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Methotrexate Induced Muco-Cutaneous Toxicity - A Rare Case Report

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ABSTRACT

We are reporting a rare case of methotrexate induced apoptosis related cytotoxic reactions in the form of painful, oedematous, erosive and ulcerative lesions involving abdomen, lumbo-sacral area, extremities and oral mucous membrane in a 70 years old male patient of psoriasis vulgaris following chronic and high dose ingestion of methotrexate.

Introduction-

Methotrexate (MTX) is one of the folic acid antagonists with potent chemotherapeutic and immunosuppressive effect.It competitively and irreversibly binds to dihydofolate reductase enzyme within 1 hour. This prevents the conversion of dihydrofolate to tetrahydofolate. Tetrahydrofolate is necessary for DNA and RNA synthesis. It also partially and reversibly inhibits thymidylate synthetase within 24 hours after administration of methotxexate. The overall effect of methotrexate is inhibition of cell division being specific for S phase of normal cell cycle.

In dermatology FDA approved indications are psoriasis and Sezary syndrome. It can be used off labely in proliferative dermatosis, immunobullous dermatosis, autoimmune connective tissue diseases, vasculitis etc.

Methotrexate has many side effects like hepatotoxicity, bone marrow suppressive effect, pulmonary toxicity, gastro intestinal side effects and reproductive side effects. Methotrexate induced cutaneous side effects have been rarely reported in the literature. With this background we present a rare case of methotrexate induced mucocutaneous side effects in a patient of Psoriasis vulgaris.

Case report -

70 year old male patient, who is known case of Psoriasis since 12 years came to our OPD with chief complaints of reddish lesions all over body since 10 days. Patient had taken 185 mg of T. Methotrexate in divided dose under supervision of private practioner in total duration of past 1 year.

As the patient was familiar with the methotrexate treatment, he took high weekly dose of methotrexate i.e 20mg/week for 7-8 month of his own. After this dosing his psoriatic plaques over abdomen and lumbo sacral area became painful oedematous , erosive with mild perilesional erythema[Fig 1 & 2]. Similar changes were also noticed on the lesions present over extrimities . Few erosive and ulcerative lesions were also present over lower lip and buccal mucous membrane[Fig 3]. Investigations were Hb –7.8 gm % ,TLC – 1700/ cumm , Platlets – 69000/cumm, FBS – 101mg%, PPBS – 153 mg%, Sr Urea – 33mg%, Creatinin – 1.6 mg%, SGOT – 23 IU/l , SGPT – 28IU/l .USG – Grade 1 Prostatomegaly with cystitis with normal hepatobiliary system. With this clinical and laboratory findings the diagnosis of methotrexate induced toxicity was made.

Immediately after admission methotrexate was stopped and patient was treated with Inj vitcofol 2cc im alternate day for 6 days and Tab Folic acid 5mg bid for 26 days.

Clinically patient gradually recovered with above mentioned treatment in 4 weeks [Fig. 4]. Routine haematological investigations after 4 weeks of treatment showed improvement in his blood counts. His Hb was10.4 gm%, TLC – 6700/cumm and platelet count was 1.55 lakhs.

Discussion –

Methotrexate induced cutaneous side effects have been rarely reported in literature and it is mostly related to dosing and duration of methotrexate. Skin eruptions following high dose of methotrexate treatment appears to result from cytotoxic T lymphocyte and mononuclear cells that induce apoptosis in keratinocytes expressing drug derived antigen at their surface. [1,2] .Regions of rapid proliferation such as the oral lining mucosa show a greater frequency of ulceration than masticatory mucosa or body skin with chemotherapy treatment [3,4,5]. Thus in our case mucosal eruptions appear to be induced by toxic effect of high dose of methotrexate on rapidly diving cells. Methotrexate's toxic effects on abdomen and extremity can be due to direct toxic effect on acral epidermis from high concentrations of chemotherapy agents in areas that are vasculat cul-de-sacs [6]. Toxicity over abdomen and back could be correlate with the fact that mitotic index correlates significantly with epithelial thickness, with a thicker region shows high rate of proliferation, albeit to a lesser extent then acral or mucosal skin [7,8].

Skin ulcerations within the psoriasis plaques usually occur within one month of starting or restarting therapy[9], however, such events have been reported following chronic administration of methotrexate.[10,11] Healing is rapid with complete re-epithelialization occurring within 10-12 days after discontinuation of methotrexate [9].

Our patient took methotrexate chronically for more than one year and specially in a higher dosing since past 7-8 months. Our patient recovered completely within 3-4 weeks after stopping methotrexate. Patient was rechallenged after 1 month of complete recovery with low dose of methotrexate without any side effects.

Conclusion

In our case methotrexate induced apoptosis related cytotoxic reactions were likely due to the result of chronic ingestion of high dose.



Fig 1

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Fig 2



Fig 3



Fig 4

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