# Leukocytoclastic vasculitis associated with methotrexate therapy

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Sir,

Chemotherapeutic agents are associated with quite diverse mucocutaneous reactions, but vasculitis is rare[1]. The most common adverse effects of methotrexate (MTX) include bone marrow depression, gastrointestinal disturbances, and cutaneous and mucosal toxicity. MTX-induced hypersensitivity reactions were occasionally seen following intermediate or high-dose regimens: the usual manifestations have been urticaria, anaphylaxis and photosensitivity and, rarely, vasculitis[1-3]. We report a patient with acute lymphoblastic leukemia (ALL) who developed leukocytoclastic vasculitis following high-dose MTX infusion.

A nine-year-old boy was admitted to Hacettepe Children's Hospital in 1996 with a diagnosis of ALL. Complete remission was achieved following ALL induction chemotherapy which included prednisone, L-asparaginase, adriamycin, vincristine and intrathecal MTX (St. Jude Total XI Study Group Protocol).The patient experienced a bone marrow relapse during the intensification phase of the treatment. A second complete remission was achieved at the end of the induction phase. During the consolidation phase, high-dose MTX infusion (2 g/m$^2$) and calcium folinate rescue were instituted. Four days after the fourth course of high-dose MTX, diffuse palpable purpuric lesions were noticed on both upper and lower extremities (Fig. 1); the patient also suffered from abdominal pain and arthralgia. A skin biopsy showed leukocytoclastic vasculitis (LCV). No therapy was given; skin lesions and other symptoms resolved spontaneously within a few days.

Leukocytoclastic vasculitis (LCV) is an immune complex vasculitis that produces vascular damage and secondary ischemic manifestations. Small blood vessels, including the postcapillary venules, are affected. Polymorphonuclear leukocytes infiltrate the necrotic vessel wall, and scattered nuclear debris accumulates around the lesion. A number of agents have been postulated as etiologic factors of LCV, including infection, foreign proteins, chemicals and certain systemic disease such as chronic active hepatitis, ulcerative colitis and bacterial endocarditis[4]. Cutaneous and systemic vasculitis can be associated with malignant disorders, before, during or after their diagnosis[5-6]. The association with lympho- or myelo- proliferative disorders is significantly higher than that with solid tumors.

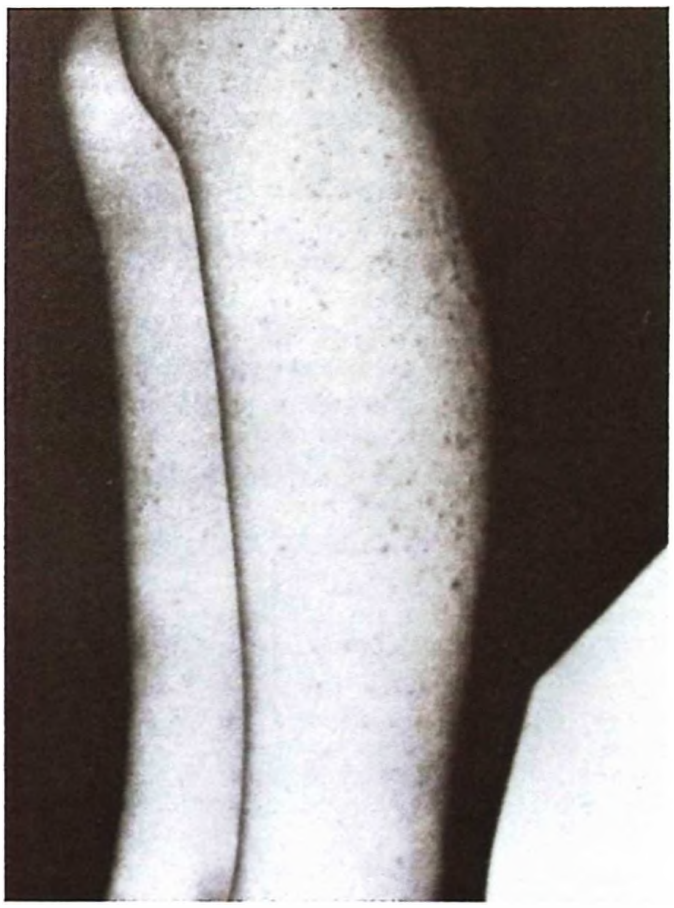

Fig. 1. Maculopapular rash in lower extremity.

The LCV of the presented patient, however, was not associated with leukemia, since the patient was in complete remission. Thus, MTX was thought to be the triggering factor in LCV, which has been reported to be associated with MTX even at low doses, suggesting a non-dose related association[3,7]. MTX is increasingly used in rheumatoid arthritis at low-doses (10-15 mg/m$^2$, weekly). We suggest that this should be a word of caution and that the drug history should be carefully investigated in similar cases.

## REFERENCES

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