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UNDERSTANDING METHOTREXATE TOXICITY: RISKS AND SIDE EFFECTS

General Medicine

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ABSTRACT

Methotrexate (MTX) is a widely used antifolate agent for treating malignancies and autoimmune disorders. Despite its efficacy, improper dosing can lead to severe toxicity. We present a case of methotrexate toxicity in a 56-year-old female with rheumatoid arthritis, who developed pancytopenia, oral mucositis, and periorbital hyperpigmentation due to a dosing error. The patient required intravenous folinic acid therapy and supportive management, leading to gradual recovery. This study emphasizes the importance of patient education, regular monitoring, and early recognition of toxicity to improve treatment safety and outcomes.

KEYWORDS

INTRODUCTION

Methotrexate (MTX) is a cornerstone drug for autoimmune diseases and malignancies. It inhibits dihydrofolate reductase, disrupting DNA synthesis and cell proliferation. However, due to its narrow therapeutic index, improper dosing can result in serious complications affecting hematopoietic, gastrointestinal, renal, hepatic, and cutaneous systems.

CASE REPORT

A 56-year-old female with rheumatoid arthritis presented with oral ulcers, multiple ecchymoses, and hair fall for 8 days. She mistakenly took methotrexate daily instead of weekly, leading to pancytopenia, oral mucositis, and periorbital hyperpigmentation.

Laboratory Findings

Day	Total WBC (cells/cumm)	Hemoglobin (g/dL)	PCV (%)	Platelet Count (cells/cu.mm)
1	2000	9.2	28	26,000
2	1000	7.4	21	34,000
3	1000	6.0	21	13,000

RESULTS

The patient developed severe oral mucositis, pancytopenia, and periorbital hyperpigmentation. With folinic acid rescue therapy, blood counts normalized by day 14, emphasizing the need for strict dosing adherence.

DISCUSSION

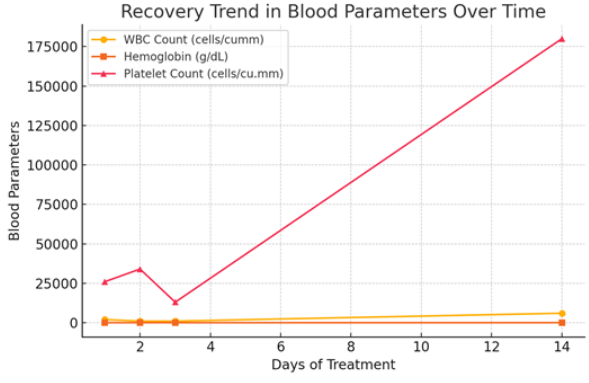
MTX may suppress the production of dihydro Folate reductase and decrease the stocks of tetrahydrofolate, both of which are required for the production of purine nucleotides and thymidylate, which are both required for cell replication and DNA synthesis, Cytotoxic MTX works mainly in rapidly multiplying cells, such as lymphocytes, which explains its significant anti-inflammatory. immunosuppressive, and apoptosis properties.

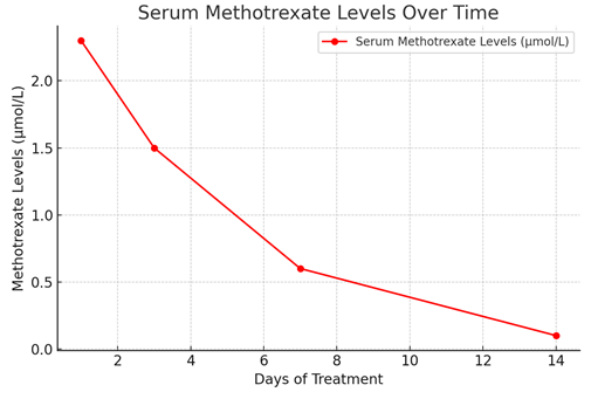
[I] When administered by the mouth, MTX is quickly but inefficiently absorbed, a process that exhibits interindividual heterogeneity. The protein bound to albumin is around 50 MTX is found in extracellular compartments, such as the synovium, as well as other organs, such as the kidney and liver. Liver aldehyde oxidase might transform MTX to 7-hydroxymethotrexate, which can later be transformed to MTX polyglutamy! (MTXPG)derivatives by the enzyme foly|polyglutamyl synthase (FPGS) and preferentially maintained within cells.

Mtx is eliminated via kidneys which are capable of excretion and re absorption within renal tubules Mtx is dangerous if administered improperly, most serious possible adverse effects is myelosuppression which causes the majority of the relatively infrequent fatalities caused by MTX. Other side effects include bone marrow suppression, liver fibrosis, pneumonitis, homeopathy, and baldness Hepatitis, kidney dystimetion, hyperglycemia, and being overweight are all risk factors for MTX. MTX is a hepatotoxic drug that may cause cirrhosis and hepatitis.

MTX toxicity may appear as bone marrow suppression and gastrointestinal ulcers. Other unusual but often observed characteristics include cutaneous ulceration within skin lesions in individuals with underlying psoriasis vulgaris;

The characteristic histology of cutaneous MTX toxicity, including keratinocyte enlargement and epidermal necrolysis, confirms clinical observations of direct toxic action. Dermatological side effeets, such as nonspocific morbilliform drug rashes, which are erythematous, macular, itchy, and limited to the neck and trunk, are reported to affect 14% to 15% of people. Under extreme circumstances, MTX may cause photoreactivation, photo intensification, and skin hyperpigmentation.





Future Directions

- Development of automated alerts in electronic health records (EHR) to prevent dosing errors.
- Personalized MTX dosing algorithms based on patient-specific factors.
- Further studies on alternative low-toxicity folate antagonists.
- Patient-centered counseling programs to reinforce adherence and safety measures.

CONCLUSION

Methotrexate toxicity can lead to life-threatening complications. Early recognition, aggressive management with folinic acid, and patient education are essential in preventing severe adverse effects. Physicians should ensure clear dosing instructions and routine blood monitoring to improve patient safety.

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