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Case Report

Methotrexate induced chronic hepatotoxicity

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ABSTRACT

55 year old male patient diagnosed to have psoriasis 2.5 years ago and was started on methotrexate 5 mg thrice weekly. Patient was symptomatically better and continued methotrexate without proper follow up. 2 months ago patient experienced abdominal pain and distension. Skin lesions worsened on discontinuing methotrexate but later subsided with treatment. 1 week ago, patient had abdominal pain, bleeding and ascites. Cumulative dose of methotrexate 1.8g; Liver function tests: total bilirubin- 2.0; direct - 1.0; platelet count: 58,000 cells/cu.mm; ascitic tap done and fresh frozen plasma was infused.

Keywords: Methotrexate, Hepatotoxicity, Psoriasis

INTRODUCTION

Methotrexate is an antifolate, antimetabolite and an immunosuppressant widely used in the treatment of leukemia, lymphoma, several solid organ tumours, psoriasis, inflammatory bowel disease and rheumatoid arthritis.[1] Methotrexate acts by inhibiting folate metabolism, by blocking dihydrofolic acid reductase. This results in inhibition of synthesis of purines and pyrimidines and decreasing DNA and RNA synthesis. The typical maintenance dose used to treat psoriasis and rheumatoid arthritis is 7.5 to 25 mg once weekly either orally or by injection. Side effects are mostly dose related and include stomatitis, oral ulcers, alopecia, fatigue, headache, gastrointestinal upset, nausea, diarrhoea hepatotoxicity and bone marrow suppression.

CASE REPORT

We report a 55 year old male diagnosed to have chronic plaque psoriasis 2½ years ago, and was started on methotrexate 5 mg thrice weekly. Folic acid (5 mg) was taken once weekly on a separate day. He had no past history of hematemesis or malena; no history of jaundice and tuberculosis. He was a non-diabetic and non-hypertensive. Patient was symptomatically better and continued methotrexate weekly without investigation. On missing the doses, there was exacerbation of lesions, so he continued methotrexate without medical follow-up. 2 weeks ago patient was admitted for complaints of abdominal pain and distension, jaundice, bleeding and ascites. Liver function tests: total/ direct bilirubin-2.0/1.1; PT/INR: 23.2/1.82; Cumulative dose of methotrexate was 1800 mg. Platelet count was 48,000 cells/cu.mm. Tests for hepatitis A, B and C were found to

be negative on autoantibody tests. Methotrexate was stopped. Paracentesis was done and fresh frozen plasma infused.

DISCUSSION

Long-term, weekly low-dose methotrexate therapy is associated with serious adverse reactions like myelosuppression, interstitial pneumonitis and hepatotoxicity. The pathogenesis of methotrexate-induced hepatic damage includes intra hepatocellular accumulation of a polyglutamated metabolite of methotrexate might be responsible for liver toxic effects. Liver histology changes are seen mostly at cumulative doses of methotrexate dosages between 1500 and 6000 mg, which necessitate close monitoring at this stage.[2]

Many studies conducted earlier, in methotrexate treated psoriatic patients reported a very high prevalence of hepatotoxicity with fibrosis occurring in up to 50% and cirrhosis in up to 20 %.[3,4]

Concerns on hepatotoxicity in psoriasis patients, laid to dermatologic guidelines that indicate monitoring periodically after every 1500 mg cumulative dose, in order to identify liver injury by means of serial liver biopsies. Liver biopsy is regarded as the gold standard method in the assessment of histological changes, but its application is complicated by some important limitations.[5]

Our patient presented with cumulative dose of methotrexate of 1800 mg with signs of liver injury and low platelet count. Patient was treated symptomatically and methotrexate was stopped temporarily. The patient recovered and the dose of methotrexate was reduced further for the management of psoriasis

CONCLUSION

Early recognition of symptoms of liver injury as a sign of methotrexate toxicity in the reported case allowed prompt reduction in dose of methotrexate and adequate care thereby avoiding serious morbidity.

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