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Antituberculosis therapy-induced liver injury: A case report and clinical management strategies

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Abstract

Drug-Induced Liver Injury (DILI) from Anti-Tuberculosis Therapy (ATT) is increasingly common and affects patient outcomes. Factors like alcohol use, existing liver conditions, and gender (especially females) influence DILI risk. Recognizing and managing DILI quickly is crucial. This case study of a 32-year-old female with ATT-induced liver injury shows the importance of management strategies and healthcare provider roles in monitoring and education. The patient, with a history of tuberculosis, started ATT for work-related annual chest X-rays. After about six weeks, she developed body swelling, yellowing skin, and itching, leading to the discontinuation of ATT. Symptomatic treatment and liver protection improved her condition, with decreasing SGOT, SGPT, and bilirubin levels. She was discharged with follow-up instructions. ATT-induced DILI is a significant challenge, requiring prompt therapy cessation and supportive care. Healthcare providers, especially pharmacists, are essential in-patient education and monitoring. Further research and collaboration are needed to reduce ATT-induced DILI risks.

Keywords: Drug-Induced Liver Injury (DILI); Anti-Tuberculosis Therapy (ATT); Clinical presentation; Risk factors; Management.

Introduction

Drug-Induced Liver Injury (DILI) is a significant clinical concern, characterized by liver damage resulting from the administration of various medications [1]. One area where DILI is of particular concern is in the context of Anti-Tuberculosis Therapy (ATT), which is used to treat Tuberculosis (TB) infections [2]. ATT-induced liver injury has been a growing issue in recent years, with numerous cases reported worldwide [3]. The prevalence of ATT-induced DILI is influenced by several factors, including patient characteristics, concomitant medication use, and individual susceptibility [4]. The primary medications implicated in ATT-induced DILI are Isoniazid (INH), Rifampicin (RIF), and Pyrazinamide (PZA) [5]. These drugs are crucial components of the standard TB treatment regimen and have demonstrated efficacy in combating the infection. However, they are also known to carry a risk of hepatotoxicity, making liver injury a potential adverse effect of ATT [6]. The exact mechanisms underlying DILI in the context of ATT remain poorly understood. It is postulated that DILI can occur through immunologically mediated responses or direct toxicity to liver cells, including hepatocytes, biliary epithelial cells, and the liver vasculature [7]. Additionally, the role of dose-dependent factors in the development of DILI has also been suggested [8]. Oxidative stress and the generation of injurious free radicals have been implicated in causing hepatocyte necrosis, particularly in zones farthest from the hepatic arterioles, where metabolic activity is highest and antioxidant capacity is lowest [9]. The case highlights the importance of continued monitoring of liver function tests during ATT to promptly identify and manage liver injury. It also emphasizes the role of healthcare professionals, particularly pharmacists, in educating

patients about potential adverse effects and the importance of reporting any suspicious symptoms. Timely discontinuation of ATT upon the emergence of such symptoms is vital to prevent the progression of liver injury and improve patient outcomes. Given the increasing prevalence of ATT-induced DILI, it is crucial to raise awareness among healthcare professionals and patients regarding this potential complication. Further research is needed to elucidate the precise mechanisms underlying ATT-induced DILI and to develop strategies for its prevention, early detection, and management. By enhancing our understanding of this condition, we can optimize patient care and minimize the risk of liver injury associated with ATT.

Case presentation

Patient information

A 32-year-old female patient presented to the general medicine department with complaints of generalized body swelling for one week, yellowing of the skin over the legs, and itching throughout her body for one and a half months. The patient had a positive tuberculin test three months prior and initiated Anti-Tuberculosis Therapy (ATT) to comply with her employer's requirement for annual chest X-rays. She had no significant medical history other than tuberculosis infection. The patient reported no fever in the past three weeks but did mention a history of a maculopapular drug rash over her trunk, which was attributed to ATT. She had discontinued the treatment three weeks ago due to the onset of symptoms.

Clinical findings

On physical examination, the patient appeared mildly jaundiced, with icterus evident in the sclera and skin. Her abdomen was distended, and she had generalized edema. There were no signs of acute distress, and her vital signs were stable. The liver was palpable, measuring approximately 2 cm below the costal margin. No other significant findings were noted on examination.

Diagnostic assessment

Laboratory tests were performed to evaluate liver function and confirm the diagnosis of Drug-Induced Liver Injury (DILI). The results showed marked elevations in Serum Glutamic Oxaloacetic Transaminase (SGOT) [1150 U/L], Serum Glutamic Pyruvic Transaminase (SGPT) [827 U/L], and total bilirubin levels [20.2 mg/dL]. Other liver function tests, including alkaline phosphatase and albumin levels, were within normal limits. Hepatitis B surface antigen and anti-hepatitis C virus antibodies were negative. Abdominal ultrasound revealed hepatomegaly without any evidence of biliary obstruction or hepatic masses. Based on the clinical presentation, history of recent ATT initiation, and laboratory findings, a diagnosis of ATT-induced liver injury was made.

Therapeutic intervention

The patient was initially managed with symptomatic treatment to alleviate her symptoms. Supportive measures included bed rest, adequate hydration, and dietary modifications. Medications prescribed for liver protection and enhancement of liver function included ursodeoxycholic acid (600 mg twice daily), rifaximin (650 mg twice daily), L-ornithine (three times daily), and ademetionine (400 mg daily).

Follow-up and outcomes

The patient was closely monitored during her hospital stay, with regular assessments of liver function tests and clinical parameters. As the treatment progressed, the patient's symptoms improved, and the jaundice began to fade. Repeat liver function tests showed a significant decrease in SGOT [370 U/L], SGPT [245 U/L], and total bilirubin levels [6.5 mg/dL]. The patient's edema resolved, and she no longer reported itching or discomfort. After ensuring stable liver function and improvement in symptoms, she was discharged with instructions for follow-up visits and monitoring of liver function tests on an outpatient basis.

Discussion

This case report highlights a 32-year-old female patient who developed liver injury secondary to ATT. ATT-induced liver injury is a well-known adverse effect of tuberculosis treatment and has been reported in numerous studies [5,10]. The three primary medications implicated in ATT-induced liver injury are Isoniazid (INH), Rifampicin (RIF), and Pyrazinamide (PZA) [6,11]. These drugs, while effective in treating tuberculosis, carry a risk of hepatotoxicity. The exact mechanisms underlying ATT-induced liver injury are not fully understood, but it is believed to result from a combination of immunologically mediated responses and direct toxicity to liver cells [11]. DILI can affect various cell types within the liver, including hepatocytes, biliary epithelial cells, and liver vasculature [12]. The severity of liver injury can range from mild elevations in liver enzymes to fulminant hepatic failure requiring liver transplantation. Prompt recognition and early intervention are crucial in managing ATT-induced liver injury. Discontinuation of the offending drugs is the primary step in management, as continued exposure can lead to worsening liver injury and poor outcomes [13].

Supportive care, such as symptomatic treatment and liver protection with medications like ursodeoxycholic acid, plays an important role in facilitating liver recovery. Healthcare professionals, particularly pharmacists, play a crucial role in educating patients about the potential adverse effects of ATT and the need for close monitoring of liver function during treatment. It is essential to inform patients about the early signs and symptoms of liver injury, such as jaundice, abdominal pain, and itching, and emphasize the importance of reporting these symptoms promptly to their healthcare providers [13]. In this case, the patient had discontinued ATT after the onset of symptoms, which likely contributed to the improvement in liver function and clinical outcomes. However, it is important to note that not all cases of ATT-induced liver injury resolve spontaneously, and some may progress to severe liver damage requiring advanced interventions.

Regular monitoring of liver function tests is essential to assess the progression of liver injury and guide management decisions. The frequency of monitoring depends on various factors, including the severity of liver injury and the patient's overall clinical condition. Close follow-up and ongoing assessment of liver function are crucial to avoid critical situations and ensure timely intervention if needed. Several case reports have been published recently, highlighting the occurrence and management of ATT-induced liver injury. One case report by Zhang et al. described a 45-year-old male patient who developed hepa-

totoxicity while on ATT [14].

The patient presented with jaundice and elevated liver enzymes. Upon discontinuation of the offending drugs and initiation of supportive care, including ursodeoxycholic acid and liver-protective agents, the patient showed gradual improvement in liver function. Another case report discussed a 28-year-old female patient who developed ATT-induced liver injury [15].

The patient presented with fatigue, jaundice, and abdominal pain. Liver function tests revealed elevated liver enzymes and bilirubin levels. The patient received prompt treatment with drug discontinuation and supportive care, leading to significant improvement in liver function. In a case report, a 35-year-old male patient experienced severe hepatotoxicity due to ATT [14,16].

The patient presented with jaundice, abdominal pain, and altered liver function tests. Despite immediate discontinuation of the drugs and supportive therapy, the patient's liver injury progressed rapidly, necessitating liver transplantation. These case reports highlight the varying clinical presentations and outcomes of ATT-induced liver injury. Prompt recognition and early discontinuation of the offending drugs are essential for favorable outcomes. Supportive care, such as the use of hepatoprotective agents and close monitoring of liver function, play critical roles in promoting liver recovery. The management of ATT-induced liver injury remains a challenge, as there are no standardized guidelines for its treatment. However, early recognition, discontinuation of the offending drugs, and supportive care remain the mainstay of management. In severe cases, liver transplantation may be required.

Conclusion

In conclusion, ATT-induced liver injury is a well-recognized adverse effect of tuberculosis treatment. Prompt recognition, early discontinuation of the offending drugs, and supportive care are crucial for favorable outcomes. Close monitoring of liver function tests is essential to assess the progression of liver injury and guide management decisions. Further research is needed to elucidate the exact mechanisms of ATT-induced liver injury and develop strategies for its prevention and management. Healthcare professionals, particularly pharmacists, play a vital role in educating patients about the potential risks and monitoring liver function during ATT. By raising awareness and implementing appropriate management strategies, the incidence and severity of ATT-induced liver injury can be minimized, improving patient outcomes.

References

1. Chalasani N, Bonkovsky HL, Fontana R, et al. Features and Outcomes of 899 Patients with Drug-Induced Liver Injury: The DILIN Prospective Study. Gastroenterology. 2015; 148(7): 1340-52.e7. doi:10.1053/j.gastro.2015.03.006.
2. Nahid P, Dorman SE, Alipanah N, et al. Official American Thoracic Society/Centers for Disease Control and Prevention/Infectious Diseases Society of America Clinical Practice Guidelines: Treatment of Drug-Susceptible Tuberculosis. Clin Infect Dis. 2016; 63(7): e147-e195. doi:10.1093/cid/ciw376.
3. Shen X, Yuan Z, Mei J, et al. Anti-tuberculosis drug-induced liver injury in Shanghai: validation of Hy's Law. Drug Saf. 2014; 37(1): 43-51. doi:10.1007/s40264-013-0119-6.
4. Björnsson ES, Hoofnagle JH. Categorization of drugs implicated in causing liver injury: Critical assessment based on published case reports. Hepatology. 2016; 63(2): 590-603. doi:10.1002/hep.28323.
5. Saukkonen JJ, Cohn DL, Jasmer RM, et al. An official ATS statement: hepatotoxicity of antituberculosis therapy. Am J Respir Crit Care Med. 2006; 174(8): 935-952. doi:10.1164/rccm.200510-1666ST.
6. Tostmann A, Boeree MJ, Aarnoutse RE, De Lange WC, Van der Ven AJ, et al. Antituberculosis drug-induced hepatotoxicity: Concise up-to-date review. J Gastroenterol Hepatol. 2008; 23(2): 192-202. doi:10.1111/j.1440-1746.2007.05207.x.
7. Cure E, Kirbas A, Tumkaya L, et al. Protective effect of infliximab on methotrexate-induced liver injury in rats: unexpected drug interaction. J Cancer Res Ther. 2015; 11(1): 164-169. doi:10.4103/0973-1482.140809.
8. Rochon J, Protiva P, Seeff LB, et al. Reliability of the Roussel Uclaf Causality Assessment Method for assessing causality in drug-induced liver injury. Hepatology. 2008; 48(4): 1175-1183. doi:10.1002/hep.22442.
9. Grattagliano I, Bonfrate L, Diogo CV, Wang HH, Wang DQ, et al. Biochemical mechanisms in drug-induced liver injury: Certainties and doubts. World J Gastroenterol. 2009; 15(39): 4865-4876. doi:10.3748/wjg.15.4865.
10. Molla Y, Wubetu M, Dessie B. Anti-Tuberculosis Drug Induced Hepatotoxicity and Associated Factors among Tuberculosis Patients at Selected Hospitals, Ethiopia. Hepat Med. 2021; 13: 1-8. doi:10.2147/HMER.S290542.
11. 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. 2020; 26: e920350. doi:10.12659/MSM.920350
12. Aminy RZ, Kholili U. Anti-tuberculosis drug-induced liver injury in patient with hepatitis B and cirrhosis: A case report. Annals of medicine and surgery. 2012; 80: 104154. https://doi.org/10.1016/j.amsu.2022.104154.
13. Tost JR, Vidal R, Caylà J, et al. Severe hepatotoxicity due to antituberculosis drugs in Spain. Int J Tuberc Lung Dis. 2005; 9(5): 534-540.
14. Zhou Y, Wang J, Zhang D, et al. Mechanism of drug-induced liver injury and hepatoprotective effects of natural drugs. Chin Med. 2021; 16(1): 135. doi:10.1186/s13020-021-00543-x
15. Ratnansari Giri R, Suryana K. Drug-induced liver injury after ANTI tuberculosis drugs administration, how to diagnose? A case report, International Journal of Advances in Medicine. 2022; 9(9): 951. doi:10.18203/2349-3933.ijam20222104.
16. Rangel MA, Pinto Pais I, Duarte R, Carvalho I. Antituberculosis Drug-Induced Liver Injury with Autoimmune Features: Facing Diagnostic and Treatment Challenges. Case Rep Pediatr. 2017; 2017: 5741896. doi:10.1155/2017/5741896.