DOI: 10.7860/JCDR/2024/67726.19102

Case Report

Internal Medicine Section

Rifampicin-induced Pancytopenia in Pulmonary Tuberculosis Patient: A Rare Presentation

YASHIKA BANSAL[1], NITIN TANGRI[2]

BY-NC-ND

ABSTRACT

Tuberculosis (TB) is prevalent throughout the world and is a major public health problem in most developing countries. In India, standardised and Directly Observed Treatment (DOT) under National Tuberculosis Elimination Programme (NTEP) is being recommended currently for drug-sensitive pulmonary TB. TB being a major health issue in developing nations like India, causes enormous death and morbidity every year. Anti-Tuberculosis Treatment (ATT) given for TB has been highly effective in fighting the disease and is generally well tolerated, with few minor side-effects. We report a 76-year-old male who was diagnosed with pulmonary TB and was on first-line four-drug anti-tubercular therapy ATT since seven days. He presented to the emergency department with loss of weight and appetite, chest tightness and vomiting. Liver Function Tests (LFT) was deranged, suggesting ATT-induced hepatitis. After normalisation of LFT, rifampicin reintroduction was initiated. Complete Blood Count (CBC) revealed pancytopenia. In bone marrow biopsy, normoblastic maturation with few micronormoblasts and megaloblast picture was seen that did not reveal any granuloma, thereby ruling out the presence of *Mycobacterium tuberculosis* (MTB). Iron profile and vitamin B12 levels were within normal limits. Rifampicin-induced pancytopenia is rare but its possibility should always be kept in mind while treating with ATT.

Keywords: Anti-tuberculosis treatment, Directly observed treatment, Drug-induced reaction, *Mycobacterium tuberculosis*

CASE REPORT

A 76-year-old male, diagnosed with pulmonary TB was on ATT since seven days, presented to the emergency department with complaints of loss of weight and appetite, chest tightness and vomiting since seven days with no significant co-morbidities. The patient was lean and thin.

Examination revealed tachycardia (heart rate 132/min), tachypnea (respiratory rate 30/min), pallor, and icterus. Chest radiograph showed bilateral infiltration with patchy consolidation in right upper zone, which were suggestive of tubercular lesions. As per the investigations, haemoglobin (Hb) was 8.8 g/dL, Total Leucocyte Count (TLC) was 8200 /mm^3, and platelet count was 1.15 lac/mm^3, Erythrocyte Sedimentation Rate (ESR) was 80 mm/hour and C-reactive Protein (CRP) was 20 mg/L. He showed increased aminotransferases {Aspartate Transaminase (AST): 364 IU/L and Alanine Transaminase (ALT): 162 IU/L} and hyperbilirubinaemia (total bilirubin was 5.6 mg/dL). Sputum for Cartridge Based Nucleic Acid Amplification Test (CBNAAT) was collected for testing that was found to be positive for *Mycobacterium tuberculosis* (MTB) with sensitivity to rifampicin.

Due to Anti-Tuberculosis Treatment (ATT) induced hepatitis, ATT was withheld. Once the parameters of LFT were normalised (total bilirubin: 1 mg/dL, AST 55 IU/L, ALT: 48 IU/L), ATT was reintroduced with single drug at a time along with monitoring. After starting the rechallenge with rifampicin, pancytopenia was noticed 48 hours after reintroduction-haemoglobin was 7.9 g/dL, TLC was 2800/mm^3 and platelet was 60,000/mm. Rifampicin was stopped in view of the same.

The patient was evaluated further to exclude the possibility of bone marrow TB. Iron profile, vitamin B12 levels were sent, which were within normal limits. Bone marrow biopsy and aspiration was done, which showed normoblastic maturation with few micronormoblasts and megaloblasts and no granuloma. Peripheral blood smear was suggestive normocytic normochromic anaemia with relative lymphopenia. Reticulocyte count was 5%. Bone marrow for Gene-Xpert- MTB not detected.

Blood picture improved after rifampicin withdrawal-haemoglobin was 8.1 g/dL, TLC was 5.2 mili/cumm and platelet count was 1 lac/mm^3. However reintroduction was not done due to the immune modulated action of rifampicin and a possibility of dreaded outcome related to it. The patient was put on oral prednisolone (1 mg/kg body weight/day which was tapered and stopped after three weeks); isoniazid (H), pyrazinamide (Z) ethambutol (E), and streptomycin (S) for two months followed by isoniazid (H), ethambutol (E) for next 10 months. The patient was regularly monitored in Outpatient Department (OPD). Chest X-Ray (CXR) showed radiological resolution of consolidation/infilterates.

DISCUSSION

Tuberculosis is a major health problem worldwide which affects primarily lungs but can affect almost any tissue and organs of the human body. About a third of the world's population is estimated to be infected with tubercle bacilli and hence at risk of developing active TB disease. The disease burden is highest in Africa and Asia, particularly in India and China (accounting for almost 40% of the world's TB cases altogether) [1]. Despite all the efforts made, TB remains one of the top 10 causes of death worldwide and the leading cause of death from a single infectious agent [2]. TB is a curable disease although drug resistance is one of the major challenges in the treatment, prevention and control of the disease. One needs to take a note that use of anti-TB drugs is not free from side-effects. These include allergic reactions, fever, rash, vasculitis, nausea, vomiting, hepatotoxicity, hepatocellular inflammation, peripheral neuropathy and others, to name a few. In addition, a wide range of haematological abnormalities have been reported as a result of administration of anti-TB drugs [1,3].

TB infection affects the production and life span of all haematologic cellular components, sometimes resulting in life-threatening complications. Iron, folate, and vitamin B12 metabolism is derailed. The pharmacological agents used for treatment of TB may also cause haematologic changes. Various aetiologies and mechanisms give rise to haematological disorders. Nearly every aspect of

haematology can be affected by drug-induced haematological disorders, which can impact platelets, Red Blood Cells (RBC), White Blood Cells (WBC), and the coagulation system [4,5]. The wide spectrum of drug-induced haematologic syndromes occur due to various mechanisms that include immune effects, enzymatic pathway interactions, and direct inhibition of haematopoiesis. It is believed that there are about four possible relationships of TB to haematological manifestations: 1) Drugs may cause idiosyncratic reactions; 2) malabsorption; 3) interference with iron metabolism; and 4) haemolysis in patients with RBC enzyme deficiencies. All these may predispose to TB reactivation. Idiosyncratic reactions manifested by depression of any or all of the three cellular blood elements (WBC, RBC and platelets) together with the coagulation system may be caused by any of the anti-TB drugs [1].

Drug reaction to ATT is like a double-edged sword as withholding ATT and initiating systemic steroids for the drug reactions can further aggravate the condition with increased risk of disseminated and multidrug resistant TB [6]. The aim of regular monitoring is to detect the factors predictive of therapeutic failure or worst outcomes at an early stage and many a times reintroduction is to be avoided to prevent immune modulated response which may at times be fatal [1]. Haematological disorder in patients with TB are possible in any age group, but predominant in elderly which is why they need more medical attention and haematological monitoring, even when on ATT, as rifampicin induced thrombocytopenia is well established but there are many rare manifestations as well [4,5].

As we know, TB itself can cause bone marrow suppression so a proper workup to rule out bone marrow TB is necessary to classify it as drug induced pancytopenia. Drug discontinuation in cases of severe adverse event is always necessary and a different regimen is to be started, as reintroduction may cause a fatal event.

CONCLUSION(S)

To conclude, TB can present in various ways, and one of the haematological manifestations is pancytopenia but once ruled out, drug induced reaction should always be suspected. Medication reactions to ATT are frequent. As a last option, halting ATT and beginning systemic steroid treatment for the reaction can worsen the disease and raise the risk of Multidrug-Resistant (MDR) and disseminated TB. Re-challenging with ATT not only identifies the drug of concern but also facilitates the resumption of a safer substitute ATT regimen. Proper survillence and a strong alternative regimen if a patient is not responding well to anti-tubercular drugs can help us fight TB in a safe and efficient manner.

REFERENCES

[1] Kassa E, Enawgaw B, Gelaw A, Gelaw B. Effect of anti-tuberculosis drugs on hematological profiles of tuberculosis patients attending at University of Gondar Hospital, Northwest Ethiopia. BMC Hematol. 2016;16:01. Doi: 10.1186/s12878-015-0037-1. PMID: 26751690; PMCID: PMC4706672.
[2] Minardi ML, Fato I, Di Gennaro F, Mosti S, Mastrobattista A, Cerva C, et al. Common and rare hematological manifestations and adverse drug events during treatment of active TB: A state of art. Microorganisms. 2021;9(7):1477.
[3] Agarwal AK, Chugh IM, Punjabi C, Dewan S, Shah A. Asymptomatic aplastic anaemia in a patient receiving anti-tuberculosis treatment. Indian J Tuberc. 2001;48:97.
[4] Mintzer DM, Billet SN, Chmielewski L. Drug-induced hematologic syndromes. Adv Hematol. 2009;2009:495863.
[5] Whitfield CL. Hematologic abnormalities in tuberculous patients. Arch Intern Med. 1970;126(4):698.
[6] Sharma RK, Verma GK, Tegta GR, Sood S, Rattan R, Gupta M. Spectrum of cutaneous adverse drug reactions to anti-tubercular drugs and safe therapy after re-challenge-A retrospective study. Indian Dermatol Online J. 2020;11(2):177-81.

PARTICULARS OF CONTRIBUTORS:
1. Postgraduate Resident, Department of Respiratory Medicine, Adesh Medical College and Hospital, Shahabad (M), Kurukshetra, Haryana, India.
2. Professor, Deptartment of Respiratory Medicine, Adesh Medical College and Hospital, Shahabad (M), Kurukshetra, Haryana, India.

NAME, ADDRESS, E-MAIL ID OF THE CORRESPONDING AUTHOR:
Yashika Bansal,
NH-1, Village- Mohri Tehsil- Shahabad (M), Kurukshetra-136135, Haryana, India.
E-mail: yashikabansal5737@gmail.com

PLAGIARISM CHECKING METHODS: [Jain H et al.]
- Plagiarism X-checker: Sep 28, 2023
- Manual Googling: Dec 19, 2023
- iThenticate Software: Jan 12, 2024 (9%)

ETYMOLOGY: Author Origin

EMENDATIONS: 7

AUTHOR DECLARATION:
- Financial or Other Competing Interests: None
- Was informed consent obtained from the subjects involved in the study? Yes
- For any images presented appropriate consent has been obtained from the subjects. NA

Date of Submission: **Sep 27, 2023**
Date of Peer Review: **Nov 24, 2023**
Date of Acceptance: **Jan 17, 2024**
Date of Publishing: **Mar 01, 2024**