Methotrexate and Mucositis: A Merry-Go-Round for Oncologists

Abstract
High-dose methotrexate is the backbone of various regimens for treating lymphoid malignancies. Mucositis is a well-known, dose-related side effect of methotrexate. Prophylactic measures such as folinic acid rescue are useful but do not prevent mucositis in all the cases. Once severe mucositis (WHO Grade IV) sets in, mortality is very high. The index case highlights the natural course of methotrexate-induced mucositis and the need for swift and preemptive intervention.

Keywords: Lymphoid malignancy, methotrexate, mucositis

Introduction
Methotrexate is a commonly used drug for lymphoid malignancies as well as connective tissue disorders. It is known to cause an array of complications including myelosuppression, mucosal ulcers, skin rash, and liver toxicity. Because Sidney Farber reported its usefulness in acute lymphoblastic leukemia, it has been used rampant and successfully in various lymphoid malignancies.[1] Although the incidence of life-threatening complications has decreased with precautionary measures such as folinic acid rescue (after high-dose methotrexate [HDMTX]), yet it is a reality. In this case report, we present a case of HDMTX-induced severe mucositis despite having received folinic acid rescue. We highlight the course of potentially life-threatening mucositis effectively managed with timely intervention with supportive care.

Case Report
A 22-year-old female, a known case of acute lymphoblastic lymphoma, on modified BFM 2000 protocol was admitted with complaints of painful, oral ulcers and difficulty in swallowing for 2 days. One week earlier, she had received HDMTX (5 g/m²) followed by folinic acid rescue. On examination, she had restricted mouth opening and multiple oral mucosal ulcers [Figure 1a] (mucositis WHO Grade IV). Her investigations revealed hemoglobin 110 g/L, total leukocyte count (TLC) 0.9 × 10⁹/L, absolute neutrophil count 0.04 × 10⁹/L, platelet 70 × 10⁹/L, and normal peripheral blood smear. Her serum urea was 22 mg/dL, creatinine 0.9 mg/dL, and alanine transaminase 42 U/L.

Discussion
Methotrexate is used as low dose (<50 mg/m²), intermediate dose (50–500 mg/m²), and high dose (>500 mg/m²).[2] HDMTX is used for central nervous system (CNS) prophylaxis in acute lymphoblastic leukemia/lymphoma. It is also used therapeutically in primary CNS lymphoma, leptomeningeal metastasis, and osteosarcoma. The intermediate-and low-dose methotrexate is used for gestational trophoblastic disease and inflammatory disorders such as rheumatoid
Methotrexate and mucositis

Conclusion

Methotrexate-induced mucositis may be fatal if not treated proactively. However, a swift and preemptive intervention results in a rewarding outcome. A resplendent clinical photograph of the index patient demonstrates the natural history of a successfully managed Grade-IV mucositis and the HDMTX cycles continued albeit at a lower dose!

Consent

Informed signed written consent was taken from the patient involved.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient has given her consent for her images and other clinical information to be reported in the journal. The patient understands that her name and initials will not be published and due efforts will be made to conceal identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

References

