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Rifampicin Causing Deep Vein Thrombosis: A Rare Case Report

P. Deepak*, D. Nagendar, B. Divya***, B. Sowjanya****, B. S. V.Manjula*****

*Assistant professor,**Associate professor,***Junior Resident,****Senior resident,*****Professor and HOD, Department of Medicine, Gandhi Medical College/Hospital, Secunderabad, Telangana state, INDIA.

Corresponding Email ID: ndevulapally@yahoo.com

Case Report

Subject: Medicine

Abstract:

Tuberculosis (TB) is an infectious disease with high prevalence in India and worldwide. In India, most of the antituberculous regimens under RNTCP are rifampicin based. Deep vein thrombosis (DVT) is a rare side effect of Rifampicin and very few cases are reported worldwide. Studies have demonstrated possible association between DVT and use of Rifampicin with a relative risk of 4.74 in patients treated with rifampicin containing regimens. Here we report a case of young adult female with pulmonary tuberculosis initiated on rifampicin based ATT presented with DVT.

Key words: Tuberculosis, Rifampicin, Deep vein thrombosis.

Introduction:

Thrombosis is the formation of a blood clot inside a blood vessel, obstructing the flow of blood through the circulatory system. When a blood vessel is injured, the body uses platelets and fibrin to form a blood clot to prevent blood loss. Even when blood vessel is not injured, blood clots may form in the body under certain conditions. Rifampicin, contribute to the hyper coagulable state by decreasing production and increasing clearance of anticoagulant hepatic proteins [5]. Rifampicin can also cause endothelial injury which favours thrombosis [6]. Very few cases are reported worldwide [1].

In our case, after ruling out other hyper coagulable states, association between Rifampicin and DVT is established and near total recovery of patient indicates the role of physician in recognizing and treating the condition in early phase.

Case Report:

A 20 year old unmarried female presented to emergency department with painful swelling of left lower limb. She had complaints of productive cough, anorexia, weight loss, low grade fever since 2 months. She was not on hormonal pills, had no history of recent surgeries, no prolonged immobilisation, with no history of similar complaints in past. Diagnosed as pulmonary tuberculosis and was started on category1 ATT under RNTCP which includes Isoniazid, Rifampicin, Pyrazinamide, Ethambutol. She noticed swelling of left lower limb after 10 days of initiation of ATT. General physical examination revealed poorly built, malnourished woman weighing 48 kg. she was febrile (axillary temperature of 38.3 degree centigrade), with tachycardia (pulse 102 /min) ,hypotension (BP 90/60 mm Hg). Her respiratory rate was 22 with oxygen saturation of 92%. Chest auscultation revealed fine crepitations in left infraclavicular, right mammary, right inframammary areas, amphoric breath sounds in right infraclavicular area .Cardiovascular and abdominal examination was normal. Her left leg was swollen, erythamatose with serous discharge oozing out and tender to touch. Laboratory findings on admission revealed low haemoglobin (Hb-8.3 gm%), leucocytosis (WBC count-13,000/cumm), normal platelet count (3,67,000/cumm), with elevated CRP (5.20mg/dl), elevated D-dimers (5.51ug/ml) and plasma fibrinogen level was normal. Renal function tests, liver function tests were normal. On evaluation for secondary causes for hyper coagulable state, direct coombs tests, rheumatoid factor, protein C and S, antithrombin 3, antiphospho lipid antibody, antineutrophilic antibody titres are normal; antibodies for HIV by ELISA are negative. Sputum examination was positive for tubercle bacilli. Chest x-ray demonstrated patchy heterogeneous opacities noted in the left upper zone and right upper and mid zones with cavitation in right upper zone suggestive of pulmonary Kochs. Ultrasonography of abdomen was normal. Electrocardiogram and 2 D echo was normal with Ejection fraction 68%. Doppler of both lower limbs done which revealed thrombus extending from left posterior tibial vein to left common iliac vein. Along with continuation of ATT, patient was treated with low molecular weight heparin and warfarin for thrombus and antibiotics for associated cellulitis. Warfarin dose was titrated to achieve target INR of 2-3. Within two weeks of hospital stay patient responded .

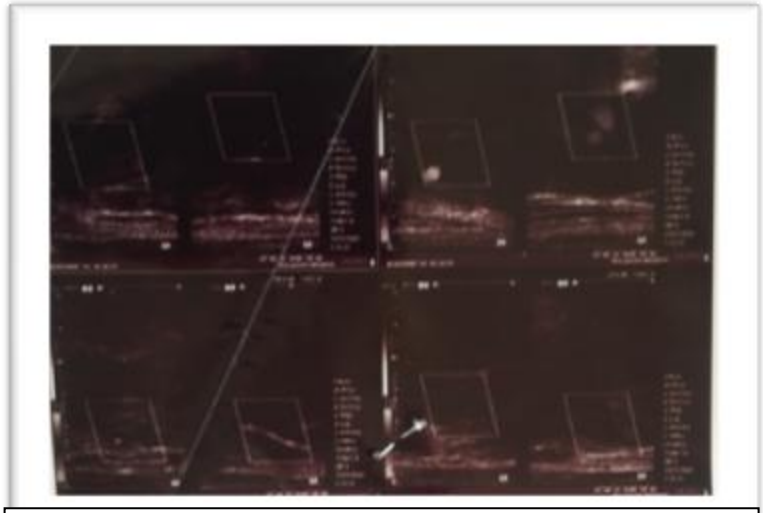

Figure 1: Doppler lower limbs

Figure 2: Chest X-ray posteroanterior view

Figure 4: At time of Admission

Figure 4: At time of Discharge

favourably with improvement in constitutional symptoms and swelling of lower limb decreased .Patient was discharged and advised regarding continuation of of ATT, regular follow up.

Discussion:

Tuberculosis (TB) remains one of the deadliest communicable diseases in the world. In 2013, an estimated 9.0 million people developed TB and 1.5 million died from the disease [2]. In India RNTCP formulated guidelines for tuberculosis treatment. Rifampicin is one of first line drugs for tuberculosis treatment. It acts by inhibiting bacterial DNA dependant RNA polymerase. Rifampicin is effective liver enzyme inducer promoting up reglation of hepatic cytochrome p450 enzymes (CYP2C9,CYP3A4), increasing the rate of metabolism of other drugs that are cleared by liver through this enzymes [3]. Frequently, a higher dose of warfarin is necessary to achieve therapeutic INR levels, because of rifampicin effects on cytochrome P450 [4]. But we have achieved target INR in this patient with low dose warfarin.

Commonly encountered side effects with rifampicin are jaundice, raised LFTs (14%), GIT symptoms (1-2%), flu like symptoms, pruritus, rash (1-5%). Thrombosis is uncommon side effect seen with Rifampicin. Studies have demonstrated a possible association between DVT and use of rifampicin with a relative risk of 4.74 in

patients treated with Rifampicin containing regimens [1]. This does not contraindicate the use of this drug in patients at risk, but patients with risk factors should be supervised. In a study on 2096 people using Rifampicin, 49 (2.34%) patients are found to have DVT as side effect. In this study group, DVT was found especially in males (89.36%), old age more than 60 years (59.57%) and in those taking Rifampicin for < 1 month [7]. FDA research report states that percentage of Rifampicin taking patients, where DVT is reported as side effect is 0.5385%.

Conclusion:

Though venous thrombosis is uncommon side effect of Rifampicin, treating physicians should be cautious during initial phase of treatment. Rifampicin should be continued along with initiation of anticoagulants.

References:

1. *White NW. Venous thrombosis and rifampicin. Lancet. 1989 Aug 19;2(8660): 434-5.*
2. *World Health organisation, global tuberculosis report 2014,211.*
3. *Katzung BG, Masters, S.B, Trevor A.J ; Basic and clinical pharmacology,12 edition, McGraw-Hill.*
4. *T.H. Self, R.B. Mann ,Interaction of rifampin and warfarin ,Chest,1975,67,490–491.*
5. *Robson SC, White NW, Aronson I, et al. Acute-phase response and the hypercoagulable state in pulmonary tuberculosis. B.r J, Haematol. 1996 Jun;93(4):943-9.*
6. *Prevention of VTE, American college of chest physicians, evidence based clinical practice guidelines,8th edition , chest 2008:133:381S-453S.*
7. *FDA research report, Feb 28, 2015.*
