Case Report

Rifampicin-induced thrombocytopenia in a patient of disseminated tuberculosis

S Vinayak Agarwal[1], Nishant Kumar[2], Rajeev Patni[3]

From [1]Resident, Department of Pulmonary Medicine, [2]Resident, [3]Consultant, Department of General Medicine, Santokba Durlabhji Memorial Hospital cum Medical Research Institute, Jaipur, Rajasthan, India

ABSTRACT

Thrombocytopenia may be associated with a variety of conditions and risks depending on its severity, ranging from mild epistaxis to life-threatening bleeding. Many drugs or herbal remedies can cause thrombocytopenia by either inhibiting platelet production and/or enhancing their destruction from the peripheral blood-mediated through an immunological mechanism implicating drug-dependent antibodies. Drugs are a common cause of acute immune-mediated thrombocytopenia in adults, the drug etiology is often initially unrecognized. Most cases of drug-induced thrombocytopenia are caused by drug-dependent antibodies that are specific for the drug structure and bind tightly to platelets by their Fab regions but only in the presence of the drug. Thrombocytopenia is an uncommon but life-threatening complication of certain antitubercular drugs. The discovery of isolated thrombocytopenia in a patient taking several medications presents a challenging clinical problem. We report a case of a young immunocompetent female who presented with disseminated tuberculosis and was found to have rifampicin-induced thrombocytopenia.

Key words: Immunocompetent, Miliary tuberculosis, Rifampicin, Thrombocytopenia

According to the new guidelines published by the government of India for END tuberculosis (TB) 2025, the prevalence of TB >15 years is 316 per lac population, while the prevalence of all forms of TB at any age is 312 per lac population. The risk factors for TB consist of an epidemiological triad of agent, host, and environment. The treatment of TB is aimed at treating the patient and reducing the risk of transmission of *Mycobacterium TB* to other persons. The individual patient and the community, in which the patient resides, have an advantage from the successful treatment of TB. The decision to initiate combination chemotherapy for TB is based on clinical, radiographic, laboratory, patient, and public health factors. Among first-line antitubercular drugs, rifampicin is one of the most widely used and effective anti-TB drugs. Adverse effects are uncommon, except for occasional hepatotoxicity, skin rash, gastrointestinal upsets, and flu-like syndrome. Rarely, allergic and other autoimmune manifestations, including thrombocytopenia, are seen especially with high-dose intermittent treatment. Thrombocytopenia is generally defined as a platelet count below the lower normal limit, $<150 \times 10^9$/L, although many suggest that a cut-off value of 100×10^9/L is more appropriate to identify clinically significant thrombocytopenia. Adverse reactions due to rifampicin are either dose-related or allergic. Serious reactions to anti-TB drugs are uncommon. Rifampicin-induced thrombocytopenia is an uncommon but potentially life-threatening complication of anti-TB treatment [1]. Rifampicin-induced thrombocytopenia was first reported by Blajchman *et al*. in 1970 [2]. Most of the described cases were observed with high-dose intermittent therapy with rifampicin (1200 mg twice weekly) [3]. Only a few cases of thrombocytopenia have occurred during daily treatment or after administration of rifampicin following an interruption of therapy [2,4].

Access this article online	
Received - 03 May 2022 Initial Review - 21 May 2022 Accepted - 02 June 2022	Quick Response code
DOI: 10.32677/ijcr.v8i6.3463	

CASE REPORT

A 30-year-old female patient was admitted with a history of fever (101°F) mainly during evening hours, non-productive cough, and pain abdomen for the past month.

At presentation, the patient was conscious, oriented with stable vitals, respiratory rate of 18 breaths/min, and SpO_2 of 96% at room air. On palpation, the right supraclavicular lymph node was enlarged (2 cm × 1.5 cm) and firm in consistency. A respiratory system examination showed bilateral air entry with no added sounds. Other systems examination was unremarkable.

Correspondence to: Dr. S Vinayak Agarwal, H. NO 1772, Khan Bari Dindli Basti Shere Punjab Adityapur, Jamshedpur, Jharkhand - 831 013, India. E-mail: svinayak.agarwal8@gmail.com

© 2022 Creative Commons Attribution-NonCommercial 4.0 International License (CC BY-NC-ND 4.0).

Her routine blood examination showed hemoglobin-9.9 g/dl, total leukocyte count – 3770/ul, and platelets – 150,000/uL. The prothrombin time was 14 s, the international normalized ratio was 1.14, and the erythrocyte sedimentation rate - 42 mm/1st h suggesting bone marrow involvement. HBs Ag, Hepatitis C virus Ag, and human immunodeficiency virus were negative.

Computed tomography chest revealed bilateral miliary opacities, multiple mediastinal, and cervical enlarged lymph nodes. Fine-needle aspiration cytology of the right supraclavicular lymph node was done which showed features of tubercular lymphnoditis. She was started on first-line antitubercular treatment. In view of deranged liver enzymes (Serum glutamic oxaloacetic transaminase [SGOT]-234 U/L, Serum glutamic pyruvic transaminase [SGPT]-300 U/L), and antitubercular drugs (Isoniazid, Rifampicin, and Pyrazinamide) causing hepatotoxicity were withheld. Streptomycin (0.75 g intramuscular injection), ethambutol (1000 mg/oral), and levofloxacin (750 mg/oral) were continued along with the addition of steroids (prednisolone 30 mg once daily).

Subsequently, the patient's liver enzymes improved (SGOT declined from 234 U/L to 30 U/L and SGPT declined from 300 U/L to 28 U/L). Hence, rifampicin was added to the ongoing treatment. The patient developed ecchymosis on the second day after restarting rifampicin. There was a sudden decline in platelet counts from 1.8 lac/mm^3 to 5000/mm^3. At the time of this presentation, clinical suspicion of rifampicin-induced thrombocytopenia was made. Confirmation of drug-induced thrombocytopenia (DITP) at the time of initial presentation is not often possible as tests for drug-dependent anti-platelet antibodies are not available in most laboratories. No other obvious cause except rifampicin was seen in our patient for the decline in platelet counts. Thrombocytopenia due to the antitubercular drug is a rare adverse effect but was observed in our patient; hence, rifampicin was withheld. The platelets count of the patient improved gradually within 5 days after stopping rifampicin. Discontinuation of the suspected drugs leading to the resolution of thrombocytopenia provided strong evidence of DITP.

After 5 days, isoniazid initially and later pyrazinamide were added to the ongoing treatment with monitoring of the platelet counts. A complete blood picture of the patient showed improvement without any decline in platelet level after introducing the isoniazid and pyrazinamide. The patient also became afebrile with improvement in her oxygen saturation levels. Hence, she was discharged. On follow-up after 4 months, no further episodes of decline in platelet were seen.

DISCUSSION

The causes of thrombocytopenia include viral infections, collagen vascular diseases, lymphoproliferative disorders, and drugs. DITP can be caused by quinidine, sulfonamides, chemotherapeutic agents, penicillin, barbiturates, heparin, digoxin, and estrogen [5]. Thrombocytopenia attributed to rifampicin, though rare, has been reported in the treatment of pulmonary TB [6-8]. In our patient, we ruled out infection by cultures and collagen vascular disease with antinuclear antibody testing. Our patient was not receiving any of the drugs except rifampicin which is known to cause thrombocytopenia.

TB Research Center, Chennai, reported only a single case of rifampicin-induced thrombocytopenia among over 8000 patients treated for TB over 30 years [9]. In our case, the patient developed thrombocytopenia after interruption of antitubercular treatment for 2 months on a daily regimen. Our patient had tolerated the initial treatment with rifampicin daily without any complaints, but since her liver function test got deranged. Hence, it was withheld for a few days. Severe thrombocytopenia was observed within 2 days after restarting rifampicin. Serious adverse reactions due to rifampicin, which is immune complex-mediated, are mostly encountered during intermittent therapy or when there is a gap in treatment [10].

In patients with clinically DITP, an etiological agent can be identified in only 10% of cases. In the remaining cases, the etiological diagnosis can be pointed out by a prompt rise in the platelet count on withdrawal of the offending drug [2]. If detected early and treated appropriately, thrombocytopenia during rifampicin therapy is usually reversible. Since in our patient, it was detected early, the drug was stopped and supportive steroid therapy was given following which the resolution occurred. It has been recommended that rifampicin-induced thrombocytopenia is an absolute contraindication to further therapy with rifampicin [11]. Rechallenging with the offending drug even in small doses is contraindicated if purpura occurs [12].

CONCLUSION

Disseminated TB is associated with high mortality despite the availability of effective treatment. Platelet counts should be monitored after starting antitubercular drugs. The clinician must be aware of these rare complications which are life-threatening, but if detected early is completely reversible.

REFERENCES

1. Garg R, Gupta V, Mehra S, Singh R, Prasad R. Rifampicin induced thrombocytopenia. Indian J Tuberc 2007;54:94-6.
2. Blajchman MA, Lowry RC, Pettit JE, Stradling P. Rifampicin-induced immune thrombocytopenia. Br Med J 1970;3:24-6.
3. Poole G, Stradling P, Worrledge S. Potentially serious side effects of high-dose twice-weekly rifampicin. Br Med J 1971;3:343-7.
4. Mehta YS, Jijina FF, Badakere SS, Pathare AV, Mohanty D. Rifampicin induced immune thrombocytopenia. Tuberc Lung Dis 1996;77:558-62.
5. Robbins SL, Kumar V, Cotran RS. Diseases of red cells and bleeding disorders. In: Robbins Pathological Basis of Diseases. 4th ed. Philadelphia: WB Saunders Co; 1989. p. 657-702.
6. Sharma TN, Gupta PR, Purohit SD, Jain BL, Durlabji P, Koolwal S. Thrombocytopenic purpura induced by daily administration rifampicin. Indian J Tuberc 1985;32:199-200.
7. Lee CH, Lee CJ. Thrombocytopenia--a rare but potentially serious side

effects of initial daily and interrupted use of rifampicin. Chest 1989;96:202-3.
8. Smock KJ, Perkins SL. Thrombocytopenia: An update. Int J Lab Hematol 2014;36:269-78.
9. BanuRekha VV, Adhilakshmi AR, Jawahar MS. Rifampicin-induced acute thrombocytopenia. Lung India 2005;22:122-4.
10. Yakar F, Yildiz N, Yakar A, Kılıçaslan Z. Isoniazid-and rifampicin-induced thrombocytopenia. Multidiscip Respir Med 2013;8:13.
11. George JN. Drug induced thrombocytopenia: A systemic review of published case reports Ann Intern Med 1998;129:886-90.
12. Aquinas M, Allan WG, Horsfall PA, Jenkins PK, Hung-Yan D, Fox W, *et al.* Adverse reactions to daily and intermittent rifampicin regimens for pulmonary tuberculosis in Hong Kong. Br Med J 1972;1:765-71.

Funding: None; Conflicts of Interest: None Stated.

How to cite this article: Agarwal SV, Kumar N, PatnSi R. Rifampicin-induced thrombocytopenia in a patient of disseminated tuberculosis. Indian J Case Reports. 2022;8(6):176-178.