Gac Méd Caracas 2023;131(Supl 2):S192-S197
DOI: 10.47307/GMC.2023.131.s2.15

Liver Cirrhosis Patient with Complications of Hepatic Hydrothorax. Case Report

Paciente con cirrosis hepática con complicaciones de hidrotórax hepático. Reporte de caso

Amie Vidyani[1a*], Titong Sugihartono[2a], Budi Widodo[3a], Herry Purbayu[4a], Ummi Maimunah[5a], Ulfa kholili[6a], Husin Thamrin[7a], Muhammad Miftahussurur [8ab], Iswan Abbas Nussi[9a], Poernomo Boedi Setiawan[10a]

SUMMARY

Introduction: *Hepatic hydrothorax is that occurs in individuals with decompensated cirrhosis of the liver. Approximately 5 % of cases of pleural effusion occur in patients with cirrhosis and ascites. Although quite rare, it is associated with higher morbidity and lower survival rates. The mechanism is not fully understood, but the most widely accepted pathogenesis involves the presence of portal hypertension, diaphragmatic defects, and negative intrathoracic pressure. In this case, the pleural effusion occurs because of the direct displacement of peritoneal fluid through the small openings in the diaphragm into the pleural space. We aimed to study its clinical features and natural history.*
Case Presentation: *We reported a 59-year-old woman with liver cirrhosis and hepatic hydrothorax complications. Patients experience shortness of breath and hematemesis. Examination of chest X-ray and chest CT scan found right pleural effusion. The patient was treated with repeated thoracocentesis, and a chest pigtail catheter was placed for pleural effusion, salt restriction, diuretics, and management of the underlying disease (liver cirrhosis). After the installation of the chest pigtail catheter, the fluid production reduced (less than 500 mL in a day). The results of the pleural fluid analysis showed an impression of the transudate.*
Conclusion: *This study reports the rare case of a patient with right pleural effusion due to hepatic hydrothorax in liver cirrhosis, who improved with comprehensive therapy (salt restriction, diuretics, repeated thoracocentesis, and then chest pigtail catheter application).*

Keywords: *Liver cirrhosis, hepatic hydrothorax, pleural effusion.*

RESUMEN

Introducción: *El hidrotórax hepático es el que se presenta en individuos con cirrosis hepática descompensada. Aproximadamente el 5 % de los*

DOI: https://doi.org/10.47307/GMC.2023.131.s2.15

ORCID: 0000-0002-7533-5652[1]
ORCID: 0000-0003-4923-9832[2]
ORCID: 0000-0003-4491-8545[3]
ORCID: 0000-0002-9603-8593[4]
ORCID: 0000-0002-2496-4336[5]
ORCID: 0000-0003-3885-8398[6]
ORCID: 0000-0002-6176-1765[7]
ORCID: 0000-0003-1415-6033[8]
ORCID: 0000-0002-4179-1545[9]
ORCID: 0000-0002-1443-3929[10]

Recibido: 23 de febrero 2023
Aceptado: 4 de marzo 2023

[a]Gastroentero-Hepatology Division, Department of Internal Medicine, Faculty of Medicine, Dr. Soetomo Teaching Hospital, Universitas Airlangga, Surabaya
[b] Institute of Tropical Disease, Airlangga University, Surabaya, Indonesia

*Corresponding author: Amie Vidyani, MD.
Department of Internal Medicine, Gastroentero-Hepatology Division, Faculty of Medicine, Dr. Soetomo Teaching Hospital, Universitas Airlangga, Surabaya Indonesia.
E-mail: amie.vidyani@fk.unair.ac.id

casos de derrame pleural ocurren en pacientes con cirrosis y ascitis. Aunque bastante raro, se asocia con una mayor morbilidad y menores tasas de supervivencia. El mecanismo no se comprende por completo, pero la patogenia más ampliamente aceptada involucra la presencia de hipertensión portal, defectos diafragmáticos y presión intratorácica negativa. En este caso, el derrame pleural se produce por el desplazamiento directo del líquido peritoneal a través de las pequeñas aberturas del diafragma hacia el espacio pleural. El objetivo fue estudiar sus características clínicas y su historia natural.

Descripción de caso: *Reportamos una mujer de 59 años con cirrosis hepática y complicaciones de hidrotórax hepático. Los pacientes experimentan dificultad para respirar y hematemesis. En el examen de radiografía de tórax y tomografía computarizada de tórax se encontró derrame pleural derecho. El paciente fue tratado con toracocentesis repetidas y se colocó un catéter pigtail (cola de cerdo) torácico por derrame pleural, restricción de sal, diuréticos y manejo de la enfermedad de base (cirrosis hepática). Después de la instalación del catéter de cola de cerdo torácico, la producción de fluidos se redujo (menos de 500 mL en un día). Los resultados del análisis del líquido pleural mostraron una impresión del trasudado.*

Conclusión: *Este estudio reporta el raro caso de un paciente con derrame pleural derecho por hidrotórax hepático en cirrosis hepática, que mejoró con terapia integral (restricción de sal, diuréticos, toracocentesis repetidas y luego aplicación de catéter de cola de cerdo torácico).*

Palabras clave: *Cirrosis hepática, hidrotórax hepático, derrame pleural*

INTRODUCTION

Hepatic hydrothorax is an excess accumulation of transudate fluid in the pleural cavity in patients with decompensated liver cirrhosis without pulmonary and pleural heart disease. The condition is localized to the right in approximately 85 % of cases and to the left alone in 13 % of cases, as only 2 % have effusions on both sides (1).

Hepatic hydrothorax is a rare complication of end-stage liver disease, accounting for 5 %-10 % of cirrhotic patients. There are already a few case reports describing the clinical features and treatment of hepatic hydrothorax, but current knowledge about this complication of cirrhosis is very limited. The pathogenesis and therapy of hepatic hydrothorax have not been well studied, and there are no randomized controlled trials that can provide the best treatment option, so evidence-based guidelines have not been published (2).

Patients with minimal pleural effusion may be asymptomatic or have pulmonary symptoms, such as shortness of breath, cough, chest discomfort, hypoxemia, or respiratory failure. Hepatic hydrothorax is prone to spontaneous bacterial pleurisy with or without spontaneous bacterial peritonitis. Hepatic hydrothorax indicates progression to decompensated cirrhosis and the need for liver transplantation consideration. The management of hepatic hydrothorax is still a problem because the condition of the liver tends to be poor (3). We present this case report to increase knowledge about liver cirrhosis complications, which are rare.

CASE PRESENTATION

A 59-year-old woman came from a hospital referral to the emergency room of Dr. Soetomo Hospital with complaints of vomiting blood one day before admission to the hospital. She vomited blood once in the form of fresh blood mixed with blood clots. The amount is approximately half a glass of mineral water (125 mL). The patient did not complain of abdominal pain, cough, or shortness of breath. There was no history of previous trauma or jaundice or urination like tea. The patient did not brush her teeth when she vomits.

The patient also complains of shortness of breath, but there was no cough or fever. The shortness of breath worsens when she sleeps, improving with a sitting position. The patient had had lung fluid removed while being treated in the internal medicine ward. The patient admitted that she had never looked yellow or had hepatitis before.

From the physical examination, the respiratory rate was 24x/minute. On examination of the head and neck, the conjunctiva was not anemic, not icteric. On chest examination, the development of the right chest wall lags behind the left. Auscultation of the thorax obtained decreased right vesicular breath sounds and no additional breath sounds. On abdominal examination,

there was no visible distention, *caput medusa*, or *collateral vein*. On auscultation, bowel sounds were normal. On percussion, neither *shifting dullness* nor undulation was found. Abdominal palpation revealed that the liver and spleen were not palpable.

From the results of laboratory tests, it was found that several tests were less or more than the reference values, which can be seen in Table 1.

Table 1. Laboratory result

Checking type	Parameters	Result
Hemoglobin	12.0-14.0 (F) 13.0-16.0 (M)	11.7 g/dL
Leukocytes	5 000-10 000	6360 u/mL
Neutrophils	39.8-70.5	76.30 %
Lymph	23.1-49.9	13.20 %
Platelets	150 000-450 000	83 000 u/mL
Blood Urea Nitrogen (BUN)	7-20	16 mg/dL
Serum creatinine	0.5-1.2	0.6 mg/dL
Sodium	136-146	140 mmol/L
Potassium	3.5-7.0	3.4 mmol/L
Chloride	94-111	102 mmol/L
AST <25 (M)	<21 (F) 149 units/L	
ALT <30 (M)	<23 (F) 70 units /L	
Albumin	3.4-5.0	2.98 g/dL
PPT	9-12	10.3 seconds
APTT	23-33	29.8 seconds
Random blood glucose	<200	117 mg/dL

From the investigation, HBsAg reactive, and COVID-19 PCR swab was not detected. The patient had undergone radiological investigations in the form of a chest X-ray with the results of pulmonary inflammation with right pleural effusion, and the heart did not show abnormalities (Figure 1). The ultrasound examination revealed normal liver size, heterogeneous increased echo-parenchymal intensity, irregular obtuse angles, no nodules, and an enlarged spleen that appeared ascites (Figure 2). There was an impression of hepatic cirrhosis with ascites. Transient elastography examination of the patient showed the results of 36.3 kPa, which is equivalent to the degree of fibrosis f4. The results of the initial ECG examination revealed rhythmic sinuses with a heart rate of 79 beats per minute, normoaxis.

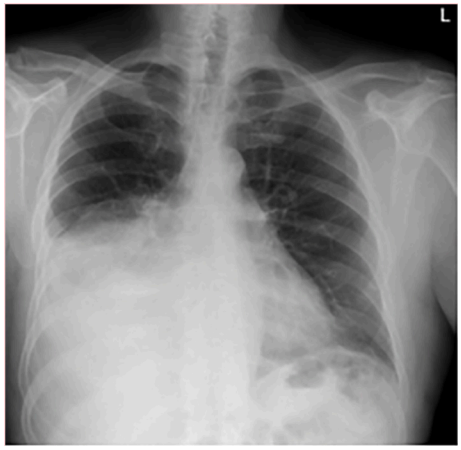

Figure 1. Chest X-ray (First admission).

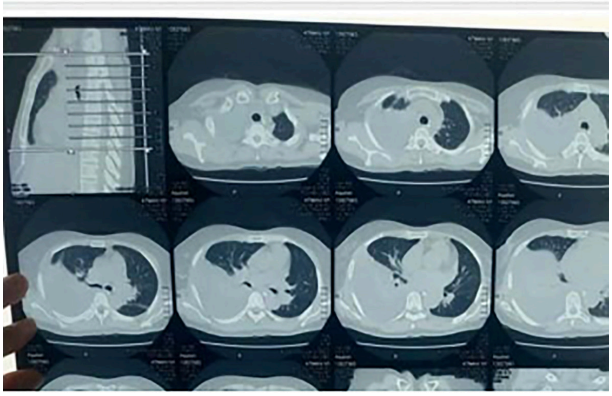

Figure 2. Thorax CT scan (First Admission).

From a chest X-ray examination and thorax CT scan, there is a right-sided pleural effusion, thickening of the left hilum, and ascites (Figures 1 and 2). On the fourth day of treatment, the patient complained of shortness of breath and black stool getting worst. The chest X-ray revealed the right pleural effusion, and the right lung was not visualized, suggesting a massive right pleural effusion. We gave additional therapy in the form of a somatostatin analog bolus of 50 mcg followed by a somatostatin analog drip of 25 mcg every hour and omeprazole in 40 mg every 6 hours and antibiotic (ceftriaxone injection of 2 g daily). On the tenth day of treatment, the

patient did not experience melena. Pleural fluid cytology results showed no malignancy, only powdered lymphocyte cells. The patient was then planned for endoscopy. The endoscopy showed esophageal and gastric varices (GOV-1) and gastropathy congestive. The patient was treated with an injection of histoacryl and lipiodol for gastric varices.

The patient was then planned for repeated fluid evacuation. On the fifth day of treatment, the patient underwent a second pleural fluid evacuation, 1 200 mL of lung fluid was obtained with a transparent color impression, and pleural fluid cytology was performed. The patient underwent a chest X-ray evaluation after the evacuation of pleural fluid. It was found on a chest X-ray of lung inflammation, right pleural effusion, and atherosclerosis. Because the estimated amount of lung fluid in the patient is still a lot, it is planned to install the right pigtail catheter in the patient. After the installation of the chest pigtail catheter, the fluid production reduced (less than 500 mL in a day). The results of the pleural fluid analysis showed an impression of the transudate.

DISCUSSION

Liver cirrhosis is a progressive, diffuse, fibrotic, and nodular condition that damages the entire liver structure (4). Cirrhosis is the final course of fibrogenesis in chronic liver disease. The liver changes from a normal state to a fibrotic condition, with cirrhosis being a complex process involving parenchymal and non-parenchymal components, the immune system, cytokines, proteinases, and their inhibitors (5).

Cirrhosis can be caused by various diseases, including alcohol, viral hepatitis infection (hepatitis B and C), and *Non-Alcoholic Fatty Liver disease* (NAFLD). Cryptogenic, metabolic (hemochromatosis or Wilson's disease), biliary disease, autoimmune, drug-induced hepatitis (e.g., methotrexate, amiodarone), and hepatic venous congestion (Budd Chiari syndrome, constrictive pericarditis) (6).

Cirrhosis and hepatocellular carcinoma (HCC) are two clinical outcomes of untreated chronic hepatitis B. This patient, although recently tested positive for hepatitis B, already has signs of chronic liver disease based on physical examination and investigations. This patient underwent a known HBsAg test in August 2020 and showed high ALT levels. The indications for treatment of hepatitis B infection were determined based on a combination of four criteria, including serum HBV DNA level, HBeAg status, ALT level, and liver histology. In patients with compensated cirrhosis, treatment was initiated in patients with HBV DNA >2 x 10^3 IU/mL. In contrast, decompensated cirrhosis should be treated promptly to prevent disease progression, regardless of HBV DNA or ALT (7). In this case, the patient is prescribed antiviral treatment in the form of tenofovir in a dose of 1 x 300 mg for life.

The natural course of cirrhosis is characterized by a phase of asymptomatic compensatory cirrhosis followed by a phase of decompensation, and this period of decompensation is characterized by the appearance of various symptoms, including ascites, bleeding, encephalopathy, and jaundice (8). The clinical picture of decompensated cirrhosis was assumed to result from a hemodynamically compromised overactive circulation syndrome caused by peripheral arterial vasodilation, particularly in the splanchnic circulation. Vasodilation impairs adequate blood volume and ultimately leads to hypoperfusion of peripheral organs, with the kidneys being the most affected (9).

One of the common complications of chronic decompensated liver disease is portal hypertension (10). Portal hypertension is defined as high pressure in the portal circulation characterized by an increased hepatic venous pressure gradient of >5 mmHg (9). Clinically, portal hypertension can be diagnosed in cirrhotic patients based on the presence of ascites, varicose veins, or both (11). In this case, the patient had minimal ascites detected by ultrasound. Endoscopic examination revealed varicose veins. The patient also experienced complications from esophageal and gastric varices. Effective volume reduction activates vasoconstrictors and water and sodium retention mechanisms such as the renin-angiotensin aldosterone system (RAAS), sympathetic system, and arginine-vasopressin secretion. This explains the main features of decompensated cirrhosis, such as sodium and

water retention, leading to ascites and Hepatorenal syndrome (HRS) (9).

Signs suggestive of portal hypertension include splenomegaly, portal vein dilatation, portal vein occlusion, decreased platelet count, and ascites with a serum albumin gradient more significant than 1.1 g/dL. The *Hepatic Venous Porto Gradient (HVPG) range* can provide useful clinical information for determining the prognosis of portal hypertension and its complications. Normal people have an HVPG range of 2-5 mmHg. Above 6 mmHg indicates portal hypertension, and an HVPG above 10 mmHg indicates significant portal hypertension (11).

Pleural effusion is a condition with excess fluid in the pleura. Fluid accumulates in the pleural space when the accumulation exceeds the absorption of the pleural fluid. Patients with suspected pleural effusion should undergo chest imaging studies to determine its severity. If a pleural effusion is found, efforts should be made to find the cause. The first step is to determine whether the fluid is transudative or exudative.

Pleural fluid was considered inflammatory fluid if it met at least one of the criteria for pleural protein level/serum protein level >0.5, pleural LDH/serum LDH >0.63, pleural LDH level more than 2-thirds of the upper limit of serum LDH (12). Based on the analysis results, the pleural fluid in the patient, in this case, did not meet the three criteria, so the patient's pleural fluid was transudate.

Hepatic hydrothorax is a complication of liver cirrhosis, which is very rare and usually has a relatively poor prognosis. Hepatic hydrothorax is a condition in which a large amount of fluid accumulates in the pleural cavity (generally more than 500 mL), which occurs in patients with cirrhosis and portal hypertension.

This patient had portal hypertension showing esophageal and gastric varices (GOV-1) and portal gastropathy on endoscopy. Physical examination showed no signs of liver chronicity, such as jaundice, redness of the palms, or the presence of collateral veins. Laboratory examination showed thrombocytopenia and hypoalbuminemia with positive hepatitis serology (HBsAg). Ultrasound revealed ascites.

The clinical examination may reveal pleural effusion in patients with ascites or without cirrhosis. We can diagnose hepatic hydrothorax early, mainly if the effusion is localized only to the right. Left-sided localization with fever and respiratory symptoms requires further investigation to rule out other diseases. Therefore, in cirrhotic patients with pleural effusion, a pleural puncture is necessary when symptoms occur to determine the type of pleural fluid transudate in the condition. The fluid in this state is similar to an ascitic fluid, but due to the difference in absorption speed, there is a slight difference in fluid analysis. Radioactive isotopes can be used to make decisions under suspicious circumstances (1).

The management principle of hepatic hydrothorax begins with salt reduction and diuretic therapy, similar to ascites, due to portal hypertension. This therapy principle is often inadequate because patients usually cannot tolerate the volume of pleural effusion. Symptomatic patients undergo thoracentesis to reduce dyspnea and/or hypoxia (13).

Diuretic therapy is usually initiated and gradually increased to furosemide 40 mg/day and spironolactone 100 mg/day, maintaining the ratio at 100 mg/day; 40 mg until the clinical response is adequate (14). In some cases, patients may be more comfortable with therapeutic thoracentesis if the pleural effusion is large enough (>1.5 L). This should be done with care to avoid drinking more than 2 liters of fluid with the risk of re-expansion, pulmonary edema, and hypotension. Diuretic therapy without repeated thoracentesis was sufficient for symptomatic relief in the natriuresis-matched group. However, in the group with significant sodium retention, thoracentesis may need to be repeated every 2-3 weeks to relieve symptoms (15).

Liver transplantation is the definitive treatment in severe cases when salt reduction and diuretic therapy have failed. Patients who are unable to undergo a liver transplant, or are waiting for an organ to become available, may experience a *transjugular intrahepatic portosystemic shunt* (TIPS) or *video-assisted thoracoscopy* (VATS) to correct a diaphragmatic defect (16). Selvan et al. (2021) reported indwelling pleural catheter-

based management for hepatic hydrothorax as a bridge to liver transplantation (17).

The patient, in this case, had been injected with Histoacryl-Lipiodol to prevent bleeding from esophageal and gastric varices (GOV-1). Salt restriction and diuretic therapy were also performed. This patient also received repeated thoracocentesis and the chest pigtail catheter for the pleural effusion. The evaluation was based on the amount of pleural fluid drained each day. The fluid production reduced (less than 500 mL) after chest pigtail catheter application and the patient got better. Diuretic therapy was gradually tapered off, and salt reduction was continued on discharge until the patient no longer produced a pleural effusion.

CONCLUSION

A 59-year-old female patient with liver cirrhosis and right pleural effusion due to hepatic hydrothorax has been reported. The patient did not find the cause of the heart and lung infection. The management of hepatic hydrothorax in this patient is comprehensive including treating the underlying disease (liver cirrhosis) and reducing the pleural effusion treated with salt reduction, diuretics, repeated thoracocentesis, and lastly chest pigtail catheter.

Acknowledgments

Thank you to the patient who has given consent to this report.

Conflict of Interest

All the authors declare no conflict of interest.

REFERENCES

1. Garbuzenko DV, Arefyev NO. Hepatic hydrothorax: An update and review of the literature. World J Hepatol. 2017;9(31):1197-1204.
2. Cardenas A, Kelleher T, Chopra S. Review article: Hepatic hydrothorax. Aliment Pharmacol Ther. 2004;20(3):271-279.
3. Yoon JH, Kim HJ, Jun CH, Cho SB, Jung Y, Choi SK. Various treatment modalities in hepatic hydrothorax: What is safe and effective? Yonsei Med J. 2019;60(10):944-951.
4. Kumar S, Burney IA, Zahid KF, Souza PC, Belushi MA, Mufti TD, et al. Colorectal cancer patient characteristics, treatment and survival in Oman - A single center study. Asian Pac J Cancer Prev. 2015;16(12):4853-4858.
5. Dooley J, Lok A, Garcia-Tsao G, Pinzani M. Sherlock's Diseases of The Liver and Biliary System. John Wiley & Sons. 2018:832.
6. Maitra T, Das SP, Barman P, Deka J. Spectrum of Complications of Chronic Liver Disease in Gauhati Medical College, and Hospital: A Hospital Based Study. J Clinical and Diagnostic Res. 2019;13(6):OC07-OC12.
7. Terrault NA, Bzowej NH, Chang KM, Hwang JP, Jonas MM, MH Murad. AASLD guidelines for treatment of chronic hepatitis B. Hepatology. 2016;63(1):261-283.
8. Sarin SK, Kumar M, Lau GK, Abbas Z, Chan HLY, Chen CJ, et al. Asian-Pacific clinical practice guidelines on the management of hepatitis B: A 2015 update. Hepatol Int. 2016;10:1-98.
9. Bernardi M, Angeli P, Claria J, Moreau R, Gines P, Jalan R, et al. Albumin in decompensated cirrhosis: new concepts and perspectives. Gut. 2020;69:1127-1138.
10. Nusrat S, Khan MS, Fazili J, Madhoun MF. Cirrhosis and its complications: Evidence-based treatment. World J Gastroenterol. 2014;20(18):5442-5460.
11. Koh C, Heller T. Approach to the diagnosis of portal hypertension. Clin Liver Dis (Hoboken). 2012;1(5):133-135.
12. Mercer RM, Corcoran JP, Porcel JM, Rahman NM, Psallidas I. Interpreting pleural fluid results. Clin Med (Lond). 2019;19(3):213-217.
13. Krok KL. Hepatic Hydrothorax: Current Concepts. Clin Liver Dis (Hoboken). 2014;4(2):35-37.
14. Ellison DH. Clinical pharmacology in diuretic use. Clin J Am Soc Nephrol. 2019;14(8):1248-1257.
15. Lv Y, Han D, Fan D. Hepatic hydrothorax. Ann Hepatol. 2018;17(1):33-46.
16. Ma B, Ma B, Shang T, Huang J, Tu Z, Wang Y, Han Y, et al. Analysis of clinical features and prognostic factors in patients with hepatic hydrothorax: A single-center study from China. BMC Gastroenterol. 2022;22:1-10.
17. Selvan M, Collins H, Griffiths W, Gelson W, Herre J. Case Report: Indwelling Pleural Catheter Based Management of Refractory Hepatic Hydrothorax as a Bridge to Liver Transplantation. Front Med. 2021;8:1-6.