Case Report

A Case of Anti-Tuberculosis Drug-Induced Liver Injury with Multi-organ Failure During Initial Therapy

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Abstract

Introduction: Anti-tuberculosis medications are widely recognized for their potential to cause hepatotoxicity. Although uncommon, this adverse reaction can result in substantial morbidity and even mortality. Reported rates of anti-tuberculosis drug-related hepatotoxicity (ATDIH) vary from 2% to 28%, with most cases arising in the early weeks of treatment.

Case: We describe a 57-year-old male with pulmonary tuberculosis who developed worsening dyspnea, right upper quadrant discomfort, abdominal swelling, nausea, and vomiting after one month of standard anti-tuberculosis therapy. Laboratory evaluation revealed markedly abnormal liver enzymes, hyperbilirubinemia, hypoalbuminemia, and prolonged INR. A diagnosis of drug-induced hepatitis was made, complicated by acute kidney injury and type 2 respiratory failure. Anti-tuberculosis medications were discontinued, and intensive supportive therapy was initiated, including continuous renal replacement therapy and mechanical ventilation. Despite these measures, the patient progressed to multi-organ failure and died.

Conclusion: This case illustrates the need for vigilant monitoring of hepatic function, especially during the first month of therapy, and timely recognition of hepatotoxicity to improve outcomes.

Key words

Hepatotoxicity, Drug-induced liver injury, Anti-tuberculosis drugs, Multiorgan failure.

Introduction

Drug-induced liver injury (DILI) is a major cause of medication-related morbidity, accounting for about 10% of acute hepatitis and representing the leading cause of acute liver failure in the United States [1, 2]. Antimicrobial agents, particularly those used in tuberculosis treatment, along with non-steroidal anti-inflammatory agents and herbal supplements, are common triggers.

Diagnostic criteria for DILI generally include alanine aminotransferase (ALT) levels exceeding five times the upper limit of normal (ULN), or ALT at least three times ULN in combination with total bilirubin more than twice ULN [3]. Two categories of DILI are recognized: intrinsic (predictable, dose-dependent, rapid onset) and idiosyncratic (unpredictable, usually independent of dose). Isoniazid typically produces idiosyncratic liver injury, while pyrazinamide more often causes dose-related toxicity [1, 4, 5, 6].

The incidence of anti-tuberculosis drug-induced hepatitis (ATDIH) is highly variable, ranging from 2% to nearly 28%, with the majority occurring during the first month of intensive therapy [7, 8]. Therefore, early laboratory monitoring is advised, ideally within the first two weeks. Delayed recognition may necessitate treatment interruption, which risks relapse and resistance [9–11].

We report a case of severe ATDIH complicated by progressive multi-organ dysfunction.

Case report

A 57-year-old male, former smoker, was diagnosed with pulmonary tuberculosis and commenced on standard quadruple therapy (isoniazid, rifampicin, ethambutol, and pyrazinamide). After one month, he presented with progressive shortness of breath, abdominal distension, nausea, vomiting, and pain in the right upper abdomen.

On admission, he was conscious but tachypneic, with bilateral coarse crepitations. Chest radiography revealed left hilar opacification. Arterial blood gases indicated partially compensated respiratory acidosis.

Initial laboratory testing showed ALT 527 U/L, AST 856 U/L, bilirubin 112 µmol/L, albumin 20 g/L, and INR 2.2. Serum creatinine was markedly elevated (955 µmol/L) with oliguria (45 mL/8 hours). ATDIH was suspected (after excluding other causes), prompting discontinuation of therapy. He was started on intravenous N-acetylcysteine, vitamin K, rifaximin, and lactulose. Because of worsening renal function, continuous renal replacement therapy (CRRT) was initiated.

Despite non-invasive ventilation, his oxygenation deteriorated, requiring intubation and mechanical ventilation, following the development of acute respiratory distress syndrome (ARDS). During his ICU stay, he underwent three sessions of CRRT. He developed hepatic encephalopathy and later developed a cardiac arrest, possibly secondary to a pneumothorax. Following resuscitation and chest tube insertion, his neurological status remained poor. Despite maximal support, he succumbed to progressive multi-organ failure.

Discussion

Older age, female sex, extensive pulmonary involvement, underlying liver disease, HIV

infection, alcohol intake, and genetic factors increase susceptibility to DILI [10, 12]. In the present case, the patient was 57 years old but had no other apparent risk factors.

Notably, up to one-third of patients with ATDIH may be asymptomatic despite significant hepatic damage, highlighting the importance of routine biochemical monitoring [10]. Genetic polymorphisms, such as those affecting NAT2 acetylator status, are known to influence risk [2, 12].

The usual Tuberculosis (TB) regimen consists of two months of quadruple therapy followed by four months of dual therapy. In cases of acute hepatic failure, drug cessation and supportive treatment are critical. Intravenous N-acetylcysteine has been shown to provide biochemical improvement in selected cases [5, 6].

This case underscores the severe consequences of ATDIH, including respiratory failure and acute kidney injury, both of which required advanced supportive therapy. Although treatment cessation was lifesaving from a hepatic perspective, it may compromise TB control, leading to relapse or resistance. Clinicians must balance the risks of hepatotoxicity against the consequences of inadequate TB therapy.

Conclusion

Anti-tuberculosis drug-induced liver injury most frequently occurs during the initial month of therapy. Close biochemical surveillance and rapid intervention are crucial to prevent catastrophic complications.

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