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Clinical pharmacist intervention on antitubercular drug induced hepatitis and dermatitis

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ABSTRACT

A 47 year old female patient with microbiologically confirmed pulmonary tuberculosis on intensive phase of anti-tubercular therapy now showed up with complaints of cough, loss of appetite, itching and loss of weight. The cutaneous reaction was a sign of dermatitis and elevation in the estimates of liver enzymes point to hepatic damage. The suspected drugs were discontinued and hepatoprotectives along with antihistamine were initiated. Faulty treatment can dive into drug-resistant strains of Mycobacterium tuberculosis and exterminate almost half of the victims within five years if left untreated. A meticulous follow-up and timely change of therapy may avert serious adverse events.

INTRODUCTION

Tuberculosis is known to be declared as a worldwide health emergency, which is the second leading infectious killer after covid 19 [1,2]. The standard treatment in line with the RNTCP guidelines for respiratory tuberculosis comprise of isoniazid, rifampicin, ethambutol and pyrazinamide for 8 weeks accompanied by 16 weeks of isoniazid, rifampicin and ethambutol [3]. Directly observed therapy endorsed by WHO has ameliorated patient's therapeutic adherence and positive outcomes but the treatment interruptions give rise to adverse reactions [4].The most prevalent lethal outcomes are hepatotoxicity, cutaneous reactions, gastrointestinal and neurological disorders [3]. Hepatic damage can range from asymptomatic transaminase elevations to fulminant hepatic failure. Drug induced skin injury is amalgamated with itching, skin rash, blisters, eosinophilia, lymphadenopathy and mucocytosis [5].

CASE REPORT

A 47 year old female patient with microbiologically confirmed pulmonary tuberculosis two weeks back was presented to the Department of pulmonary medicine of Government medical college hospital. The fluorescence microscopy for presumptive tuberculosis of sputum revealed appearance of acid fast bacilli with grade 1+. The patient showed up with complaints of cough, loss of appetite, itching and loss of weight .While obtaining family history, we ascertained extrapulmonary tuberculosis in father 12 years back, h/o tuberculosis eye in daughter of sister and h/o extrapulmonary tuberculosis in aunty. She commenced anti -tubercular regimen in the intensive phase with isoniazid 75mg, pyrazinamide 400mg, rifampicin 150mg and ethambutol 275mg.

Upon investigation the patient was conscious and unveiled with pallor, the vitals were stable with blood pressure 130/80mmHg, pulse rate 78/minute and fasting blood sugar

76mg/dL .The following lab investigations were done; blood routine examination, liver profile, renal profile, HBsAg-CLIA, HIV-CLIA, HCV-CLIA, hepatitis panel-AHBC, arthritis-ANA, USG abdomen. Hemoglobin level was found to be 11g/dL and liver function test was deranged [table 1] . The ultrasonography study of abdomen exhibited the liver span as 13.8cm and gall bladder wall thickness as 4mm.The renal function test was ascertained to be normal. The estimates of Hepatitis B Surface Antigen, Human Immunodeficiency Virus and Hepatitis C antigen was accounted to be 0.25COI, 0.22COI and 0.04 COI each to each which was non-reactive. The test for hepatitis panel and antinuclear antibodies viewed as normal.

DISCUSSION

The cutaneous reaction of itching over the chest was a sign of dermatitis. The elevation in the estimates of liver enzymes such as aspartate aminotransferase, alanine transaminase and alkaline phosphatase along with aberrant values of liver proteins-serum albumin and serum globumin is a pointer to hepatic damage.

Isoniazid, pyrazinamide and rifampicin are grievous hepatotoxic drugs. Hepatotoxicity to isoniazid cause elevation of serum transaminases, bilirubinemia, bilirubinurea, jaundice in conjugation with dermatological, gastrointestinal, hypersensitivity, neurological, hematological and renal reactions [6]. Pyrazinamide is the most hepatotoxic than isoniazid and rifampicin and has been marked out to cause various skin reactions like maculopapular rash, erythema multiforme, exfoliative dermatitis and DRESS syndrome [7]. Other complications include hyperuricemia, flushing, arthralgia, dysurea and sideroblastic anemia. The complexity in association with rifampicin involves the skin and gastrointestinal system. May cause epigastric distress, anorexia, psuedomembranous colitis and pancreatitis [8]. Hepatitis and transient bilirubinemia occur with the co-administration with isoniazid. Serious vision problems like visual acuity and optic neuritis are the reported side effects of ethambutol. The incidence rate of CADR among the first line Antitubercular drugs - Pyrazinamide is the commonest offending drug(2.38%) followed by streptomycin(1.45%), ethambutol(1.44%), rifampicin(1.23%) and isoniazid(0.98%) [7]. The incidence rate of liver toxicity is 1.1% with rifampicin alone and 1.6% with isoniazid alone but 2.6% with isoniazid and rifampicin co-administration [9].

As a clinical pharmacist we proposed the incidence of antitubercular drug induced hepatitis and dermatitis. The initiative was to withdraw the antitubercular medications owing to aftereffect and to observe the refinement. This ensued in the lessening of cutaneous reaction and normalizing of liver function tests. We conducted investigations to rule out other alternative causes and thus to put a period to the diagnosis. The advancement in the outcomes with the discontinuation of the suspected drugs pilot us to scrutinize the adverse reaction by Naranjo adverse drug reaction probability scale in which Antitubercular drug induced hepatitis was deemed to be a probable ADR and Antitubercular drug induced dermatitis was a possible ADR.

The drugs allocated in the course of therapy is given in table below [table 2]. The hepatoprotective drug URSODEOXYCHOLIC ACID is given which tweak the manifestations. The itching was truncated by the antihistamine CETIRIZINE. N-ACETYL CYSTEINE replenishes the glutathione level which act as antioxidant. VITAMIN-B COMPLEX possess antioxidative properties which is a mandatory supplement in drug-induced toxicity in tuberculosis patient. The antitubercular drug regimen was substituted with LEVOFLOXACIN 750mg, ETHAMBUTOL 800mg and Intramusular injection STREPTOMYCIN 0.75g on daily doses and the patient was discharged. The patient was counseled regarding the need to complete the course of ATT medication. A meticulous follow-up and timely change of therapy may avert serious adverse events. Levofloxacin may cause diarrhea, pounding heartbeats, headache, dizziness, shortness of breath and ethambutol may lead to blurred vision, loss of vision, colour blindness which makes the patient obliged to inform the physician. Streptomycin is given by intramuscular injection from the local hospital and directed to be monitored for ototoxicity and nephrotoxicity.

CONCLUSION

Prompt commencement of potent therapy for pulmonary

Table 1 : Liver Function Test

TEST	DAY 1	DAY 3	DAY 6	NORMAL RANGE
Serum bilirubin total	0.7	0.5	0.5	0.2-1.0mg%
Serum bilirubin direct	0.1	0.1	0.1	<0.25 mg%
SGPT	223	323	165	5-42 IU/L
SGOT	511	295	59	5-38 IU/L
Serum ALP	138	144	96	20-112 IU/L
Serum total protein	8.6	7.5	6.5	5.5-8.5 gm%
Serum albumin	2.9	3.2	3.5	3.0-5.0 gm%
Serum globulin	4.9	4.3	3.7	2.5-3.5 gm%

Table 2 : Drug Chart

DRUGS	Dose	Frequency	1	2	3	4	5	6
T.Ursodeoxycholic acid	150 mg	1-0-1	+	+	+	+	+	+
T.Ranitidine	150 mg	1-0-1	+	+	+	+	+	+
T.Vitamin B Complex	B1-1.1mg B2-1.1mg B3-14mg B5-5mg B6-1.5mg B7-30mcg B9-400mcg B12-2.4mcg	1-0-1	+	+	+	+	+	+
T.Cetirizine	10 mg	SOS	+	+	+			
T.N-acetyl cysteine	600 mg	1-0-1	+	+	+	+	+	
Inj.Glutathione	600 mg	OD				+	+	
Inj.Streptomycin	0.75 g IM	OD						+
T.Ethambutol	800 mg	OD						+
T.Levofloxacin	750 mg	OD						+

tuberculosis terminate the transmission of Mycobacterium tuberculosis from one to many. The antitubercular treatment is requisite for one's well-being along with communal health intercession. Tuberculosis can be fatal and exterminate almost half of the victims within five years if left untreated. The active disease may proliferate to other body organs due to deprivation of therapy. Faulty treatment can dive into drug-resistant strains of Mycobacterium tuberculosis that are comparatively strenuous to cure. Hence patient should be adherent to regimen for finer net result.

LIMITATIONS

Further follow-up of the case was not achievable and cases with similar prodromes were arduous to pile up.

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

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