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Case study of Methotrexate induced oral ulcers

Dr. Amit Dubey[1] (PG Resident), Dr. Ankur Singh Baghel[2] (PG Resident) & Dr. Ashish Sharma[3] (F.I.A.E Head & Professor), Dr. Rahul Bharaskar (PG Resident)

Department of Medicine, RDGMC Ujjain, M.P.[1,2,3&4]

Corresponding Author: Dr. Amit Dubey

Abstract
Methotrexate is well established drug in the treatment of various neoplastic diseases. More recently it has become use full as once-weekly, low-dose treatment of disorders such as psoriasis and rheumatoid arthritis. Clinical trials have shown its effectiveness in these conditions and it is likely that dentists will encounter patients taking this drug in general dental practice. Oral ulceration can occur as a side effect of methotrexate therapy. This may be due to lack of folic acid supplementation or overdosage due to confusion regarding its once-weekly regime.

1. INTRODUCTION

MTX is an antimetabolite, antifolate agent developed in 1948, used to treat certain forms of cancer. It is also commonly used to treat rheumatoid arthritis in both adults and juveniles and severe psoriasis. MTX interrupts the synthesis of both DNA and RNA and slows or stops the growth of rapidly dividing cells, including mucosal, cancer and bone marrow cells. MTX induces a deficiency of folate-dependent co-enzymes and suppresses the immune system.MTX is a bicarboxylic acid, a folic acid analogue that inhibits dihydrofolate reductase enzyme. The later is required to reduce folate to an active form, which acts as a co-factor in the production of nucleic acids essential for DNA synthesis. Inhibition of this enzyme by MTX causes a reduction in DNA formation and cell turnover and is responsible for both its therapeutic and the more common side effects, such as myelosuppression and mucositis. Psoriasis is a chronic, inflammatory, non-contagious skin condition usually affecting the skin of the elbows, knees, and scalp. The cells in the superficial skin layer multiply more quickly than normal, causing thickened areas of skin, and producing thick scaling plaque. It has a variable course with periodic periods of remission and exacerbation. Both biologic and non-biologic agents are used in its treatment. Non-biologics, such as MTX, suppress the immune system and are considered first line treatments. Biologics target certain aspects of the immune system contributing to the pathogenesis of psoriasis.

Regular blood and liver function tests are required for patients undergoing systemic treatment to monitor the toxicities of these medications, all of which must be avoided in pregnancy.
Oral ulceration is reported in 14% of patients on long-term, low-dose MTX treatment. The lesions may be caused by a lack of folic acid supplementation or an over-dosage of the MTX drug. While the lesions are aggravated by chronic drug administration, they will disappear three weeks after suspension of the MTX administration. This adverse effect of MTX is mostly dose-dependent and usually occurs due to an accidental over dosage.
Oral side effects are of importance to the patient not only because of the associated pain, but also because it affects the ability to eat. This aggravates the folate deficiency, causes weight

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loss and leads to a general weakening of health.[7] Folic acid supplementation can reduce MTX-induced mucosal and gastrointestinal side effects by 79%.

Most of the cases of ulceration induced by methotrexate have been described in patients treated with low-dose (7.5-25mg/wk) instead of a higher dose of methotrexate (100-250mg/m2/wk), probably because hyperproliferative psoriatic plaques are more susceptible to the influence of folate antagonism.

One of the primary toxic effects of methotrexate is myelosuppression. MTX suppressed hematopoiesis has been confirmed to cause anemia, aplastic anemia, leukopenia,pancytopenia,neutropenia,thrombocytopenia, lymphadenopathy, and lymphoproliferative disorders. MTX is thus contraindicated in patients with low hematologic cell counts or pre-existing myelosuppression. Regular monitoring of a complete blood count (CBC) is compulsory and some cases may require temporary discontinuation of the therapy. In addition, folate therapy or leucovorin rescue may prevent or palliate side effects. Low dose methotrexate is increasingly being administered in the control of psoriasis. It is generally an effective and safe medication, with oral ulceration being its most common side effect. Oral ulceration may be due to dosage error or folate deficiency and these problems should be clarified in patients who present with oral ulceration while using methotrexate.

Presenting case-

- Patient name Dayaram 48/male resident of ghattiya shajapur,farmer by occupation,hindu by religion admitted at ucth ujjain at 22/12/2021 with complain of oral cavity ulcers since 10 day which was acute in onset, progressive in nature. Firstly presently over tongue and then progress to hard palate, single ulcer is present over hard palate, Painful ulcer, associated with slouging and crusting with no h/o of local trauma and no h/o of bleeding and pus discharge.
- Patient is a case of plantar eczema for which he was prescribed methotrexate 5mg, patient is ignorant took 10mg of methotrexate, diagnosed in 2013 no significant past medical illness, No history of previous hospitalization
- GENERAL EXAMINATION- BP-130/80MMHG, PULSE-102/MIN,SPO2-97%ON RA,PALLOR,ICTERUS,CYANOSIS,CLUBBING,LYMADNOPATHY,JVP NOT RAISED,EDEMA= ABSENT
- SYSTEMIC EXAMINATION- WNL
- **INVESTIGATION**-HB-11.9,TLC-26.2,platelets-1.09LACS,SGOT-41.5,SGPT-82,SODIUM- 134,POTASSIUM- 4.8, UREA-64, CREATININE- 7.8→4.6
- MRI PNS- DIFFUSE EDEMA/THICKENING INVOLVING RIGHT BUCCAL MUCOSA AND BUCCINATOR MUSCLE EXTENDING IN SOFT TISSUE FAT OF CHEEK REGION. FOCAL MARROW EDEMA INVOLVING ALVEOLAR ARCH OF MAXILLA IN RELATION TO MOLAR TOOTH REGION
- On basis of these a provisional diagnosis of methotrexate induced oral ulcer, ? Stevens johnsons syndrome,? oral tb was made

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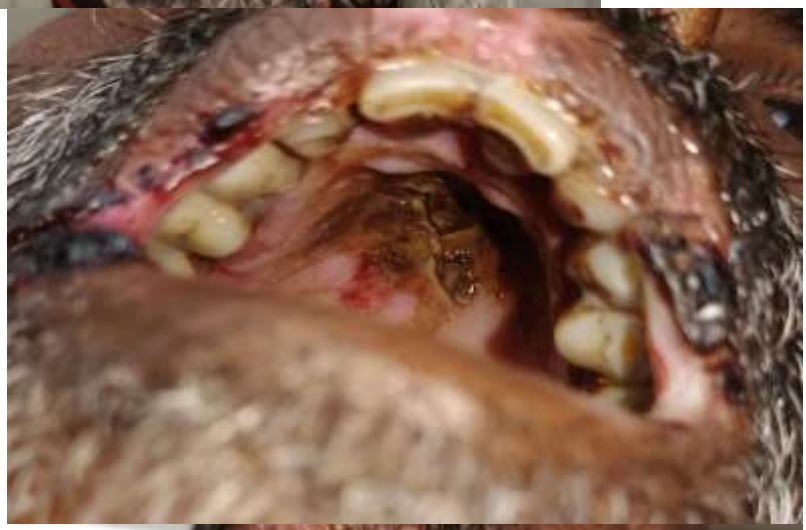

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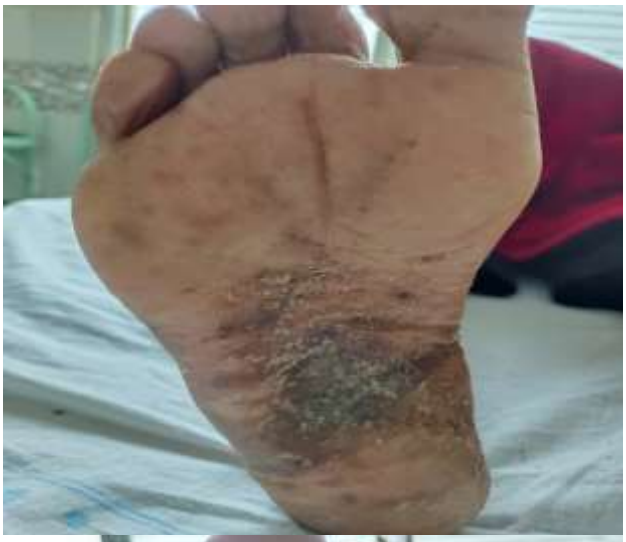
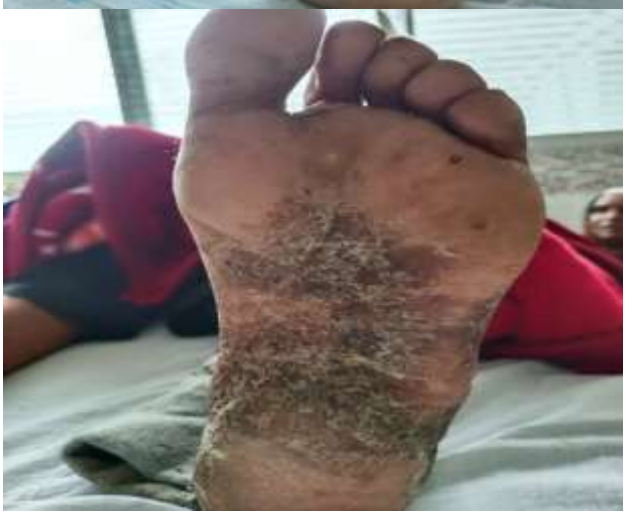
PLANTAR ECZEMA(BILATERAL FOOT PLANTARS)





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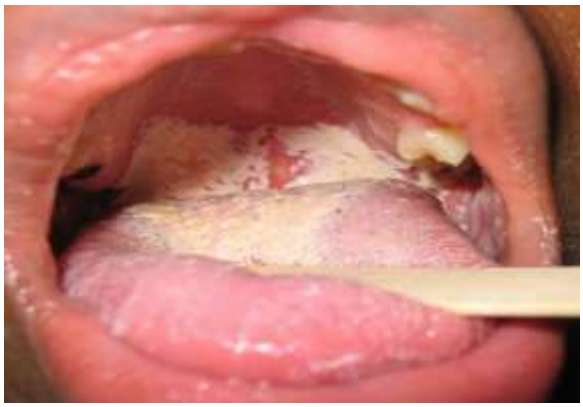
2. DISCUSSION:

Differential diagnosis

➢ ORAL THRUSH-

- Creamy white lesion over tongue, inner cheeks
- Painful
- Slightly raised lesion with a cottage cheese like
- Whitish in apperance
- Slight bleeding when rubbed



➢ **TRAUMATIC ULCER**

- Single/multiple
- Spontaneous healing after elimination of traumatic factors
- Inflammed basis,shallow or deep ulcers,margins slightly elevated

➢ **STEVEN JOHNSON SYNDROME**

- Flu like symptoms
- Followed by a red or purple rash
- That spread and form blisters.
- Affect **less than 10%** of entire body

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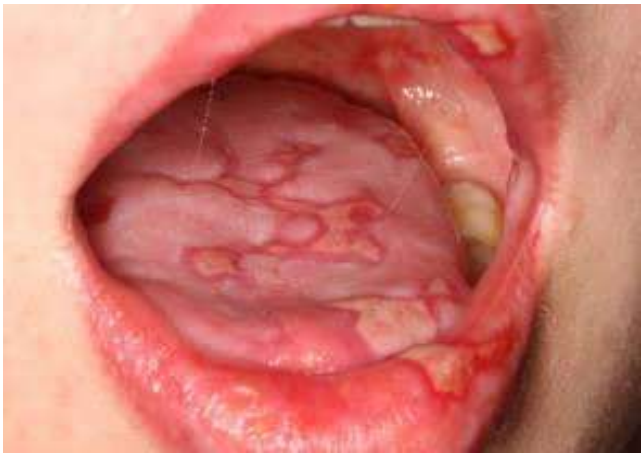
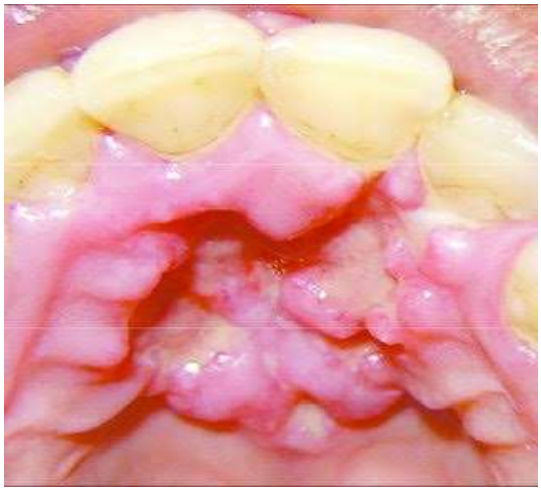


- **ORAL TUBERCULOSIS**

- Single ulcer
- Chronic ulcer lasting more than 3 weeks.
- Ragged,indurated and irregular margins,cobblestone appearance.
- Overhanging edges and pale floor



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