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Letter to Editor

Acute Methotrexate Toxicity in a Case of Generalised Lichen Planus

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Dear Editor,

Methotrexate (MTX) toxicity occurring in cases of psoriasis and rheumatoid arthritis has been widely reported. Here, we report a case of generalised lichen planus (LP), who presented with ulceration of skin lesions, mucosal ulceration and haematological derangements after treatment with MTX. This report is unprecedented as MTX toxicity in LP has been hitherto unreported to the best of our knowledge.

A 60-year-old male presented with itchy skin lesions all over the body for 6 months. The patient had uncontrolled diabetes mellitus (haemoglobin A1C - 10.3%) and was on oral metformin for the past 12 years. On examination, multiple well-defined violaceous flat-topped scaly papules and plaques were present over the trunk and upper extremities and lichenified plaques over the lower extremities involving a body surface area of 30–40%. There were no lesions in oral cavity. Nail examination revealed multiple longitudinal ridges over all fingernails and pincer nail deformity with subungual hyperkeratosis of both great toenails. Skin biopsy for histopathological examination was advised, but the patient refused. Polarised dermoscopy using handyscope (FotoFinder™ systems GmbH, Bavaria, Germany) showed violaceous background with linear white streaks and peripheral brown dots [Figure 1]. A diagnosis of LP was established based on the clinical and dermoscopic features. The patient was advised oral MTX 15 mg/week after necessary investigations.

The patient developed ulceration and pain over skin lesions and mucosal erosions 2 days after the second MTX dose. On examination, multiple erosions and crusting over few existing skin lesions were present. Few erosions were present over buccal mucosa [Figure 2a and b].

On evaluation, the patient was found to have leucopenia, thrombocytopenia, albuminuria and glycosuria [Table 1]. Liver and renal function tests were normal. Serum MTX levels could not be measured. A provisional diagnosis of acute MTX toxicity was made, and the patient was started on intravenous leucovorin 20 mg every 6 h, along with vigorous hydration under intensive care. Prophylactic antibiotics and a single subcutaneous dose of pegfilgrastim 6 mg were administered. Skin lesions were cleaned, and topical antibiotic dressing was done.

The patient experienced a full recovery with haematological abnormalities returning to normal after 2 days and resolution of mucocutaneous ulceration after 10 days of treatment [Table 1, Figure 2c and d]. Systemic retinoid was started for the management of LP.

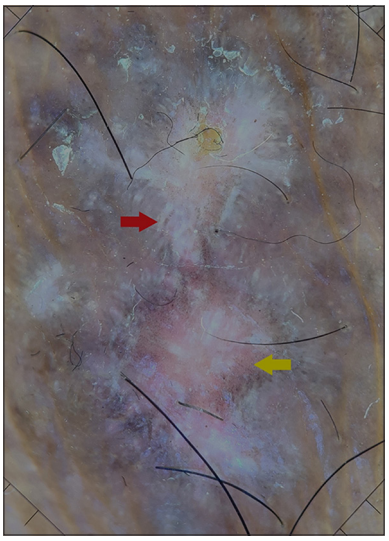

Figure 1: Dermoscopy showing a violaceous background with linear white streaks (Wickham's striae, red arrow) and peripheral brown dots (yellow arrow) (FotoFinder™ systems GmbH, Bavaria, Germany. Polarised ×20).

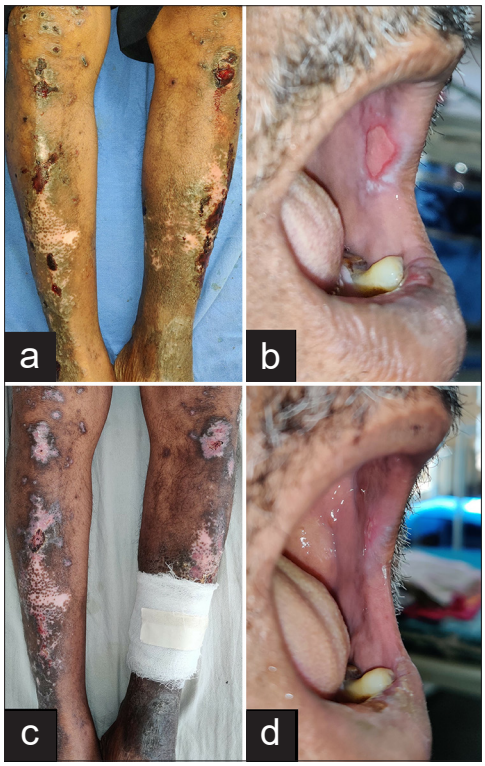

Figure 2: Clinical images showing (a) ulceration over lichen planus lesions over legs and (b) erosions in oral cavity at presentation (c) resolution of cutaneous ulceration and (d) resolution of erosions in oral cavity after 10 days of treatment initiation.

Table 1: Haematology at baseline and over the course of therapy.

	At baseline	After 48 h of administering pegfilgrastim	After 10 days of administering pegfilgrastim
TLC	1490/μL	4980/μL	13960/μL
Neutrophils	56.1%	48.2%	75.0%
Platelets	54000/μL	82000/μL	547000/μL

TLC: Total leucocyte count

LP is an immunological disorder involving skin, mucosa, hair and nails. Treatment of LP is directed towards the resolution of symptoms and is essential for preventing complications such as scarring and rarely carcinoma. According to the European guidelines, corticosteroids are the first-line treatment, which is also most commonly employed by treating physicians. MTX at a dose of 15–20 mg/week is the third-line treatment for cutaneous LP.[1] MTX acts on dihydrofolate reductase, an enzyme required for the synthesis of purines and pyrimidines and inhibits it, thereby hindering the proliferation of activated T-cells and keratinocytes. The use of this drug for inflammatory disorders is a common practice due to its low cost and high efficacy. Multiple studies conducted on LP patients have shown that MTX is safe.[2]

MTX toxicity commonly occurs due to dosage errors either by the patient or physician. Other causes include renal impairment, hypoalbuminaemia, use of drugs interacting with MTX and genetic polymorphisms in folate pathway.[3,4] In the present case, there was no clear identifiable cause.

Prolonged intracellular presence of the drug is due to polyglutamination, seen in cells such as leukemic myeloblasts, synovial macrophages, lymphoblasts and epithelia. Acute toxicity causes dermatitis, mucositis, gastrointestinal bleeding, diarrhoea and myelosuppression. Other features include neutropenic fever, ischaemia, haemorrhage, electrolyte and fluid losses, hepatotoxicity and pulmonary toxicity. Precipitation of MTX and its metabolites in renal tubules occurs in acidic environment which leads to renal damage.[3] In the present case, the patient had developed mucocutaneous ulceration, leucopenia and thrombocytopenia. Ulceration of psoriatic plaques maybe due to higher uptake of MTX by hyperproliferative lesions.[5] Ulceration of LP lesions could be mediated by a similar mechanism.

Prompt recognition of symptoms and signs of MTX toxicity and admission to intensive care unit for further management is necessary to prevent complications. Treatment requires rapid hydration, alkalinisation of urine, haemodialysis

(facilitates rapid elimination of drug), leucovorin and glucarpidase. Granulocyte colony-stimulating factor can be used for the management of neutropenia. Barrier dressings and oral care should be practiced.[3] This patient was successfully managed with vigorous hydration, leucovorin and a single dose of pegfilgrastim.

Although the safety profile of MTX in LP has been proven in multiple studies, risk of toxicity still persists, and the patient should be monitored carefully for early detection and prompt treatment.

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