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Acute hepatitis B infection in patients with graves' disease a case report

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Abstract

Acute hepatitis B infection remains a clinical concern due to its potential progression to fulminant hepatitis and acute liver failure, particularly in patients with comorbid conditions requiring hepatotoxic medications. Graves' Disease, an autoimmune disorder characterized by hyperthyroidism, is commonly managed with antithyroid drugs such as propylthiouracil or methimazole, both of which carry a risk of liver injury. The coexistence of acute hepatitis B infection and Graves' Disease therefore presents a complex therapeutic challenge. We report a case of a 53-year-old woman presenting with acute hepatitis B infection in the setting of Graves' Disease and hypoparathyroidism. The patient presented with gastrointestinal symptoms and markedly elevated transaminase levels. Serological testing confirmed acute hepatitis B infection with positive HBsAg and IgM anti-HBc, while imaging and Fibroscan showed no evidence of chronic liver disease. Graves' Disease was confirmed by suppressed TSH, elevated free thyroxine, and high TRAb levels. The patient was managed conservatively with supportive therapy for acute hepatitis B without antiviral treatment, in accordance with international guidelines, while antithyroid therapy was modified from propylthiouracil to methimazole to minimize hepatotoxic risk. Clinical and laboratory improvement was observed, and follow-up demonstrated HBsAg clearance and anti-HBs seroconversion. This case highlights the importance of careful monitoring and individualized management strategies in patients with acute hepatitis B infection and concurrent Graves' Disease to prevent progression to severe liver injury while maintaining adequate control of thyroid function.

Keywords: Acute hepatitis B, Graves' disease, Antithyroid drugs, Hepatotoxicity

Introduction

Hepatitis B Virus (HBV) infection remains a major global public health challenge, despite the availability of effective vaccines and antiviral therapies. It is estimated that approximately 300 million people worldwide are living with chronic hepatitis B infection, contributing to around 820,000 deaths annually due to complications such as liver cirrhosis and hepatocellular carcinoma (Jeng et al., 2023). The burden of hepatitis B is particularly high in endemic regions, including Southeast Asia, China, and most African countries, where more than 6% of the population are chronic carriers of HBV (Feldman et al., 2020). Indonesia, as part of the Southeast Asian region, remains among the countries with a high prevalence of hepatitis B, making HBV infection a significant clinical and epidemiological concern.

Acute hepatitis B infection in adults is generally self-limiting, with more than 90% of patients achieving spontaneous recovery and viral clearance. However, a small proportion of cases may progress to severe clinical manifestations, including fulminant hepatitis and acute liver failure, which are associated with high mortality rates (Dooley et al., 2011). Furthermore, asymptomatic or unrecognized acute infections may evolve into chronic hepatitis B, ultimately leading to cirrhosis or hepatocellular carcinoma and accounting for up to 500,000 deaths annually worldwide. These potential outcomes highlight the importance of careful clinical assessment, close monitoring, and timely decision-making regarding antiviral therapy in patients with acute hepatitis B infection.

Graves' Disease is a systemic autoimmune disorder characterized by the presence of thyroid-stimulating hormone receptor antibodies (TRAb), which stimulate thyroid follicular cells, resulting in diffuse goiter, hyperplasia, and excessive production of thyroid hormones. Graves' Disease represents the most common cause of hyperthyroidism and is associated with multisystem involvement, including cardiovascular, neurological, and metabolic complications (Kahaly et al., 2018). Standard management strategies aim to reduce thyroid

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hormone production and include radioactive iodine therapy, thyroidectomy, and antithyroid medications such as propylthiouracil (PTU) and methimazole.

Although antithyroid drugs are widely used and generally effective, their administration is not without risk. Hepatotoxicity is a recognized adverse effect of thionamide antithyroid drugs, particularly propylthiouracil, which has been associated with severe liver injury and, in rare cases, acute liver failure. Methimazole is considered to have a more favorable hepatic safety profile, but liver dysfunction may still occur, especially in patients with pre-existing liver disease (Kahaly et al., 2018). Consequently, the management of Graves' Disease in patients with concurrent acute liver conditions poses a significant clinical challenge.

In the context of acute hepatitis B infection, the risk of progression to fulminant hepatitis necessitates careful evaluation of all potentially hepatotoxic medications. The continuation or modification of antithyroid therapy must be balanced against the risk of worsening liver injury and the need to control thyrotoxicosis, which itself may exacerbate systemic stress and hepatic dysfunction. Close clinical observation, serial monitoring of liver function tests, and individualized therapeutic adjustments are essential in such complex clinical scenarios.

This case report aims to highlight the clinical considerations and management challenges of acute hepatitis B infection in a patient with Graves' Disease, emphasizing the importance of multidisciplinary decision-making and vigilant monitoring to prevent severe hepatic complications while maintaining adequate control of thyroid function.

Case report

A 53-year-old woman came to the emergency room with the main complaint of nausea accompanied by vomiting, which she had been experiencing for the past 3 days. She vomited more than five times a day. The vomit contained food, with each episode amounting to approximately 200 ml. The patient had previously visited a local clinic and was prescribed antiemetic medication, but she found it difficult to take due to the nausea and vomiting. Additionally, the patient reported having loose stools twice, with a brownish-yellow color, starting one day before presenting to the ER, with a volume of approximately 100 ml per bowel movement. The patient did not report jaundice on her skin or eyes.

Upon further history taking, the patient denied any history of liver disease or previous jaundice. The history of vaccination against Hepatitis B virus is unclear. One month prior, the patient had been hospitalized twice with a diagnosis of Impending Thyroid Storm + Hypocalcemia on 10/2/2022 and with a diagnosis of Grave's Disease + AF Rapid Ventricular Response + Hypocalcemia on 10/6/2023. During both hospitalizations, HBsAg test results were negative. The patient has never undergone a thyroidectomy or blood transfusion. There is no family history of liver disease, Hepatitis B, or jaundice. The patient also denies alcohol consumption or herbal medicine use. The patient is sexually active with her husband.

From further investigation during the previous hospitalization period, it was found that the patient had undergone a thyroidectomy in 1994 at a local health center. Since 2021, the patient has been diagnosed with hyperthyroidism and has been regularly treated with PTU, Vitamin D3, Calcium, Calcitriol, and Potassium tablets. The patient was hospitalized in the two previous periods with the main complaint of stiffness and difficulty moving. The patient was diagnosed with suspected hypoparathyroidism and was discharged after her calcium levels were successfully corrected.

The patient is conscious (GCS 456) with vital signs showing BP 137/84 mmHg, pulse 84 beats per minute, RR 18 breaths per minute, body temperature 36.6°C, and SpO2 98% without supplemental oxygen. On examination of the head and neck, the patient's eyes appear protruding with icteric sclera. There is no anemia of the conjunctiva, signs of dyspnea, or cyanosis. On the front of the neck, there is a lump the size of a chicken egg, 3 to 4 cm in diameter, with a firm, rubbery consistency that moves when the patient swallows. Chest wall movement was symmetrical, and no retraction was observed. Heart sounds I and II were heard singly without murmurs or gallops. Vesicular breath sounds were heard throughout the lung fields, and no wheezing or rhonchi were heard. Physical examination of the

abdomen revealed a flat abdomen. Auscultation revealed bowel sounds eight times per minute. There is tenderness in the right hypochondrium and epigastrium without enlargement of the liver or spleen. There are no signs of cirrhosis such as ascites, collateral veins, or caput medusae. The patient's extremities are warm, dry, and red with *a capillary refill time* of less than two seconds. *Chvostek's* and *Trosseau's* signs are positive.

Laboratory results upon arrival showed: Hb 13.6 g/dL; HCT 41.4%; MCV 86.8 fL; MCH 28.5 pg; WBC 8,930 /µL; NEUT 83.1%; LYMPH 9.2%; PLT 262,000 µL; PT 12.9 s (control 11.5 s); APTT 28.2 s (control 28.6 s); INR 1.1 (based on PT); BUN 10.8 mg/dL; Cr 0.68 mg/dL; Na 137 mmol/L; K 3.9 mmol/L; Cl 103 mmol/L; Ca 7.11 mmol/L; P 5.17 mmol/L; AST 2873.8 U/L; ALT 1810 U/L; D-Bil 1.2 mg/dL; T-Bil 1.9 mg/dL; Alb 4.22 g/dL; Glucose 120 mg/dL; HBsAg reactive; anti-HCV non-reactive; FT4 1.74 ng/dL; TSH 0.014 mIU/L.

Abdominal ultrasound examination shows: Liver: normal size, sharp angle, smooth edges, slightly increased echogenicity of the parenchyma, no dilation of the inferior vena cava/superior vena cava, portal vein/hepatic vein appear normal, portal vein size +/- 1 cm (normal < 1.3 cm) with *portal vein velocity* 19.9 cm/s (normal > 16 cm/s), no nodules/cysts/masses visible; Gallbladder: normal size, no wall thickening visible, no stones/nodules/sludge visible; Pancreas: normal size, parenchymal echo intensity appears normal, no pancreatic duct dilation visible, no masses/cysts/calcifications visible. The results of the description of other organs were within normal limits. The radiologist concluded that the abdominal ultrasound results were consistent with *mild parenchymal liver disease*.

Based on the results of clinical, laboratory, and ultrasound examinations, we concluded the initial diagnosis as acute hepatitis B + Graves' disease + hypocalcemia due to hypoparathyroidism. We then planned additional laboratory tests, including Ig-M anti-HBc, IgM anti-HAV, HBV-DNA, and HBeAg tests. These tests aim to rule out other causes related to elevated transaminase levels. The patient is admitted to the internal medicine ward for observation and improvement of conditions related to the risk of progression to fulminant hepatitis and acute liver failure. The patient is administered supportive therapy with an H1 diet and aminofusin hepar infusion. For hypoparathyroidism, the patient was given therapy to maintain blood calcium levels with calcium CaCO3 preparations and vitamin D preparations in the form of D3 and Calcitriol. Graves' Disease was controlled with the administration of the beta blocker propranolol accompanied by Thiamazole 2x10 mg as a substitute for propylthiouracyl to prevent worsening of liver function. DL, LFT, and SE were evaluated periodically.

Table 1. Clinical development of acute hepatitis B in patients with hyperthyroidism and hypoparathyroidism

	11/22 (in the emergency room)	**11/23 (in the ward)**	**11/27**	**November 29**	**November 30**	**7/2 (at the outpatient clinic)**
Hb (g/dL)	13.6		11.7			13.7
WBC (/µL)	8930		7510			9880
NEUT (%)	83.1		61			63.9
LYMPH (%)	9.2		29.8			29.4
PLT (/µL)	262,000		283,000			398,000
ALT (U/L)	1810	4155	996.2	505.7		18
AST (U/L)	2873.8	5180	188.2	57.3		23
Albumin (g/dL)	4.22		3.01	3.58		5.37
Bilirubin (mg/dL)	1.9	4.3	1.9			0.37
Bil D (mg/dL)	1.2	3.2	1.3			0.11
Blood Sugar (mg/dL)	120		91.1			113
PT (sec)	12.9		11.2			

aPTT (sec)	28.2		31.3			
INR	1.1					
BUN (mg/dL)	10.8		12.1			11
Cr (mg/dL)	0.68		0.53			0.8
Na (mmol/L)	137		139	139		
K (mmol/L)	3.9		3	4.5		
Cl (mmol/L)	103		104	102		
Ca (mmol/L)	7.11		6.8	7.17		
P (mmol/L)	5.17		4.98	6.11		
HBsAg	Reactive					Non-reactive
HBeAg	Reactive 820.76					
HBV-DNA (IU/mL)	Detected 5.46 x 10^3					
IgM anti-HBc	Reactive (12.87)					
Anti-HBs (mIU/mL)						Reactive
IgM anti-HAV	Non-reactive					
Anti-HCV	Non-reactive					
TRAb (IU/L)					26.08	
PTH Intact (pg/mL)					2.14	
FT4 (ng/dL)	1.74		2.04			
TSH (mIU/L)			0.014			

Note: HB = hemoglobin; WBC = white blood cell count; NEUT = neutrophil count; LYMPH = lymphocyte count; PLT = platelet count; ALT = alanine transaminase; AST = aspartate transaminase; Bil D = direct bilirubin; Bil T = total bilirubin; PT = prothrombin time; APTT = activated partial thromboplastin time; INR = international normalized ratio; BUN = blood urea nitrogen; Cr = creatinine; Na = sodium; K = potassium; Cl = chloride; HBsAg = hepatitis B surface antigen; HBeAg = hepatitis B envelope antigen; IgM = immunoglobulin M; anti-HBc = anti-hepatitis B core; anti-HAV = anti-hepatitis A; TRAb = thyroid hormone receptor antibody; PTH = parathyroid hormone; FT4 = Free T4;

The IgM anti-HAV test result was negative. IgM anti-HBc showed a reactive result with a value of 12.87 (ECLIA; reference value <0.1). HBeAg was reactive with a value of 820.76 and HBV-DNA was reactive with a result of 5.46 x 10^3IU/mL. These results confirm the suspicion of acute hepatitis B infection in the patient. The patient remains under supportive care and observation without nucleoside analog administration. A *Fibroscan* examination was also performed with a *liver stiffness* result of 5.3 kPa, which is normal; that is, there is no fibrosis process in the liver. The patient also underwent TRAb level testing with a result of 26.08 IU/L (ECLIA; normal reference <=1.75 IU/L) and intact PTH level of 2.14 pg/mL (normal reference 10–65 pg/mL), confirming the suspicion of hypoparathyroidism in the patient. During the observation period in the ward, we observed clinical improvement in the patient day by day, with reduced nausea and vomiting and improvement in jaundice. Transaminase levels increased during the first two days of treatment but subsequently showed a downward trend, followed by a decrease in bilirubin levels. Other parameters monitored for acute liver failure, such as blood sugar levels and hemostasis function (PT and APTT), also showed good results during treatment. On day 10, the patient was discharged and scheduled for a follow-up appointment at the hepatology clinic.

During the *follow-up* at the outpatient clinic, the patient was in stable and good condition with no complaints. Laboratory results also showed improvement. The patient underwent a repeat HBsAg

test accompanied by HBsAB. HBsAg showed a negative result with a level <0.1 (negative reference <1) accompanied by positive HBsAB with a level of 164.18 mIU/mL (non-reactive reference <8). These results indicate seroconversion and that the patient did not develop chronic hepatitis B infection.

Result And Discussion

The hepatitis B virus is a *double-stranded* DNA virus from the *Hepadnaviridae* family with a specific tropism for hepatocytes. After entering the cell through the *sodium-taurocholate cotransporting polypeptide* receptor, hepatitis B virus DNA integrates into the host hepatocyte nucleus as *covalently closed circular DNA* (cccDNA), which remains indefinitely and can be reactivated later under immunosuppressed conditions (Jeng et al., 2023; Castaneda et al., 2021). Hepatitis B virus has long been understood to be *non-cytopathic*, with damage to hepatocytes primarily caused by the immune response itself (Castaneda et al., 2021). Hosts with a strong and widespread immune response will experience a *self-limited* condition known as acute hepatitis. Meanwhile, hosts with a deviant immune response may develop a life-threatening condition called fulminant hepatitis. In hosts with a poor immune system, it can progress to chronic hepatitis B infection (Altaf et al., 2023).

Graves' disease is a disease caused by a disorder of the immune system and is characterized by the proliferation and hypersecretion of thyroid hormones (hyperthyroidism). Hyperthyroidism in *Graves' disease* is caused by autoantibodies against the thyrotropin receptor (TRAb), so measuring TRAb levels is very important for diagnosis and management. TRAb is not controlled through negative feedback mechanisms, so thyroid stimulation by TRAb often causes thyrotoxic conditions in *Graves' disease* (Cui et al., 2016).

A 53-year-old woman came to the emergency room with the main complaint of nausea accompanied by vomiting, which she had been experiencing for the past 3 days. She vomited more than five times a day. The vomit contained food, with each episode amounting to approximately 200 ml. The patient had sought treatment at a local clinic and was given antiemetic medication, but she had difficulty taking it due to nausea and vomiting. Additionally, the patient complained of loose stools twice, with a brownish-yellow color, starting one day before coming to the emergency department ( ), with a volume of approximately 100 ml per bowel movement. The patient did not experience jaundice in her body or eyes.

Hepatitis B infection has an average incubation period of approximately 1 to 6 months and can develop into several spectrums of clinical manifestations. Approximately 70% of patients will experience asymptomatic infection, 30% of patients will go through the icteric phase, and <1% of the rest will develop fulminant manifestations to acute liver failure (Dekker et al., 2021; Jeng et al., 2023). The initial symptoms of acute hepatitis B infection are nonspecific, such as weakness, loss of appetite, nausea, and pain in the upper right abdomen. In the icteric phase, complaints of weakness and loss of appetite worsen and last from weeks to several months. Improvement in jaundice indicates progression to the convalescent phase (Jindal et al., 2013).

Laboratory test results upon the patient's arrival showed elevated transaminase enzymes, increased direct and total bilirubin, and reactive HBsAg. Initial test results indicated liver dysfunction and suspicion of acute hepatitis B infection.

Table 2. Laboratory results at initial presentation suggestive of acute hepatitis B

	11/22 (in the ER)
ALT (U/L)	1810
AST (U/L)	2873.8
Total Bilirubin (mg/dL)	1.9
Bilirubin D (mg/dL)	1.2
Ca (mmol/L)	7.11
P (mmol/L)	5.17
HBsAg	Reactive

Patients with acute hepatitis B infection may experience an increase in transaminase enzymes of up to 500-5000 IU/L, which decreases after the acute phase of the infection. The increase in bilirubin levels varies, ranging from relatively normal levels in *anicteric* patients to high levels in patients experiencing the icteric phase, although it rarely exceeds 10 mg/dL. Serum albumin may be normal or

slightly decreased, particularly in more severe manifestations. (Dekker et al., 2021; Jindal et al., 2013). An INR increase >1.5 indicates coagulation dysfunction and is an important sign of disease progression toward fulminant hepatitis, in addition to prolonged disease course (visible and persistent jaundice symptoms >4 weeks) (Lampertico et al., 2017; Schaefer & John, 2023; Wang et al., 2021). Persistently elevated ALT levels accompanied by detectable HBsAg beyond 6 months from symptom onset indicate disease progression to chronicity (Castaneda et al., 2021; Koffas, 2023).

The anti-HBc IgM level test showed a reactive result with a value of 12.87 (ECLIA; reference value <0.1). HBeAg was reactive with a value of 820.76 and HBV-DNA was reactive with a result of 5.46 x 10^3IU/mL. A fibroscan test was also performed with a liver stiffness result of 5.3 kPa, which is normal; indicating no fibrosis process in the liver. The patient also underwent TRAb level testing with a result of 26.08 IU/L (ECLIA; normal reference <=1.75 IU/L) and intact PTH level of 2.14 pg/mL (normal reference 10–65 pg/mL), confirming the suspicion of hepatitis B infection, Graves' disease, and hypoparathyroidism in the patient.

The diagnosis of acute hepatitis B infection is established through HBsAg and anti-HBc IgM testing (Castaneda et al., 2021). HBV DNA and HBeAg, as markers of active hepatitis B virus replication, can be detected in the early stages and disappear as the patient's condition improves. Resolution of acute hepatitis B is marked by seroconversion; beginning with HBeAg becoming anti-HBe, followed by HBsAg becoming anti-HBs. In fulminant cases where HBsAg clearance occurs more rapidly, anti-HBc IgM becomes the sole marker of acute infection (Lampertico et al., 2015; Sedano et al., 2021).

Distinguishing acute hepatitis B from acute exacerbation of chronic hepatitis B is difficult, mainly because these two conditions share similarities in terms of clinical manifestations, biochemistry, and serology (Baek, 2020). In hepatitis B endemic areas, acute exacerbation of chronic hepatitis B is common, and the acute symptoms of this exacerbation are often the first manifestations of chronic hepatitis B or long-standing cirrhosis in patients. Even in endemic areas, acute exacerbation of chronic hepatitis B is estimated to account for up to 50% of all cases initially diagnosed as primary infection (Lall et al., 2020; Orenbuch-Harroch et al., 2008). Anti-HBc IgM has long been considered a specific marker for acute hepatitis B infection. However, with advances in diagnostic technology, anti-HBc IgM is positive in some patients with chronic hepatitis B infection, albeit at low levels (Lall et al., 2020). Although this poses a dilemma, the two conditions differ in terms of management strategies, prognosis, and impact on public health, making it crucial to distinguish between them (Baek, 2020).

Table 3. Comparative analysis of various studies evaluating the role of serological tests in distinguishing acute hepatitis B from acute exacerbation of chronic hepatitis B

Study	Technique	IgM anti-HBc	HBV-DNA	Other findings
Rodella et al. 2006	Chemiluminiscent Immunoassay (CLIA)	S/Co=10, avidity index=0.7 diagnostic for HBA	Not performed	HBsAg levels differ significantly. HBA > HBK-EA
Huang et al. 2006	MEIA HBV DNA-qPCR	Average index value 2.9 HBA – 1.5 HBK-EA	Comparable in both groups	*Cut-off* for IgM anti-HBc 2.4-2.5 shows 90% sensitivity and specificity
Han et al. 2008	Enzyme Immunoassay (EIA)	At a dilution of 1:10,000, high sensitivity and specificity (96.2% and 93%)	No significant difference was found	Combining HBV DNA and HBeAg enhances diagnostic accuracy
	HBV DNA = qPCR			Low HBeAg levels are more useful than negative HBeAg
Kumar et al. 2006	Enzyme Immunoassay (EIA)	Titers >1:1,000 were found in 80% of HBA patients	<0.5 pg/mL was found in HBK-EA patients	

Dao et al. 2012	Enzyme Immunoassay (EIA)	*S/N* ratio is higher in HBA=88.2	HBA 3.9 log_{10}IU/mL; HBK-EA 5.2 log_{10}IU/mL	*S/N* ratio cutoff point of 5.0 for IgM
Park et al. 2015	Chemiluminiscent Immunoassay (CLIA)	The S/Co ratio of anti-HBc IgM was significantly higher in the HBK-EA group	HBV DNA levels were significantly higher in the HBK-EA group	The optimal cutoff values for anti-HBc IgM and HBV DNA levels to distinguish between the two conditions are an S/Co ratio of 8 and 5.5 log10 IU/mL, respectively
Thanage et al. 2019	Chemiluminiscent Immunoassay (CLIA) HBV DNA = PCR	≥12.14 S/Co	>15,390 IU/mL in HBK-EA	
Lall et al. 2020	Chemiluminiscent Immunoassay (CLIA)	The S/Co ratio of anti-HBc IgM is higher in the HBA group	Not performed	S/Co ratios of 20.5 for anti-HBc IgM and 1.27 for INR may help distinguish HBA from HBK-EA

Note: HBA = Acute Hepatitis B; HBK-EA = Acute Exacerbation of Chronic Hepatitis B; CLIA = Chemiluminiscent Immunoassay; EIA = Enzyme Immunoassay; MEIA = Microparticle Enzyme Immunoassay; IgM anti-HBc = Immunoglobulin M antibody against hepatitis B core antigen; HBV = Hepatitis B Virus, HBeAg = Hepatitis B e antigen; S/CO = *signal cut-off*; qPCR = *quantitative real-time polymerase chain reaction*; S/N = *signal-to-noise ratio*

Table 2 summarizes the optimal *cut-off* values, sensitivity, and specificity from studies comparing serological tests in distinguishing acute hepatitis B and acute exacerbation of chronic hepatitis B. Studies conducted by Rodella et al, Huang et al, Han et al, Kumar et al, Dao et al., and Park et al showed that a combination of the S/Co and S/N ratios of anti-HBc IgM and HBV DNA is useful for distinguishing acute hepatitis B from acute exacerbation of chronic hepatitis B, despite different *cut-off* values. A recent 2020 study by Lall et al. included INR as a variable and tested other marker combinations to distinguish acute hepatitis B from acute exacerbation of chronic hepatitis B. However, this recent study showed that these combinations did not improve the ability of serological tests to distinguish between the two, and anti-HBc IgM remained the most significant factor in distinguishing between them (Lall et al., 2020). In our patients, a different method was used compared to those studies, so the results of quantitative anti-HBc IgM tests cannot be compared proportionally. *Fibroscan* results showing no fibrosis, no signs of chronic liver disease, and an INR <1.27 helped point to a diagnosis of acute hepatitis B. The patient had a history of negative HBsAg tests during previous treatment periods. Likewise, the absence of a history of procedures such as transfusions during the patient's treatment period eliminated the possibility of transmission via transfusion. Although transmission through *invasive* procedures such as injections cannot be completely ruled out due to the patient's history of readmission, in areas with high hepatitis B endemicity such as Indonesia, the possibility of horizontal transmission within a family is quite high with the presence of family members who are asymptomatic carriers with positive HBsAg or asymptomatic chronic hepatitis B (Athalye et al., 2023; Lloyd & Franco, 2023; Roberts et al., 2021; Zhao et al., 2021).

The patient was treated in the internal medicine ward for observation and improvement of conditions related to the risk of fulminant development leading to acute liver failure. The patient was given supportive therapy with an H1 diet and aminofusin hepar infusion. For hypoparathyroidism, patients are given therapy to maintain blood calcium levels with calcium CaCO3 preparations and vitamin D preparations in the form of D3 and Calcitriol. Graves' Disease is controlled with the administration of the beta blocker propranolol accompanied by Thiamazole 2x10 mg as a substitute for propylthiouracyl to prevent worsening of liver

function. DL, LFT, and SE are evaluated periodically.

The American Association for the Study of Liver Diseases (AASLD), the Asian Pacific Association for the Study of the Liver (APASL), the European Association for the Study of the Liver (EASL), and the World Health Organization (WHO) agree that antiviral treatment for acute hepatitis B infection is only indicated in patients with clinical conditions that lead to fulminant or acute liver failure; which can be characterized by a clinical course lasting >4 weeks, coagulopathy (marked by an INR increase >1.5), or the onset of encephalopathy symptoms (Dekker et al., 2021; Huang & Lim, 2020; Jeng et al., 2023; Lampertico et al., 2017; Sarin et al., 2016; Terrault et al., 2018; World Health Organization (WHO), 2015). The lack of recommendations for antiviral use as therapy for acute hepatitis B infection is based on the high rate of spontaneous *recovery* in adult patients without *immunocompromised* conditions who suffer from acute hepatitis B. In addition, a study reported that in order to achieve spontaneous *recovery*, the immune system must be exposed to hepatitis B antigen in the early phase to induce antibody production, and antiviral administration can inhibit this process. However, there have also been reports of cases where antibodies did not form in patients who did not receive therapy, resulting in different management approaches between patients (Dooley et al., 2011; Feldman et al., 2020; Jindal et al., 2013). The results of our evaluation showed gradual clinical improvement within a relatively short period of time, so antiviral therapy was not administered to the patient.

Thionamide drugs such as propylthiouracil (PTU), carbimazole (CBZ), and methimazole (MMI) are the first line of treatment for hyperthyroidism (Kahaly et al., 2018; Katzung & Trevor, 2015). Although rare (<0.1% to 1%), cases of severe to fatal hepatitis due to thionamide use, particularly PTU, have been reported. Unlike PTU, hepatitis caused by thionamide use with MMI has been reported to have milder symptoms and a cholestatic pattern. A study with a sample of >70,000 patients treated with antithyroid drugs found that the risk of hepatitis and cholestasis with MMI use is *dose-dependent* compared to PTU (Butt et al., 2023; Ichiki et al., 1998; Kahaly et al., 2018).

During follow-up at the outpatient clinic, the patient was stable and well with no complaints. Laboratory results also showed improvement. The patient underwent a repeat HBsAg test accompanied by HBsAB. HBsAg showed a negative result with a level <0.1 (negative reference <1) accompanied by positive HBsAB with a level of 164.18 mIU/mL (non-reactive reference <8).

In patients with acute hepatitis B, serum transaminase levels and HBsAg decrease and return to normal levels and disappear at the same time. In about 80% of cases, HBsAg will be undetectable within 12 weeks after the onset of the disease. The continued detection of HBsAg after 6 months implies the development of chronic infection and the possibility of *recovery* within 6 to 12 months is quite small (Dooley et al., 2011; Feldman et al., 2020). In patients, seroclearance and seroconversion are obtained with the undetectable HBsAg and the appearance of anti-HBs.

Conclusion

A case has been reported of a 53-year-old woman with acute hepatitis B infection who had Graves' disease. The diagnosis of acute hepatitis B was confirmed based on positive results from anti-HBc IgM testing. As a differential diagnosis for acute hepatitis B, we ruled out acute exacerbation of chronic hepatitis B based on the absence of signs of chronic liver disease, *Fibroscan* results that did not indicate fibrosis, and an INR level <1.27. In addition to supportive management of acute hepatitis B infection, we initiated Graves' Disease therapy in the patient to reduce the risk of acute liver failure and further liver damage from the thionamide drug PTU, which was converted to MMI in the patient.

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