

# Rifampicin-induced Thrombocytopaenia Purpura

Hamed Bashir, Shahid Mahdi and Alok Anand

Max Hospital, Saket, New Delhi, India

## Abstract

We report the case of a 28-year-old resident doctor with no past history of having taken rifampicin, who presented with thrombocytopaenic purpura occurring after the initiation of anti-tuberculosis therapy (isoniazid, rifampicin, pyrazinamide and ethambutol) for tubercular lymphadenopathy. [Indian J Chest Dis Allied Sci 2016;58:189-190]

**Key words:** Rifampicin, Thrombocytopaenia.

## Introduction

Serious reactions to anti-tuberculosis drugs are uncommon. Thrombocytopaenia induced by rifampicin in the absence of prior sensitisation is exceptional, especially when it occurs in a patient without risk factors.<sup>1</sup>

## Case Report

A 28-year-old resident doctor presented with complaints of swelling in the region of right supra-clavicular region. It was associated with generalised malaise, loss of appetite and weight loss for last few weeks. There was also history of low grade fever. There was no history of cough, expectoration, chest pain, or haemoptysis. He had taken a course of antibiotics along with supportive treatment but without any clinical response. The past medical history was not significant.

General examination of the patient was not remarkable, except for a 2.5mm x 2.0mm lymph node in the left supra-clavicular region (Figure 1). Systemic examination revealed no abnormalities. Chest radiograph (postero-anterior view) showed a right para-tracheal soft tissue shadow suggestive of right para-tracheal adenopathy (Figure 2). Laboratory investigations revealed a normal haemogram with an erythrocyte sedimentation rate of 55 mm in 1<sup>st</sup> hour. Sputum was negative for acid-fast bacilli on smear examination. Fine needle aspiration cytology (FNAC) of lymph node was done which revealed epitheloid granulomas suggestive of tuberculosis (Figures 3,4).

Based on the above findings, anti-tuberculosis therapy (ATT) was advised with isoniazid 300mg, rifampicin 600mg, pyrazinamide 1.5g, ethambutol 1200mg. There was marked clinical improvement and all symptoms were relieved within three weeks. Three weeks later, the patient noticed purpuric rash on his arms and legs. There was no bleeding from any site. Haemogram was done which revealed thrombocytopaenia with platelet count of 30,000. It was decided to stop all anti-tuberculosis drugs. Liver function tests, renal function tests, and anti-nuclear antibodies



Figure 1. Photograph of the patient showing supra-clavicular lymph node.

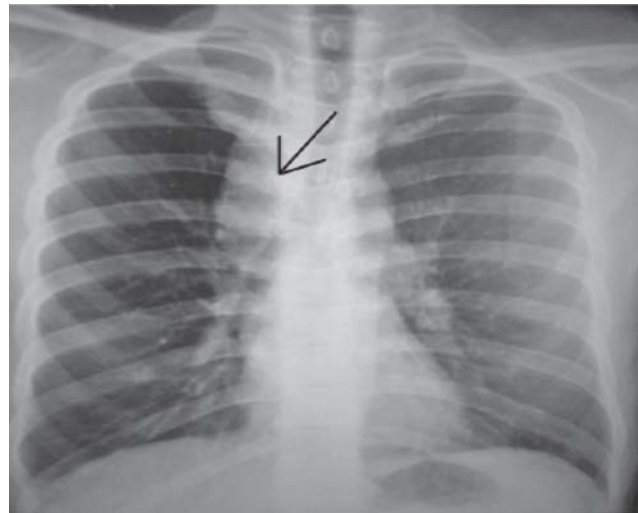


Figure 2. Chest radiograph (postero-anterior view) showing right para-tracheal lymph node.

tests were normal. Dengue viral markers were also negative. There were no further purpuric rashes. After three days ATT was resumed with levofloxacin

[Received: July 10, 2015; accepted: August 3, 2015]

**Correspondence and reprint requests:** Dr Hamed Bashir, Consultant, Max Hospital, 2-Press Enclave Road, Saket, New Delhi-110 017, India; E-mail: hamedkhan001@gmail.com

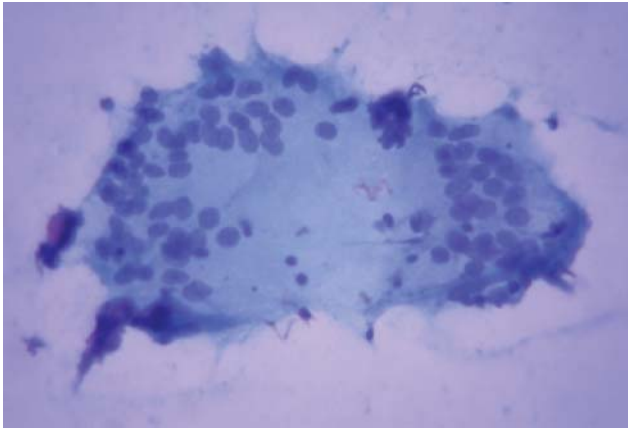


Figure 3. Photomicrograph showing giant cell on pap smear (Pap stain  $\times$  400).

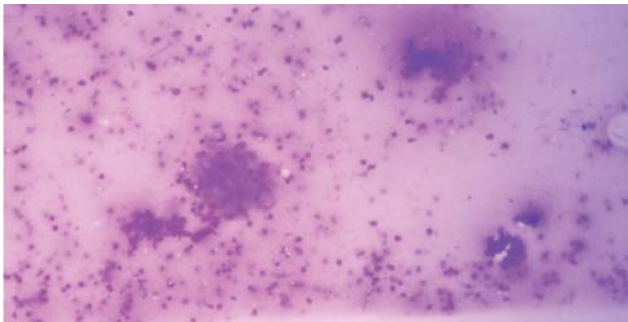


Figure 4. Photomicrograph showing epitheloid granuloma (Geimsa stain  $\times$  100).

in place of rifampicin. Platelet count was repeated after three days which revealed an upward trend. After one week, the platelet count was above 100,000/cmm. On follow-up now at two months, the platelet count has been in the normal range.

## Discussion

Serious reactions to anti-tuberculosis drugs are uncommon. Rifampicin-induced thrombocytopenia is an uncommon but potentially life-threatening complication of ATT.<sup>2</sup> Rifampicin-induced thrombocytopenia was first reported by Blajchman and co-workers<sup>3</sup> in 1970. Most of the described cases were observed with high dose intermittent therapy with rifampicin (1200mg twice weekly).<sup>4</sup> Only a few cases of thrombocytopenia have occurred during daily treatment or after administration of rifampicin following an interruption of therapy.<sup>2,6</sup> Tuberculosis Research Centre, Chennai, reported only a single case of rifampicin-induced thrombocytopenia among over 8000 patients treated for tuberculosis over 30 years.<sup>7</sup> Thrombocytopenia induced by rifampicin in the absence of prior sensitisation is exceptional, especially when it occurs in a patient without risk factors.<sup>1</sup>

It has been observed that rifampicin-induced thrombocytopenia is caused by the presence of anti-rifampicin antibodies<sup>6</sup> These antibodies fix a complement on the platelets in the presence of rifampicin resulting in platelet destruction.<sup>8</sup> A sizeable number of patients taking anti-tuberculosis drugs interrupt treatment prematurely

due to various reasons and although most are subsequently re-started on the same drugs, thrombocytopenia is very uncommon.<sup>9</sup> It has been found that antibodies against rifampicin can be demonstrated in a significant number of patients after stopping the drugs. Yet rifampicin-induced thrombocytopenia is still relatively rare.<sup>2,3,7</sup> Low incidence of thrombocytopenia-inducing effect of rifampicin during daily dosage has been attributed to the possible presence of development of neutralising antibodies formed during continuous treatment or it may be that the antigen-antibody complex is continuously removed without causing an allergic reaction.<sup>10</sup> Thus, daily dosing of rifampicin may result in immunologic tolerance, whereas intermittent dosing favors sensitisation.<sup>1</sup> Interruption of treatment may be a risk factor for such complication in daily regimen of rifampicin.

In patients with clinically drug-induced thrombocytopenia, an aetiological agent can be identified in only 10% cases. In the remaining cases, the aetiological diagnosis can be suspected by a prompt rise in the platelet count upon withdrawal of the offending drug.<sup>2</sup> This case recorded a score of 9 on Naranjo ADR Probability scale<sup>11</sup> incriminating the drug as a definite cause for the reaction.

It has been recommended that rifampicin-induced thrombocytopenia is an absolute contraindication to further therapy with rifampicin.<sup>5</sup> However, Bhasin and co-workers<sup>12</sup> suggested that re-challenges should be done before finally withdrawing rifampicin.

## References

1. Neino Mourtala Mohamed A, Tummino C, Gouitaa M, Chanez P. Thrombocytopenia induced by rifampicin not previously sensitized: a case presentation. *Rev Mal Respir* 2013;30:785–8.
2. Garg R, Gupta V, Mehra S, Singh R, Prasad R. Rifampicin induced thrombocytopenia. *Indian J Tuberc* 2007;54:94–6.
3. Blajchman MA, Lowry RC, Pettit JE, Stradling P. Rifampicin-induced immune thrombocytopenia. *Br Med J* 1970;3:24–6.
4. Poole G, Stradling P, Worledge S. Potentially serious side effects of high-dose twice-weekly rifampicin. *Br Med J* 1971;3:343–7.
5. George JN. Drug induced thrombocytopenia: a systemic review of published case reports. *Ann Intern Med* 1998;129:886–90.
6. Mehta YS, Jijina FF, Badakere SS, Pathare AV, Mohanty D. Rifampicin induced immune thrombocytopenia. *Tuberc Lung Dis* 1996;77:558–62.
7. Banu Rekha VV, Adhilakshmi AR, Jawahar MS. Rifampicin-induced acute thrombocytopenia. *Lung India* 2005;22:122–4.
8. Hadfield JW. Rifampicin-induced thrombocytopenia. *Postgrad Med J* 1980;56:59–60.
9. Verma AK, Singh A, Chandra A, Kumar S, Gupta RK. Rifampicin-induced thrombocytopenia. *Indian J Pharmacol* 2010;42:240–2.
10. Bassi L, di Bernardino L, Perna G, Silvestre LG. Antibodies against rifampicin in patients with tuberculosis after discontinuation of daily treatment (note). *Am Rev Respir Dis* 1976;114:1189–90.
11. Naranjo CA, Busto U, Sellers EM, Sandor P, Ruiz I, Roberts EA, et al. A method of estimating the probability of adverse drug reactions. *Clin Pharmacol Ther* 1981;30:239–45.
12. Bhasin DK, Sarode R, Puri S, Marwaha N, Singh K. Can rifampicin be restarted in patients with rifampicin-induced thrombocytopenia? *Tubercle* 1991;72:306–71.