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ACUTE METHOTREXATE TOXICITY DUE TO ACCIDENTAL OVERDOSE : A CASE REPORT

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Abstract : *Methotrexate (MTX) is widely used for managing autoimmune diseases and certain malignancies but has a narrow therapeutic index. This report highlights a case of acute MTX toxicity in a 50-year-old female due to a prescription error, presenting with pancytopenia, gastrointestinal symptoms, and systemic toxicity. Early recognition and treatment with leucovorin, urine alkalinization, and supportive care led to favorable outcomes. The case underscores the need for patient education and cautious prescribing to prevent such errors.*

INTRODUCTION

Methotrexate (MTX) is a folate antagonist that inhibits dihydrofolate reductase (DHFR), leading to reduced tetrahydrofolate (THF) levels and impairing thymidylate and purine synthesis. This mechanism underlies its effectiveness in treating autoimmune diseases such as rheumatoid arthritis and psoriasis, as well as malignancies like leukemia and lymphoma[1]. However, MTX's narrow therapeutic index predisposes it to dosing errors, potentially resulting in severe toxicity, including pancytopenia, hepatotoxicity, mucositis, and renal failure [1-3].

Acute MTX toxicity is often linked to accidental overdose or prescription errors, particularly in distinguishing MTX from folic acid tablets. Risk factors include renal impairment, concurrent use of nephrotoxic drugs, and delayed MTX clearance due to drug interactions [4,5]. This case highlights the clinical features, diagnosis, and management of acute MTX toxicity caused by a dosing error in a resource-limited setting.

CASE PRESENTATION

A 50-year-old female presented to the emergency department with complaints of loose stools for four days, high-grade fever for three days, and nausea, vomiting, abdominal pain, and skin rashes for one day. She also reported hematochezia. Two days before admission, she realized that she had mistakenly taken MTX 7.5 mg twice daily for seven days, believing it to be folic acid, as prescribed for her joint pain.

On examination, the patient was tachycardic (heart rate: 130 beats per minute), hypotensive (blood pressure: 100/60 mmHg), febrile (temperature: 101°F), and had a respiratory rate of 20 breaths per minute. Arterial blood gas analysis showed hypoxemia with primary respiratory alkalosis. Laboratory investigations revealed pancytopenia: hemoglobin was 8.2 mg/dL, total leukocyte count was 410/mm³, and platelet count was 60,000/mm³. Other findings included mild elevations in liver transaminases and a urine pH of 5.9.

A diagnosis of acute MTX toxicity was made based on clinical presentation and laboratory findings. Treatment was initiated with high-dose folinic acid (leucovorin) at 50 mg intravenously every six hours, alongside urine alkalinization with sodium bicarbonate to maintain a urinary pH above 7. Intravenous fluids were given for hydration, and broad-spectrum antibiotics were administered to prevent infections. Supportive care included antiemetics and monitoring of renal and hepatic functions.

Over the next five days, the patient's condition improved significantly. Fever and gastrointestinal symptoms resolved, and her pancytopenia showed gradual improvement. The patient was discharged in stable condition with strict instructions on medication use and follow-up monitoring.

DISCUSSION

Methotrexate toxicity is a dose-limiting complication often exacerbated by errors in prescribing or administering the drug. MTX inhibits DNA synthesis by blocking DHFR, with rapidly dividing cells, such as those in the bone marrow, gastrointestinal tract, and epithelium, being particularly vulnerable [6]. Acute toxicity manifests as pancytopenia, mucositis, hepatotoxicity, nephrotoxicity, and systemic inflammatory responses [7,8].

The risk of MTX toxicity is heightened in patients with renal dysfunction or concurrent use of nephrotoxic drugs, such as nonsteroidal anti-inflammatory drugs (NSAIDs) or antibiotics like trimethoprim-sulfamethoxazole, which inhibit MTX clearance [9]. Leucovorin rescue and urine alkalinization are the mainstays of management, aiming to reduce systemic toxicity and enhance MTX elimination. Timely initiation of these measures is crucial for preventing life-threatening complications [10].
This case underscores the importance of patient education regarding MTX dosing, especially in regions where prescription errors are common. Physicians should exercise caution when prescribing MTX and consider strategies such as distinct packaging or labeling to differentiate it from folic acid.

CONCLUSION

Acute MTX toxicity is a preventable yet potentially fatal condition that requires early recognition and prompt intervention. This case highlights the importance of patient education, judicious prescribing practices, and awareness of toxicity management. Further emphasis on healthcare provider training and robust prescription protocols can help reduce the incidence of such errors.

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