

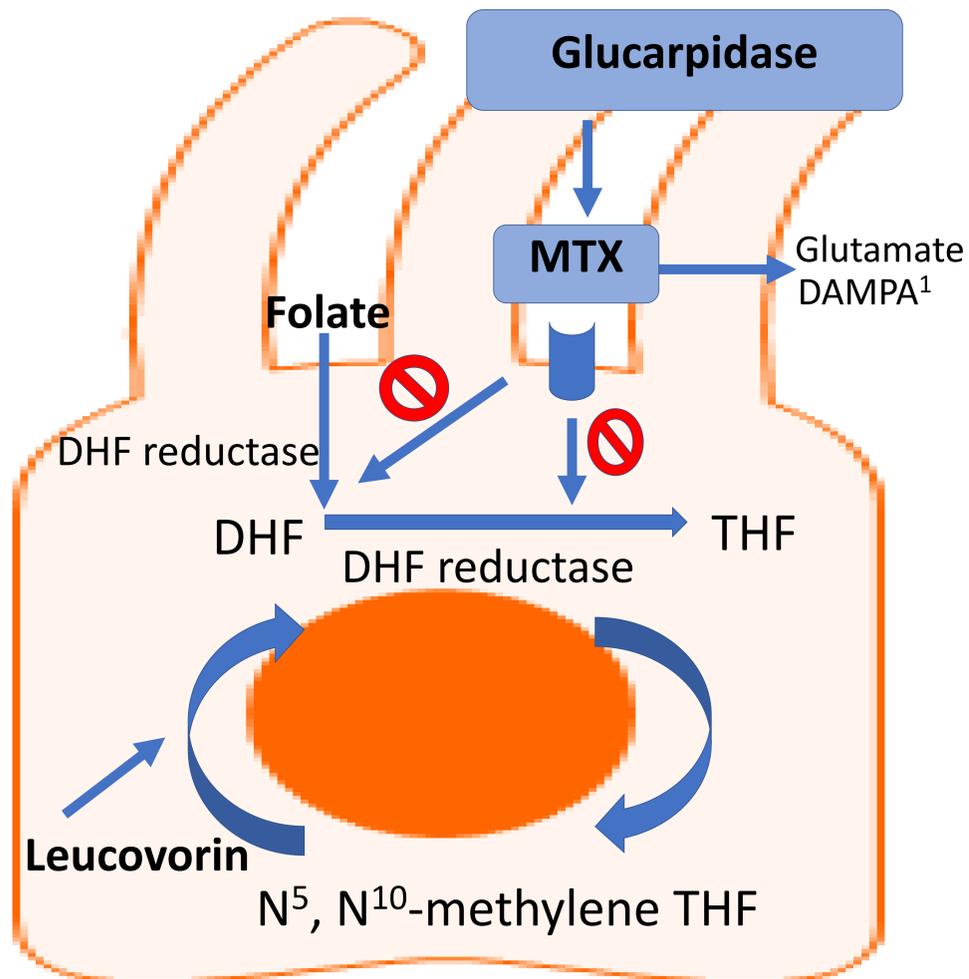
Rescue Glucarpidase Therapy in Low-dose Methotrexate Toxicity

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Introduction

- ❖ Methotrexate (MTX) is a folate antagonist used to treat certain malignancies (high dose) and autoimmune disorders (low dose).
- ❖ Its toxic effects are predominantly seen in higher division rate cells, such as the gastrointestinal (GI) epithelium and bone marrow stem cells.
- ❖ Glucarpidase is a recombinant bacterial enzyme that inactivates MTX and is approved as rescue therapy in high dose MTX toxicity with decreased renal clearance. However, little is known about its use in low-dose regimens.
- ❖ We present a case of a patient with low-dose acute MTX toxicity and kidney injury successfully treated with glucarpidase and supportive therapy.



Case presentation

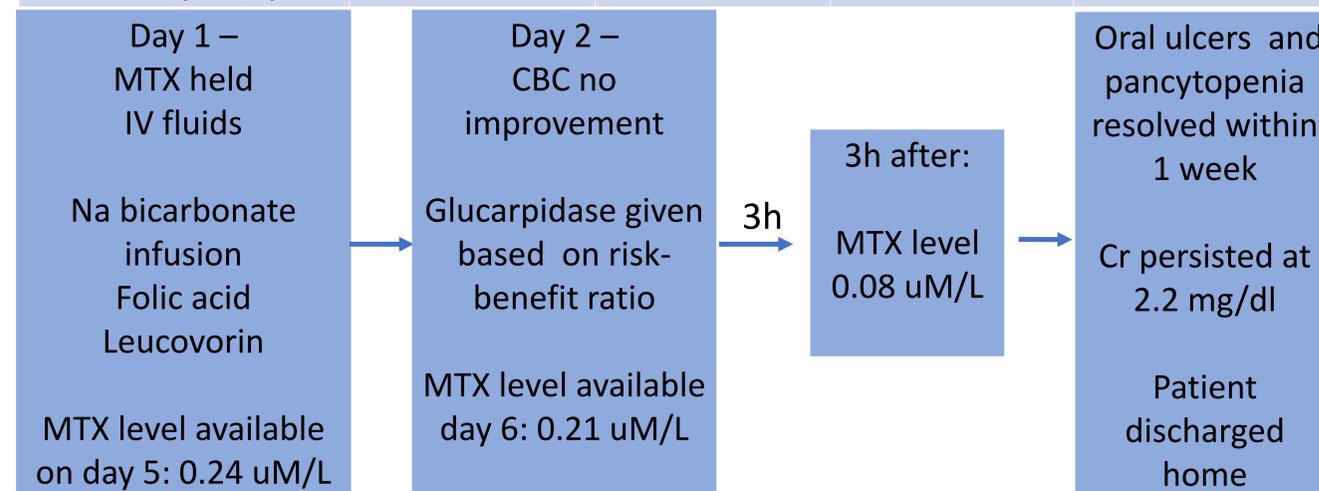
A 54-year-old male with rheumatoid arthritis (RA), type 2 diabetes, CKD2, HTN, HLD presented with one week of generalized weakness, diarrhea, fevers, and three days of painful oral ulcers and a violaceous rash on upper extremities (Fig.1).

Recently admitted to another hospital with acute kidney injury and had continued taking MTX 5 mg three times a week. He was not taking folic acid.



Fig.1

	Day 1	Day 2	Day 3	Day 6
Hb (g/dL)	6.7	7.3	8.9	7.3
WBC (/mcl)	1,840	2,800		10.4
ANC (/mcl)	1,000	1,156		5,800
Platelets (x10 ³ /mcl)	36	38	38	119
Cr (mg/dL)	2.2	2.3		
Alb (g/dl)	2.3			
MTX level (uM/L)	0.24	0.21	0.08	



Discussion

- ❖ Common side effects of MTX include skin, oral mucosa, and GI lesions. Pancytopenia occurs in < 1% of patients with low-dose MTX and usually resolves after stopping the drug. Sustained bone marrow suppression can occur in cases with hypoalbuminemia or impaired renal function, both seen in our patient.
- ❖ Most of the evidence for glucarpidase use refers to high-dose MTX toxicity, but little is known on low-dose toxicity management.
- ❖ Glucarpidase decreases MTX plasma level by 98% in the first 30 minutes. It is approved for MTX levels >1 uM/L with concomitant impaired kidney function.
- ❖ In our case, it was administered before MTX level results due to high mortality risk with a favorable response and good patient outcome.

Educational objectives

- ❖ Low dose MTX toxicity is treated supportively with IV fluids, alkalization and rescue therapy with leucovorin.
- ❖ Glucarpidase can be considered as off-label in life-threatening situations.
- ❖ There are published case reports of fatal outcomes in similar cases which did not receive glucarpidase.
- ❖ Low dose MTX should be prescribed once a week and should be accompanied by folic acid daily for lower risk of toxicity.

References

- ❖ Ramsey, L. B., Balis, F. M., O'Brien, M. M., et al (2018). Consensus guideline for use of glucarpidase in patients with high-dose methotrexate induced acute kidney injury and delayed methotrexate clearance. *The oncologist*, 23(1), 52.
- ❖ Shaikh N, Sardar M, Raj R, Jariwala P. A Rapidly Fatal Case of Low-Dose Methotrexate Toxicity. *Case Rep Med*. 2018;2018.