

LETTER TO THE EDITOR

Acute Vesico-Bullous Eruption from Methotrexate Overdose in a Psoriasis Patient

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Dear Editor:

Methotrexate (MTX) is a folic acid analog that potently blocks folate-dependent enzymes integral to DNA synthesis¹. It is one of the most common systemic immunosuppressive agents used by dermatologists, particularly in the control of psoriasis. Fatal complications are rare in a dermatological low dose regimen. We herein report a case of acute cutaneous toxicity of MTX representing bullous eruption after a weekly dose of MTX was taken daily for a short period.

A 73-year-old male had been treated for psoriasis since 2008 with narrow band ultraviolet B phototherapy. His psoriatic arthritis had been well controlled with etanercept subcutaneous injection for 1 year and he had stopped etanercept for 1 year. MTX was considered after the psoriatic arthritis worsened, and a rheumatologist prescribed 10 mg/week MTX for 5 days. He accidentally misunderstood the prescription and took 10 mg/day MTX for a period of 5 days. After 1 week, he presented with erythematous vesicobullae and erosions on the arms and face and ulcers in mucosal areas, including the lips (Fig. 1). There was no other skin disease history except psoriasis. Laboratory studies revealed thrombocytopenia (110,000/mm³) and alanine aminotransferase (ALT) was elevated to 99U/L, whereas all laboratory data prior to MTX therapy, including

complete blood count, liver function test, had been within normal limits. Other laboratory results including levels of albumin, blood urea nitrogen, and creatinine were within normal limits. With discontinuation of MTX and methylprednisolone 24 mg/day taken for a week, the skin bullous eruption and labial ulceration rapidly resolved without sequelae (Fig. 2), and the platelet count and ALT value returned to normal. Unfortunately, the patient refused pathologic evaluation. Clinical history, however, indicated MTX overdose-associated bullous eruption; the onset of the eruption was 5 days after initiation of MTX ingestion, and the eruption began to resolve immediately after discontinuation of MTX. After 2 weeks, MTX was restarted at a dose of 10 mg/week and he is taking MTX without misunderstanding or adverse events.

Although MTX's precise mechanism of action in cutaneous autoimmune disease remains unclear, the effects are believed to include inhibition of cell division of tumoral, hematopoietic, and other rapidly proliferating cells¹.

MTX has been associated with a number of mucocutaneous side effects, such as photosensitivity, erosions, necrosis, and diffuse noninflammatory alopecia¹. More rarely, cutaneous ulceration within diseased skin has been reported^{2,3}. In this case, the latest psoriatic lesions of the patient were mainly on his arms, and the MTX cutaneous toxicity occurred on the diseased skin. Lawrence and Dahl³ reported that histologic evaluation of the ulcer edge showed swollen epidermal cells with vacuolated or dyskeratotic cells, indicating incipient epidermal necrosis. Although rare, severe side effects, such as bone marrow suppression, liver failure, and pulmonary fibrosis can occur even in low-dose therapy⁴.

As was the case in this instance, drugs available in once-weekly formulations require extra vigilance⁵. One of the once-weekly dosing drugs, MTX, can be life-threatening when the drug is administered daily as a result of physician,

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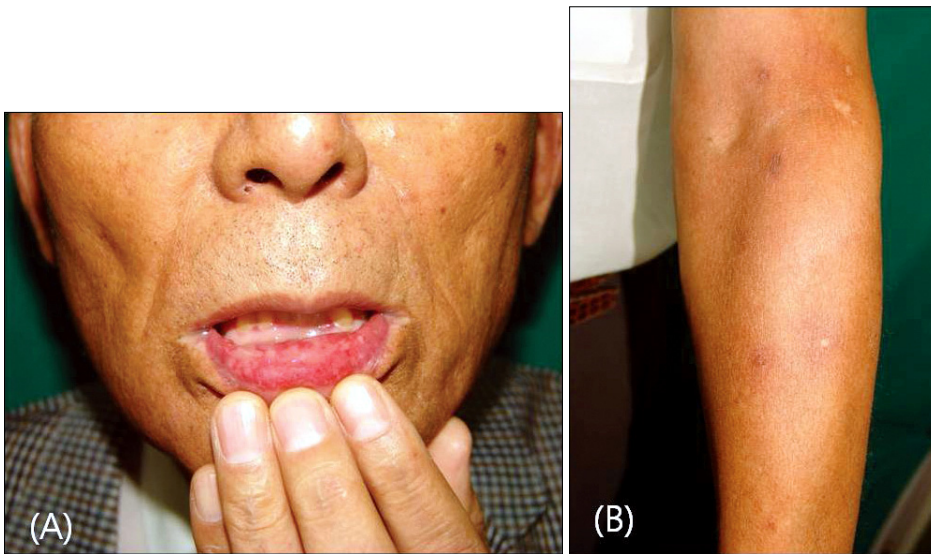


Fig. 1. Acute vesicobullous eruption after administration of methotrexate for 5 consecutive days (A) on oral mucosa (B) on the left arm.



Fig. 2. Ruptured bullous eruption healing with re-epithelization on the left arm.

pharmacy, or patient error. Pre-MTX counseling needs to focus on ensuring that patients clearly understand this dosing schedule¹. In order to avoid a significant risk, patients should be given written, personalized information about the use of a once-weekly drug, and preparation of a time table can help the patient to establish a routine for taking doses as prescribed⁵.

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