Case report

METHOTREXATE INDUCED ORAL MUCOSITIS AND BONE MARROW SUPPRESSION IN PSORIATIC PATIENT

ABSTRACT

Methotrexate is an antimetabolite that binds to the dihydrofolate reductase enzyme and is 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 a 67-year-oldmale patient diagnosed with psoriasis and wrongly takingmethotrexate 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 counseling to ensure the understanding of prescriptions and to prevent drug toxicity.

INTRODUCTION

From the 1950s, Methotrexate (MTX) wasa widely used systemic immunosuppressive agent, and by 1951, MTX was introduced as an antipsoriaticagent, it was approved by FDA(please write the official name of this federation) for this indication in 1972. MTX is a folate antimetabolite that binds to dihydrofolate reductase enzyme which leads to impaired DNA synthesis and repair[1,2]. Apart from the use of MTX in malignant disorders, it is also taken orally in low doses to control conditions like rheumatoid arthritis and psoriasis[3]. MTX is considered a drug that is relatively safe when it is prescribed at a low dose regimen that does not exceed 25mg/weekly. The severe acute toxicity is rare and mostly presents with cutaneous ulceration, bone marrow suppression, and mucositis[4]. Approximately 78% of MTX-treatedpsoriasis patients develop adverse drug reactions (ADR) where nausea and vomiting are common adverse reactions with ecchymosis, reversible alopecia, pruritus, and in severe cases acute ulcerations of psoriatic plaques, toxic epidermal necrolysis, and mucosal erosions[5]. Most cases occur as a result of inadvertent overdosing due to erroneously taking drugs daily[4].

CASE REPORT

A 67-year-old, male patient with a 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 7.5mg tablet once weekly, but the patient had wrongly taken once daily for 4 days and then 7.5mg BD for 3 days. The cumulative dose was 75 mg MTX. He developed oral mucositis and psoriasis vulgaris over the 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 to the hospital and treated with IV fluids NS,RL, Inj. Folinic acid, Inj. Vitamin B complex, T.Pantoprazole, Ointment Clobetasol, T.Folic acid, and Antibiotics were given.

DISCUSSION

In dermatology, MTX has been used as a relatively safe drug dosage(7.5mg to 25mg/week), with toxicity and side effects associated with dose-dependentmechanisms 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 toxicity is higherif additional doses of MTXare administered than the usual scheduled weekly dose[6]. 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 of folinic acid, and other supportive treatment within 6-8 days. MTXtoxicity has an impact on the skin, gastrointestinal mucosa, bone marrow, liver, and kidneys. Skin ulceration due to MTX toxicity isrestricted to psoriatic plaques by higher uptake of MTX by hyperproliferative psoriatic plaques than the normal skin.[6].

In renal impairment cases, low doses are enough to cause bone marrow suppression, and also diabetes mellitus may have a role inaltering the pharmacokinetics of MTX by physiological environment altering of the body[7]. In the year 1996, a literature review by Pearce and Wilson identified 47 cases of MTX-inducedskin ulceration which were reported between the years 1951 and 1967 and further of 17 cases between the years1967 and 1996 (including two of their patients and those of Roenigk et al. and Lawrence and Dhal) [8].

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 acid is an antidote of choice used for the MTX toxicity. It is said that the earlier the treatment of folinic acid, the higher the success rate, mainly concerning the venture to avoid or to interrupt myelosuppressive effects[2]. In most cases, bone marrow toxicity is dose-dependentand responds to folinic acid. Pancytopenia, leukopenia, anemia, and thrombocytopenia rarely occur. In a review by Gutierrez-Urea and associates clinically significant pancytopenia was found in 1% to 2% of rheumatoid arthritis on MTX therapy[9].

Management of delayed Methotrexate excretion: Glucarpidase (carboxy-peptidase, CPDG2) which was approved by theUS 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[6].

Methotrexate is the best option with great therapeutic value for psoriasis and most importantly it should be well guided by the physician[2].

CONCLUSION

Our case presented with complaints of psoriasis vulgarise, and oral mucositis with MTX-induced bone marrow suppression shows that the improper dosage of methotrexate will lead to toxicity as it has a low therapeutic index. Therefore it is important to ensure the correct understanding of prescription. Dispensing the MTX drug in weekly dosage packsand communicating effectively with the patients about unusual administration of dosage regimen can reduce adverse effects. Physicians should embolden the feedback of patients to ensure that patient understands the weekly dosage regimen schedule and this medication should not used “as needed” for symptomatic control. MTX is well well-establishedelement of the dermatology therapeutic arsenal governed by robust guidelines for introduction and monitoring which aims to minimize the patient risk **[6,8].**

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