ORIGINAL RESEARCH PAPER
Volume - 10 | Issue - 03 | March - 2021 | PRINT ISSN No. 2277 - 8179 | DOI : 10.36106/ijsr
INTERNATIONAL JOURNAL OF SCIENTIFIC RESEARCH

RARE COMPLICATION OF RIFAMPICIN- THROMBOCYTOPENIA- A CASE REPORT

General Medicine

Dr Vinus Taneja MD Internal Medicine (Associate Consultant), Department of Internal Medicine, Sir Ganga Ram Hospital, New Delhi, India.

Dr Rishikesh Dessai* MD Internal Medicine (Associate Consultant), Department of Internal Medicine, Sir Ganga Ram Hospital, New Delhi, India.*Corresponding Author

Dr Vikas Kumar DNB Family Medicine (Medicine Senior Resident), Department of Internal Medicine, Sir Ganga Ram Hospital, New Delhi, India.

Dr Ambuj Garg DNB Medicine (Consultant), Department of Internal Medicine, Sir Ganga Ram Hospital, New Delhi, India.

ABSTRACT

Rifampicin is one of the important anti-tubercular drugs used in the treatment of Tuberculosis (Tb). The complications of anti-tubercular drugs are very well known to all, but, there are a few complications which are rare and also life threatening . There are a few life threatening complications of Rifampicin, especially when used in intermittent regime like- acute kidney injury, thrombocytopenia, anemia and agranulocytosis. We hereby, report a case of Rifampicin induced thrombocytopenia, in a patient on anti-tubercular treatment for pulmonary tuberculosis. The thrombocytopenia in this patient recovered after stopping the culprit drug (rifampicin). We hereby, want to increase the awareness of this rare and life threatening complication of rifampicin, especially when used in the intermittent regime, amongst the physicians, who are treating tuberculosis.

KEYWORDS

Thrombocytopenia, Rifampicin, Tuberculosis, Anti-tubercular therapy, Rifampicin induced thrombocytopenia, drug induced thrombocytopenia.

INTRODUCTION

Anti- tubercular drugs are mostly safe to use, but, their life threatening complications are rare. One of such life threatening complication is Thrombocytopenia. Thrombocytopenia can occur with any of the primary anti-tubercular drugs- isoniazid, rifampicin, ethambutol and pyrazinamide.[1] There are two mechanisms known-hematological reactions in case of Isoniazide and immunological reactions for Ethambutol, Pyrazinamide and Rifampicin.[2,3,4] These drugs either cause suppression of platelets production or immunological platelet distruction. The commonest complication of rifampicin are – gastro-intestinal effects, hepatotoxicity and flu like symptoms. There are a few rare serious complications of rifampicin, which are seen especially with intermittent regime , like Thrombocytopenia and acute kidney injury.[5,6] Rifampicin induced thrombocytopenia was first ever reported in the year 1970.[7]

We hereby, report a case in which the patient was started on anti-tubercular treatment, including Rifampicin, when the patient stopped the treatment and then restarted, during the course, only to realize that his platelet count was decreasing and upon stopping Rifampicin the platelet count showed improvement. Diagnosis such case, of drug induced complications, in a patient on multiple drugs is a challenging task, to identify the offending drug.[8,9] What is important is to have high level of suspicion and awareness and discontinuation of the offending drug will improve the patient's condition, as we did in our case. Hence, detection at an initial level is very important to treat the thrombocytopenia.

CASE REPORT

57 years old female patient, was bought to our hospital with chief complaints of fevef sice one and a half months, generalized weakness, decreased appetite and weight loss (approximately 3 kgs) over the period of one and a half months. The patient was evaluated at a private hospital in her home-town, approximately 25 days before getting the patient to our hospital and her investigations revealed sputum AFB positive with chest X-ray suggestive of pulmonary tuberculosis, and so the patient was started on 4 drug anti-tubercular therapy (Rifampicine, Isoniazide, Pyrazinamide, Ethambutol) as per body weight. After taking the treatment for 10 days, patient developed mild rashes over the lower limbs, so the patient was re-evaluated and was found to have low platelet count of 5000 per cubic millimeter, which was previously normal. Her hemoglobin was 11.9 gm per decilitre, total leukocyte counts 11400 cells per cubic millimeter. Patient complaint of persistent fever. Malarial parasite, dengue NS1/IgM were negative. The anti-tubercular treatment was stopped and the patient was given multiple platelet transfusions and the platelet count increased to 100500 per cubic millimeter after 3 days. CT chest was also done which showed fibrocavitatory lesions on bilateral upper lobes of lungs with mediastinal lymphadenopathy suggestive of pulmonary tuberculosis. So now the patient was restarted on anti-tubercular treatment (4 drugs) and re-investigated after 3 day. He investigations revealed hemoglobin was 10.3 gm per decilitre, total leukocyte counts 3900 cells per cubic millimeter, platelet count 13000 per cubic millimeter. The patient was then shifted to critical care unit , in view of respirstory distress.Her repeated investigations revealed persistent thrombocytopenia, so she had received multiple blood product transfusions. Patient underwent bone marrow examination which revealed microcytic normoblastic erythropoisis ??thrombocytopenic purpura/?? Viral etiology. Her anaemia profile was normal, direct and indirect Coombs test was negative. The patient was started on low dose steroid (methyl prednisolon 20mg twice a day) and then was shifted to our hospital for further management. Patient was a known asthmatic and was on bronchodilaters. On examination; patient was afebrile, pulse:88 per minute, blood pressure:126/80 mm of Hg, respiratory rate:18 per minute. Systemic examination; respiratory system: bilateral basal creptations, other systems were within normal limits. On presentation, a provisional diagnosis of pulmonary tuberculosis with thrombocytopenia?drug induced, ? Thrombocytopenic purpura, ?vasculitis was considered. Her investigations revealed Haemoglobin was 9.7 gm per decilitre, total leukocyte counts 4200 cells per cubic millimeter, platelets 25000 cells per cubic millimeter, ESR was 68 mm at the end of 1st hour, serum creatinine 0.62 mg per decilitre, aspartate aminotransferase 69 U per litre, alanine aminotransferase 43 U per litre, thyroid function test was within normal limits, anti-nuclear antibody was negative, Chest X-ray showed cavitatory lesions. Patient was started on empirical antibiotic (cefoparazone) and 3 drug anti-tubercular treatment (without rifampicin) was started with great precautions. The bone marrow slides were reviewed which showed cellular haemopeotic elements with erythroid hyperplasia. Patients platelet count improved after 3 days, increased to 223000 cells per cubic millimeter and the patient was discharged. Then the patient started having rifampicin on her own, without medical consult. When the platelet count was repeated after3 days, her counts had again reduced to 10000 cells per cubic millimeter. Patient came for follow-up, rifampicin was stopped and solumedrol was started, platelets were transfused, anti-tubercular treatment was modified to streptomycin, levofloxacin, ethambutol, pyrazinamide (as per body weight). Platelet counts were monitored daily, which showed increasing trend and the patient was discharged in good health with a final diagnosis of Pulmonary Tuberculosis with Rifampicin induced Thrombocytopenia.

DISCUSSION

The common causes of thrombocytopenia are- drug induced (heparin, quinine, sulfonamides, acetaminophen, ibuprofen, glycoprotein IIb/IIIa inhibitor), infections (HIV, hepatitis-C, Ebstein-baar virus, sepsis with DIC), rheumatological, autoimmune disorders and myelodysplasias.[5] All first line anti-tubercular drugs can cause thrombocytopenia. There are two mechanisms known-hematological reactions in case of Isoniazide and immunological reactions for Ethambutol, Pyrazinamide and Rifampicin.[10,11] Rifampicin induced Thrombocytopenia was first ever reported in 1970.[7] According to a study at Tuberculosis Centre, Chennai, only one case of rifampicin induced thrombocytopenia was observed in 30 years.[12,13] Thrombocytopenia causes due to Rifampicin is more commonly witnessed with intermittent regime or any gap in the treatment.[14,15] Possible mechanism postulated is, when the drug is given, immune complexes adsorb to the platelet membrane, leading to platelet distruction.[16,17] Glycoprotein Ib/IX complex with the Immunoglobulin G (IgG) antibody is the target in rifampicin-induced immune thrombocytopenia.[18]

Such patients should be treated with 3 drug therapy which should include one parentral agent (aminoglycoside) and two safe oral agents.[9] As such cases closely resemble many other conditions, which are difficult to differentiate and identify the culprit drug, one can give corticosteroids only in case of severe thrombocytopenia.[9] Regular monitoring of the platelet count should be done..Once the diagnosis of drug induced thrombocytopenia is done, the culprit drug should never be restarted, as it has the potential of life threatening complications.[19]

REFERENCES:

[1] Garg R, Gupta V, Mehra S, Singh R, Prasad R. Rifampicin induced thrombocytopenia. Indian J Tuberc 2007;54:94-6.
[2] Ross JD, Horne NW. Drugs used in chemotherapy. In: Horne NW, editor. Modern drug treatment of tuberculosis. 1st Indian ed. New Delhi: Oxford University Press 1992. pp 1-17.
[3] Prasad R, Mukerji PK. Rifampicin induced thrombocytopenia. Indian J Tuberc 1989;36:44.
[4] Jain VK, Vardhar H, Prakash OM. Pyrazinamide induced thrombocytopenia. Tubercle 1988;69:217-8.
[5] Blumberg HM, Burman WJ, Chaisson RE, Daley CL, Etkind SC, Friedman LN, et al. American Thoracic Society, Centers for Disease Control and Prevention and the Infectious Diseases Society. Treatment of tuberculosis. Am J Respir Crit Care Med 2003;167:603-62.
[6] Friedman LN. Chemotherapeutic agents for mycobacterial infections. In: Tuberculosis: Current concepts and treatment. 2nd ed. Boca Raton, Florida: CRC Press LLC; 2001. pp 301-32.
[7] Ferguson GC. Rifampicin and thrombocytopenia. BMJ 1971;3:638.
[8] Wazny LD, Ariano RE. Evaluation and management of drug induced thrombocytopenia in the acutely ill patients. Pharmacotherapy 2000;20:292-307.
[9] Pedersen-Bjergaard U, Andersen M, Hansen PB. Drug induced thrombocytopenia: Clinical data on 309 cases and the effect of corticosteroid therapy. Eur J Clin Pharmacol 1997;52:183-9.
[10] Prasad R, Mukerji PK. Rifampicin induced thrombocytopenia. Indian J Tuberc 1989;36:44.
[11] Ross JD, Horne NW. Drugs used in chemotherapy. In: Horne NW, editor. Modern drug treatment of tuberculosis. 1st Indian ed. New Delhi: Oxford University Press 1992. pp 1-17.
[12] Banu Rekha VV, Adhilakshmi AR, Jawahar MS. Rifampicininduced acute thrombocytopenia. Lung India 2005;22:122-4.
[13] Verma A, Singh A, Chandra A, Kumar S, Gupta R. Rifampicininduced thrombocytopenia. Indian J Pharmacol 2010;42:240.
[14] Poole G, Stradling P, Worrledge S. Potential serious side effects of high-dose twice-weekly rifampicin. BMJ 1971;3:343-7.
[15] Hong Kong Tuberculosis Treatment Services/Brompton Hospital/ British Medical Research Council. A controlled trial of daily and intermittent rifampicin plus ethambutol in the retreatment of patients with pulmonary tuberculosis. Results up to 30 months. Tubercle 1975;56:179-89.
[16] Blajchman MA, Lowry RC, Petil JE, Stradling P. Rifampicin induced immune thrombocytopenia. BMJ 1970;3:24-6.
[17] Marcus AJ. The Cecil textbook of medicine. 16th ed. Philadelphia: W.B. Saunders Co. 1982. p p 983.
[18] Pereira J, Hidalgo P, Ocqueteau M, Blacutt M, Marchesse M, Nien Y, et al. Glycoprotein Ib/IX complex is the target in rifampicin induced immune thrombocytopenia. Br J Haematol 2000;110: 904-10.
[19] Das S, Roy A, Maiti A. Rifampicin induced thrombocytopenia. Indian J Dermatol 2006;51:222.