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Case Report

Anti-tuberculosis drug-induced liver injury in patient with hepatitis B and cirrhosis: A case report

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ABSTRACT

Background: Pulmonary tuberculosis patients infected with hepatitis B are at high risk for drug-induced liver injury.

Case presentation: A 42-year-old Indonesian female complained of sclera icterus, tea-colored urine, vomiting, dyspnea, and swollen stomach and legs. The patient experienced this condition after taking anti-tuberculosis drugs for five days. Her medical history showed hepatitis B and cirrhosis. Follow-up examination included chest X-ray and GeneXpert supported a diagnosis of pulmonary tuberculosis. However, abdominal ultrasonography indicated ascites and cirrhosis. We diagnosed the patient with anti-tuberculosis DILI, cirrhosis Child-Pugh C (score 12) related to hepatitis B, and pulmonary tuberculosis. We decided to stop the anti-tuberculosis drug. We treated the patient using tenofovir, hepatoprotective drug, diuretics, and albumin infusion. On the third day, the patient received new anti-tuberculosis drugs, including levofloxacin 750 mg, ethambutol 1000 mg, and streptomycin 1000 mg (LES). The patient's condition then gradually improved.

Discussion: The dilemma of treating tuberculosis in liver disease is treating tuberculosis without ignoring hepatitis B and cirrhosis.

Conclusion: Administration of anti-tuberculosis drugs based on liver tolerance of hepatotoxic drug in patients with hepatitis B and cirrhosis.

1. Introduction

Pulmonary tuberculosis is an infectious disease caused by infection of *Mycobacterium tuberculosis*. Indonesia has a very high estimated incidence of tuberculosis, as much as 647 per 100,000 population [1,2]. Several studies reported that treating pulmonary tuberculosis has a side effect of damaging the liver, known as Drug-Induced Liver Injury (DILI) [3,4]. Anti-tuberculosis DILI was reported at 2–28% globally [5]. In addition, hepatitis and cirrhosis are risk factors for the severity of anti-tuberculosis DILI [6,7]. We reported a case of an Indonesian female with anti-tuberculosis DILI, hepatitis B and cirrhosis. We reported based on SCARE 2020 guidelines [8].

2. Case presentation

For two days, a 42-year-old Indonesian female complained of sclera icterus, tea-colored urine, vomiting, dyspnea, swollen stomach and legs. The patient also had a cough and a low food intake for three days. The patient experienced this condition after taking anti-tuberculosis drugs for five days. Anti-tuberculosis drugs used included isoniazid 300 mg, rifampicin 600 mg, and ethambutol 1000 mg. The patient had a medical history of pulmonary tuberculosis with pleural effusion, hepatitis B, and cirrhosis. The patient had also been taking tenofovir regularly for two months. A month ago, laboratory history showed aspartate aminotransferase (AST) of 73 U/L, alanine aminotransferase (ALT) of 20 U/L, total bilirubin of 3.22 mg/dL, direct bilirubin of 1.76 mg/dL, and alkaline phosphatase of 121 IU/L.

Vital sign investigation showed a pulse rate of 108 × /min, respiratory rate of 24 × /min, and SpO2 of 96%. The physical analysis included the chest showing low breath sound in 1/3 hemithorax lungs, abdomen showing ascites, and lower extremities having pitting oedema. Laboratory investigation reported AST of 234 U/L, ALT of 208 U/L, total bilirubin of 11.16 mg/dL, direct bilirubin of 7.76 mg/dL, and alkaline phosphatase of 282 IU/L. HBsAg test was reactive, and the HBeAg test was positive. Ascites fluid analysis showed polymorphonuclear 230 cells, albumin of 0.3 g/dL, and serum ascites albumin gradient of 2.0 g/

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dL. The adenosine deaminase (ADA) test results in pleural fluid showed a 38.7 IU/L value. Ziehl Neelsen and GeneXpert tests were positive [9,10]. Chest X-ray showed minimized bilateral pleural effusion (Fig. 1). Abdominal ultrasonography showed reduced liver size, increased echoparenchyma, irregular margins, splenomegaly, and ascites (Fig. 2).

We diagnosed the patient with anti-tuberculosis DILI, cirrhosis Child-Pugh C (score 12) related to hepatitis B, and pulmonary tuberculosis. We decided to stop the anti-tuberculosis drug. Moreover, we treated the patient using tenofovir, hepatoprotective drug, diuretics, and albumin infusion. Because ascites were not getting better, we performed paracentesis on day-3. The anti-tuberculosis drugs were started again with levofloxacin 750 mg, ethambutol 1000 mg, and streptomycin 1000 mg (LES). The patient's condition gradually improved, marked by resolution of nausea, vomiting, icteric, appetite, decreased volume of ascites, and improved AST, ALT, and bilirubin, so the patient was discharged on the eighth day of treatment. The LES regimen was continued for two months, followed by levofloxacin and ethambutol for ten months (2LES/10LE). Other drugs for hepatitis B and cirrhosis were continued.

3. Discussion

Anti-tuberculosis drugs consist of first-line and second-line, including isoniazid, rifampicin, and pyrazinamide, which hepatotoxic drugs cause liver injury in patients with pre-existing liver disease [11,12]. However, based on their efficacy, isoniazid and rifampicin are generally recommended to be used whenever possible. Of these drugs, rifampicin is least likely to cause hepatocellular damage, although it is sometimes associated with cholestatic-type damage. Isoniazid monotherapy may be safe in patients with hepatitis B virus infection. However, more than one hepatotoxic anti-tuberculosis drug is associated with significant liver injury and is further associated with fulminant disease, increased mortality and delayed onset hepatotoxic effects. Pyrazinamide is the most hepatotoxic and should be avoided in patients with chronic liver disease [13,14].

Managing pulmonary tuberculosis in cirrhosis patients is a challenge for clinicians because therapy could be a double-edged sword. Anti-tuberculosis drugs caused by hepatotoxicity and progressive tuberculosis can further liver decompensation due to inadequate therapy. The tuberculosis treatment should ideally either isoniazid or rifampicin, as both are the most potent anti-tuberculosis drugs. In patients with advanced liver disease with complications of cirrhosis and signs of liver failure, the use of hepatotoxic drugs may be best avoided [15,16]. Administration of anti-tuberculosis drugs in patients with chronic liver disease should be used with caution. The choice of regimen should be based on the severity of the underlying liver disease. The selection of the proposed anti-tuberculosis drugs should follow the liver disease stage (Child-Pugh) [14,15]. Recommendation for patients with tuberculosis and cirrhosis Child-Pugh C (advanced cirrhosis) should be given anti-tuberculosis drugs without hepatotoxic drugs from the start of treatment [15,17].

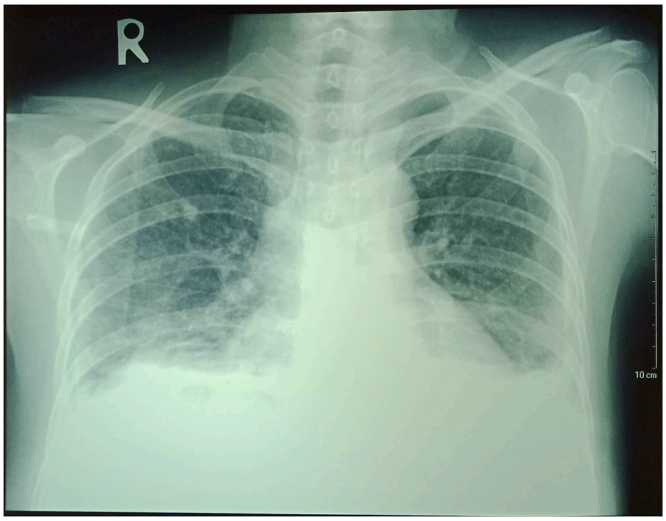

Fig. 1. Chest X-ray showing bilateral pleural effusion in lungs.

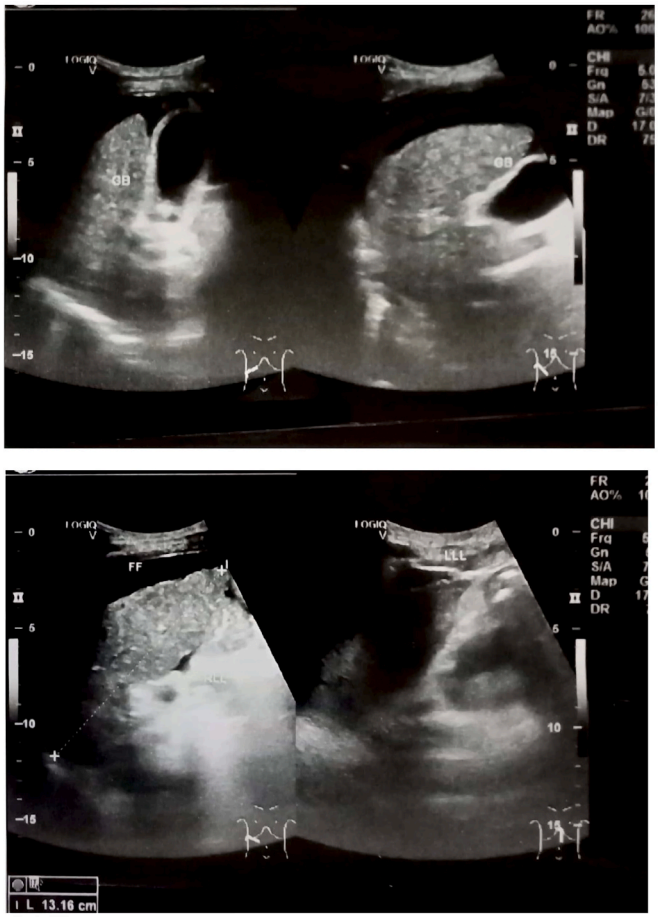

Fig. 2. Abdomen ultrasound showing ascites and liver cirrhosis.

4. Conclusion

Hepatitis B and cirrhosis are risk factors for anti-tuberculosis DILI. The management of anti-tuberculosis DILI is stopping anti-tuberculosis drugs and resetting the treatment. Administration of anti-tuberculosis drugs should follow the liver disease (Child-Pugh) stage by considering liver tolerance.

Provenance and peer review

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Conflicts of interest

Rusdi Zakki Aminy and Ulfa Kholili declare that they no conflict of interest.

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Ethical approval

Not applicable.

Consent

Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

Author contribution

All authors contributed toward data analysis, drafting and revising the paper, gave final approval of the version to be published and agree to be accountable for all aspects of the work.

Registration of research studies

1. Name of the registry: -.
2. Unique Identifying number or registration ID: -.
3. Hyperlink to your specific registration (must be publicly accessible and will be checked): -.

Guarantor

Ulfa Kholili is the person in charge of the publication of our manuscript.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.amsu.2022.104154.

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