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RIFAMPICIN-INDUCED HEMOLYTIC ANEMIA: A RARE CASE REPORT

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ABSTRACT

Drug induced immune hemolytic anemia can be either dependent on drug or induced by drug. There are few case reports on Immune Hemolytic Anemia associated with Tuberculosis. Rifampicin induced hemolytic anemia is very rare. Here we report a case of 32 year female who presented with anemia, jaundice, raised reticulocyte count, LDH, serum urea & creatinine. Immunohematological work up of this patient showed direct antiglobulin test(DAT) to be positive, autocontrol negative, elution negative and drug testing positive for rifampicin, negative for other antitubercular drugs. It was confirmed to be a case of Rifampicin induced hemolytic anemia. Thus drug history is to be taken with proper evaluation of the case for better management of hemolytic anemia.

Keywords: Direct Antiglobulin Test, Drug-induced hemolytic anemia, Elution, Rifampicin

INTRODUCTION

Tuberculosis (TB) is a wide spread infectious disease in India that can affect any organ system. Anemia is commonly seen in TB patients and it is usually anemia of chronic disease. However, the incidence of autoimmune hemolytic anemia or treatment related anemia is very rare in the settings of tubercular infection. Acute hemolysis as an adverse reaction to Rifampicin is a very rarely encountered complication.[1,2] Acute hemolysis is sometimes associated with acute renal failure.[3,4] Here we reported a case of rifampicin induced hemolytic anemia with drug induced nephritis and hepatitis.

CASE REPORT:

A 32 year female presented to the Pulmonary Medicine Department with low grade fever, cough with sputum, breathlessness, easy fatigability and yellowish discoloration of eye and urine after taking category-I antitubercular drug(ATT) for ten days. On examination, pallor was found along with icterus, no lymphadenopathy, no edema. On auscultation bilateral crepitation and rhonchi with right side bronchial breath sound was heard. ATT was stopped and the patient was treated symptomatically. On laboratory examination, hemoglobin 4gm/dl, indirect bilirubin 4.2mg/dl, total bilirubin 12.4mg/dl, raised liver enzyme(SGOT 1260U, SGPT 620U, ALP 698U) urea 153mg/dl & creatinine 5.1mg/dl, LDH 898U and reticulocytosis 2.8%. With the features of hemolysis, the case was referred to Dept of Transfusion Medicine to rule out any immunological cause. After doing detailed immunohematological work up , blood group of the patient was found to be B Rh D Positive. DAT(direct antiglobulin test) was found to be positive along with monospecific DAT positive for C3d only, auto control, antibody screening & elution negative. Suspecting it to be a case of drug induced hemolytic anemia, test was done

for rifampicin & isoniazid in adherence to AABB Methods.(Table-1)

TABLE1: AABB testing methods for patient serum in presence of drug(IPOD), All test tubes incubated at 37^0c for 2hour and then the result was interpreted.

Test tube 1	2	3	4	5	6
Patient serum	Patient serum	Patient serum	Patient serum	Normal serum	Normal serum
Normal serum	Normal serum	------	-------	---	---
PBS	drug	drug	PBS	PBS	drug
0	4+	4+	0	0	0

TABLE2: Different lab parameters on day1, 4, 7 of hospitalization.

	DAY1	DAY4	DAY7
Hb (gm/dl)	4	5.2	5.1
Billirubin (T) (mg/dl) (D)	12.6 8.7	8.1 4	2.2 1.3
ALP(U)	696	324	239
SGOT(U)	1260	626	84
SGPT(U)	620	296	101

The test tubes containing patient's plasma with rifampicin only and both rifampicin & normal plasma showed agglutination with pooled O cell, but negative in other test tubes. There was no agglutination when tested for other antitubercular drugs. All the hemolytic pictures were corrected on stopping ATT (HB% and LFT were as mentioned in Table-2) . It was confirmed to be a case of rifampicin induced hemolytic anemia.

DISCUSSION:

Drug induced hemolytic anemia(DIHA) is a rare condition most commonly occurs with cephalosporin group of drugs and the trend is increasing with cotrimoxazole, diclofenac, fludarabine and lorazepam.[5] There are about 17 literatures on AIHA due to antitubercular drug that to rifampicin induced hemolytic anemia is extremely rare.[6] There are four basic principles of occurrence of DIHA like drug adsorption, immune complex formation, autoantibody development, non-immune adsorption of drug.[7] In the immune complex mechanism, circulating drug stimulates the immune system to produce antibody directed against the drug.[8] The antibody binds to the circulating drug and the resulting immune complex can then bind to a red cell. It is unknown whether binding to the red cell is specific or nonspecific. The red cells coated by antibody–drug complexes, are typically removed via brisk, intravascular hemolysis.[9] Rifampicin is like the prototypic drug quinidine for this mechanism as described by Shulman and Rall.[10] The different type of DIHA and the serological findings with the prototype drugs is described in the Table-3.[11]

Volume 1, Issue 2; July-August 2018; Page No. 221-223

TABLE 3

DIHA TYPE	Monospesific DAT		ELUTION	Prototype Drug	Testing Method
	IgG	C3d			
Drug adsorption	++	+/-	Positive	Pencillin	IPOD/DTRC
Immune complex	+	++	Negative	Quinine	IPOD/DTRC
Autoantibody	+++	+/-	Positive	α-Methyldopa	IA
Nonimmunologic adsorption	--	--	--	β Lactamase	DTRC/IPOD

IPOD: In Presence Of Drug, DTRC: Drug Treated Red Cell, IA: Induction of Autoimmunity

In this case, patient had anemia and jaundice with raised reticulocyte count & LDH suggestive of hemolyic anemia, hepatomegaly with raised indirect bilirubin suggestive of hepatitis, raised urea creatinine suggestive of nephritis.The only finding of DAT positive with strong suscipision of drug induced haemolytic anemia open up the Pandora box. To find out the cause of DAT positivity, tests were done to rule out presence of auto or alloantibody. Monospecific DAT was positive for C3d only. Negative autocontrol & elution were suggestive of drug induced IHA. IPOD testing method found out to be presence of drug antibody against rifampicin, not isoniazid or ethambutol. Drug withdrawal also reduced the sign & symptoms and so also the laboratory findings of hemolysis. In tuberculosis, the patient is with utmost need of antitubercular drug. As the offending drug was identified, patient was again treated with ATT with titrated dose of rifampicin and discharged with follow-up advice.

CONCLUSION:

Strong suspicion and complete immunohematological work up is helpful in diagnosing a case of drug induced haemolytic anemia. In TB patients ,drug adverse reactions are common. But drug induced haemolytic anemia is rare. Identifying the causative drug will make the pulmonary physician easy to treat the patient effectively.

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Volume 1, Issue 2; July-August 2018; Page No. 221-223