# Accidental high-dose methotrexate toxicity due to an electronic prescribing error

Sir,

Methotrexate is widely used in psoriatic patients and methotrexate toxicity is a relatively frequent problem. High-dose methotrexate intoxication, however, is rarely reported.[1] Most cases are patients who have taken several times the usual doses due to misinterpretation of complex weekly oral schedules.

A 45-year-old man was referred to our clinic with oral ulcerations and pustular lesions on his psoriatic plaques. He had been treated variously over 10 years with cyclosporine, acitretin, as well as psoralen ultraviolet A (PUVA), and methotrexate had been prescribed recently. Five days after the 1st intramuscular injection of what was supposed to be a 25 mg dose (half of a 50 mg vial), he developed mouth sores and his psoriatic plaques flared, becoming reddish, itchy and painful.

On the 7th day after the injection, his psoriatic lesions were seen to be scaly and surrounded by a vivid erythema; there were also tiny pustules within these lesions [Figure 1]. Although his vital signs were stable, and complete blood counts as well as routine biochemistry were normal, he was admitted to our hospital for suspected methotrexate toxicity. We could not determine his serum methotrexate levels but his records in the nationwide electronic prescription system revealed that 5 g/50 ml of methotrexate had been prescribed. Sodium bicarbonate was therefore started for alkalization of urine; however, leucovorin rescue therapy was not initiated as the injection had been given more than seven days earlier.

By the third day of hospitalization, his absolute neutrophil count (ANC) had decreased to 400/mm$^3$ and he developed a high fever. Granulocyte-colony stimulating factor (G-CSF) therapy and prophylactic imipenem were initiated. The skin and oral lesions subsequently worsened and total parenteral nutrition had to be added. On the sixth day, the pustular lesions began to crust and ulcerate. A unit of platelet suspension was transfused since the platelet count had decreased to 12000/ml and a fecal occult blood test was found positive. Liver enzymes were elevated at this point (ALT: 155 U/L, AST: 72 U/L), while renal function tests remained normal. On day 8, his lesions began to resolve and the hematologic parameters started to improve. On day 10, the ANC had risen to 3270/mm$^3$. Granulocyte-colony stimulating factor and antibiotic treatments were stopped, and oral feeding was resumed. By day 12 of his hospital stay, the liver enzymes had regressed to normal values and he was discharged on the 14th day with almost complete clinical remission.

A computerized prescriber order entry system was recently introduced in our country. The use of computerized prescriptions appears to be a promising strategy to reduce prescription errors. A study in Spain showed that medication errors were minimized after implementation of an e-prescription system, especially dosage related errors.[2] The authors attributed this to the e-system providing the usual doses of drugs by default. The software in our country, however, does not include default dosages. We believe that the unfamiliarity of the prescribing dermatologist with this system coupled with a numerical similarity between the intended dose (50 mg) and volume of the vial (50 ml) [Figure 2] caused confusion in both the prescribing dermatologist and the nurse injecting the dose, leading to a very high dose being administered inadvertently.

High-dose methotrexate is used in the treatment of malignant diseases along with appropriate preventive measures such as leucovorin rescue. Accidental high-dose methotrexate intoxication has rarely been reported. In a Pubmed search, we found only one report of toxicity probably due to a high dose of methotrexate,[1] in which a psoriatic patient self-administered an unknown dose and subsequently developed ulcerative lesions which were considered a diagnostic clue.

Pustular and ulcerative lesions are a rare but striking manifestation of methotrexate toxicity;[1,3-5] pathogenic mechanisms beyond direct toxicity are yet to be elucidated. Almost all reported cases are patients who were on oral methotrexate.[2-5] Pearce *et al*., have also described two patients with erosions of their psoriatic lesions as a sign of methotrexate toxicity.[3] They stated that the clinical features in their patients were similar to those in patients described previously and emphasized that erosions on psoriatic plaques constitute an early sign of methotrexate toxicity. In our case too, the pustular

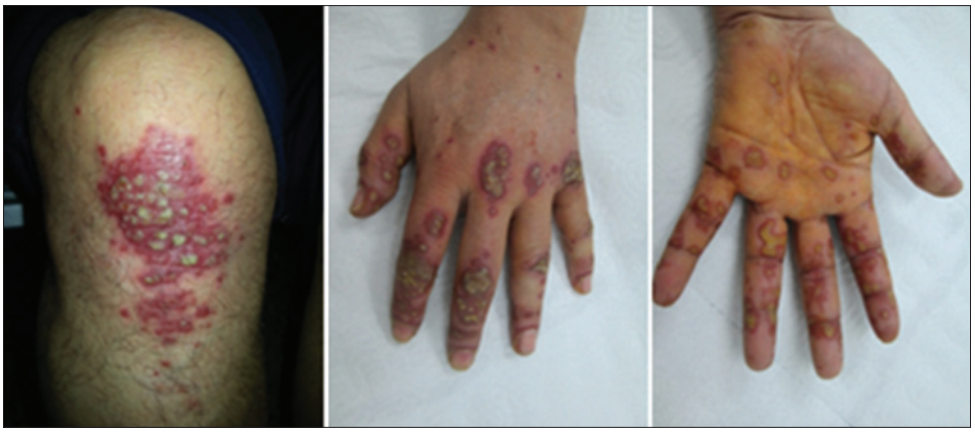

**Figure 1: Pustular eruptions of MTX toxicity. Initial pustular lesions of psoriatic plaques following MTX injection located on the knees and hands**

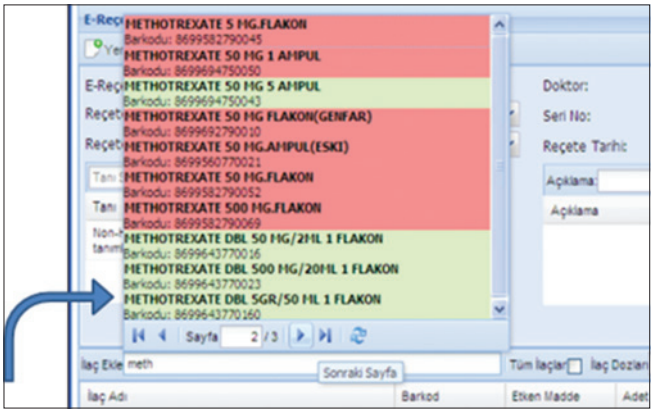


**Figure 2: Computer-assisted order entry of methotrexate. The screen shot of the e-recipe showing the drugs with different methotrexate doses**

eruptions on psoriatic plaques served as a herald of possible methotrexate toxicity leading us to hospitalize the patient despite the limited number of lesions and initially normal laboratory findings. Clinicians should therefore recognize pustular lesions evolving into ulceration in a psoriatic patient on methotrexate as a warning sign.

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