Case Report

From cure to crisis: Rifampicin-induced thrombocytopenia in spinal tuberculosis

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ABSTRACT

Thrombocytopenia, a rare adverse reaction of rifampicin, requires prompt detection and management. We report the case of a 16-year-old female with spinal tuberculosis who developed thrombocytopenia after temporarily discontinuing antitubercular treatment. Upon stopping the treatment after admission, her platelet counts normalized. However, re-administration of rifampicin alone led to a recurrence of thrombocytopenia within 1 day, confirming rifampicin-induced thrombocytopenia. The patient fully recovered after discontinuing rifampicin and tolerated a modified regimen of isoniazid, ethambutol, pyrazinamide, and levofloxacin. This case highlights the need to monitor platelet count in patients receiving rifampicin.

Key words: Adverse drug reaction, Antitubercular therapy, Drug-induced thrombocytopenia, Rifampicin, Spinal tuberculosis

Rifampicin, a crucial drug used in the treatment regimens for tuberculosis, is generally well-tolerated [1,2]. It commonly causes minor adverse reactions such as gastrointestinal upset, cutaneous reactions, and hepatotoxicity [3]. However, in rare cases, it can lead to life-threatening complications such as acute renal failure or thrombocytopenia [2]. The prevalence of adverse reactions to first-line antitubercular drugs ranges from 8.0 to 85% [4]. Thrombocytopenia is defined as a platelet count below 150×10^9/L, although many clinicians consider 100×10^9/L a more appropriate threshold for identifying clinically significant cases [5]. The exact cause of thrombocytopenia is often unclear, and clinicians face challenges in distinguishing among various possible pathologies such as sepsis, disseminated intravascular coagulation (DIC), microangiopathic processes, or autoimmune disease [6]. Drugs, nutritional supplements, or herbal remedies can cause thrombocytopenia by inhibiting platelet production or enhancing their destruction through drug-induced immune thrombocytopenia [6]. The condition is reversible if diagnosed at an early stage and treated appropriately [7].

This case report presents a rare and novel instance of rifampicin-induced immune thrombocytopenia in a 16-year-old female undergoing treatment for spinal tuberculosis. The temporal association between rifampicin administration and thrombocytopenia, along with the exclusion of other potential causes, determines the uniqueness of this case. This is the first such report from our institution, contributing valuable insights into the rare hematological adverse effects of rifampicin. We confirmed rifampicin as the causative agent and presented a detailed case report of this rare adverse effect.

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CASE PRESENTATION

A 16-year-old female with spinal tuberculosis, who was on antitubercular treatment (ATT), presented to our Pediatric department with a history of fever for 2 days, along with the appearance of bruising on the lips, subconjunctival hemorrhage, ecchymosis (Fig. 1a), purpura, (Fig. 1b), and menorrhagia. The patient's past medical history was negative. However, a detailed review of her treatment history revealed that she had temporarily discontinued ATT for 8 days due to the unavailability of medications and restarted the regimen after the interval.

On admission, her vital signs were stable, and systemic examination findings were normal. Laboratory investigations revealed hemoglobin of 7 g/dL and platelet count of 9000/mm^3, with a normal coagulation profile, antinuclear antibodies profile, and bone marrow findings.

According to her medical history and clinical presentation, we suspected the diagnosis of drug-induced thrombocytopenia. After discontinuing ATT, we found a marked improvement in her platelet count and normalized over time. We then reintroduced ATT with Rifampicin alone. Within 1 day of restarting it, her platelet counts again dropped to 16000/mm^3. Rifampicin was then stopped, and

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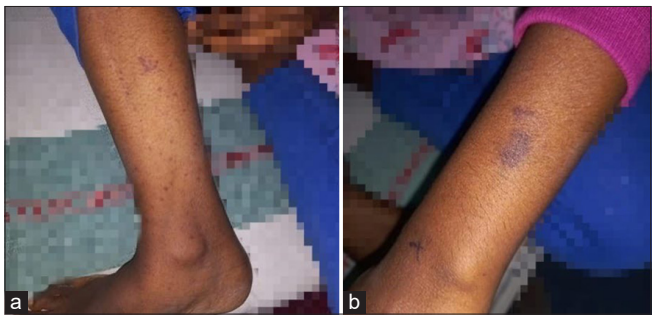

Figure 1: (a) Ecchymosis on upper limbs; (b) Purpura on lower limbs

the platelet count normalized again. Subsequently, isoniazid, along with ethambutol, was reintroduced, with the platelet count remaining stable. This pattern suggested that thrombocytopenia observed in the patient was most likely induced by rifampicin.

We continued to regularly monitor the patient in our outpatient department, treating her with a modified ATT regimen consisting of pyrazinamide, ethambutol, levofloxacin, and isoniazid.

DISCUSSION

Rifampicin-induced thrombocytopenia has been documented in recent literature, highlighting its potential severity even upon first exposure [2]. Rifampicin-induced thrombocytopenia is thought to occur due to the presence of anti-rifampicin antibodies [8]. These antibodies bind to platelets in the presence of rifampicin and trigger platelet destruction [8]. This condition is common with high-dose intermittent treatment or reintroducing rifampicin after treatment interruption rather than a daily regimen [9]. A case report highlighted the importance of careful evaluation for temporal association with the suspected drug that is required to diagnose drug-induced immune thrombocytopenia. The authors have presented a case report of pediatric female cases [3]. Which is in conjunction with another case report [10].

In the present study, our patient who was receiving ATT treatment for spinal tuberculosis developed immune-mediated thrombocytopenia after temporary disruption for 8 days. This suggests that treatment interruptions may increase the risk of thrombocytopenia, as observed in our patient. Even rifampicin-induced thrombocytopenia was seen in a patient with a medical history of brucellosis who was treated with rifampicin and doxycycline [11]. Most patients on ATT often halt and resume treatment; however, thrombocytopenia remains rare. While antibodies against rifampicin may still be detectable in some patients after discontinuing the drug, the occurrence of thrombocytopenia is infrequent [12]. The low incidence of this condition during continuous rifampicin use may be due to the presence of neutralizing antibodies [12]. This suggests that continuous dosing leads to immunologic tolerance, while intermittent dosing increases sensitivity.

Nagashima *et al*. [13] reported an unusual occurrence of miliary tuberculosis with thyroid tuberculosis in a 75-year-old male patient. The patient experienced rifampicin-induced thrombocytopenia, however successfully completed the treatment with rifabutin. George *et al*. collected case reports of drug-induced thrombocytopenia and defined criteria to explain the association between drugs and thrombocytopenia [14]. Recent case reports have highlighted the occurrence of rifampicin-induced thrombocytopenia even upon first exposure, emphasizing the need for vigilance [2]. Another study documented a similar case, reinforcing the importance of monitoring platelet counts during rifampicin therapy [3].

The findings in our case support a definitive diagnosis of drug-induced thrombocytopenia. Firstly, the patient who received ATT, including rifampicin on hospital admission, experienced a rapid onset of thrombocytopenia. After discontinuing rifampicin, the patient's platelet counts showed complete and sustained recovery, suggesting a causal relationship. Notably, the patient was not taking any other medications prior to the onset of symptoms, thereby minimizing confounding factors.

The differential diagnosis for thrombocytopenia in this patient includes infectious, autoimmune, hematologic, and drug-related causes. Viral infections such as dengue, HIV, hepatitis B, and C, and cytomegalovirus are known to reduce platelet counts, but the patient tested negative for all of these. Autoimmune disorders like systemic lupus erythematosus, which can lead to immune-mediated platelet destruction, were considered but deemed unlikely as her antinuclear antibody profile was negative. Hematologic causes such as aplastic anemia or leukemia were excluded based on a normal bone marrow examination. DIC was ruled out owing to a normal coagulation profile and the absence of clinical signs of systemic clotting or bleeding. Given the clear temporal association between the reintroduction of rifampicin and the recurrence of thrombocytopenia, along with resolution upon its withdrawal, drug-induced immune thrombocytopenia emerged as the diagnosis.

Furthermore, when the patient was re-exposed to the rifampicin alone after initial recovery, a rapid recurrence of thrombocytopenia was observed. This rechallenge provides strong evidence that the drug was the causative agent. Collectively, these findings fulfill all four criteria necessary for a definitive diagnosis of drug-induced thrombocytopenia, emphasizing the need for clinicians to identify and discontinue the drug to prevent recurrence and its associated complications. Subsequently, the patient was given ATT without rifampicin, and no further episodes of thrombocytopenia occurred. This supports our conclusion that thrombocytopenia was induced by rifampicin.

CONCLUSION

Thrombocytopenia is a potentially life-threatening complication of intermittent rifampicin therapy. Therefore, clinicians must be vigilant for signs of rifampicin-induced thrombocytopenia. However, early diagnosis and prompt drug discontinuation can completely reverse the condition. Additionally, if rifampicin must be reintroduced, frequent monitoring of platelet counts is essential, and treatment should proceed under close supervision.

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