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CASE REPORT

Thrombocytopenia induced by intermittent therapy with Rifampicin – A case report

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Introduction

Rifampicin is one of the most widely used and effective antituberculosis/antileprosy drugs. Adverse effects are uncommon, except for occasional hepatotoxicity, skin-rash, gastrointestinal upsets, and flu-like syndrome.[1] It is rarely allergic, and other autoimmune manifestations including thrombocytopenia are seen especially with intermittent treatment.[2] Here we report a case of thrombocytopenia caused by intermittent administration of rifampicin in view of its rare occurrence.

Case Report

A 50 year old male diagnosed with Hansen's disease was administered with multibacillary multidrug therapy (MB-MDT) in August 2017. After a month when he took the second dose of monthly MB-MDT he developed a few purpuric lesions over the inner aspect of his lower lip, left arm and right leg associated with fever, myalgia and cough with hemoptysis.

On Investigation it was discovered that he had thrombocytopenia (8000), other essential baseline investigations were normal including Prothrombin time and INR.

With the differential diagnosis of viral fever induced thrombocytopenia or rifampicin induced thrombocytopenia, the patient was admitted and evaluated. Dengue (rapid card test) and antiplatelet antibody test for rifampicin (Ranbaxy lab) was negative. Six units of platelets were transfused. Since he had hemoptysis sputum culture & sensitivity, chest X ray and HRCT lung was normal. Post transfusion his platelets improved to 1,01,000 hence he was discharged and advised to continue MB MDT after 1 week.

A month later he presented to the emergency room, with severe body pain, chills, sweating, nausea, and one episode of vomiting after taking rifampicin.

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On examination he had hypotension, tachycardia, ECG was in sinus rhythm. On investigation he again had severe thrombocytopenia (4000) and mild hyperbilirubinemia without any purpuric lesions. He was admitted in intermediate care and was started on platelet transfusion (4 units). On day 2 his platelet count further dropped to 3000. He developed numerous purpuric lesions over hand and legs, along with hemoptysis. He was treated with short course of steroids. After 17 units of platelets transfusion platelets improved to 84,000. The patient improved symptomatically. Hence he was diagnosed as Rifampicin induced thrombocytopenia. Clarithromycin was replaced in the place of rifampicin in MB MDT and the patient was discharged. On follow-up his platelet count was normal and he had no bleeding manifestations.

Discussion

Rifampicin is a semisynthetic derivative of rifamycin B which is an antibiotic produced by Streptomyces meditteranei. It is a potent bactericidal drug which has broad antibacterial spectrum including mycobacterium species. It has a rapid action on *Mycobacterium leprae* by inhibiting DNA dependent RNA polymerase.

Rifampicin is commonly known to cause discoloration of body fluids like tears and urine to an orange or red colour. The most serious complications are hepatotoxicity, cutaneous syndrome, abdominal syndrome, respiratory syndrome, and flu like symptoms. Thrombocytopenia is rarely seen.

Rifampicin induced thrombocytopenia is an uncommon but life threatening complication. Only one case has been reported with anti-leprosy treatment.[3] Rifampicin binds non-covalently to specific membrane glycoprotein IX present on the platelets and induces conformational changes thereby activating the complement pathway which leads to destruction of the platelets.

Rifampicin-induced thrombocytopenia is more common in intermittent therapy than in continuous therapy because in continuous therapy there is neutralisation of antibodies, and antigen – antibody complex is being continuously removed without causing an allergic reaction, whereas intermittent therapy allows a sufficient quantity of antibody to be built up during the drug free interval.

Drug induced throbocytopenia is assessed by using standard criteria to define three levels of severity of bleeding.[4]

1. Major bleeding – defined as intracranial or retroperitoneal bleed or overt bleed with decrease in haemoglobin by more than 2 gm% or require two or more units of blood transfusion.
2. Minor bleeding – Overt bleeding that does not meet the criteria of major bleeding (Malena, gross hemoturia epistaxis, gingival bleeding that is prolonged for 30 mins or requires medical intervention) excessive menstrual bleeding or vaginal bleeding other than menses.
3. Trivial bleeding – Petechiae, purpurae, brief epistaxis or gingival bleed, guaic test positive stool or microscopic hematuria.

The direct assay for measurement of platelet bound antibodies can be performed but its sensitivity is 49–66% and specificity is 78–92%. In our case this test was negative so we

restarted Rifampicin again and the patient had a severe episode of thrombocytopenia. Hence confirming our diagnosis of rifampicin induced thrombocytopenia. So the negative test cannot be used to rule out the diagnosis.

In these patients Rifampicin should be stopped. Platelet counts should be monitored regularly, and most of the patients recover with platelet transfusion. Occasionally patients with severe thrombocytopenia and hemorrhagic manifestations may require temporary support with corticosteroids.[5] Plasmapheresis can be helpful in some cases. The offending drug should not be reused as only minute quantities of the drug are needed to set up a subsequent immune reaction. Even death has been reported.

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