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Methotrexate induced Toxic Epidermal Necrolysis in a Rheumatoid Arthritis Patient: A Case Report

Dr Lili Joarder[1], Dr. Lopamudra (Dhar) Chowdhury[2], Dr. Koustuv Chowdhury[3], Dr. Sanjit Mal[4], Abhik Saha[5]

[1]Second Year Post Graduate Trainee, Department of Pharmacology, R G Kar Medical College and Hospital, Kolkata
[2]Professor and Head, Department of Pharmacology, Coordinator of PvPI, R. G. Kar Medical College and Hospital, Kolkata, India
[3]Assistant Professor, Department of Pharmacology, Deputy Coordinator of PvPI R. G. Kar Medical College and Hospital, Kolkata, India
[4]Assistant Professor, Department of General Medicine, R. G. Kar Medical College and Hospital, Kolkata, India
[5]Junior Pharmacovigilance Associate, Indian Pharmacopoeia Commission, National Coordination Centre, R. G. Kar Medical College and Hospital, Kolkata, India

Corresponding Author: Dr. Lili

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ABSTRACT

Methotrexate (MTX), a folate antagonist, is a first-line disease-modifying antirheumatic drug (DMARD) used in the treatment of Rheumatoid arthritis (RA), a chronic autoimmune disorder characterized by synovial inflammation and joint destruction[1]. Despite its efficacy, MTX is associated with severe adverse drug reactions (ADRs), which are classified as Type B reactions—idiosyncratic or hypersensitivity reactions that are unpredictable and often dose-independent. Toxic epidermal necrolysis (TEN), a rare but life-threatening ADR, is a severe mucocutaneous condition characterized by extensive epidermal detachment and mucosal erosions, often triggered by medications. This case highlights the potential for MTX to induce TEN, hepatic failure, and renal failure, emphasizing the critical need for vigilant monitoring, early recognition, and prompt management of MTX toxicity, particularly in high-risk populations with comorbidities

Adverse drug reaction was reported to Adverse drug reaction monitoring centre (AMC) and severity was assessed by WHO-UMC Scale. Patient died after 3 days of admission. Score of Toxic epidermal necrolysis (SCORTEN Scale) is used to assess severity of the illness and to predict mortality[4].Early diagnosis, withdrawal of offending agent& timely proper supportive management can help in lowering the mortality.

Keywords: Methotrexate, Toxic Epidermal Necrolysis, Rheumatoid Arthritis, Adverse Drug Reaction, Hepatic Failure, Renal Failure.

INTRODUCTION

Methotrexate (MTX) is a cornerstone in the treatment of Rheumatoid arthritis (RA), psoriasis, and other inflammatory conditions due to its immunomodulatory and anti-inflammatory effects[5]. However, MTX is associated with significant toxicity, particularly in elderly patients and those with comorbidities such as chronic kidney disease (CKD). MTX toxicity primarily affects rapidly dividing cells, leading to mucocutaneous, hepatic, renal, and hematological complications[2]. Toxic

epidermal necrolysis (TEN) is a rare but life-threatening ADR characterized by widespread skin necrosis and mucosal involvement

CASE PRESENTATION

Patient Information:

A 61-year-old female with a history of rheumatoid arthritis (RA), non-hemorrhagic cerebrovascular accident (CVA), hypertension, and CKD was admitted to the medicine inpatient department (IPD) with generalized erythematous and ecchymotic rashes, oral mucositis, and small joint deformities. She reported a 7-day history of loose stools, hematuria, and dysphagia. Her medications included Tab Methotrexate, Ecosprin AV, Telmisartan, and folic acid.

Clinical Findings:

On admission, the patient exhibited generalized non-pruritic rashes, oral mucosal ulcers, and signs of systemic toxicity. Laboratory investigations revealed impaired renal and hepatic functions, pancytopenia, and a positive rheumatoid factor (RF). ENT evaluation for dysphagia suggested video laryngoscopic investigation under anesthesia.

Timeline:

Day 1: Patient admitted with rashes, oral mucositis, and systemic symptoms. MTX toxicity suspected.

Day 2: Oral mucosal ulcers progressed to necrotic ulcers. Dermatological consultation confirmed MTX-induced TEN. MTX was discontinued, and leucovorin rescue were initiated.

Day 3: Pancytopenia worsened, creatinine levels raised to 2.7 mg/dL, and hepatic function deteriorated further. The patient developed icterus and bleeding from rashes. Despite aggressive management, the patient succumbed to death.

Diagnostic Assessment:

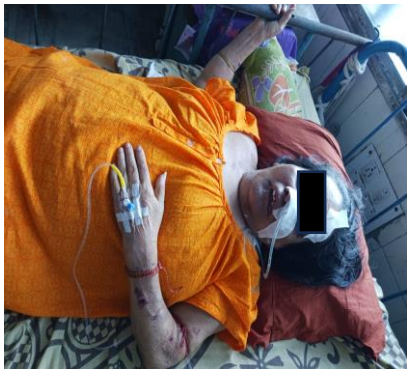
The diagnosis of MTX-induced TEN was based on clinical findings, Scorten scale[4], including widespread skin necrosis, mucosal involvement, and systemic toxicity. Laboratory findings supported the diagnosis, with elevated urea (105 mg/dL), creatinine (3.5 mg/dL), and pancytopenia (WBC: 900/μL).

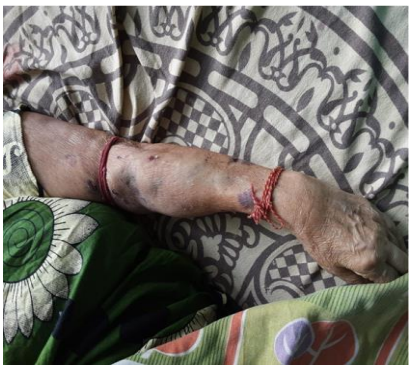
Therapeutic Intervention:

Management included discontinuation of MTX, folic acid supplementation, leucovorin rescue, and supportive care for hepatic and renal failure. Despite these measures, the patient's condition deteriorated rapidly.

Outcome:

The patient died on day 3 of admission due to multi-organ failure secondary to MTX-induced TEN.





Bullous lesions with multiple ecchymotic patches with oral mucosal involvement

DISCUSSION

MTX toxicity is a well-documented complication, particularly in patients with impaired renal functions. In this case, the patient's age, CKD, and concomitant use of other medications likely contributed to the TEN is a rare but serious ADR associated with MTX, characterized by widespread epidermal necrosis and mucosal involvement. Early recognition and prompt discontinuation of the offending drug are critical in managing such cases.

MTX toxicity involves inhibition of dihydrofolate reductase, leading to impaired DNA synthesis and cellular replication. This mechanism explains the involvement of rapidly dividing tissues such as the skin, gastrointestinal mucosa, and bone marrow[3]. The patient's pancytopenia, oral mucositis, and TEN are consistent with this mechanism.

This case highlights the importance of:

1. Monitoring high-risk patients (e.g., elderly, CKD) closely for signs of MTX toxicity.
2. Early recognition and intervention in cases of suspected ADR and reporting to the AMC.
3. Patient education regarding the risks of MTX and the importance of adherence to monitoring protocols.

CONCLUSION

MTX-induced TEN is a rare but life-threatening ADR that requires immediate recognition and intervention. This case underscores the need for vigilant monitoring of patients on MTX, particularly those with comorbidities such as CKD. Healthcare providers should maintain a high index of suspicion for ADRs and implement strategies to mitigate risks, including dose adjustments, folic acid supplementation, and regular monitoring of renal, hepatic and dermatological system.

Adverse drug reaction was reported to Adverse drug reaction monitoring centre (AMC). Causality assessment was done by WHO- UMC Scale and it was found to be probable.

Declaration by Authors

Conflict of Interest: The authors declare no conflict of interest

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