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The Management of Hepatotoxicity due to Antituberculotic Therapy in a Patient with Cerebral Tuberculosis: Case Report and Literature Review

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ABSTRACT

Hepatotoxicity is the main problem of antituberculotic treatment like isoniazid, rifampicin and pyrazinamide. We evaluate the outcomes of re-challenge for anti-tuberculosis drug in order to manage hepatotoxicity due to antituberculotic therapy in a patient with cerebral tuberculosis. A female patient was diagnosed with cerebral tuberculosis and had been treated with 5 regimens of antituberculotic drug: isoniazid, rifampicin, pirazinamid, ethambutol, and streptomycin. After four days, the patient felt several adverse reactions such as abdominal discomfort, nausea, and vomiting. Following this, a liver function test was performed. The levels of SGOT and SGPT elevated 15 times higher cted on day than the normal upper limit, which also indicated antituberculotic drug induced hepatotoxicity. A sequential rechallenge method was performed to overcome this problem. The method was successful to manage hepatotoxicity induced by antituberculotic therapy.

INTRODUCTION

Hepatotoxicity is the main problem of antituberculosis treatment like isoniazid, rifampicin and pyrazinamide because it can seriously contribute to nonadherence, eventually contributing to treatment failure, relapse, or the emergence of drug resistance [1]. Anti-TB drug–induced hepatotoxicity is associated with a mortality of 6%–12% if these drugs are continued after the onset of symptoms [2]. There were several mechanism of antituberculosis that caused hepatotoxicity. Interaction of rifampicin and isoniazid can induced toxic metabolit of isoniazid that damage liver, and also the interaction increase hydrazine-production that toxic to liver. Pyrazinamide inhibit CYP450 and nicotinamide adenine dinucleotide [3]. According to American Thoracic Society the patients who experienced hepatotocity induced by antituberculosis can be given rechallenge methods to overcome it [4]. In Indonesia, antituberculosis hepatotoxicity often occurs but is not well documented. The aim of this study was to evaluate the outcomes of rechallenge for anti-tuberculosis drug in order to manage hepatotoxicity due to antituberculosis therapy in a patient with cerebral tuberculosis.

METHODS

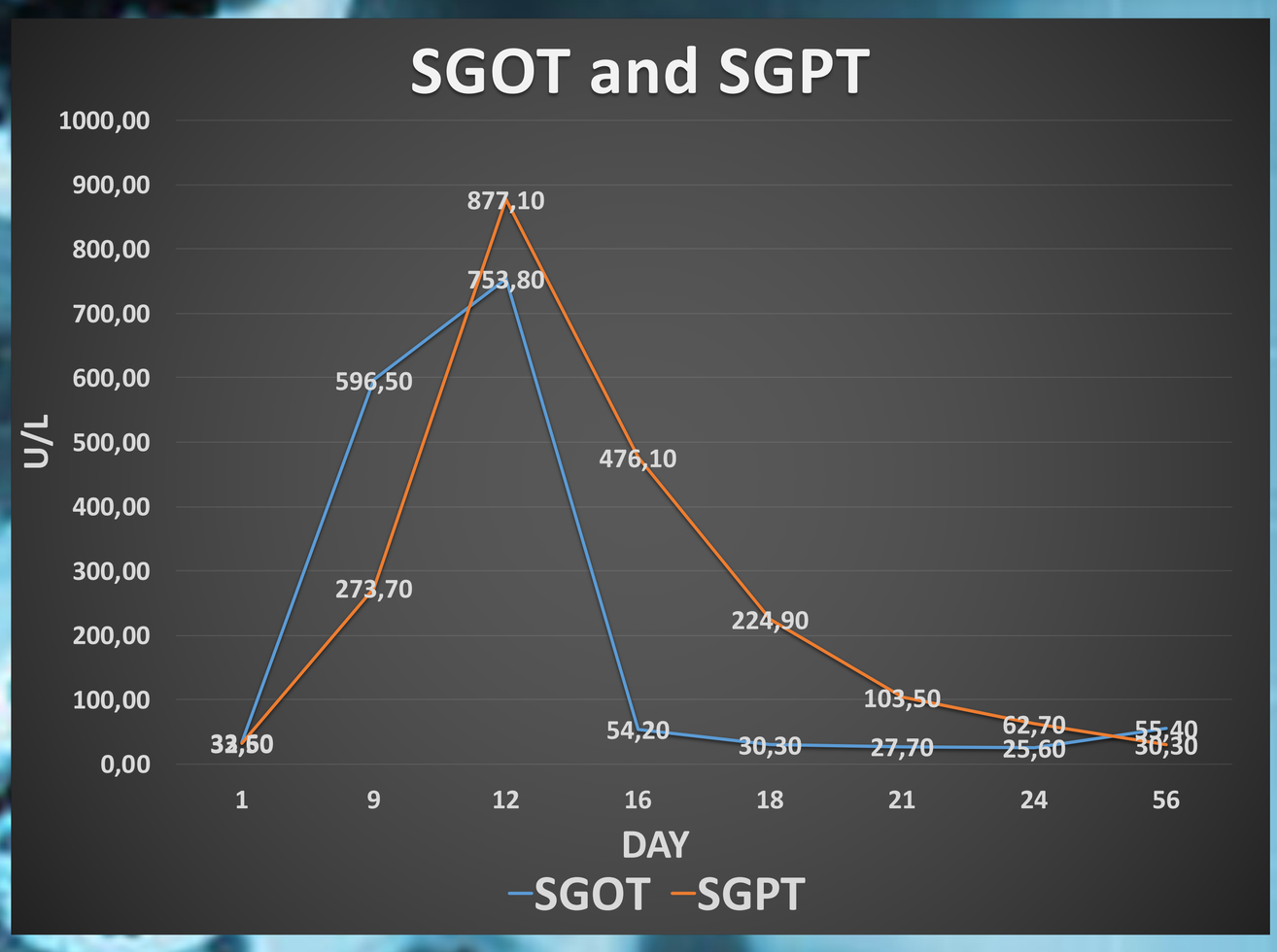
This was a case report. Hospital X approved this study. Informed consent was obtained from the patient

CASE PRESENTATION

A female patient **(age: 45, weight: 45 kg, height : 145 cm)** was diagnosed with cerebral tuberculosis and had been treated with 5 regimens of antituberculosis drug: isoniazid **225 mg(H), rifampicin 450 mg(R), pyrazinamide 1200 mg(Z), ethambutol 825 mg(E), and streptomycin injection 1000 mg(S).** The initial laboratory test for SGOT and SGPT performed on the patient prior to the administration of antituberculosis drug was normal (SGOT 33.6 U/L and SGPT 32.5 U/L). After four days, the patient felt several adverse reactions such as abdominal discomfort, nausea, and vomiting. Following this, a liver function test was conducted on day 9. The levels of SGOT and SGPT elevated to 596.7 U/L and 273.7 U/L respectively**. These were approximately 15 times higher than the normal upper limit, which also indicated antituberculosis drug induced hepatotoxicity.**

A sequential **rechallenge method** was performed on day 9 by suspending isoniazid, rifampicin, and pyrazinamide. The liver function test on day 12 still showed the increasing levels of SGOT and SGPT (753.8 U/L and 877.1 U/L respectively), and therefore the administration of ethambutol was discontinued. After evaluating for 9 days, another liver function test was performed on day 21. The SGOT and SGPT levels decreased to 27.7 U/L and 103.5 U/L respectively. In turn, ethambuthol was reinitiated to the patient. On Day 24, the liver enzyme was within the normal range of values: SGOT 25.6 U/L and SGPT 62.7 U/L. Subsequently, on that day, isoniazid and rifampicin were readministered to the patient. Finally, on day 56, the laboratory test for SGOT and SGPT showed 55.4 U/L and 30.3 U/L respectively, pyranzinamid were readministered to the patient accordingly.

RESULTS



Note :

Day 1: RHZES	Day 9: ES	Day 12: S
Day 21: ES	Day 24: RHES	Day 56: RHZES

There were some strategy to do rechallenge in patient tuberculosis but the evidence was still little other that expert opinion to guide the re-introduction of TB medications [5]. In this study the clinicians used sequential method by adding one by one the anti-TB drug. When when hepatotoxic occurs first, the clinicians stop the use of isoniazid, rifampicin and pyrazinamid due to high potential of hepatotoxicity of these drug [6]. But after few days the SGOT and SGPT still increase then the clinician stop the ethambutol. There was one evidence showed ethambutol increase liver function test but the mechanism still unknown [7]. And clinician still use streptomycin because it has no effect on hepatotoxicity [3]. When the liver function was normal the clinician first re-introduced ethambutol then give isoniazid and rifampicin and the last one was pyrazinamid because it was the most potential hepatotoxic [8]. The dose given in this rechallenge used American thoracic society methods which given in full dose from the first day it was re-introduce and from the study comparison of American thoracic society with british thoracic society guideline showed no difference [9]. These sequential was success showed by normal liver function test after the treatment.

CONCLUSION

In this study, sequential rechallenge to manage hepatotoxicity induced by antituberculosis therapy was successful. It should be carried out cautiously by monitoring liver function test in patient receiving antituberculosis drug to prevent morbidity and mortality

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10. Picture available at http://theconversation.com/how-your-genes-influence-what-medicines-are-right-for-you-46904

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Conflict of Interest : All authors have none to declare