Case Report

Drug-Induced Liver Injury During First-Line Anti-Tubercular Therapy (Isoniazid, Rifampicin, Pyrazinamide, and Ethambutol): A Case Report with De-challenge and Rechallenge

Sridevi Chokkakula[1*], Ashwitha Balasani[1], Sathwika Reddy Ammana[2]

Article Info

[*]***Corresponding Author:***
Sridevi Chokkakula
Department of Pharmacy Practice, Malla Reddy Pharmacy College, Maisammaguda, Hyderabad, Telangana, India.
E-mail: sridevisamireddy92@gmail.com
Phone: 7780659802

Keywords

ADR (adverse drug reaction), Anti-tubercular therapy, De-challenging, HRZE (isoniazid, Rifampicin, Pyrazinamide, Ethambutol), Re-challenging, TB (Tuberculosis)

Abstract

Background: The primary treatment for tuberculosis, which includes isoniazid, rifampicin, pyrazinamide, and ethambutol, is vital for managing the disease but often leads to drug-induced liver injury (DILI), especially in older adults. It is important to accurately identify and manage hepatotoxicity caused by this treatment to safely continue therapy.

Objective: This report discusses a case of liver injury induced by first-line anti-tubercular drugs in an elderly patient, emphasizing the importance of de-challenge, alternative non-hepatotoxic treatments, and a carefully monitored stepwise rechallenge.

Methods: An 84-year-old woman with pulmonary tuberculosis and hypertension (treated with amlodipine) experienced abnormal liver function tests after starting first-line anti-tubercular therapy. A thorough clinical evaluation, laboratory tests, causality assessment, de-challenge, alternative treatment, and stepwise rechallenge were conducted with close biochemical monitoring.

Results: Initial tests showed significant hyperbilirubinemia (total bilirubin 5.2 mg/dL), elevated aspartate aminotransferase (AST 176–247 U/L), slightly increased Alanine Aminotransferase (ALT 40–55 U/L), and an R-ratio of about 2.6, indicating a predominantly cholestatic pattern with mixed features of liver injury. After discontinuing the hepatotoxic treatment and starting alternative medications (Moxifloxacin, Streptomycin, and Ethambutol), liver function tests improved significantly within 3–5 days. Once liver parameters normalized, Rifampicin was gradually reintroduced, and liver function tests remained stable four days after rechallenge, with no return of hepatotoxicity.

Conclusion: This case illustrates that early detection of liver injury from anti-tubercular therapy, prompt de-challenge, use of alternative non-hepatotoxic drugs, and a carefully monitored stepwise rechallenge can enable the safe continuation of tuberculosis treatment in elderly patients. Close biochemical monitoring, along with consideration of therapeutic drug monitoring, may further improve patient safety.

Introduction

Tuberculosis ranks as a significant infectious disease globally and is one of the top causes of illness and death around the world. The World Health Organization reports that millions of new tuberculosis cases emerge each year, especially in low- and middle-income nations. Successful treatment necessitates extended multidrug therapy to ensure recovery and prevent the development of resistance [11]. ”Hepatitis” is a term referring to inflammation of the liver, a condition that can result from various causes, including viral infections, alcohol consumption, drug reactions, or autoimmune disorders. It’s a swelling of the liver tissue, which can damage its function [1]. ATT (antitubercular therapy)-induced drug-induced liver injury is defined as an increase in liver enzymes such as alanine transaminase (ALT) and aspartate transaminase (AST) to more than 2-3 times the upper normal limit in individuals taking antitubercular medication in the absence of other causes of liver injury [2]. Among the first-line drugs, isoniazid (H), rifampicin (R), and pyrazinamide (P) have potential for hepatotoxicity, with pyrazinamide being the most hepatotoxic, followed by isoniazid and rifampicin [3]. ATT-induced hepatitis is due to metabolic idiosyncrasy, where the metabolites are released and accumulated during the metabolic process; this may be facilitated by polymorphism of metabolizing enzymes [4]. The pathogenesis of isoniazid-induced hepatotoxicity is not fully understood and involves hepatic metabolism. Isoniazid is metabolized by N-acetyltransferase (NAT2) and CYP2E1 to form acetyl hydrazine and other intermediates. These metabolites produce reactive toxic species that bind to hepatic macromolecules, leading to liver injury [5]. Rifampicin enhances the hepatotoxicity of other anti-tubercular drugs. It activates the pregnane X receptor, leading to induction of drug-metabolizing enzymes such as CYP3A4. This increases isoniazid metabolism and the formation of toxic metabolites, contributing to liver injury. [6]. Rifampicin also induces isoniazid hydrolases, leading to increased hydrazine levels in slow acetylators, thus increasing toxicity [7]. Compared to other primary antitubercular medications, ethambutol-induced liver toxicity is infrequent and unusual. The precise mechanism remains unclear, and ethambutol is not regarded as a direct intrinsic liver toxin. Current evidence indicates that liver damage is primarily idiosyncratic and immune-mediated, rather than related to dosage. Moxifloxacin as an alternative anti-tubercular drug works by inhibiting DNA gyrase (topoisomerase II) and topoisomerase IV, which are crucial for bacterial DNA replication and transcription, thereby preventing the growth of Mycobacterium tuberculosis. Streptomycin is utilized as a second-line tuberculosis medication, primarily targeting extracellular mycobacteria, and is used when hepatotoxic drugs need to be avoided. It irreversibly attaches to the 30S ribosomal subunit, leading to mRNA misreading and blocking protein synthesis, which results in the death of bacterial bactericidal effect [6,8]. Hepatotoxicity is often observed as part of hypersensitivity reactions, such as DRESS syndrome, suggesting an immunological component. Since ethambutol is typically used in combination with other drugs, determining its specific role in liver damage is challenging [12]. Pyrazinamide leads to liver damage primarily due to its dose-dependent metabolic toxicity. Inthe liver, it is converted to pyrazinoic acid and subsequently to 5-hydroxypyrazinoic acid, metabolites that are directly toxic to hepatocytes. These metabolites induce oxidative stress, disrupt mitochondrial function, and impair cellular energy production, resulting in hepatocellular injury and necrosis, which clinically manifests as elevations in alanine aminotransferase and aspartate aminotransferase levels resembling acute hepatitis. Compared to other first-line antitubercular drugs, pyrazinamide is more hepatotoxic because its liver injury is strongly dose dependent, occurs through direct metabolic toxicity rather than idiosyncratic reactions, and lacks a safe metabolic detoxification pathway. The risk is further amplified in elderly patients, those with pre-existing liver disease, and when pyrazinamide is used in combination with other hepatotoxic antitubercular agents [13]. Antitubercular drug–induced liver injury occurs due to multiple biochemical mechanisms. During hepatic metabolism, these drugs form reactive metabolites that can damage mitochondria, leading to reduced energy production and hepatocyte injury. These metabolites induce oxidative stress by generating reactive oxygen species, leading to lipid peroxidation and cell membrane damage. They may also trigger immune-mediated liver injury, with combined effects of mitochondrial dysfunction, oxidative stress, and immune activation contributing to hepatocellular or cholestatic injury [10]. The various risk factors for ATT (anti-tubercular therapy)-induced hepatitis include advanced age, female gender, pregnancy, comorbidities such as diabetes and obesity, underlying liver diseases, genetic factors such as acetylator polymorphism, concomitant viral infections such as HIV and hepatitis B and C, and underlying nutritional status such as malnutrition [8].

While liver injury caused by anti-tubercular drugs is well recognized, there is a scarcity of detailed accounts on how it is managed in older patients, especially concerning the use of alternative medications and the careful, monitored reintroduction of first-line treatments. This case report aims to detail a liver injury caused by medication in an elderly patient undergoing first-line anti-tubercular treatment. It also emphasizes the importance of dechallenge, the use of alternative therapies that do not harm the liver, and a carefully monitored step-by-step rechallenge to ensure the safe continuation of tuberculosis treatment.

Materials and methods

Study Design

This manuscript is a descriptive, single-patient case report documenting drug-induced liver injury associated with first-line anti-tubercular therapy.

Study Setting and Duration

The case was identified and managed in the Department of General Medicine at Malla Reddy Hospital, Suraram, Hyderabad, Telangana, India. The clinical evaluation, management, and follow-up were carried out during the patient’s hospital admission in 2024.

Patient Selection

The patient was selected based on the clinical presentation of

abnormal liver function tests following initiation of first-line anti-tubercular therapy.

Inclusion Criteria

Patients were included if they:
We're receiving first-line anti-tubercular therapy (isoniazid, rifampicin, pyrazinamide, and ethambutol)
Developed abnormal liver function tests temporally associated with anti-tubercular drug exposure
Showed improvement in liver function tests following dechallenge of suspected hepatotoxic drugs

Exclusion Criteria

Patients were excluded if they:
Had pre-existing chronic liver disease
Had confirmed viral hepatitis or obstructive hepatobiliary disease as the primary cause of liver dysfunction
Had liver injury attributable to causes other than anti-tubercular drugs

Case

An 84-year-old woman was admitted to the General Medicine department with complaints of loose stools, vomiting, poor oral intake, and epigastric abdominal pain for the past three days. She had been diagnosed with pulmonary tuberculosis two months earlier and was receiving first-line anti-tubercular therapy comprising isoniazid, rifampicin, pyrazinamide, and ethambutol. She was also a known hypertensive for several years and was on regular treatment with amlodipine 5 mg once daily. The therapy was temporarily discontinued during the evaluation of liver injuryas a precautionary measure in the context of polypharmacy, although it is not commonly associated with hepatotoxicity. There was no history of chronic liver disease, alcohol use, or intake of other hepatotoxic medications.

Lab investigations

Her lab data showed IgG Ab positive (8.81). A normal value of <1.00 to rule out infectious causes of liver damage, viral hepatitis screening was conducted. The test for Hepatitis A IgM came back negative, while Hepatitis A IgG was positive (8.81), suggesting previous exposure and immunity rather than a current infection. Tests for Hepatitis B surface antigen (HBsAg) and anti-Hepatitis C virus (anti-HCV) antibodies were also negative. These results effectively exclude acute viral hepatitis as the source of the liver injury. Due to the swift biochemical recovery after stopping the medication and the clear timing with antitubercular treatment, autoimmune markers were not assessed, as the rapid biochemical improvement following drug withdrawal strongly supported a drug-induced etiology, making alternative causes such as autoimmune hepatitis less likely. An abdominal ultrasound revealed that the liver's echotexture was normal, with no signs of biliary blockage, gallstones, or dilation within the intrahepatic bile ducts; this excludes obstructive cholestasis. Reduced Hb levels to 9.7 gm% and reduced RBC levels to 3.1 m/cmm with an increased ESR. Liver function tests showing the rise in ALT, AST, and bilirubin levels and decreased total protein levels. Electrolytes showing hyponatremia and hypokalemia with urine culture positive for E. coli. Child-Pugh test score 5. Renal function tests were found to be normal.

Table 1: Liver function test results at baseline before de-challenge of first-line anti-tubercular therapy.

LFT	Day1	Day2	Reference Values
Total Bilirubin	5.2	5.0	0.3-1.3mg/dL
Direct Bilirubin	3.1	3.8	0.1-0.3mg/dL
Indirect Bilirubin	2.1	1.2	0.2-0.8md/dL
AST	176	247	10-40U/L
ALT	40	55	7-56U/L
ALP	63	63	44-147U/L
Total protein	5.6	5.4	6-8.3g/dL
Albumin	3.2	3.1	3.5-6.5g/dL
Globulin	2.4	2.3	2-3.5g/dL
A/G	1.33	1.37	1.5-2.5

Table 2: Liver function test trends following de-challenge and treatment with alternative anti-tubercular agents (Day 3–Day 5).

LFT	Day3	Day4	Day5	Reference Values
Total Bilirubin	1.8	1.8	1.6	0.3-1.3mg/dL
Direct Bilirubin	1.2	1.2	1.1	0.1-0.3mg/dL
Indirect Bilirubin	0.6	0.6	0.5	0.2-0.8md/dL

LFT	Day3	Day4	Day5	Reference Values
AST	89	59	33	10-40U/L
ALT	68	61	38	7-56U/L
ALP	57	60	53	44-147U/L
Total protein	5.3	5.7	5.4	6-8.3g/dL
Albumin	3.0	3.3	3.2	3.5-6.5g/dL
Globulin	2.3	2.4	2.3	2-3.5g/dL
A/G	1.30	1.37	1.39	1.5-2.5

Table 3: Liver function test results four days after stepwise rechallenge with rifampicin.

LFT	Four days after administration of rifampicin	Reference Values
Total Bilirubin	1.6	0.3-1.3mg/dL
Direct Bilirubin	1.4	0.1-0.3mg/dL
Indirect Bilirubin	0.2	0.2-0.8md/dL
AST	24	10-40U/L
ALT	17	7-56U/L
ALP	54	44-147U/L
Total protein	5.6	6-8.3g/dL
Albumin	3.2	3.5-6.5g/dL
Globulin	2.4	2-3.5g/dL
A/G	1.33	1.5-2.5

Table 4: Showing Serum Electrolyte Levels.

Electrolytes	DAY 1	DAY 4	Reference Values
Sodium	131 mEq / L	136 mEq/L	135-145mEq/L
Potassium	2.5 mEq/L	3.6 mEq/L	3.5-5mEq/L
Chloride	97 mEq/L	97 mEq/L	98-106mEq/L

Upon initial examination, liver function tests revealed marked hyperbilirubinemia, with a total bilirubin concentration of 5.2 mg/dL, alongside increased aspartate aminotransferase (AST) and slightly raised alanine aminotransferase (ALT) levels. To characterize the pattern of liver injury, the R-ratio was calculated using the formula R = (ALT/ULN) ÷ (ALP/ULN). The peak ALT level was 55 U/L (ULN 40 U/L), and ALP was 63 U/L (ULN 120 U/L). The calculated R-ratio was therefore (55/40) ÷ (63/120) ≈ 2.63, indicating a mixed hepatocellular–cholestatic pattern of liver injury. This biochemical pattern, along with marked hyperbilirubinemia and modest transaminase elevation, supported a predominantly cholestatic pattern with mixed features,consistent with drug-induced liver injury. This was corroborated by the significant rise in bilirubin levels, modest elevation in transaminases, and nearly normal ALP levels. After discontinuing the suspected hepatotoxic antitubercular medications, there was a gradual return to normal of bilirubin and liver enzyme levels, indicating a reversible drug-induced liver injury. Due to abnormal liver function tests indicating potential liver damage from anti-tubercular drugs, all first-line anti-tubercular medications (isoniazid, rifampicin, and pyrazinamide) with hepatotoxic potential were discontinued (dechallenge). The patient was then started on alternative anti-tubercular drugs that are not harmful to the liver, such as moxifloxacin, streptomycin, and ethambutol.

Liver function was closely monitored, and within three to five days of beginning the new treatment, there was a noticeable improvement in serum bilirubin and transaminase levels, suggesting a successful de-challenge response. After liver function tests returned to normal, the initial anti-tubercular treatment was gradually reintroduced, beginning with rifampicin, and no signs of hepatotoxicity reappeared during the first fourdays of this process.

Initial serum electrolyte tests showed slight hyponatremia (Na: 133 mEq/L) and hypokalemia (K: 2.5 mEq/L), which improved upon retesting (Na: 134 mEq/L, K: 3.6 mEq/L) after supportive care. These imbalances were linked to gastrointestinal losses and decreased oral intake and were resolved before resuming anti-tubercular treatment.

Table 5: RUCAM Causality Assessment for Anti-Tubercular Therapy-Induced Liver Injury.

RUCAM Criteria	Clinical Findings in present case	Score
Time of onset of liver injury after starting the drug	Patient developed abnormal liver function tests approximately 2 months after initiation of ATT, which falls within the typical time frame for ATT-Induced DILI	+2
Course of ALT after stopping the drug (DECHALLENGE)	ALT and Bilirubin levels improved significantly within 3-5 days after withdrawal of hepatotoxic drugs	+3
Risk factors	Age>55 years (84 years)	+1
Concomitant drugs	Amlodipine was used but discontinued and not strongly associated with significant hepatotoxicity	0
Exclusion of non-drug causes	Viral hepatitis screening performed (Hepatitis A IgM negative, HBsAg negative, Anti-HCV negative); no history of alcohol use or chronic liver disease; imaging excluded biliary obstruction.	+2
Previous hepatotoxicity information for the drug	Hepatotoxicity of Isoniazid, Rifampicin, and Pyrazinamide is well documented in literature	+2
Response to re-administration (RECHALLENGE)	Rifampicin rechallenge did not reproduce hepatotoxicity during the monitored period.	0
TOTAL SCORE		10

Causality assessment was performed using the RUCAM (Roussel Uclaf Causality Assessment Method) scale, which yielded a score of 10, indicating highly probable drug-induced liver injury.

Treatment

In view of markedly abnormal liver function tests suggestive of drug-induced liver injury, first-line anti-tubercular therapy was withheld (dechallenge). Alternative treatment with non-hepatotoxic drugs of Inj. MOXIFLOXACIN 400 mg IV OD, initiated as an alternative treatment for tuberculosis, particularly when primary medications are unsuitable due to side effects or drug resistance. Inj. STREPTOMYCIN 0.75 g IM OD is utilized as a second-line tuberculosis medication, primarily targeting extracellular mycobacteria, and is used when hepatotoxic drugs need to be avoided. and Inj. ETHAMBUTOL 800 mg is employed as a supplementary antitubercular drug to avert drug resistance and boost treatment effectiveness. It is given along with liver protectants such as Inj.

L-ORNITHINE-L-ASPERTATE 6 amp in 10 DNS slow IV over 8 hours, T. URSODEOXYCHOLIC ACID 300 mg PO BD, and T. GLUTATHIONE 500 mg PO BD. On the third day the patient was administered Inj. N-ACETYL CYSTINE 600 mg PO BD.

On the fifth day, MOXIFLOXACIN was stopped, and T. LEVOFLOXACIN 500 mg OD was administered. Liver function tests were performed until optimal results were obtained.

After normalization of liver function tests, a cautious stepwise rechallenge of first-line anti-tubercular therapy was initiated, beginning with low-dose rifampicin under close biochemical monitoring: RIFAMPICIN 150 mg on day 1, and the dose was incrementally increased to T. RIFAMPICIN 300 mg on day 2 and 400 mg on day 4. Along with FAROPENAM 200 mg P/O OD, T. LEVOFLOXACIN and Inj. STREPTOMYCIN were withheld, and LFTs were repeated, and they showed normal results. The ophthalmologist's opinion was taken, and a fundoscopy was performed: There is no evidence was found of retinopathy changes; a psychiatrist's opinion was taken in view of the past history of delirium. They advised T. ZOLPIDEM 5 mg SOS (when the patient is unable to sleep).

DISCHARGE MEDICATION

T. RIFAMPICIN 450mg PO OD

T. ETHAMBUTOL 800mg PO OD

T. URSODEOXYCHOLIC ACID 300mg PO BD x 5 days

T.PANTOPRAZOLE 40mg PO OD x 5 days
T. ZOLPIDEM 5mg PO SOS

Discussion

Drug-induced liver injury is a known complication of first-line antitubercular therapy, especially in older patients who may experience altered drug metabolism and diminished liver function. In this case, the liver injury's biochemical pattern, its timing with the start of antitubercular therapy, and the quick recovery after stopping the medication strongly indicate ATT-associated DILI. As the patient also had a urinary tract infection caused by Escherichia coli and electrolyte disturbances, including hyponatremia and hypokalemia, likely related to gastrointestinal losses and reduced oral intake. Although systemic infection and metabolic disturbances can occasionally influence liver enzyme levels, the rapid normalization of liver function tests following withdrawal of hepatotoxic drugs suggests that antitubercular therapy remained the most plausible cause of liver injury in this case. The successful gradual reintroduction of rifampicin without the return of liver toxicity further confirmed the diagnosis while enabling the continuation of tuberculosis treatment.

The treatment for ATT-induced liver diseases should be initiated at an appropriate time; if not, this may lead to life-threatening conditions such as resistant TB. Once the diagnosis of ATT-induced hepatitis is established, it is essential to first stop all potentially hepatotoxic drugs till the LFTs become normal. In the interim period, at least three non-hepatotoxic drugs, such as ethambutol, streptomycin, and quinolones such as levofloxacin, ofloxacin, and moxifloxacin, can be used after evaluation of renal function and visual acuity.

The liver injury pattern observed in this patient is consistent with hepatotoxicity associated with first-line antitubercular therapy. The marked elevation in bilirubin levels with relatively lower transaminases suggests a predominantly cholestatic pattern rather than hepatocellular injury. The patient's clinical improvement following drug withdrawal, along with the absence of worsening upon cautious rechallenge, further supports the diagnosis of drug-induced liver injury. These findings highlight the importance of early recognition and timely management to prevent complications.

According to National Tuberculosis Eradication Programme (NTEP) guidelines and recommendations from the World Health Organization (WHO), rechallenge with antitubercular drugs is generally initiated once transaminase levels return to less than two times the upper limit of normal, with stepwise reintroduction of drugs and adequate monitoring intervals. In the present case, a rechallenge strategy was implemented; however, the duration of monitoring between drug reintroductions was shorter than typically recommended in standard guidelines. This deviation was a pragmatic clinical decision, necessitated by the patient's advanced age and the urgent need to resume effective tuberculosis therapy. Rifampicin was selected as the initial drug for rechallenge due to its comparatively lower hepatotoxic potential relative to isoniazid and pyrazinamide and its established role as the backbone of antitubercular therapy, in alignment with national and WHO guidance. However, rechallenge was limited to rifampicin alone, and isoniazid and pyrazinamide were not reintroduced. This limits definitiveattribution of hepatotoxicity to a specific agent. Despite the shortened rechallenge period, close clinical and biochemical monitoring was performed to ensure patient safety. The approach reflects a balance between guideline recommendations and real-world clinical urgency. Based on the WHO-UMC causality assessment scale, this case was categorized as a probable adverse drug reaction.

The World Health Organization–Uppsala Monitoring Centre (WHO-UMC) causality assessment scale was utilized to evaluate causality. A distinct temporal link was identified between the start of first-line antitubercular treatment and the emergence of liver dysfunction. Clinical and laboratory assessments ruled out other potential causes of liver damage, such as viral hepatitis and obstructive hepatobiliary disease. During a stepwise rechallenge, rifampicin was reintroduced, and liver function tests remained normal four days after reintroduction, with no recurrence of hepatotoxicity. Given the temporal correlation, positive dechallenge outcome, and exclusion of other causes, the reaction was deemed a probable adverse drug reaction according to WHO-UMC criteria. A structured causality assessment using the Roussel Uclaf Causality Assessment Method (RUCAM) yielded a score, indicating a highly probable drug-induced liver injury. Most studies published on liver injury caused by anti-tubercular drugs focus on mixed-age or relatively younger groups and mainly report hepatocellular or mixed liver injury patterns. These studies typically involve stopping the problematic drugs, with limited documentation of stepwise rechallenge, as it is often avoided due to safety concerns. In contrast, the current case involves a very elderly patient (84 years old), a demographic often under-represented in the literature, and shows a mixed liver injury pattern was observed, with features suggesting a predominantly cholestatic component, while most reports focus on hepatocellular injury. Additionally, this case includes a well-documented laboratory timeline, showing baseline abnormalities, improvement after de-challenge from Day 3 to Day 5, and stable liver function tests four days after a stepwise rechallenge. The successful continuation of first-line anti-tubercular therapy following a carefully monitored rechallenge underscores a practical management strategy that goes beyond diagnosis and may provide valuable clinical guidance.

With the stated objective, this case highlights that cautious rifampicin rechallenge may be feasible even in very elderly patients with suspected anti-tubercular drug-induced liver injury when careful monitoring is undertaken.

Limitations

This report is constrained by its focus on a single patient, which limits its applicability to a broader population. Additionally, procedures such as liver biopsy, therapeutic drug monitoring, and pharmacogenetic testing (such as NAT2 polymorphism analysis) were not conducted. Furthermore, the multiple hepatotoxic antitubercular drugs were discontinued simultaneously, making it difficult to identify the causative agent, and the rechallenge period was relatively short. Despite these constraints, the case offers a clear temporal relationship, and a positive dechallenge

response, exclusion of alternative causes, and supportivecausality assessment provide reasonable evidence and also provide valuable clinical insights into managing anti-tubercular drug-induced liver injury in an elderly patient.

Conclusion

This case report discusses a drug-induced liver injury linked to first-line anti-tubercular treatment in an elderly patient, characterized by a cholestatic liver injury pattern. Early identification, swift withdrawal of hepatotoxic medications, and the introduction of alternative non-hepatotoxic anti-tubercular drugs led to a quick biochemical recovery. A cautious, gradual reintroduction of rifampicin with close laboratory monitoring was well-tolerated without a return of hepatotoxicity, allowing for the safe continuation of tuberculosis therapy. This case emphasizes the significance of personalized management strategies for elderly patients and highlights the importance of close biochemical monitoring and therapeutic drug monitoring as essential tools to improve the safety of de-challenge–rechallenge strategies in cases of anti-tubercular drug-induced liver injury.

Conflict of interest

None.

Funding Statement

Nil.

Ethical Approval Statement

This paper presents a case study involving a single patient, based on standard clinical practice. According to the ethical guidelines of Malla Reddy Hospital in Suraram, Hyderabad, Telangana, India, individual case reports are considered clinical documentation rather than research involving human subjects and thus do not require a formal reference number from the Institutional Ethics Committee. The committee has reviewed and approved the publication of this case. The patient provided written informed consent for the publication.

Patient Consent Statement

Written informed consent was obtained from the patient for publication of the case report.

Acknowledgement

The authors would like to thank the guide, Dr. CH. Sridevi, and Dr. G. Tulja Rani, principal of Malla Reddy Pharmacy College, for their kind support and encouragement, and the physicians of the general medicine department, Malla Reddy Hospital, Suraram.

Credit Author Statement

Author 1*: Supervision, final approval of manuscript, and support in case interpretation.
Author 1: Conceptualization, Data Collection, Clinical Examination, Investigation, Writing-Original Draft Preparation.
Author 2: Literature search, editing and validation of clinical details, reference management, and proofreading.

Data Availability Statement

The data supporting this case report are not publicly available due to patient privacy and confidentiality. Anonymized information may be provided by the corresponding author upon reasonable request.

References

1. Zhao H, Wang Y, Zhang T, Wang Q, Xie W. Drug-induced liver injury from anti-tuberculosis treatment: A retrospective cohort study. Med Sci Monit [Internet]. 2020;26:e920350. Available from: http://dx.doi.org/10.12659/MSM.920350
2. Giannini EG, Testa R, Savarino V. Liver enzyme alteration: a guide for clinicians. CMAJ [Internet]. 2005;172(3):367–79. Available from: http://dx.doi.org/10.1503/cmaj.1040752
3. Hoofnagle JH, Björnsson ES. Drug-induced liver injury - types and phenotypes. N Engl J Med [Internet]. 2019;381(3):264–273. Available from: http://dx.doi.org/10.1056/NEJMra1816149
4. Knowles SR, Uetrecht J, Shear NH. Idiosyncratic drug reactions: the reactive metabolite syndromes. Lancet [Internet]. 2000;356(9241):1587–1591. Available from: http://dx.doi.org/10.1016/S0140-6736(00)03137-8
5. Huang Y-S, Chern H-D, Su W-J, Wu J-C, Lai S-L, Yang S-Y, et al. Polymorphism of the N-acetyltransferase 2 gene as a susceptibility risk factor for antituberculosis drug-induced hepatitis. Hepatology [Internet]. 2002;35(4):883–889. Available from: http://dx.doi.org/10.1053/jhep.2002.32102
6. Shen C, Meng Q, Zhang G, Hu W. Rifampicin exacerbates isoniazid-induced toxicity in human but not in rat hepatocytes in tissue-like cultures. Br J Pharmacol [Internet]. 2008;153(4):784–791. Available from: http://dx.doi.org/10.1038/sj.bjp.0707611
7. Chen J, Raymond K. Roles of rifampicin in drug-drug interactions: underlying molecular mechanisms involving the nuclear pregnane X receptor. Ann Clin Microbiol Antimicrob [Internet]. 2006;5(1):3. Available from: http://dx.doi.org/10.1186/1476-0711-5-3
8. Anand AC, Seth AK, Paul M, Puri P. Risk factors of hepatotoxicity during anti-tuberculosis treatment. Med J Armed Forces India [Internet]. 2006;62(1):45–49. Available from: http://dx.doi.org/10.1016/S0377-1237(06)80155-3
9. Centers for Disease Control and Prevention. Clinical guidelines for TB. Available from: https://www.cdc.gov/tb/. Accessed: 04/12/2025.
10. Knowles SR, Uetrecht J, Shear NH. Idiosyncratic drug reactions: the reactive metabolite syndromes. Lancet [Internet]. 2000;356(9241):1587–1591. Available from: http://dx.doi.org/10.1016/S0140-6736(00)03137-8
11. Global tuberculosis reports [Internet]. Who.int. [cited 2026 Jan 6]. Available from: https://www.who.int/teams/global-tuberculosis-programme/tb-reports
12. Ethambutol. In: LiverTox: Clinical and Research Information on Drug-Induced Liver Injury. Bethesda (MD): National Institute of Diabetes and Digestive and Kidney Diseases; 2012.

13. Hussain Z, Zhu J, Ma X. Metabolism and hepatotoxicity of pyrazinamide, an antituberculosis drug. Drug Metab Dispos [Internet]. 2021;49(8):679–682. Available from: http://dx.doi.org/10.1124/dmd.121.000389