International Journal of Advances in Medicine
Adrian SJ et al. Int J Adv Med. 2022 Sep;9(9):935-938
http://www.ijmedicine.com
pISSN 2349-3925 | eISSN 2349-3933
DOI: https://dx.doi.org/10.18203/2349-3933.ijam20222100

Case Report

Congestive hepatopathy secondary to graves' disease: a case report

Steven Johanes Adrian*, I. Made Suma Wirawan

Department of Internal Medicine, Wangaya General Hospital, Denpasar, Bali, Indonesia

Received: 29 June 2022
Accepted: 28 July 2022

***Correspondence:**
Steven Johanes Adrian,
E-mail: stevenjohanes15@gmail.com

Copyright: © the author(s), publisher and licensee Medip Academy. This is an open-access article distributed under the terms of the Creative Commons Attribution Non-Commercial License, which permits unrestricted non-commercial use, distribution, and reproduction in any medium, provided the original work is properly cited.

ABSTRACT

Graves' disease is a common cause of hyperthyroidism in iodine-sufficient parts of the world. Excessive thyroid hormone is known to have multiple effects on various organs, including the liver. We reported a case of 49-year old male patient with worsening jaundice, ascites, tremor, and palpitation, with previous history of uncontrolled Graves' disease. Findings from examination reveals signs of congestive hepatopathy, such as positive hepatojugular reflux and dilated hepatic vein. Treatment options for hyperthyroidism in patients with liver dysfunction includes methimazole and radioactive iodine-131. Liver dysfunction in patients with thyrotoxicosis is commonly found in daily practice, but establishing the cause of liver dysfunction can be a challenge because of the multiple cause of liver injury in hyperthyroidism.

Keywords: Congestive hepatopathy, Graves' disease, Hyperthyroidism

INTRODUCTION

Graves' disease is a common cause of hyperthyroidism in iodine-sufficient parts of the world, with prevalence ranging from 0.2% to 1.3%.[1] In Indonesia, the reported prevalence of hyperthyroidism is 6.9%.[2] Excessive thyroid hormone is known to have multiple effects on various organs, including liver. Hepatic dysfunction in patients with thyroid disease is a common condition. Possible causes of hepatic dysfunction in Graves' disease includes effect of thyroid hormone excess, anti-thyroid drug related hepatic injury, and presence of concomitant liver disease.[3,4]

CASE REPORT

A 49-year old Indonesian male presented with worsening jaundice, abdominal pain, and distension since 1 week. He also complained of dyspnea, nausea, tremor, and palpitation since past 2 months. His history of disease was Graves' disease since 5 years ago, but he hadn't visited the hospital since 2-years ago because of the COVID-19 pandemic. He previously had visited the outpatient clinic for the same symptoms, and had started his anti-thyroid medication again since then.

On physical examination, his blood pressure was 120/80 mmHg, heart was rate 107 bpm (irregular), respiratory rate was 22 times per minute, temperature was 37.3°C, oxygen saturation in room air was 98%. Ophthalmic examination showed bilateral exophthalmos and jaundice on the sclera. Thyroid gland was diffusely enlarged. Cardiac auscultation revealed pansystolic murmur on tricuspid valve. Abdominal examination shows normal bowel sounds, with positive shifting dullness and hepatomegaly. Patient also had pitting edema on both legs. Hepato-jugular reflux was also present on this patient.

Laboratory findings were: Haemoglobin 8.9 g/dl, white blood cell 4.000/µl, thrombocyte 223.000/µl. ALT 17 U/l, AST 44 U/l, total bilirubin 4.56 mg/dl, direct bilirubin 3,8 mg/dl, and indirect bilirubin 0,76 mg/dl. Patient has normal blood sugar and kidney function. Thyroid function test showed hyperthyroidism: thyroid-stimulating-hormone (TSH) 0.16 mIU/l (0.35-5.10), free thyroxine (FT4) 3.6 ng/dl (0.5-1.4). HBsAg and anti-HCV test was negative. Postero-anterior chest X-ray showed

cardiomegaly with minimal right pleural effusion. Electrocardiography (ECG) showed atrial fibrillation with normal ventricular response, while his ECG from 2 years ago showed no atrial fibrillation (sinus tachycardia). Abdominal ultrasonography suggested that he had congestive liver, with suspected cardiac cirrhosis (dilatation of the hepatic vein with normal portal vein and portal velocity), ascites, and splenomegaly. No dilatatation of intrahepatic and extrahepatic bile duct was found. Echocardiography examination revealed dilated left atrium, right atrium, and right ventricle, moderate tricuspid and mitral regurgitation, normal left ventricle ejection fraction/LVEF (61%), and normal right ventricle systolic function 9 [Tricuspid anullar plane systolic excursion (TAPSE) 29 mm].

Patient was treated with methimazole 10 mg BID, spironolactone 50 mg QID, bisoprolol 2.5 mg QD, clopidogrel 75 mg QD, candesartan 8 mg QD, and intravenous furosemide 20 mg BID. Patient was also given 2 units of packed red cell. After 5 days of treatment, his ascites was resolved, along with normalization of bilirubin. Patient was discharged after the 6 days of treatment with stable condition.

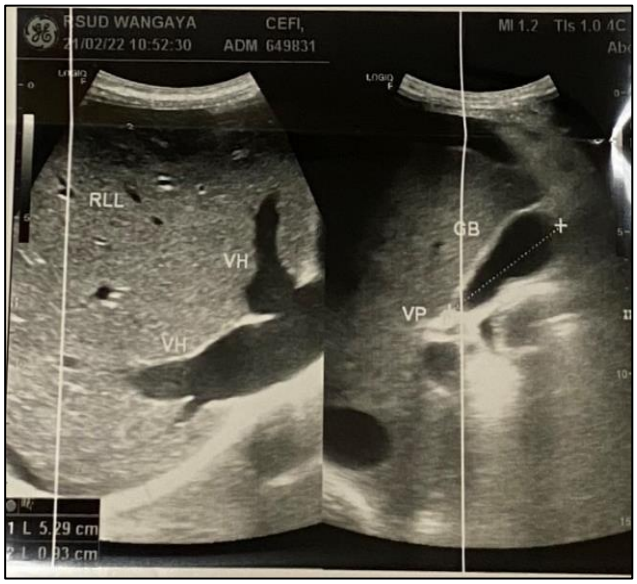

Figure 1: Abdominal USG of dilatation of hepatic veins.

DISCUSSION

Liver is one of the affected organs in patients with hyperthyroidism, with 15% to 79% patients with untreated hyperthyroidism suffering from severe liver damage and impaired synthetic function. There are multiple interactions of thyroid hormones and the liver in maintaining homeostasis. About 80% T3 is formed by 51-deiodination of T4 in extrathyroidal tissue, such the kidney and liver. The liver also produced serum proteins (thyroxine-binding globulin/TBG, transthyretin, albumin, and lipoproteins) required by thyroid hormones to maintain serum free thyroid and availability to the tissues. Thyroid hormones are needed by the liver to perform its metabolic functions, by regulating the levels of ligandin that affects the enzymatic activity of glucoronyltransferase. Liver dysfunction in patients with hyperthyroidism can be caused by multiple mechanisms: (1) direct liver toxicity from exposure of excess thyroid hormones; (2) liver cell degeneration from accelerated decomposition of liver glycogen and protein; (3) congestive hepatopathy from thyrotoxic heart failure; (4) previous underlying liver disease; (5) toxicity and injury by antithyroid medications; (6) autoimmune-related liver injury.[5,6] Retrospective studies also reported that the risk factors of liver dysfunction were age, course of Graves' disease, heart rate, weight of the thyroid gland, FT4 level, TR-antibodies, and TPO-antibodies.[7]

Congestive hepatopathy is described as manifestations of chronic, passive congestion of the liver in the setting of heart failure or other cardiac defects that result in elevation of central venous pressure.[6,8] Circulatory system disorders may cause hepatic dysfunction due to several mechanisms. First, right ventricular dysfunction increases preload or central venous pressure that can cause direct liver damage. From the right heart chamber, the pressure is then transmitted to the hepatic vein and sinusoids, which leads to intrahepatic edema, decreased perfusion, oxygen diffusion, hemorrhagic injury, and modification of the hepatic architecture and atrophy, which appear as elevation of hepatic enzymes. If the left side of the heart is also affected, perfusion and tissue hypoxia occurs, causing elevation of hepatic enzymes, LDH, and prolongation of coagulation status. These process caused the clinical manifestation of cardiac cirrhosis, such as shortness of breath, leg swelling, paroxysmal nocturnal dyspnea, and orthopnea, combined with symptoms due to liver dysfunction: abdominal pain, nausea, vomiting, jaundice, hepatomegaly, abdominal distention, and ascites. Hepatocytes, bile ducts, and biliary epithelium are sensitive to increase of lobular pressure, causing elevated bilirubin suggesting cholestasis. Thyrotoxicosis may also cause congestive heart failure secondary to atrial fibrillation and sinus tachycardia.[9] Ascites is caused by the enlargement of sinusoidal fenestrae secondary to sinusoidal congestion and exudation of protein rich fluid into the space of Disse, which subsequently overwhelms the lymphatic vessels.[10] Hepatojugular reflux can be demonstrated by sustained abdominal pressure, causing increase in venous return, shown by paradoxical rise in jugular venous pressure (JVP), usually correlated with right heart failure.[11]

Chest radiographs findings in congestive hepatopathy are not specific, but pericardial calcification may suggest constrictive pericarditis. Abdominal ultrasonography shows dilated inferior vena cava and dilated hepatic veins. Abdominal CT scan findings are hepatomegaly, dilatation of inferior vena cava and hepatic veins, hepatic vein-to-hepatic vein shunts, and abnormal enhancement of the liver parenchyma with contrast CT scan.[12]

Graves' disease is treated with anti-thyroid medications such as propylthiouracil (PTU) and thiamazole. These drugs, especially PTU, was associated with liver damage and failure.[3] Methimazole has also been associated with transient asymptomatic elevations of serum aminotransferase, especially during first 3 months after starting the high dose therapy. Methimazole is also reported to cause liver injury with cholestatic or mixed pattern, but fatalities are rare.[13] Studies have reported normalization liver enzymes (ALT, AST, GGT) in patients with liver function abnormalities after starting anti-thyroid medications.[14] The American thyroid association (ATA) recommends checking baseline liver enzyme and reconsider the initiation of anti-thyroid medication if baseline liver enzymes are above 5×ULN.[15] Treatment modalities for Graves' disease with liver injury also includes radioactive iodine (RAI) and surgery. Radioactive iodine-131 (^{131}I) treatment usually does not cause radiation damage to the liver, and was reported to return hepatic function indices after 6 months.[16]

In our case, this patient had stable course of Grave's disease for 5 years, until he stopped taking anti-thyroid medication for the last 2 years. This patient didn't have history of heart and liver failure, and the development of atrial fibrillation was presumed to occur after stopping the anti-thyroid medication. Patient manifested with exophthalmos, jaundice, ascites, pitting edema, and positive hepatojugular reflux, suggesting congestive hepatopathy. He has normal ALT and AST, with hyperbilirubinemia and jaundice. Normal or mildly elevated liver enzymes can be found in liver dysfunction due to congestive hepatopathy, even though acute congestion may lead to marked increases in levels of aminotransferases and bilirubin as high as viral and toxic hepatitis. Drug-induced liver dysfunction associated with anti-thyroid medication may be excluded because the patient has stopped taking drugs for the last 2 years. Other causes of liver dysfunction in patients with thyrotoxicosis cannot be ruled out yet, because of the many mechanisms of thyroid hormones interacting with liver function. Liver dysfunction in patients with thyrotoxicosis is commonly found in daily practice. However, establishing the cause of hepatic dysfunction can be a challenge. Managing thyrotoxicosis in patients with hepatic dysfunction is also a difficult decision, considering both PTU and thiamazole may cause hepatic complications.

CONCLUSION

Graves' disease is a common cause of hyperthyroidism in iodine-sufficient parts of the world, with prevalence ranging from 0.2% to 1.3%, and 6.9% patients in Indonesia is diagnosed with hyperthyroidism. Congestive hepatopathy is on of the causes of liver dysfunction in patients with Graves' disease. However, management of hyperthyroidism itself such as methimazole and PTU can sometimes cause further hepatotoxicity. Thyroid dysfunction should also be assessed in patients with unexplained liver dysfunction, especially in patients with history of previous thyroid disease.

ACKNOWLEDGEMENTS

Author would like to thank Ketut Suryana as chairman of internal medicine department, Wangaya general hospital, Denpasar, Bali, Indonesia for reviewing our work and general support.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: Not required

REFERENCES

1. Taylor PN, Albrecht D, Scholz A, Gutierrez-Buey G, Lazarus JH, Dayan CM et al. Global epidemiology of hyperthyroidism and hypothyroidism. Nat Rev Endocrinol. 2018;14(5):301-16.
2. Diseases TIS of ETF on T. Indonesian Clinical Practice Guidelines for Hyperthyroidism. JAFES. 2014;27(1):34.
3. Mazo DF de C, de Vasconcelos GBS, Pereira MAA, de Mello ES, Bacchella T, Carrilho FJ et al. Clinical spectrum and therapeutic approach to hepatocellular injury in patients with hyperthyroidism. Clin Exp Gastroenterol. 2013;6(1):9.
4. Wafa B, Faten H, Mouna E, Fatma M, Mohamed A. Hyperthyroidism and hepatic dysfunction: Report of 17 cases. JGH Open. 2020;4(5):876-9.
5. Opoku-Akyeampong NAAS, Agyei-Nkansah A, Yorke E. Liver dysfunction associated with hyperthyroidism: Lessons from 2 Case reports. Clin Case Rep. 2021;9(6).
6. Yorke E. Hyperthyroidism and Liver Dysfunction: A Review of a Common Comorbidity. Clin Med Insights Endocrinol Diabetes. 2022;15.
7. Li C, Tan J, Zhang G, Meng Z, Wang R, Li W. Risk factors of hyperthyroidism with hepatic function injury: A 4-year retrospective study. Horm Metab Res. 2015;47(3):209-13.
8. Hilscher M, Sanchez W. Congestive hepatopathy. Clin Liver Dis. 2016;8(3):68.
9. Ziccardi MR, Pendela VS, Singhal M. Cardiac Cirrhosis. StatPearls. 2021.
10. Khemichian S, Fong T-L. Hepatic Dysfunction in Hyperthyroidism. Gastroenterol Hepatol (NY). 2011;7(5):337.
11. Vaidya Y, Bhatti H, Dhamoon AS. Hepatojugular Reflux. BMJ. 2021;318(7192):1172.
12. Wells ML, Fenstad ER, Poterucha JT, Hough DM, Young PM, Araoz PA et al. Imaging Findings of Congestive Hepatopathy. Radiographics. 2016;36(4):1024-37.
13. National Institute of Diabetes and Digestive and Kidney Diseases. Methimazole. 2020.
14. Lee SY. Clinical thyroidology ® 70 l Liver Enzymes Are Commonly Elevated in Untreated Hyperthyroidism and Improve after Correction of the

Hyperthyroidism. Volume. 2021;33(2):2329-9711.
15. Ross DS, Burch HB, Cooper DS, Greenlee MC, Laurberg P, Maia AL et al. 2016 American Thyroid Association Guidelines for Diagnosis and Management of Hyperthyroidism and Other Causes of Thyrotoxicosis. Thyroid. 2016;26(10):1343-421.
16. Wang R, Tan J, Zhang G, Zheng W, Li C. Risk factors of hepatic dysfunction in patients with Graves' hyperthyroidism and the efficacy of 131iodine treatment. Medicine (Baltimore). 2017;96(5).

Cite this article as: Adrian SJ, Wirawan IMS. Congestive hepatopathy secondary to graves' disease: a case report. Int J Adv Med 2022;9:935-8.