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Rifampicin-Induced Anaemia with Thrombocytopenia in a Patient with Pulmonary Tuberculosis: A Rare but Serious Adverse Drug Reaction

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Conflict of interest: Nil

Abstract

Background: Rifampicin is an essential component of first-line antitubercular therapy owing to its potent bactericidal activity. Despite its widespread use and favourable safety profile, rifampicin has been infrequently associated with immune-mediated haematological adverse effects. Thrombocytopenia is most commonly described manifestation, whereas rifampicin-associated haemolytic anaemia is exceedingly rare. The simultaneous occurrence of anaemia and thrombocytopenia represents an unusual and potentially fatal adverse drug reaction that warrants prompt recognition.

Case Presentation: We describe a rare case of patient with microbiologically confirmed pulmonary tuberculosis (PTB) who developed acute onset anaemia with severe thrombocytopenia following initiation of rifampicin-containing antitubercular therapy. The patient presented with breathlessness, generalized weakness, mucocutaneous bleeding and pallor within 25days of starting rifampicin. Haematological evaluation revealed marked thrombocytopenia, significant drop in haemoglobin, reticulocytosis, elevated lactate dehydrogenase, indirect hyperbilirubinemia, and a positive direct antiglobulin test, consistent with immune-mediated haemolysis. Extensive evaluation excluded alternative causes of bicytopenia, including bone marrow suppression, nutritional deficiencies, sepsis, autoimmune disease, and viral infections.

Management and Outcome: Rifampicin was promptly discontinued and supportive management with blood component therapy and short-term corticosteroids was initiated. The patient demonstrated rapid clinical and haematological improvement, with normalization of

platelet counts and haemoglobin levels over subsequent days. Antitubercular therapy was successfully continued using a rifampicin-free regimen without recurrence of cytopenias.

Conclusion: This case underscores a rare but serious immune-mediated complication of rifampicin therapy. Sudden onset anaemia with thrombocytopenia in patients receiving rifampicin should raise suspicion for drug-induced immune cytopenia. Early diagnosis and immediate drug withdrawal are crucial to prevent life-threatening haemorrhagic or haemolytic complications.

Keywords: Rifampicin, Pulmonary tuberculosis, Drug-induced thrombocytopenia, Immune haemolytic anaemia, Bicytopenia, Adverse drug reaction

Introduction

Tuberculosis remains a major global health concern, particularly in developing regions, with pulmonary tuberculosis accounting for the majority of cases and disease transmission. The implementation of standardized multidrug antitubercular therapy has markedly improved treatment outcomes, with rifampicin forming the backbone of first-line regimens due to its potent sterilizing activity against Mycobacterium tuberculosis [1]. Despite its widespread use and favourable safety profile, rifampicin has been associated with a spectrum of adverse effects, including hepatotoxicity, hypersensitivity reactions, renal dysfunction, and, rarely, haematological abnormalities [2].

Haematological adverse reactions to rifampicin are uncommon and frequently underdiagnosed. Among these, immune-mediated thrombocytopenia is the most frequently reported, whereas rifampicin-associated haemolytic anaemia is extremely rare. The simultaneous occurrence of anaemia and thrombocytopenia represents an unusual form of immune cytopenia with potentially serious consequences [3,4].

Diagnosing drug-induced cytopenias in tuberculosis patients is challenging due to the wide differential diagnosis, including bone marrow infiltration, chronic inflammation, nutritional deficiencies, hypersplenism, and coexisting infections such as HIV [7]. Awareness of this rare adverse reaction is therefore crucial. We report a rare case of rifampicin-induced immune-mediated anaemia with thrombocytopenia in pulmonary tuberculosis to highlight diagnostic considerations and management strategies.

Case Presentation

A 19-year-old female with no known comorbidities was clinically and microbiologically diagnosed with pulmonary tuberculosis at a primary health centre and initiated on first-line anti-tubercular therapy (isoniazid, rifampicin, pyrazinamide, and ethambutol) 25 days prior to presentation, with a documented baseline complete blood count showing haemoglobin 11.3 g/dL, total leukocyte count 6000/mm³, and platelet count 5.4 lakh/mm³. She presented to our hospital with progressively worsening breathlessness of insidious onset for 20 days (MMRC grade 3), associated with generalized weakness and chest pain, along with cough producing blood-tinged mucoid sputum for 4 days (approximately 2–3 teaspoons per episode, 5–6 episodes per day), gum bleeding and epistaxis for 1 day. There was no history of prior bleeding disorders, blood transfusions, alcohol abuse, or exposure to other myelotoxic drugs.

On clinical Examination, patient was hemodynamically stable, pallor was present, petechiae present over both lower limbs, with no lymphadenopathy. Haemoglobin was 5G/dL, platelet count <10,000, reticulocyte count was 8%, peripheral smear showed thrombocytopenia with

features of haemolysis, LDH was 1200, indirect bilirubin 2.8, positive Direct Coombs test, PT/INR normal, Vitamin B12/Folate normal, ANA negative, viral markers (HIV, hepatitis B, C) Negative. and bone marrow examination Normocellular marrow with megakaryocytes. Based on the temporal relationship, laboratory findings, and exclusion of other causes, a diagnosis of rifampicin-induced immune-mediated anaemia with thrombocytopenia was made.

Management and Outcome

Rifampicin was immediately discontinued, while other antitubercular drugs were temporarily withheld. The patient received platelet transfusions, packed red blood cells, and short-course corticosteroids. Haematological parameters began to improve within 5 days, with normalization of platelet count and haemoglobin over the next two weeks. ATT was re-introduced using a rifampicin-free regimen. The patient was followed up till 6 months where she completed the tuberculosis treatment without further complications.

Discussion

Rifampicin remains a cornerstone in tuberculosis management due to its ability to rapidly sterilize mycobacterial populations and shorten treatment duration. While adverse effects such as hepatotoxicity and gastrointestinal intolerance are relatively common, haematological complications remain rare and are often under recognized in routine clinical practice [1]. Among these, rifampicin-induced thrombocytopenia is the most frequently reported, whereas immune-mediated haemolytic anaemia is distinctly uncommon [2].

The pathogenesis of rifampicin-associated immune cytopenias is predominantly antibody mediated. Rifampicin acts as a hapten, inducing the formation of drug-dependent antibodies that target platelet membrane glycoproteins or red blood cell antigens only in the presence of the drug [3]. These antibodies result in rapid peripheral destruction of platelets and erythrocytes through complement activation and reticuloendothelial clearance. The coexistence of anaemia and thrombocytopenia suggests a broader immune response rather than isolated lineage involvement, making such presentations particularly rare [4].

Most reported cases of rifampicin-induced thrombocytopenia have been associated with intermittent dosing schedules or re-exposure after a drug-free interval [5]. However, increasing evidence indicates that immune cytopenias can also develop during continuous daily therapy, as observed in the present case [6]. This highlights the importance of maintaining vigilance even in patients receiving standard dosing regimens without prior exposure.

The clinical presentation is often abrupt, with patients developing petechiae, ecchymoses, mucosal bleeding, fatigue, or symptoms related to anaemia. Laboratory findings typically demonstrate severe thrombocytopenia, evidence of haemolysis including elevated lactate dehydrogenase and indirect bilirubin, reticulocytosis, and occasionally a positive direct antiglobulin test [7]. Bone marrow examination, when performed, usually reveals preserved cellularity with adequate megakaryocytes, supporting peripheral immune destruction rather than marrow failure [8].

The differential diagnosis of bicytopenia in tuberculosis patients is broad and includes bone marrow infiltration by tuberculosis, hypersplenism, nutritional deficiencies, sepsis-associated cytopenias, haemophagocytic lympho histiocytosis, and viral infections such as HIV or hepatitis viruses [9]. Careful exclusion of these conditions is essential before attributing cytopenias to rifampicin

toxicity. The temporal association between drug initiation and symptom onset, along with rapid recovery following drug withdrawal, strongly supports the diagnosis of rifampicin-induced immune cytopenia.

Management primarily involves immediate discontinuation of rifampicin, which is the single most critical intervention [10]. Supportive therapy with platelet transfusions and packed red blood cells may be required depending on the severity of cytopenias and bleeding risk. Corticosteroids are frequently used in severe cases to suppress immune-mediated destruction, although evidence for their routine use remains limited [11]. Re-challenge with rifampicin is contraindicated due to the risk of rapid recurrence and potentially fatal bleeding complications [12].

Alternative rifampicin-free antitubercular regimens should be instituted to ensure completion of tuberculosis treatment. With early recognition and appropriate management, the prognosis is favourable, and haematological recovery is typically rapid and complete[13].

Conclusion

Rifampicin-induced immune-mediated anaemia with thrombocytopenia is an exceptionally rare but reversible adverse drug reaction. Clinicians managing tuberculosis patients should maintain a high index of suspicion for drug-induced cytopenias when sudden haematological abnormalities occur. Early diagnosis and immediate withdrawal of rifampicin are essential to prevent serious complications.

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