

Methotrexate (MTX) Induced Pancytopenia - A Rare Serious Adverse Effect

Sourya Acharya¹, Samarth Shukla², Amrutha Garikapati³, Aishwarya Ghule⁴, Amol Andhale⁵

¹Department of Medicine, Datta Meghe Institute of Medical Sciences (Deemed to Be University), Sawangi (Meghe), Wardha, Maharashtra, India. ²Department of Pathology, Datta Meghe Institute of Medical Sciences (Deemed to Be University), Sawangi (Meghe), Wardha, Maharashtra, India. ³Department of Medicine, Datta Meghe Institute of Medical Sciences (Deemed to Be University), Sawangi (Meghe), Wardha, Maharashtra, India. ⁴Department of Medicine, Datta Meghe Institute of Medical Sciences (Deemed to Be University), Sawangi (Meghe), Wardha, Maharashtra, India. ⁵Department of Medicine, Datta Meghe Institute of Medical Sciences (Deemed to Be University), Sawangi (Meghe), Wardha, Maharashtra, India.

PRESENTATION OF CASE

A 65-year-old woman presented to us with complaints of fatigability and appearance of red spots on extremities since 6 days. She was a known case of rheumatoid arthritis since 5 years and was on tablet prednisolone 5 mg OD and tablet hydroxychloroquine 200 mg bid orally. Two months back she had exaggerated symptoms in the form of increased joint pains for which tablet methotrexate 7.5 mg was started weekly once and was increased to 7.5 mg bid (15 mg) per week 2 weeks back along with folic acid 5 mg per day.

Methotrexate (MTX) is a folate antagonist used to treat various malignancies, and autoimmune disorders including rheumatoid arthritis. It enters cell by an active cellular uptake and inhibits dihydrofolate reductase (DHFR) enzyme that converts dihydrofolate (DHF) to tetrahydrofolate (THF) affecting purine and ultimately DNA synthesis. Cell with capability of polyglutamylation like myeloblasts and lymphoblasts are most susceptible to the effects of MTX because polyglutamylation prolongs its intracellular presence.^{1,2}

On Examination

Pulse - 112 / min, regular. BP - 100 / 66 mm of Hg, pallor was present. Icterus, cyanosis, clubbing, oedema feet were absent. JVP was normal. There were petechial spots in palate and oral cavity (Figure 1) and ecchymosis and petechiae in the upper and lower extremities. (Figure 2 & 3)

Lab Investigations

Hb - 5.2 gram %, TLC - 400 / mm³, DLC - 12 % neutrophils, 68 % lymphocytes, absolute neutrophil count - 48 / mm³, absolute platelet count - 11,000 / mm³. Blood culture, urine culture were negative, CXR was normal. Serum procalcitonin was normal. Coagulation profile was normal. KFT and LFT were normal. A possibility of MTX induced pancytopenia was kept and the patient was treated with 3 units of PRC transfusions, 10 units of platelet transfusions, 3 doses of Granulocyte colony stimulating factor and IV antibiotics. Five days after therapy, her haemoglobin level became 9.8 gm %, TLC improved to 4,800 / mm³ with 55 % neutrophils. MTX was stopped and she was discharged on 6th day.

Corresponding Author:

Dr. Sourya Acharya,
Professor, Department of Medicine,
Jawaharlal Nehru Medical College,
DMIMS (Deemed to Be University),
Sawangi (Meghe), Wardha-442001,
Maharashtra, India.
E-mail: souryaacharya74@gmail.com

DOI: 10.14260/jemds/2020/604

How to Cite This Article:

Acharya S, Shukla S, Garikapati A, et al.
Methotrexate (MTX) induced pancytopenia
- a rare serious adverse effect. *J Evolution
Med Dent Sci* 2020;9(37):2776-2777, DOI:
10.14260/jemds/2020/604

Submission 08-05-2020,
Peer Review 06-08-2020,
Acceptance 13-08-2020,
Published 14-09-2020.

Copyright © 2020 JEMDS. This is an open
access article distributed under Creative
Commons Attribution License [Attribution
4.0 International (CC BY 4.0)]

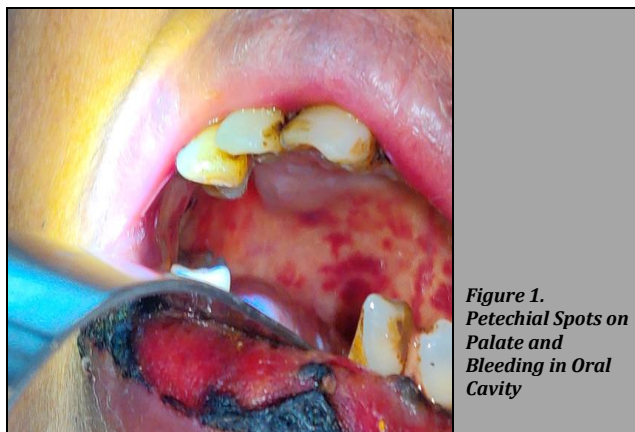


Figure 1.
*Petechial Spots on
Palate and
Bleeding in Oral
Cavity*



Figure 2.
*Bruising,
Ecchymosis and
Petechial Spots in
Arm and Forearm*



Figure 3.
*Petechial Spots in
Lower Limbs*

DISCUSSIONS

Adverse effects of MTX are pneumonitis, liver failure and myelosuppression as in this patient.³ Oral mucositis appears early and later bleeding occurs. Renal impairment aggravates the toxic effects especially when NSAIDs are concomitantly used.² Routine blood count should be done every four to eight weeks.⁴ Concomitant administration of folic acid (1 to 3 mg / day) decreases the frequency of toxicities.

In elderly patients aged more than 65 years, initial doses should be around 5 to 7.5 mg / wk. and should not exceed 20 mg / wk. Dosage adjustments for CrCl should be done and MTX should not be prescribed when CrCl is less than 10 mL / min. MTX dose should be gradually increased by no more than 2.5 mg every 1 to 2 weeks. In this case the dose was increased rather fast. Monitoring for toxicity should be done every 2 to 4 weeks for the first 3 months.⁵ Bone marrow toxicity is dose dependent but overt pancytopenia is very rare. According to a review, clinically significant pancytopenia was found in 1 % to 2 % of RA patients on MTX therapy.³

Financial or Other Competing Interests: None.

REFERENCES

- [1] Brunton LL, Chabner BA, Knollmann BJ. Goodman and Gilman's the pharmacological basis of therapeutics. 12th edn. New York: McGraw-Hill 2013.
- [2] Kremer JM, Hamilton RA. Effects of nonsteroidal anti-inflammatory drugs on methotrexate (MTX) pharmacokinetics: impairment of renal clearance of MTX at weekly maintenance doses but not at 7.5 mg. J Rheumatol 1995;22(11):2072-7.
- [3] Gutierrez-Urena S, Molina JF, Garcia CO, et al. Pancytopenia secondary to MTX therapy in rheumatoid arthritis. Arthritis Rheum 1996;39(2):272-6.
- [4] Simms RW, Kwok CK, Anderson LG, et al. Guidelines for monitoring drug therapy in rheumatoid arthritis. American College of Rheumatology Ad Hoc Committee on Clinical Guidelines. Arthritis Rheuma 1996;39(5):723-31.
- [5] Bressolle F, Bologna C, Kinowski JM, et al. Total and free methotrexate pharmacokinetics in elderly patients with rheumatoid arthritis. A comparison with young patients. J Rheumatol 1997;24(10):1903-9.