

Safety of Rifabutin in patients with rifampicin-induced thrombocytopenia

Sir,

Rifampicin (RIF) is a key drug in the treatment of drug-susceptible tuberculosis;^[1] however, RIF associated adverse reactions pose a threat to effective anti-tuberculosis treatment.^[2]

Thrombocytopenia due to RIF is well known since 1970, is a rare, immunologically mediated serious adverse reaction, and is usually reversible if detected early and treated appropriately.^[3]

Rifabutin (RIB) is structurally and pharmacokinetically similar to RIF. Although RIB substitution for RIF-induced drug-drug interaction is well established, RIB substitution for RIF-induced thrombocytopenia is poorly explored.^[4]

We report a successful substitution with RIB in a case of extrapulmonary tuberculosis patient who developed RIF-induced thrombocytopenia.

A 35-year-old Indian male presented with complaints of left leg pain, hip pain, and weight loss for a month. His pain persisted despite symptomatic treatment, magnetic resonance imaging (MRI) of sacroiliac joint with whole spine screening was performed which showed changes of sacroiliitis with incidental finding of enlarged mediastinal lymph nodes. Hence to complete the diagnostic work-up, MRI brain was done which revealed multiple ring enhancing lesions in bilateral cerebral, cerebellar hemispheres, and thalamus. He was started on the first-line anti-tuberculosis treatment: RIF, isoniazid, ethambutol, pyrazinamide, and steroids based on his radiology and a positive Mantoux test from an outside private center.

Three weeks into the treatment he developed petechiae on his extremities and back with no signs of active bleeding. On evaluation, his platelet count was found to be 1000/mm³, RIF was stopped and moxifloxacin was added and with platelet transfusions his counts picked up. A clinical diagnosis of RIF-induced thrombocytopenia was made and he was discharged with isoniazid, ethambutol, pyrazinamide, and moxifloxacin, with tapering doses of oral steroids. Repeat cerebral MRI after a month, showed significant resolution in the size and number of granulomas.

However, a month later, he developed blurring of vision and flashes of light, ethambutol was withheld, and in order to complete the regimen a decision was made to

carefully introduce RIB in place of RIF. RIB was added after a platelet count of 100,000 was achieved and the patient was monitored daily with complete blood count (CBC) and platelet count.

The patient improved clinically and radiologically and the treatment was continued for a year in view of brain involvement and anti-tubercular drug-induced toxicity with monthly CBC and platelet monitoring. Figure 1 shows progressive drop in platelet count after addition of rifampicin, but rifabutin was safely tolerated with no further drop in platelet count.

RIF-induced thrombocytopenia is an uncommon and potentially life-threatening complication with majority of cases reported due to intermittent therapy, with only a few cases occurring during daily regimen or administration after interruption of therapy. The identification of the offending agent in drug-induced thrombocytopenia poses a clinical challenge. Discontinuation of the suspected drug leading to resolution of thrombocytopenia provides a strong evidence of the causal drug. Reuse of the offending drug should be avoided as only minute amounts of the drug are needed to set up subsequent immune reactions.^[5]

RIB is a rifamycin structurally related to RIF and is active against a variety of mycobacteria. It is a less potent inducer of cytochrome P3A, hence commonly used to treat tuberculosis in human immunodeficiency virus-positive patients. There have been case reports of successful re-challenge with RIB in patients who developed cutaneous adverse drug reactions including drug reaction with eosinophilia and systemic symptoms syndrome (DRESS), but to our knowledge,

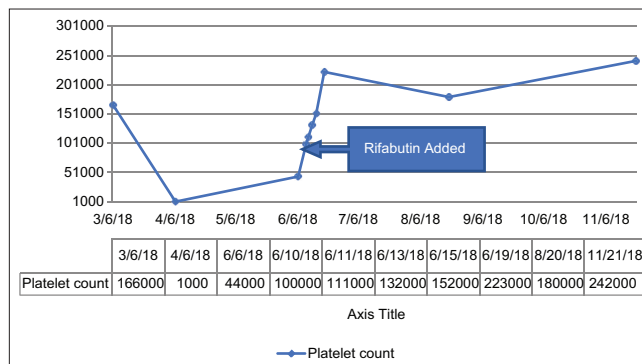


Figure 1: Progressive drop in platelet count after addition of rifampicin, rifabutin however was safely tolerated without any drop in platelet count

only one case report of RIB substitution for RIF-induced flu-like syndrome and thrombocytopenia with subsequent withdrawal due to cross-reactivity in a 42-year-old woman for treatment of leprosy relapse with a known past history of the development of rash and thrombocytopenia with both RIF and RFB.^{16,71}

In our case report, a clinical diagnosis of RIF-induced thrombocytopenia was made and the platelet count improved after RIF was stopped. However, due to adverse effects to other antitubercular drugs, an effective first-line regimen could not be constructed, hence RIB was added and the patient successfully completed the treatment with clinical and radiological improvement and no further episodes of thrombocytopenia.

Hence, the usefulness of RIB may be further studied for patients with RIF-induced thrombocytopenia to maintain optimum treatment regimen and cure rates.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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