Methotrexate induced Pancytopenia with Oral ulcer and skin lesion

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***Abstract*—Methotrexate (MTX) is commonly used disease modifying antirheumatic drugs (DMARD) for the treatment of Autoimmune disorders such as Rheumatoid Arthritis and Psoriasis. While generally well tolerated at low doses, MTX can rarely lead to severe adverse effects including Pancytopenia. A 52-year-old female patient was admitted with complaints of multiple boils in the kin, mouth ulcer for 1 week. She recently diagnosed with Rheumatoid arthritis and was started on NSAIDs (Polmacoxib), Methotrexate, Hydroxychloroquine and Deflazacort.**

***Index Terms*—Methotrexate, Pancytopenia, Oral Ulcer, Skin lesion**

I. INTRODUCTION

Methotrexate (MTX) is a folic acid antagonist widely used in the management of autoimmune diseases such as rheumatoid arthritis, psoriasis, and certain malignancies [1,2,3]. At low doses, it functions as an immunomodulatory agent and is generally well tolerated. However, despite its efficacy and frequent use, MTX can cause significant adverse effects, including hepatotoxicity, pulmonary toxicity, and hematological complications. Pancytopenia, though rare, is a potentially life-threatening side effect that warrants early recognition and immediate intervention.[4,5,6]

Methotrexate (MTX) is considered the first-line disease-modifying antirheumatic drug (DMARD) for the treatment of rheumatoid arthritis (RA). It has been widely used for over three decades due to its efficacy in reducing disease activity, slowing joint damage, and improving long-term functional outcomes. MTX is commonly started early in the disease course, often within months of diagnosis, and can be used as monotherapy or in combination with other DMARDs or biologic agents.[8,9]

MTX exerts its effect by inhibiting dihydrofolate reductase, interfering with DNA synthesis and cellular replication, particularly affecting rapidly dividing immune cells. At low doses (typically 7.5 to 25 mg once weekly), it has a predominantly anti-inflammatory and immunosuppressive action, helping control the chronic autoimmune inflammation characteristic of RA. It is usually administered orally or subcutaneously and is supplemented with folic acid to reduce adverse effects like gastrointestinal symptoms and mucositis.[10]

Despite its benefits, MTX therapy requires close monitoring due to potential side effects, including hepatotoxicity, pulmonary toxicity, gastrointestinal upset, and hematologic abnormalities such as leukopenia and pancytopenia. Regular monitoring of complete blood counts, liver and renal function tests is essential. Patient education on the importance of weekly dosing (not daily), adherence to folic acid supplementation, and early recognition of toxicity signs like oral ulcers or fatigue is critical for safe and effective use.[11]

The clinical presentation of MTX-induced pancytopenia is often nonspecific and may include fatigue, fever, mucosal ulcerations, bleeding tendencies, and increased susceptibility to infections. Mucocutaneous manifestations such as painful oral ulcers and skin lesions may be among the earliest signs of toxicity[12]. These symptoms are sometimes mistaken for the underlying disease activity or other common conditions, delaying appropriate diagnosis and management. Risk factors for toxicity include renal impairment, advanced age, folate deficiency, and drug interactions[13].

II. CASE REPORT

A 52-year-old female patient was admitted in the General medicine department with the complaints of multiple boils in the skin, mouth ulcer for 1 week. She had medical history of Rheumatoid Arthritis which was recently diagnosed and the medication history include T. POLMACOXIB 2mg, T. METHOTREXATE 7.5mg, T. HYDROXYCHLOROQUINE 200mg, T. DEFLAZACORT 6mg and T. FOLIC ACID 45mg. She had no social history and family history.

She was conscious, oriented and afebrile. On examination the chest was clear, she was able to move all limbs, mouth ulcer present. During the admission time, she had a pulse rate of 72 beats/minute, Respiratory rate of 16 breaths/minutes and had a Blood pressure of 130/80mmHg. On monitoring the elevated parameters include CRP (167mg/L), Rheumatoid Factor (203.1IU/mL), T. Bilirubin (1.67mg/dl), AST (137U/L), ALT (314U/L). The declined parameters include Total count (2540cells/cumm). The peripheral smear study showed Dimorphic anemia (Normocytic Normochromic to Microcytic hypochromic), Moderate leukopenia with relative eosinophilia, reactive lymphocytes and Thrombocytopenia. The USG Abdomen and Pelvis showed Umbilical Hernia.

The patient developed the reaction after the use of T. METHOTREXATE and the tablet were stopped and supportive treatment were given to the patient. Then the patient was diagnosed with Methotrexate induced Pancytopenia with Oral ulcer and Skin lesions. The patient was treated with INJ. POLYBION (MULTIVITAMIN) 1AMPOULE IV OD, INJ. PACTIV (PARACETAMOL) 1g IV TID, T. FLUCONAZOLE 150mg 1-0-0, T. UDISHINE (URSODEOXYCHOLIC ACID) 300mg PO BD, T. RIFAGUT (RIFAXIMIN) 550mg PO BD, T. MONTEK LC (MONTELUKAST + LEVOCETRIZINE) PO 0-0-1, CANDID MOUTH PAINT (CLOTRIMAZOLE) TID, CHLORHEXIDINE MOUTH WASH TID, METROGYL ORAL GEL (METRONIDAZOLE) L/A BD, SYP. LACTIHEP (LACTITOL) 15ml HS, T. DEXA (DEXAMETHASONE) 4mg 1-0-1, T. HYDROXYCHLOROQUINE 200mg PO 0-0-1, INJ. FOLINIC ACID 50mg IV Q6H, INJ. MUCINAC (ACETYL CYSTEINE) 1.2g IV Q12H, MAXTRA GARGLE (BENZYDAMINE) PO 1-1-1, SYP. SUCRALATE O (SUCRALFATE + OXETACAINE) 15ml PO Q6H. After 10 days the patient became symptomatically better and hence being discharged. The discharge medications include T. FOLIC ACID 5mg 1-0-0 (Monday/Wednesday/Friday), T. DEXA (DEXAMETHASONE) 1mg 1-0-1, T. HYDROXYCHLOROQUINE 200mg 0-0-1, SYP. LACTIHEP (LACTITOL) 0-0-15ml/SOS, ZYTEE GEL for L/A TID, MUPIROCIN CREAM BD, MAXTRA GARGLE (BENZYDAMINE) TID, SYP. SUCRALFATE 10ml-10ml-10ml(30minutes before food), T. UDISHINE (URSODEOXYCHOLIC ACID) 300mg 1-0-1, T. RIFAGUT 550mg 1-0-1, T. MONTEK LC (MONTELUKAST + LEVOCETRIZINE) 0-0-1, T. FLUCONAZOLE 150mg once a week for 3weeks.

III. DISCUSSION

Methotrexate (MTX) is a well-established anchor drug in the treatment of rheumatoid arthritis (RA), due to its immunosuppressive and anti-inflammatory properties. Though generally well tolerated in low weekly doses, MTX carries the risk of severe adverse effects, especially when risk factors like renal impairment, improper dosing, folate deficiency, or drug interactions are present. Pancytopenia, although rare, is a potentially fatal complication. In our case, a 52-year-old woman developed MTX-induced pancytopenia, preceded by oral ulcers and skin lesions, despite being on a standard low-dose regimen. The absence of overt renal dysfunction in this patient emphasizes that toxicity may occur even without classical risk factors.

Malaviya et al. (2002) described a 60-year-old female with rheumatoid arthritis on 15 mg/week MTX who presented with oral ulcers, fever, and pancytopenia. Her renal impairment, which had not been previously detected, contributed to drug accumulation and hematologic toxicity. Withdrawal of MTX and administration of folinic acid, antibiotics, and supportive care resulted in complete recovery[14].

Similarly, Saito et al. (2015) reported a 55-year-old man with psoriasis who mistakenly took methotrexate daily instead of weekly. He developed severe mucositis, skin desquamation, and pancytopenia, necessitating aggressive treatment with granulocyte colony-stimulating factor (G-CSF),

intravenous antibiotics, and leucovorin. His case highlights the dangers of miscommunication regarding MTX dosing schedules, which remain a common cause of toxicity[15].

IV. CONCLUSION

Methotrexate, while being a highly effective and commonly prescribed drug for rheumatoid arthritis, carries the risk of serious hematological toxicity such as pancytopenia, even at low weekly doses. This case highlights the importance of recognizing early mucocutaneous manifestations—such as painful oral ulcers and skin lesions—as potential warning signs of underlying marrow suppression. Timely identification and withdrawal of the offending agent, along with appropriate supportive care, are critical to prevent life-threatening complications.

Clinicians must ensure routine monitoring of hematological parameters, assess renal function regularly, and emphasize patient education regarding the correct dosing schedule and potential adverse effects. This case reinforces the need for vigilance, even in patients who appear clinically stable, to ensure the safe use of methotrexate in long-term therapy

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