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Methotrexate Induced Oral Mucositis and Bone Marrow Suppression in Psoriatic Patient

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Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

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Case Report

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ABSTRACT

Methotrexate is an antimetabolite which binds to the dihydrofolate reductase enzyme and used in the treatment of malignant disorders and autoimmune diseases. Myelosuppression is a serious complication of methotrexate toxicity. The following case describes a case of 67 year old male patient diagnosed with psoriasis and wrongly taken methotrexate 7.5 mg daily for 3 days and twice daily for 4 days. He presented with oral mucositis and his lab reports showed myelosuppression. Our case emphasizes the significance of effective patient counselling to ensure the understanding of prescription and to prevent drug toxicity. The key learning points of our case report include the importance of adhering to prescribed medication regimens, awareness of MTX toxicity, early initiation of folinic acid as an antidote, vigilant monitoring of toxicity, and effective patient education on proper medication use. Adherence to established MTX therapy guidelines in dermatological conditions is crucial to minimize the risk of patient.

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Keywords: Methotrexate; psoriasis; myelosuppression; mucositis.

1. INTRODUCTION

From the 1950s, Methotrexate (MTX) is a widely used systemic immunosuppressive agent and by 1951, MTX was introduced as antipsoriatic agent, it is approved by FDA (Food and Drug Administration) for this indication in 1972. MTX inhibits dihydrofolate reductase, disrupting DNA synthesis and impeding cell proliferation, particularly in rapidly dividing cells such as those in immune system and skin. Additionally, it can supress pro-inflammatory cytokines, contributing to its anti-inflammatory effects [1,2]. Apart from the use of MTX in malignant disorders, it is also taken orally in low doses to control the conditions like rheumatoid arthritis and psoriasis [3]. MTX is considered as a drug that is relatively safe when it is prescribed at low dose regimen that is not exceeding 25mg/weekly. The severe acute toxicity is rare and mostly presents with cutaneous ulceration, bone marrow suppression and mucositis [4,5,6]. Approximately 78% of MTX treated psoriasis patient develop adverse drug reactions (ADR) where nausea and vomiting are common adverse reaction with ecchymosis, reversible alopecia, pruritus and in severe cases include acute ulcerations of psoriatic plaques, toxic epidermal necrolysis and mucosal erosions [7]. Most cases occurs as a result of the inadvertent overdosing due to erroneously taking drugs daily [4].

2. CASE REPORT

A 67 year old, male patient with known case of Diabetes mellitus and psoriasis was admitted to the hospital with complaints of psoriasis vulgaris. He was newly prescribed MTX, with advice to take MTX 7.5 mg tablet once weekly, but the patient had wrongly taken once daily for 4 days and then 7.5mg BD for 3 days. Cumulative dose was 75 mg MTX. He developed oral mucositis and psoriasis vulgaris over lower limb, elbow and leg. His laboratory investigations revealed myelosuppression with Hb:10.2 g/dl, WBC:3540/ mm^3, RBC:3.5 million/mm^3, platelets:71,000/mcL, also the creatinine was 1.5 mg/dL, urea:65 mg/dl and sodium 133 mmol/L. Based on physical and laboratory findings and temporal association, MTX toxicity was diagnosed. The patient was admitted in the hospital and treated with IV fluids NS, RL, Inj. Folinic acid, Inj. Vitamin B complex, Pantoprazole, Ointment Clobetasol, T.Folic acid and Antibiotics. The patient showed good improvement, and discharged with follow up for psoriasis with the dermatologist.

3. DISCUSSION

In dermatology, MTX has used as a relatively safe drug dosage (7.5 mg to 25 mg/week), with the toxicity and side effects associated with dose dependent mechanisms or idiosyncratic. The latter occurs mostly in cells that proliferate faster, like hematopoietic bone marrow cells, and epidermal cells [2]. A low dose of MTX in psoriasis infrequently produces toxicity, and most of those occur due to the failure to adhere to the recommended guidelines. The risk of the toxicity is more if additional doses of methotrexate administered than the usual scheduled weekly dose [8]. In our case, the patient took 7.5mg once daily for 4 days and then 7.5mg BD for 3 days following he developed oral mucositis and psoriasis vulgaris. The patient has been recovered on treatment with IV fluids, injection folinic acid and other supportive treatment within 6-8 days. Methotrexate toxicity has its impact on skin, gastrointestinal mucosa, bone marrow, liver and kidneys. Skin ulceration due to MTX toxicity are restricted to psoriatic plaques by higher uptake of MTX by hyperproliferative psoriatic plaques than the normal skin [8].

In renal impairment cases, low doses are enough to cause bone marrow suppression and also diabetes mellitus may have role for altering the pharmacokinetics of MTX by physiological environment altering of the body [9]. In the year 1996, a literature review by Pearce and Wilson have identified 47 cases of MTX induced skin ulceration which was reported between the years of 1951 and 1967 and further of 17 cases between the year 1967 and 1996 (including two of their own patients and those of which by Roenigk et al. and Lawrence and Dhal) [10].

The treatment is done with the immediate suspension of the drug and administration of parenteral folinic acid in the dose of 10mg/m^2 of body surface Folinic acidic is an antidote of choice used for the MTX toxicity. It is said that earlier the treatment of folinic acid, higher the success rate, mainly concerning the venture to avoid or to interrupt myelosuppressive effects [2].

In most cases bone marrow toxicity is dose dependent and responded to folinic acid. Pancytopenia, leukopenia, anemia and thrombocytopenia are rarely occur. In a review by Gutierrez-Urea and associates the clinically significant pancytopenia was found in 1% to 2% of rheumatoid arthritis on MTX therapy [11].

Management of delayed Methotrexate excretion: Glucarpidase (carboxy-peptidise, CPDG2) which was approved by US FDA for treatment of the increased plasma MTX concentration (>1µmol/l) in patients with delayed MTX clearance due to the impaired kidney function that may result in bone marrow suppression [8]. Methotrexate is the best option with great therapeutic value for psoriasis and most importantly it should be well guided by the physician [2].

4. CONCLUSION

In our case report, the patient presented with complaints of psoriasis vulgarise, oral mucositis with MTX induced bone marrow suppression shows that the improper dosage of methotrexate will lead to toxicity as it has low therapeutic index. Therefore it is important to ensure the correct understanding of prescription. Providing MTX drug in weekly dosage pack and effectively communicating with the patients about unusual administration of dosage regimen can reduce adverse effects. Physicians should encourage patient feedback to ensure comprehension of the weekly dosage regimen, emphasizing that this medication should not be employed on an “as-needed” basis for symptomatic relief. MTX constitutes a cornerstone of dermatological therapy, adhering to rigorous guidelines for initiation and monitoring to mitigate patient risk effectively.

CONSENT

As per international standards or university standards, patient(s) written consent has been collected and preserved by the author(s).

ETHICAL APPROVAL

As per international standards or university standards written ethical approval has been collected and preserved by the author(s).

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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