METHOTREXATE INDUCED NEUTROPENIA : A CASE REPORT

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Abstract

Methotrexate is now the most popular second line therapy utilized in the USA for the treatment of rheumatoid arthritis. It has been 10 years since the initial randominzed placebo controlled trials were published which established the short term efficacy of low dose weekly Methotrexate in rheumatoid arthritis. But it is timely to re-emphasizes the toxicity profile of methotrexate therapy. Thus my current standard practice, toxicity is the major reason for methotrexate discontinuation.

Introduction

Rheumatoid arthritis (RA) is a common diseases[1] that causes substantial morbidity is most patients[2] and premature mortality in many[2-4]. RA is the commonest form of inflammatory arthropathy[5], and characterized by a chronic recurrent synovitis that affects the small joints of the hands and feet and spreads to knee joints in time and often end in deformity, disability and premature death[6]. The concept that polyarthritis especially rheumatoid arthritis should be treated, as early as possible with therapy to reduce inflammation and increase function has been fostered in the rheumatological community for several years.[7] In USA weekly low dose of methotrexate (MTX) has emerged as most frequently used second line drug. Methotrexate was originally designed to interfere with folate dependent synthesis of purine and pyrimidine required for cell division. MTX had been primarily used to treat malignancies including leukemia, lymphoma osteosarcoma and choriocarcinoma[8]. Since then MTX of in low week dose 5-30 mg /m^2 has been used to treat many rheumatic diseases as well as other illness such as asthma and inflammatory conditions of the skin and intestinal tract[9]. In this report the toxicity of MTX has highlighted when a 70 years old lady having RA was treated with MTX developed severe neutropenia, oral ulcer and respiratory tract infection that imposed a great threat to her life.

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Case report

Mrs. Jobeda begum, a 70 years old lady, non diabetic, non hypertensive, hailing from Brahmanbaria presented with symmetrical polyarthritis involving the small joint of hands, wrists, elbows knees and ankles for the last 2 years. Every involved joint were moderately swollen and tenderness score was > 3. After taking relevant history and on the basis of clinical examination of the locomotors system, she was diagnosed as a case of rheumatoid arthritis as she fulfils the ACR criteria for rheumatoid arthritis. Her laboratory investigations were also in favours of RA bearing the scenario as-

- Urine analysis reveals no abnormality
- Hematological profile showed -

WBC	8.50 K/uL
Neutrophils	65%
Eosinophils	20%
Basophils	00%
Lymphocytes	32%
Monocytes	01%
Hb	11%
Platelet count	240.00 K/uL
ESR	92 mm is 1st hour
C-reactive protein	22mg/dl
ANA and RW test	negative
SGPT, Serum Creatinine	within normal limit
CXR P/A view	normal study
MT test	negative

As these laboratory investigations were in favour of active rheumatoid arthritis, soon she was started low dose MTX of 7.5 mg weekly, diclofenac sodium, with weekly folic acid of 5 mg day after MTX ingestion. Just one and half months later the patient presented a disastrous condition having severe oral ulcer, high fever with marked respiratory embarrassment. Immediately she was hospitalized and a good life support was ensured. As to find out the cause her all laboratory investigations were done including urine analysis, haematological profile, renal function, hepatic function and X-ray examination of chest. Investigation report reveals mild impairment of hepatic and renal function but she developed severe acute neutropenia manifested as:

- WBC 2.00 K/uL
- Neutrophils 05%
- Monocytes 03%
- Lymphocytes 83%
- Eosinophils 09%
- Basophils 00%
- HB% 67%
- ESR 112 mm in 1st hour
- Platelet 180 k/uL

Considering these reports her all medication were stopped and she was managed successfully under the guidance of an internist. Meanwhile she was transfused two units of whole blood with proper nutritional support. With these measures her general condition improved oral ulcer healed and respiratory embarrassment settled and haematological profile came to normal within 10 days after stopping MTX. After 14 days she was discharged from the hospital with normal haematological profile and good hepatic and renal function.

Conclusion

Haematological toxicity with methotrexate is uncommon. Leucopenia, thrombocytopenia, megaloblastia anaemia and pancytopenia may occur. However, serious side effects such as bone marrow suppression are uncommon[10]. The most common side effects of low dose methotrexate are gastrointestinal toxicities including anorexia, nausea, stomatitis and diarrhoea. Central nervous system toxicity including headache, dizziness, fatigue and mood alterations may occur. Many of these side effects can be reduced by supplemental folic acid 1mg/d. Pulmonary toxicity remains a concern but study suggest that there was no significant change in pulmonary function in patients receiving low dose weekly methotrexate for rheumatoid arthris.[11] It is gratifying to observe the world wide interest in methotrexate. There are still many unanswered questions about this exciting compound. Further clinical and basic research with this drug is warranted to establish its safety profile.

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