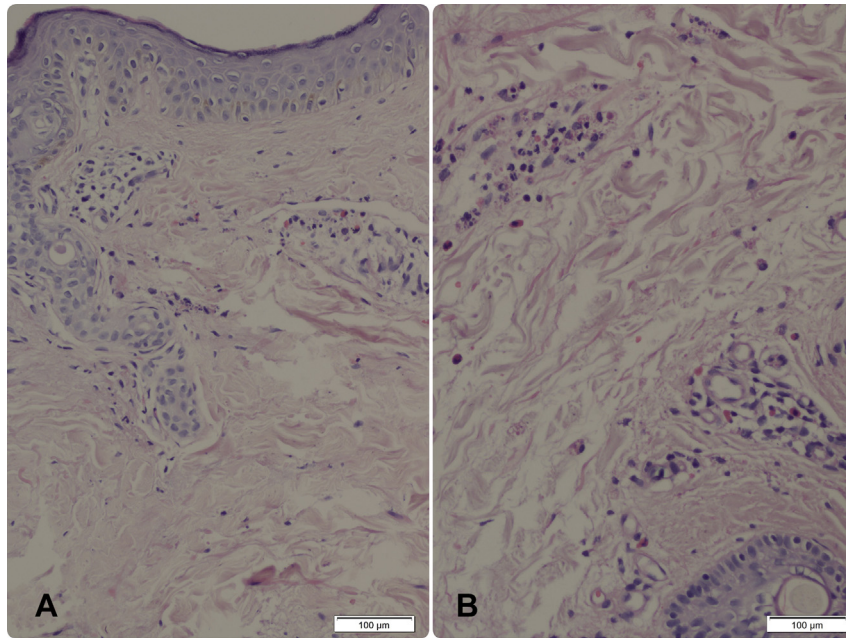

Figure 1 (A) Purpuric macules and papules on the legs, diameters ranging from 5-mm to 10-mm; (B) closer image of the lesions.

Figure 2 (A, B) Intradermal vasculopathic reaction with neutrophils and scattered eosinophils (H&E, original magnification ×200).

Thalidomide has several pharmacologic and immunologic effects involving down-regulation of tumor necrosis factor-α, up-regulation of adhesion molecules, and inhibition of angiogenesis.[1] It is used in the treatment of various autoimmune diseases and hematological diseases. The most common cutaneous side effect is maculopapular rash; vasculitic eruption in response to thalidomide has previously been reported only twice.[2−5]

Drug-induced vasculitis is characterized by inflammation of blood vessels due to the use of various pharmacological agents.[6] The most common drugs responsible are penicillin, nonsteroidal anti-inflammatory drugs, sulfonamides, and cephalosporins. Drug-induced vasculitis is considered to be triggered by the deposition of immune complexes in postcapillary venules. Drug-induced vasculitis generally occurs within 7−21 days of the first use of the drug, however, it can occur within 3 days of the second use of the responsible drug.[7] Histopathological examination demonstrating inflammatory infiltration involving eosinophils and challenge tests may be useful in distinguishing drug-induced vasculitis from idiopathic vasculitis.[6] In our patient, the repeated use of thalidomide resulted in the vasculitic rash on the legs. The histopathological analysis with eosinophilic infiltration confirmed our diagnosis as drug-induced leukocytoclastic vasculitis.

In the differential diagnosis, insect bites, erythema multiforme, pityriasis lichenoides and varioliformis acute, acute meningococcemia, rickettsial infections, and viral exanthemas should be considered.[8]

Although systemic steroid treatment may be required in the case of vasculitis with systemic involvement, drug-induced vasculitis generally improves with the withdrawal of the responsible drug.[7] In our patient, the eruption cleared in a short time with the discontinuation of thalidomide and initiation of antihistamine therapy. To the best of our knowledge, our patient is the third case of vasculitic drug eruption due to thalidomide. The outcome of the disease and the therapeutic approach are altered in drug-induced vasculitis, therefore a detailed investigation should be carried out on the medical history and drug use. Physicians should be aware of the possibility of leukocytoclastic vasculitis due to thalidomide.

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