Case Report

A rare case of adverse drug reaction and drug interaction in a human immunodeficiency virus patient

Kaza Kavya[1], M. V. S. Subbalaxmi[1], Mutnuru Phani Chakravarty[2], Soanker Radhika[3], Mallika Goyal[4]

Departments of [1]General Medicine, [2]Radiology and Imageology and [3]Clinical Pharmacology and Medical Therapeutics, Nizam's Institute of Medical Sciences, [4]Department of Ophthalmology, Apollo hospitals, Hyderabad, Telangana, India

Abstract

We are reporting a case of rifabutin-induced uveitis in a woman with human immunodeficiency virus (HIV)-tuberculosis (TB) coinfection involving the right hip. Identifying the culprit drug and tailoring the appropriate regimen was a challenge to the clinicians. We described the clinical features, ophthalmological findings, laboratory findings and radiological findings in skeletal TB and follow-up in a woman with HIV-TB coinfection. Improvement of vision on stopping rifabutin with rifampicin confirmed our diagnosis. This case highlights about adverse drug reactions and drug interactions in case of HIV and TB coinfection. Patients receiving therapy with combinations of any of these agents should be warned about signs and symptoms of uveitis and monitored closely for the development of rifabutin toxicity.

Keywords: Human immunodeficiency virus, rifabutin, tuberculosis, uveitis

Address for correspondence: Dr M. V. S. Subbalaxmi, Additional Professor, Department of General Medicine, Nizam's Institute of Medical Sciences, Hyderabad, Telangana, India.
E-mail: subbalaxmimvs@gmail.com

Submitted: 24-Jan-2020 **Accepted:** 11-Apr-2020 **Published:** 25-Oct-2021

INTRODUCTION

Usual causes of uveitis include autoimmune disorders and infections. Medications in various forms of administration are recognised as increasingly important causes of uveitis. We are presenting a case of rifabutin-induced uveitis in the case of human immunodeficiency virus (HIV) infection and improvement following stopping the drug. Rifabutin is usually well tolerated[1] and is used in the management of tuberculosis (TB) in special situations. Cases of rifabutin-induced uveitis in HIV-infected patients have been reported since 1994,[2-5] but it is still a rare occurrence.

CASE REPORT

A 38-year-old homemaker was diagnosed to have HIV 1 infection 12 years ago. After 5 years, she was evaluated at a government antiretroviral therapy (ART) centre and was started on first-line ART. The patient used ART irregularly for 5 years following which she developed failure of first-line ART and CD4 cell count dropped to 24 cells/μL. She was started on second-line ART from 2017, consisting of tenofovir-, lamivudine- and ritonavir-boosted atazanavir. After 4 months, the patient presented to our institute with pain in the right hip. Magnetic resonance imaging of the right hip (Figure 1) and bone scan revealed findings suggestive of TB. She was started on anti-tuberculosis treatment (ATT), consisting of isoniazid 300 mg once

Access this article online	
Quick Response Code:	Website: www.jcsr.co.in
	DOI: 10.4103/JCSR.JCSR_6_20

How to cite this article: Kavya K, Subbalaxmi MV, Chakravarty MP, Radhika S, Goyal M. A rare case of adverse drug reaction and drug interaction in a human immunodeficiency virus patient. J Clin Sci Res 2021;10:249-51.

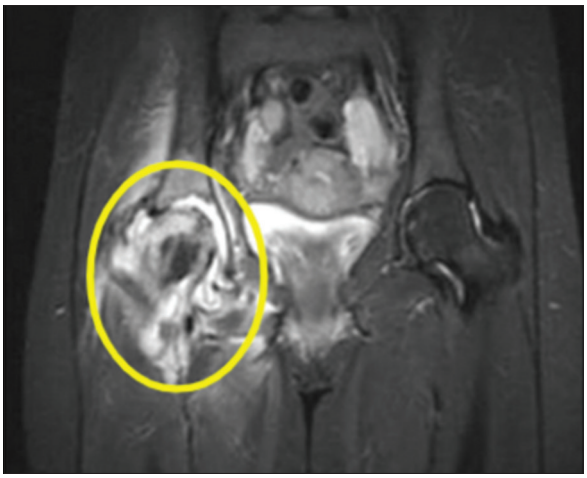

Figure 1: Magnetic resonance imaging pelvis short-T1 inversion recovery coronal view showing right femoral head (yellow circle) with hyperintensities within (oedema) and adjacent soft-tissue oedema with joint effusion. Hyperintensities also noted in the right acetabulum features suggesting tubercular aetiology

a day (OD), rifabutin 150 mg OD, ethambutol 800 mg OD and pyrazinamide 1000 mg OD. After 1 month, the patient presented with a complaint of pain in the left eye and blurred vision for 4 days. In view of her HIV status, cytomegalovirus retinitis was suspected. Expert opinion of an ophthalmologist revealed visual acuity: right eye 6/6, N6; left eye 6/6, N6 and intraocular pressure: 14 mmHg in the right eye and 16 mmHg in the left eye. In the left eye, there are conjunctival trace congestion, anterior chamber and vitreous cells occasional, inferior settled vitreous exudates, and the fundus is normal. Based on the above findings, it was opined that the uveitis of the left eye was due to rifabutin. Hence, we stopped rifabutin, and the patient was started on rifampicin in the place of rifabutin. In view of drug interactions, ART was changed to dolutegravir 50 mg BD, lamivudine 150 mg BD and abacavir 300 mg BD. The patient was discharged and advised for follow-up. On follow-up, the patient's vision improved, and the same treatment strategy was continued. ATT was given for 18 months, considering multiple interactions and interruptions. Whole-body positron emission tomography-computed tomography scan done for the patient on follow-up showed no metabolically significant active disease.

DISCUSSION

Clinicians should be aware of the development of adverse drug reactions while starting any treatment, especially if the patient needs several drugs in TB and HIV infection like in our case. Drug–drug interactions are commonly encountered often in HIV patients, as we have to treat opportunistic infections and HIV simultaneously.

Immune reconstitution inflammatory syndrome (IRIS) should also be a concern in these patients, which is defined as the paradoxical worsening of pre-existing undiagnosed infectious and autoimmune conditions following the initiation of ART due to immediate improvements in immune function that occurs as levels of HIV RNA drop, and immunosuppressive effects of HIV infection are controlled and is most common in patients with CD4+ T-cell counts <50 cells/μL. In our patients, the second-line ART was started as the first-line ART failed and resulted in a low CD4 cell count of 24 cells/μl. Later, TB manifested with an improved CD4+ cell count, and we considered it as TB IRIS.

Rifampicin plays a fundamental role in the management of patients with active TB. It is possible for patients with isoniazid-resistant TB to respond well to short-course (6 months) chemotherapy, even without the benefit of INH, while those with rifampicin-resistant TB, do not.[6] No treatment course shorter than 18 months has an acceptable success rate without a rifamycin in the regimen. Rifampicin should always be used in initial ATT unless the patient has documented rifampicin-resistant TB. Standard ATT regimens for patients infected with HIV pose a special challenge when protease inhibitors (PIs) are also indicated. PI and rifampicin usually should not be taken together, as rifampicin induces the enzymes metabolising PI.

As the patient was on PIs, rifabutin was started as rifampicin markedly lowers the serum levels of PI and non-nucleoside reverse-transcriptase inhibitors (NNRTIs) by inducing the activity of cytochrome P450 CYP3A.[7] It may result in suboptimal antiretroviral activity and subsequently acquired drug resistance.[8] Thus, the use of rifampicin to treat tuberculous disease in a patient receiving a PI or an NNRTI is not recommended. Rifabutin has been shown to be as effective against TB as rifampicin[9-11] and has the advantage of being a less potent inducer of the hepatic CYP 450 enzyme system.[12,13]

Causes of uveitis in patients infected with HIV are frequently associated with opportunistic infections and rarely due to HIV itself.[14] However, uveitis, as a side effect of rifabutin therapy, has been recognised. Possible pathogenic mechanisms may be an immune reaction or direct drug toxicity. Direct rifabutin toxicity was advocated by dose dependency, cumulative time dependency and involvement of both eyes in most cases and reversibility on drug discontinuation.[15] Ophthalmologists and physicians treating HIV, and TB should be aware of this adverse drug

reaction. If uveitis develops, rifabutin therapy should be discontinued promptly.

We are reporting this case to bring awareness about drug interactions and a rare adverse drug reaction of rifabutin. The risk of rifabutin-associated uveitis may be increased in patients receiving concurrent therapy with clarithromycin or fluconazole because of drug interactions. Patients receiving therapy with combinations of any of these agents should be warned about signs and symptoms of uveitis and be monitored closely for the development of rifabutin toxicity. This case also highlights the adverse drug reaction and drug–drug interaction in the case of HIV and TB coinfection.

Financial support and sponsorship
Nil.

Conflicts of interest
There are no conflicts of interest.

REFERENCES

1. Nightingale SD, Cameron DW, Gordin FM, Sullam PM, Cohn DL, Chaisson RE, et al. Two controlled trials of rifabutin prophylaxis against Mycobacterium avium complex infection in AIDS. N Engl J Med 1993;329:828-33.
2. Shafran SD, Deschenes J, Miller M, Philips P, Toma E. The MAC study Group of the Canadian HIV Trial Network: Uveitis and pseudo jaundice during a regimen of clarithromycin, rifabutin andethambutol. N Engl J Med 1994;330:438-9.
3. Jacobs DS, Piliero PJ, Kuperwaser MG, Smith JA, Harris SD, Flanigan TP, et al. Acute uveitis associated with rifabutin used in patients with human immunodeficiency virus infection. Am J Opthalmol 1994;118:717-22.
4. Saran BR, Maguire AM, Nichols C, Frank I, Hertle RW, Brucker AJ, et al. Hypopyon uveitis in patients with acquired immunodeficiency syndrome treated for systemic Mycobacterium avium complex infection with rifabutin. Arch Ophthalmol 1994;112:1159-65.
5. Havlir D, Torriani F, Dube M. Uveitis associated with rifabutin prophylaxis. Ann Intern Med 1994;121:510-2.
6. Mitchison DA, Nunn AJ. Influence of initial drug resistance on the response to short-course chemotherapy of pulmonary tuberculosis. Am Rev Respir Dis 1986;133:423-30.
7. Centers for Disease Control and Prevention CDC. Clinical update: Impact of HIV protease inhibitors on the treatment of HIV-infected tuberculosis patients with rifampin. MMWR Morb Mortal Wkly Rep 1996;45:921.
8. Vanhove GF, Schapiro JM, Winters MA, Merigan TC, Blaschke TF. Patient compliance and drug failure in protease inhibitor monotherapy. JAMA 1996;276:1955-6.
9. Gonzalez-Montaner LJ, Natal S, Yongchaiyud P, Olliaro P. Rifabutin Study Group rifabutin for the treatment of newly-diagnosed pulmonary tuberculosis: A multinational, randomized, comparative study versus rifampicin. Tuber Lung Dis 1994;75:341-7.
10. McGregor MM, Olliaro P, Wolmarans L, Mabuza B, Bredell M, Felten MK, et al. Efficacy and safety of rifabutin in the treatment of patients with newly diagnosed pulmonary tuberculosis. Am J Respir Crit Care Med 1996;154:1462-7.
11. Schwander S, Rusch-Gerdes S, Mateega A, Lutalo T, Tugume S, Kityo C, et al. A pilot study of anti-tuberculosis combinations comparing rifabutin with rifampicin in the treatment of HIV-1 associated tuberculosis: A single blind randomized evaluation in Ugandan patients with HIV-1 infection and pulmonary tuberculosis. Tuber Lung Dis 1995;76:210-8.
12. Perucca E, Grimaldi R, Frigo GM, Sardi A, Monig H, Ohnhaus EE. Comparative effects of rifabutin and rifampicin on hepatic microsomal enzyme activity in normal subjects. Eur J Clin Pharmacol 1988;34:595-9.
13. Li AP, Reith MK, Rasmussen A, Gorski JC, Hall SD, Xu L, et al. Primary human hepatocytes as a tool for the evaluation of structure-activity relationship in cytochrome P450 induction potential of xenobiotics: Evaluation of rifampin, rifapentine and rifabutin. Chem Biol Interact 1997;107:17-30.
14. Mwanza JC, Kayembe DL. Uveitis in HIV-infected patients. Eur J Ophthalmol 2001;11:53-6.
15. Shafran SD, Singer J, Zarowny DP, Deschenes J, Phillips P, Turgeon F, et al. Determinants of rifabutin-associated uveitis in patients treated with rifabutin, clarithromycin, and ethambutol for Mycobacterium avium complex bacteria: A multivariate analysis. Canadian HIV Trial Network Protocol Study Group. J Infect Dis 1998;177:252-5.