International Journal of Research in Dermatology
Suresh S et al. Int J Res Dermatol. 2023 Sep;9(5):304-306
http://www.ijord.com

DOI: https://dx.doi.org/10.18203/issn.2455-4529.IntJResDermatol20232549

Case Report

Rescue therapy in methotrexate toxicity: case report

Shruthi Suresh, Namratha C. Manjunath*, Sharath Kumar B. C.

Department of Dermatology, Kempegowda Institute of Medical Sciences, Bangalore, Karnataka, India

Received: 03 June 2023
Accepted: 10 July 2023

***Correspondence:**
Dr. Namratha C. Manjunath,
E-mail: drnamratamanjunath@gmail.com

ABSTRACT

Methotrexate (MTX) is widely used for the treatment of psoriasis. It has an antiproliferative action by inhibiting dihydrofolate reductase enzyme, therefore interferes with folic acid synthesis. MTX toxicity is rarely reported and the most common cause of it is accidental overdosage by the patient. This is a case report of a 51-year-old male, a known case of psoriasis, who presented with multiple erythematous tender plaques associated with burning sensation. He self-medicated with tablet MTX 5 mg daily for 10 days when the lesions got exacerbated and was found to be leucopenic. On skin biopsy, diagnosis of psoriasis with MTX induced epidermal necrolysis was established. Patient was treated with filgrastim 300 µg which was given subcutaneously 1 day apart. On follow up, lesions subsided and repeat counts were within normal limits. Patients should be explained about the selected treatment regime and discouraged from self-medicating.

Keywords: Drug toxicity, Erythematous plaques, Filgrastim, MTX

INTRODUCTION

Methotrexate (MTX) is widely used in psoriatic patients. However, reports of MTX intoxication are uncommon.[1] The majority of cases involve individuals with accidental overdosage as a result of complicated weekly oral regimen being misunderstood.[2] The objectives of present study are to identify early features of MTX toxicity [MTX induced epidermal necrolysis (MEN)], to establish early diagnosis and prompt treatment to prevent further worsening and to discuss diagnostic modalities in MEN.

CASE REPORT

A 51-year-old male patient, known case of psoriasis presented with chief complaints of peeling of skin since 15 days and raw areas in the mouth since 5 days. Lesions were associated with itching and were insidious in onset. Patient had history of application of native medication, history of drug intake prior to worsening of lesions and history of peeling of skin in the past. Patient reported self-medication with tablet MTX 5 mg for 10 consecutive days following which lesions got aggravated.

On cutaneous examination, multiple erythematous tender plaques were observed over the scalp, trunk, bilateral upper and lower limbs; multiple erosions were present on the buccal mucosae (Figure 1), lower lip, hard palate; PASI was 20.8 and BSA was 28%. Patient was a known case of psoriasis since 15 years and was started on topical steroid clobetasol ointment. He had history of admission for exacerbation of psoriasis 12 years back and was started on MTX 5 mg 1-0-1 once a week (2 tablets once a week) since then. But he reported non-compliance with medication. On general examination, bilateral pedal edema was detected. Skin biopsy revealed hyperkeratosis, focal mild acanthosis and plasma crusting with trapped neutrophilic debris (Figure 2). Epithelial cells exhibit dysmaturation with mild pleomorphism and occasional civette bodies. Also seen is mild spongiosis and basal cell vacuolar degeneration (Figure 3). Upper dermis shows vascular proliferation and mixed inflammatory infiltrate

with eosinophils (Figure 3). Diagnosis of psoriasis with MTX induced epidermal necrolysis was established.

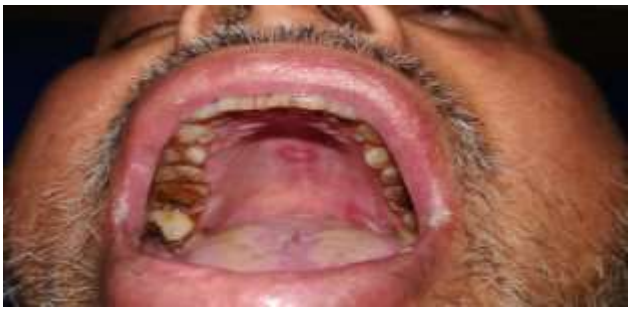

Figure 1: Buccal mucosal ulcerations on day 1.

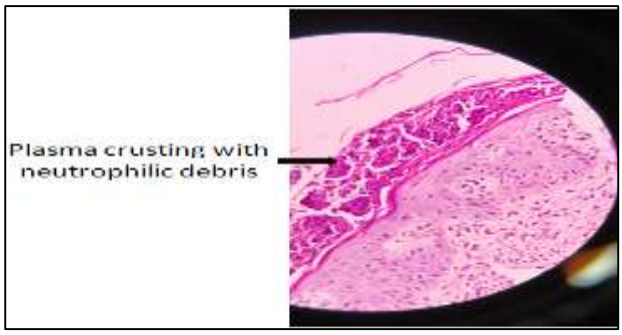

Figure 2: HPE showing plasma crusting with neutrophilic debris in epidermal layer of skin.

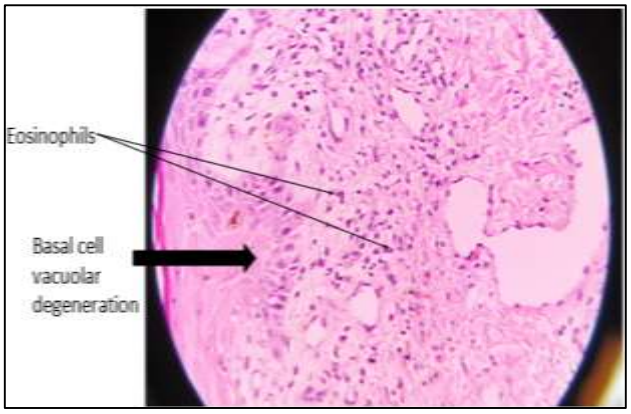

Figure 3: Edge biopsy of basal cell vacuolar degeneration and mixed inflammatory infiltrate with eosinophils.

Investigations revealed leucopenia (3940 cells/mm^3). In view of absolute neutrophil count <1500/mm^3, two doses of injection Filgrastim 300µg was given subcutaneously 1 day apart. On follow up, lesions subsided (Figure 4) and repeat counts were within normal limits (Table 1).

On discharge, patient was started on T. apremilast starter pack (for 1 week) along with topical agents for psoriasis. After the starter pack, patient was started on T. apremilast 30 mg 1-0-1. Patient was advised against self-medication and counselled regarding the consequences.

Table 1: Haematological profile of the case from day 1 to day 6.

Day	TC (cells/mm^3)	DC	Absolute neutrophil count (cells/mm^3)	Platelet (lakh/mm^3)
1	3940	N86 L10 E3 M1	3388	0.74
2	3040			0.81
3	2700	N70.6 L21.5 M5.9 E2 B0	1890	0.90
4	2090	N65 L28 M2 E5	1358	0.92
	Day 4-Inj. filgrastim 300 µg stat dose given SC			
5	Day 5-Inj. filgrastim 300 µg stat dose given SC			
6	10,270	N73 L19 M5 E3	7497	1.10

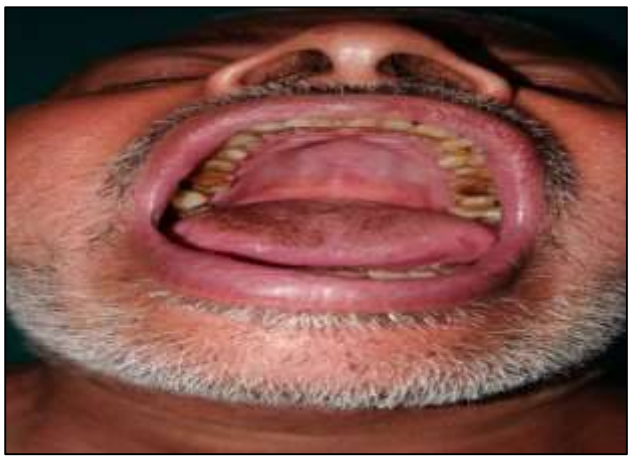

Figure 4: Buccal mucosa showing ulcerations on follow up.

DISCUSSION

Unintentional overdose of pills is the most frequent cause of acute methotrexate toxicity.[3] The most frequent reason for overdosing was listed as the long-term psoriasis treatment through self-medication.[4] Long-term usage of MTX has produced positive results with a high level of safety if used properly as well as under strict supervision.[5]

In our case, mucocutaneous lesions served as the warning sign for early detection of drug toxicity. Laboratory investigations revealed leucopenia and on skin biopsy, diagnosis of psoriasis with MTX induced epidermal necrolysis was established. Skin biopsy in our case served as a vital diagnostic modality for the diagnosis of MTX toxicity.

Our case was treated with injection filgrastim 300 µg S/C on day 4 and 5 in view of leucopenia. Hematologic profile showed improvement from day 1 to day 6 (Table 1). Other treatment modalities in acute MTX toxicity include folinic acid (leucovorin) and glucarpidase. Folinic acid rescue regimen replenishes intracellular stores of reduced folate and attenuates the MTX toxicity.[6] Glucarpidase enzyme works by rapidly metabolizing circulating (not intracellular) MTX to two inactive metabolites: Glutamate and 2,4-diamino-N-10-methylpteroic acid (DAMPA).[7] Patient was started on T. apremilast on discharge. Due to its immunomodulatory properties, apremilast partially inhibits the expression of proinflammatory cytokines thereby promoting the production of anti-inflammatory cytokines that play a pathogenic role in psoriasis.[8]

In our case, self-medication was the cause for overdosage of the drug. This highlights the importance of advising on illness chronicity, particular dose and the effects of overdosing.

CONCLUSION

MTX toxicity, though rare, if addressed on time, can prevent further complications like multi organ failure and mortality. In our case, muco-cutaneous lesions served as a warning sign for early detection of drug toxicity which was further confirmed by skin biopsy and the presence of leucopenia and hence can be considered as vital diagnostic modalities for the diagnosis of MTX toxicity. Our case was treated with T. apremilast after discharge. On follow up, lesions subsided and repeat counts were within normal limits. Hence, we conclude that early diagnosis and prompt treatment prevented further complications in our case and helped in reverting the condition of the patient. Also, patients should be explained about the selected treatment regime and discouraged from self-medicating. Side effects should also be explained.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: Not required

REFERENCES

1. Fridlington JL, Tripple JW, Reichenberg JS, Hall CS, Diven DG. Acute methotrexate toxicity seen as plaque psoriasis ulceration and necrosis: A diagnostic clue. Dermatol Online J. 2011;17(11).
2. Caliskan E, Tunca M, Açikgöz G, Arca E, Akar A. Accidental high-dose methotrexate toxicity due to an electronic prescribing error. Indian J Dermatol Venereol Leprol. 2014;80:268.
3. Agarwal KK, Nath AK, Thappa DM. Methotrexate toxicity presenting as ulceration of psoriatic plaques: a report of two cases. Indian J Dermatol, Venereol Leprol. 2008;74:481.
4. Pearce HP, Wilson BB. Erosion of psoriatic plaques: an early sign of methotrexate toxicity. J Am Academy Dermatol. 1996;35(5):835-8.
5. Chavan RB, Belgaumkar V, Gosavi AP, Deshmukh NS, Bhatt N, Agrawal K. Mucocutaneous ulcerations as a first sign of methotrexate toxicity. Dermatol Rev/ Przegląd Dermatologiczny. 2012;108(1):74-6.
6. Madke B, Singh AL. Acute methotrexate toxicity. Indian J Drugs Dermatol. 2015;1(1):46.
7. BTG International, Inc. Voraxaze (glucarpidase) intravenous injection, product information. West Conshohocken, PA: BTG International, Inc. 2013.
8. Paul C, Cather J, Gooderham M, Poulin Y, Mrowietz U, Ferrandiz C et al. Efficacy and safety of apremilast, an oral phosphodiesterase 4 inhibitor, in patients with moderate-to-severe plaque psoriasis over 52 weeks: a phase III, randomized controlled trial (ESTEEM 2). Brit J Dermatol. 2015;173(6):1387-99.

Cite this article as: Suresh S, Manjunath NC, Kumar SBC. Rescue therapy in methotrexate toxicity: case report. Int J Res Dermatol 2023;9:304-6.