UCLA Health

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Abstract Form

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Project Title:	A Case of Subacute Methotrexate Toxicity in a Patient with Rheumatoid Arthritis

Research Category (please check one):

☐	**Original Research**	☒	**Clinical Vignette**	☐	**Quality Improvement**	☐	**Medical Education Innovation**

Abstract

Introduction:
Methotrexate (MTX) is an antimetabolite medication that disrupts folic acid synthesis. Its anti-cancer, anti-inflammatory, and immunosuppressive properties are commonly used to treat many hematological, rheumatological, and dermatological conditions. It is typically dosed once a week to prevent hepatic toxicity associated with daily dosing. MTX toxicity includes myelosuppression, mucositis, hepatotoxicity, neurotoxicity, pulmonary toxicity, impaired renal function and in severe cases, multiorgan failure, sepsis, and death. Risk factors for toxicity include impaired renal function, low albumin levels, and concomitant administration of drugs that alter MTX metabolism. Approximately 1.4% of patients can develop pancytopenia when being treated with low dose MTX. We present a case of mucositis and severe myelosuppression due to subacute methotrexate toxicity in a patient with rheumatoid arthritis (RA) due to accidental daily dosing of MTX.

Case Report:
A 66-year-old female with RA, hypertension, diabetes, and aortic stenosis presented to the emergency department with three days of painful, bleeding oral lesions and subjective fevers and chills. Her vital signs were stable. Her exam was notable for ulcerative lesions of the upper and lower lips covered by dried blood and erosive lesions of the buccal mucosa. Labs were notable for a new pancytopenia with white blood cell count (WBC) of 3.3 K/cumm, hemoglobin (hgb) 9 g/dL, and platelets 98 K/cumm. Her creatinine, albumin, and liver function tests were within normal limits. Six weeks prior to presentation she started 20mg of MTX weekly with folic acid daily for a new diagnosis of seronegative RA. During a pharmacist phone visit with the patient a week after initiation, it was noted that the patient was taking eight tablets of MTX weekly (4 tablets in the morning and 4 tablets in the evening one day a week) as prescribed. During the patient's hospitalization, rheumatology was consulted and it was discovered that she was taking four tablets of MTX daily due to misunderstanding the prescription instructions (total dose 420mg in 6 weeks). Her mucositis and pancytopenia were consistent with MTX toxicity. Thus, MTX was discontinued and she was started on leucovorin rescue therapy. The next day, her mucositis progressed with new oral and nasal lesions as well as overlying oral candidiasis and eight new erythematous vesicular lesions on her right upper chest. She was started on a low dose IV methylprednisolone taper to expedite healing of her oral lesions per recommendations of Dermatology. Her pancytopenia progressively worsened, with nadir of WBC of 0.9 K/cumm (absolute neutrophil count of 400), hgb 7.5 g/dL, and platelet count of 13 K/cumm on hospital day six. Hematology/Oncology was consulted for severe pancytopenia and recommended supportive management during bone marrow recovery. She was discharged on hospital day six after completing a five-day course of Leucovorin 20mg intravenous every six hours (regardless initial MTX level <0.2 umol/L). A week after discharge, her mucositis resolved and laboratory studies showed WBC of 5.3 K/cumm, hgb of 9.0 g/dL, and platelet count of 659 K/cumm. She was subsequently switched to daily hydroxychloroquine for treatment of RA.

Discussion:
Our patient had mucositis, dermatological toxicity, and severe myelosuppression from erroneously taking MTX daily instead of weekly. Daily accidental ingestion instead of weekly dosing is not an uncommon cause of subacute MTX toxicity. The mainstay of treating MTX toxicity includes prompt administration of folinic acid supplementation with leucovorin to prevent further cellular damage. Glucarpidase can be used in patients with renal dysfunction to help eliminate MTX. In some cases, granulocyte colony-stimulating factor has been used to treat the neutropenia and prevent severe infection. Our patient was treated with leucovorin rescue therapy with resolution of her symptoms and gradual improvement in pancytopenia. This case illustrates the multiple factors that contributed to this adverse event and identifies areas of improvement to prevent MTX overdose in the future. Clearer instructions (emphasized) regarding medication use and medication reconciliation by providers and pharmacists could prevent severe, or any, toxicity. Providers can limit the amount and number of refills (if any) they provide for new prescriptions and pharmacies can prevent early refills (electronic alerts, etc.).