Case Report

Antituberculosis Therapy (ATT) induced thrombocytopenia: a case report

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ABSTRACT

Thrombocytopenia is a rare adverse effect seen with anti-tubercular drugs. We report an 80 year old male with tubercular right pleural effusion, on Category I Anti-tubercular therapy (ATT) for 3 weeks who presented with melena and epistaxis. On evaluation, he had thrombocytopenia which was found to be rifampicin-induced. ATT was restarted without rifampicin and there were no bleeding episodes. Though, rifampicin is well tolerated, but on rare occasions it can cause thrombocytopenia.

Key words: Tuberculosis, ATT, thrombocytopenia, rifampicin, intermittent regimen.

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INTRODUCTION

While treating tuberculosis, clinicians often encounter problems like adverse effects of drugs, noncompliance to treatment and microbial resistance. Moreover, determining toxicity of a particular drug is always challenging as tuberculosis is treated with combination of several drugs. Thrombocytopenia though rare, is seen when the incriminating dose of an antitubercular drug is taken by a susceptible individual.[1] The first report of rifampicin induced thrombocytopenia was published in 1970.[2] Rifampicin, being a bactericidal drug, is highly active against *tubercle bacilli*. The side effects of rifampicin are encountered more frequently with intermittent than daily regimens.[3] We report a case of rifampicin-induced thrombocytopenia, which needed timely intervention.

CASE REPORT

Our case was an eighty year old male who presented with bleeding gums, bleeding per nose, rectum and purpuric rashes over the trunks and extremities. The patient was taking Category I ATT with rifampicin 600 mg, isoniazid 300 mg, pyrazinamide 1500 mg and ethambutol 1200 mg thrice weekly for the last 3 weeks for right tubercular pleural effusion. On examination, he was hemodynamically unstable and there were petechiae over the soft palate, pharyngeal wall and bilateral subconjunctival haemorrhages. Systemic examination revealed no abnormality except for diminished vesicular breath sounds over right lower lung fields.

Investigations revealed grade IV thrombocytopenia (platelet < 25000 cells/cu.mm) and anaemia with haemoglobin - 6.2 g%, platelet count - 16,000 cells/cu.mm and erythrocyte sedimentation rate was 40 mm/h. Pseudothrombocytopenia was excluded with the peripheral smear which showed mild anisocytosis, microcytic normochromic anaemia with polychromatophilia and severe thrombocytopenia. Liver function showed mild hyperbilirubinemia (1.4 mg%). Bleeding time was 12 min with normal coagulation profile. Pleural fluid showed exudative effusion with adenosine deaminase of 75 U/L suggestive of tuberculosis. Coombs test for hemolysis was negative. His

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past records showed normal haemoglobin and platelet counts which was done before the initiation of ATT.

After hemodynamic stabilization, the patient was transfused with whole blood and platelet concentrates with regular monitoring of cell counts. Antitubercular drugs were withdrawn completely as drug induced thrombocytopenia was suspected and methylprednisolone 1 mg/kg was given. The patient condition gradually improved and there were no fresh bleeds after 3 days. Haemoglobin and platelets gradually increased and by 5th day platelets count reached 80,000 cells/cu.mm and haemoglobin to 9.0 g%. By 8th day platelet count increased to 1.5 lakhs cells/cu.mm and haemoglobin increased to 12.0 g%. A diagnosis of ATT induced thrombocytopenia was made.

The next step was to find out the causative drug for thrombocytopenia. Considering the reported incidences of thrombocytopenia with different ATT drugs, ethambutol (E) was first introduced followed by pyrazinamide (Z).[4] There were no bleeding episodes after 3 days of E+Z. Then Isoniazid (H) was introduced in half the recommended dose followed by full dose. No bleeding episode was noticed. Rifampicin was not given as it was the offending drug. Based on the WHO-UMC criteria the causality of rifampicin induced thrombocytopenia is probable. Patient was discharged with 3 drugs H, E and Z on daily regimen. Follow up after 15 days showed no bleeding manifestation and platelets were adequate. Thereafter he was followed up every month for 9 months and he completed the course of ATT without any consequences.

DISCUSSION

Thrombocytopenia can be seen with any of the primary anti-tubercular drugs. With isoniazid, it occurs as a haematological reaction.[5] Ethambutol and pyrazinamide induced thrombocytopenia could be due to an immunological mechanism.[6,7] Though adverse reactions to rifampicin are uncommon on daily regimens but are commonly seen with intermittent regimens.[8] These include various syndromes like, cutaneous syndrome, respiratory syndrome, abdominal syndrome, a flu like syndrome and purpura and elevated liver enzyme levels.[9] Other rare side effects include haemolytic anaemia, renal damage and acute renal failure. Thrombocytopenia can occur with intermittent and daily rifampicin regimens. The dose of rifampicin required to cause thrombocytopenia has not been established. However, studies have shown correlation between presence of rifampicin-dependent antibodies and the occurrence of adverse reactions with 1200 mg of rifampicin twice weekly.[10]

Table 1: Showing complete blood picture before and 3 weeks after ATT therapy

Blood parameters	Before initiation of ATT (08.Sept.2012)	3 weeks after ATT (30.Sept.2012)
Hemoglobin (g%)	14.2	6.2
Total white blood cell (WBC) count(cells/cu.mm)	6800	4,800
Differential WBC count (%)	P - 65, L - 32, M - 1, E - 2	P - 77, L - 20, M - 1, E - 2
TRBC (million/cu.mm)	2.3	1.83
Platelet	2.0 lakhs	16,000
ESR (mm/ 1st hr)	22	45
RCDW (%)	11.5	17.6
Peripheral smear	Normocytic normochromic, platelets adequate, no hemoparasites.	Mild anisocytosis, microcytic normochromic with polychromatophilia, severe thrombocytopenia, no hemoparasites.

ATT - Anti-tubercular therapy, P - polymorphonuclear neutrophil, L - lymphocyte, M - monocyte, E - Eosinophil
TRBC - tagged red blood cell, ESR - Erythrocyte sedimentation rate
RCDW - Red cell distribution width

Drug induced thrombocytopenia is either due to suppression of platelet production or platelet destruction which is immunologically mediated. Latter mechanism is responsible for thrombocytopenia seen with most of the drugs. Causative drug can be identified only in 10% of patients with certain laboratory investigations. However, there are reports which conclude that the best proof of a drug-induced aetiology is a prompt rise in the platelet count when the suspected drug is discontinued.[11]

According to WHO-UMC, causality categories, the association of rifampicin as the causal drug for this adverse reaction is probable.[12] There is no time limit for the occurrence of thrombocytopenia. It can occur within days to weeks or months after initiation of rifampicin therapy. It is usually reversible if treated appropriately at the early stage.

In our case , rifampicin was implicated as the likely cause of thrombocytopenia and there was no recurrence of thrombocytopenia when ATT was restarted without rifampicin. Follow up for 9 months was uneventful and the patient completed the course of ATT with complete resolution of pleural effusion.

ATT can induce severe thrombocytopenia which can be life threatening. In our case, rifampicin as a cause of thrombocytopenia was diagnosed. By timely withdrawal of the drug and supportive treatment, serious complications were prevented. ATT was re-introduced without rifampicin and there was no recurrence of thrombocytopenia.

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