

CASE REPORT

Symptomatic hepatic hydrothorax successfully treated with transjugular intrahepatic portosystemic shunt (TIPS)–role of titration of portosystemic gradient reduction to avoid post-TIPS encephalopathy

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A 64-year old Indian female with Child's B liver cirrhosis secondary to nonalcoholic steatohepatitis (NASH) presented to our hospital with symptoms of increasing breathlessness over 5 days. Clinical examination revealed tachypnea and decreased air entry over the right chest wall. Chest X-ray (CXR) showed a massive right pleural effusion with “white-out” of the right hemithorax (Fig. 1). Therapeutic thoracentesis drained 1.4 L of clear straw colored fluid. Biochemical analysis revealed a transudative effusion (pleural fluid LDH 64 U/L, serum LDH 564 U/L, pleural fluid total protein <10 g/L, serum total protein 66 g/L). Microbiological and cytological analyses were unyielding. Her albumin was 26 g/L, bilirubin 12 μ mol/L, and prothrombin time 11.9 sec. She was negative for viral hepatitis, autoimmune hepatitis, Wilson's disease and did not consume alcohol. CT abdomen revealed liver cirrhosis, splenomegaly, and ascites. Gastroscopy revealed nonbleeding small esophageal varices, fundal varices, and portal gastropathy. A clinical diagnosis of right hepatic hydrothorax (HH) was made and she was treated with spironolactone 100 mg om, intravenous furosemide 40 mg bd and was maintained on a low salt

Key Clinical Message

We describe a challenging case of hepatic hydrothorax secondary to nonalcoholic steatohepatitis cirrhosis. Our management involved successfully treating the hydrothorax with a transjugular intrahepatic porto-systemic shunt but having to manage the subsequent complication of hepatic encephalopathy. We conclude with a review of the available literature.

Keywords

Hepatic encephalopathy, hepatic hydrothorax, liver cirrhosis, pleural effusion, TIPS.

diet of less than 88 mmol/day. Repeat CXR showed reduction in the right pleural effusion with resolution of breathlessness and she was discharged 3 days later.

Two days after discharge, her breathlessness recurred. CXR showed re-accumulation of the right pleural effusion, requiring a second thoracentesis which drained 1.6 L of clear transudative fluid. She could not tolerate prolonged increases in her diuretics (spironolactone 100 mg om and furosemide 40 mg om) due to worsening renal function that normalized on withdrawal of said diuretics. Despite close follow up at 1–2 weekly intervals and serial CXRs, she was readmitted a further three times over the next 2 months for respiratory compromise due to re-accumulation of the right pleural effusion. None of these admissions were accompanied by any significant accumulation of ascites.

CT thorax and pleural biopsy were performed to exclude any underlying lung or pleural pathology. Trans-thoracic echocardiography demonstrated normal cardiac function. A peritoneo-pleural scintigraphy study was attempted but failed to show significant accumulation of radiotracer in the thorax. This study was, however, per-

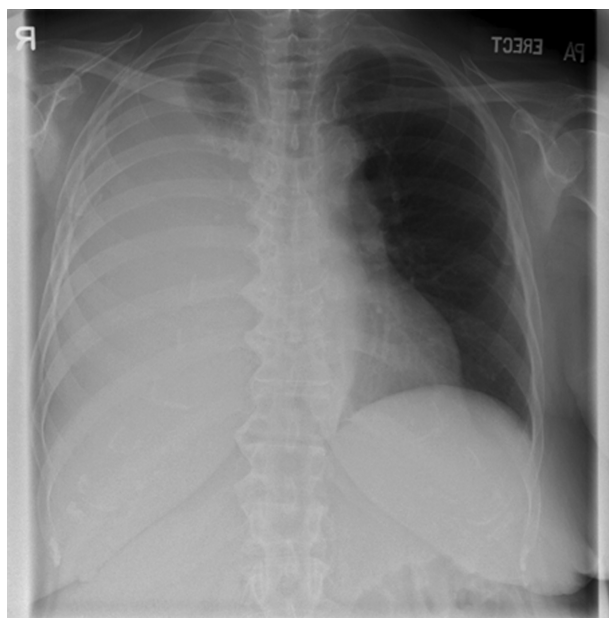


Figure 1. Initial CXR demonstrating a large right hydrothorax.

formed when the right pleural effusion was maximal. This is likely to have resulted in a false negative test due to a reduced gradient of ascitic fluid flow across the diaphragm. Hepatic venous pressure gradient (HVPG) measurement was 19 mmHg, confirming the presence of significant sinusoidal portal hypertension.

In view of the recurrent HH despite adequate salt restriction and intolerance of diuretics, the decision was made to insert a transjugular intrahepatic portosystemic shunt (TIPS) for treatment of her symptomatic HH. She had no prior episodes of hepatic encephalopathy and was Child's B (9 points) with a Model for Endstage Liver Disease (MELD) score of 13. Her bilirubin level was 1.7 mg/dL (29 μ mol/L) with a serum sodium of 129 mmol/L and a serum creatinine of 1.4 mg/dL (124 μ mol/L). TIPS was performed from the right hepatic vein to the portal vein with an initial post-TIPS portosystemic gradient of 6 mmHg (Fig. 2).

Forty-eight hours after TIPS insertion, the patient developed grade 3 hepatic encephalopathy. Plasma ammonia had increased from 50 μ mol/L pre-TIPS to 147 μ mol/L post-TIPS. She responded to fleet enema and lactulose but had two further episodes of encephalopathy within 1 month. The TIPS was thus revised using a 10 \times 58 mm atrium V12 stent placed across the previous stents. The new stent was sequentially inflated to leave a residual waist in the centre (Fig. 3). The resultant post procedure HVPG was 14 mmHg. She rapidly recovered from the encephalopathy with normalization of plasma ammonia but the HH re-accumulated and her breathlessness recurred within 2 weeks.



Figure 2. TIPS procedure—The three stents can be seen bridging the hepatic vein to the right portal venous system.



Figure 3. The V12 stent can be seen within the proximal portion of the TIPS with the residual waist (at the level of the arrows) to moderate the level of HVPG reduction.

A further TIPS revision was carried out by balloon dilatation of the V12 stent to reduce the HVPG from 14 mmHg to 9 mmHg. At this level of portosystemic gradient, the patient's HH and ascites resolved completely, allowing discontinuation of diuretics. The TIPS revision significantly reduced the frequency and severity of

encephalopathy and she has remained encephalopathy-free for the past 12 months. She is currently well and is awaiting listing for liver transplantation.

Discussion

HH is an uncommon but well recognized complication of liver cirrhosis [1]. This condition presents as a pleural effusion in a cirrhotic patient without any significant underlying cardiac or pulmonary disease. The incidence is 5–12% in patients with cirrhosis. Presentation is usually right sided (85%) but can be left sided (13%) or bilateral (2%) [2].

The underlying pathophysiology is believed to involve the presence of microscopic defects within the diaphragm. Small peritoneal herniations may occur through these diaphragmatic defects leading to the formation of pleuro-peritoneal blebs. Subsequent rupture of these blebs allows passage of ascitic fluid into the pleural space. Ruptured blebs may also act as one-way valves to prevent the passage of ascitic fluid back into the peritoneum. Furthermore, the negative intrathoracic pressure relative to the peritoneal space perpetuates the sequestration of ascitic fluid preferentially into the thoracic cavity [3]. Patients with a HH usually have clinically significant ascites but HH can occur in patients without clinically evident ascites [4].

The management of HH is based on treating the underlying ascites, that is, diuretics, salt and fluid restriction and large volume abdominal paracentesis with intravenous albumin. Chest tube insertion should be avoided as it may result in prolonged drainage due to the large amount of ascites produced daily resulting in increased risk of empyema and massive fluid and protein loss. Thoracocentesis is recommended if urgent drainage of the hydrothorax is required [5].

For patients whom the HH proves recalcitrant to medical treatment, alternative measures are required. Pleurodesis has been reported as a potential treatment option for HH. However, despite the wide availability and relative ease of chemical pleurodesis, there is a dearth of literature supporting this treatment. Evidence is limited to observational case series or case reports [6, 7]. Significant complications included acute renal failure, pneumonia, pneumothorax, and encephalopathy with a reported mortality of 27.2% at 30 days [8]. Video-assisted thorascopic surgery (VATS) and repair of diaphragmatic defects with or without chemical pleurodesis has been purported as an alternative to medical or TIPS management of recalcitrant HH. The data in this area is limited to retrospective analyses and case series [9, 10]. Overall reported success ranges from 63–85% but with high associated morbidity (e.g., empyema, pleuro-cutaneous

fistulae, pain) and mortality approaching that of 40% at 40 days.

TIPS has been used to treat refractory ascites and HH. Meta-analyses of randomized controlled trials (RCTs) evaluating the efficacy of TIPS against repeated large volume paracentesis in patients with refractory ascites demonstrate a reduction in mortality favoring TIPS [11, 12]. However, there have been no RCTs investigating the use of TIPS specifically for the treatment of HH. Retrospective evidence suggests that TIPS is efficacious for treatment of HH [13, 14] with a complete and partial response rate of 65% and 15% rate, respectively, and a 1 year survival ranging between 48 and 64% [15].

Our patient was deemed a suitable candidate for TIPS as she had diuretic refractory ascites and recurrent symptomatic hydrothorax despite diuretics and multiple paracentesis. She had a bilirubin level of less than 3 mg/dL, a relatively low MELD score and no prior history of hepatic encephalopathy. Although the TIPS effectively resolved her hydrothorax, our patient developed significant hepatic encephalopathy which occurs in up to 30–50% of patients post-TIPS. Crucial to avoiding this complication is patient selection and moderation in the degree of portosystemic shunting across the TIPS [15].

Factors associated with encephalopathy post-TIPS are advanced age, renal impairment, and a history of encephalopathy prior to TIPS insertion [15]. Pre-TIPS bilirubin predicts a 40% rise in mortality for each rise of 1 mg/dL (17 μ mol/L) above 3 mg/dL (51 μ mol/L) [16]. Bilirubin levels of 3 mg/dL (51 μ mol/L) and 5 mg/dL (86 μ mol/L) are relative and absolute contraindications for TIPS, respectively [17].

A reduction in the HVPG to below 12 mmHg is not always necessary and may precipitate post-TIPS encephalopathy. Thalheimer *et al* have demonstrated that a modest reduction in portal pressure gradient by 25–40% may result in satisfactory outcomes while reducing the incidence of HE in patients with refractory ascites [18]. Various studies assessing the technical quality of TIPS have demonstrated a high success rate in excess of 90% for reductions in HVPG of 50–60%.

Repeat intervention to manipulate portal pressures following initial TIPS placement is uncommon but has been reported in a retrospective case series of patients with refractory ascites and bleeding esophageal varices. The use of hourglass shaped balloon expandable stent grafts was demonstrated to be effective not only in reducing portal blood flow but also in allowing for future options of portal pressure manipulation [19].

In our patient, the initial TIPS placement achieved a 68% reduction in the baseline HVPG with a reduction in the portal pressure from 19 mmHg to 6 mmHg. While this level of portosystemic decompression successfully treated the HH and ascites, it resulted in significant encephalopathy.

Initial revision of the TIPS using the technique of an hourglass shaped balloon expandable stent graft increased the portal pressure to a level of 14 mmHg; expectedly this improved the encephalopathy but resulted in re-accumulation of the HH. Further revision to the final HVPG target of 9 mmHg (53% reduction in baseline HVPG) provided the appropriate balance to prevent recurrence of HH and avoid hepatic encephalopathy.

Our experience with TIPS for the management of cirrhosis-related HH in this patient affirms that excessive reduction in the portal pressure gradient is unnecessary and carries a high risk of post-TIPS encephalopathy. A reduction in approximately 40–50% of the initial HVPG should provide the optimal outcome of resolution of hydrothorax and ascites while avoiding significant hepatic encephalopathy. Studies on TIPS for treatment of variceal bleeding have clearly delineated a target reduction in the portosystemic gradient to <12 mmHg to prevent risk of rebleeding [20]. However, the target reduction in HVPG for HH has not been determined. The results of this case report provides a guide to the target reduction in portosystemic gradient after insertion of a TIPS for treatment of HH taking into account the desired balance between resolution of hydrothorax and occurrence of hepatic encephalopathy.

Conflict of Interest

All the authors listed above have no declarations to make concerning conflicts of interest; financial or otherwise. No external sources of funding were utilized for the production of this manuscript. The patient concerned has given her written consent for the use of her anonymized data in producing this case report and its publication. A copy of the written consent can be supplied if required.

References

1. Strauss, R. M., and T. D. Boyer. 1997. Hepatic hydrothorax. *Semin. Liver Dis.* 17:227–232.
2. Roussos, A., N. Philippou, G. J. Mantzaris, and K. I. Gourgouliannis. 2007. Hepatic hydrothorax: pathophysiology diagnosis and management. *J. Gastroenterol. Hep.* 22:1388–1393.
3. Cárdenas, A., and V. Arroyo. 2007. Management of ascites and hepatic hydrothorax. *Best Pract. Res. Clin. Gastroenterol.* 21:55–75.
4. Serrat, J., J. J. Roza, and T. Planella. 2004. Hepatic hydrothorax in the absence of ascites: respiratory failure in a cirrhotic patient. *Anesth. Analg.* 99:1803–1804.
5. Orman, E. S., and A. S. F. Lok. 2009. Outcomes of patients with chest tube insertion for hepatic hydrothorax. *Hepatol. Int.* 3:582–586.
6. Milanez de Campos, J. R., L. O. Filho, E. de Campos Werebe, H. Sette Jr, A. Fernandez, L. T. Filomeno, et al. 2000. Thoracoscopy and talc poudrage in the management of hepatic hydrothorax. *Chest* 118:13–17.
7. Helmy, N., Y. Akl, S. Kaddah, H. A. Hafiz, and H. E. Makhzangy. 2010. A case series: Egyptian experience in using chemical pleurodesis as an alternative management in refractory hepatic hydrothorax. *Arch. Med. Sci.* 6:336–342.
8. Lee, W. J., H. J. Kim, J. H. Park, D. I. Park, Y. K. Cho, C. I. Sohn, et al. 2011. Chemical pleurodesis for the management of refractory hepatic hydrothorax in patients with decompensated liver cirrhosis. *Korean J. Hepatol.* 17:292–298.
9. Cerfolio, R. J., and A. S. Bryant. 2006. Efficacy of video-assisted thoracoscopic surgery with talc pleurodesis for porous diaphragm syndrome in patients with refractory hepatic hydrothorax. *Ann. Thorac. Surg.* 82:457–459.
10. Ferrante, D., M. R. Arguedas, R. J. Cerfolio, B. G. Collins, and D. J. van Leeuwen. 2002. VATS with talc pleurodesis in the management of symptomatic hepatic hydrothorax. *Am. J. Gastroenterol.* 97:3172–3175.
11. D'Amico, G., A. Luca, A. Morabito, R. Miraglia, and M. D'Amico. 2005. Uncovered transjugular intrahepatic portosystemic shunt for refractory ascites: a meta-analysis. *Gastroenterology* 129:1282–1293.
12. Salerno, F., C. Camma, M. Enea, M. Rossle, and F. Wong. 2007. Transjugular intrahepatic portosystemic shunt for refractory ascites - A meta-analysis of individual patient data. *Gastroenterology* 133:825–834.
13. Dhanasekaran, R., J. K. West, P. C. Gonzales, R. Subramanian, S. Parekh, J. R. Spivey, et al. 2010. Transjugular intrahepatic portosystemic shunt for symptomatic refractory hepatic hydrothorax in patients with cirrhosis. *Am. J. Gastroenterol.* 105:635–641.
14. Wilputte, J. Y., P. Goffette, F. Zech, A. Godoy-Gepert, and A. Geubel. 2007. The outcome after transjugular intrahepatic portosystemic shunt (TIPS) for hepatic hydrothorax is closely related to liver dysfunction: a long-term study in 28 patients. *Acta Gastroenterol. Belg.* 70:6–10.
15. Rössle, M., and A. L. Gerbes. 2010. TIPS for the treatment of refractory ascites, hepatorenal syndrome and hepatic hydrothorax: a critical update. *Gut* 59:988–1000.
16. Rajan, D. K., Z. J. Haskal, and T. W. Clark. 2002. Serum bilirubin and early mortality after transjugular intrahepatic portosystemic shunts: results of a multivariate analysis. *J. Vasc. Interv. Radiol.* 13:155–161.
17. Gerbes, A. L., and V. Gulberg. 2005. Benefit of TIPS for patients with refractory ascites: serum bilirubin may make the difference. *Hepatology* 41:217.
18. Thalheimer, U., G. Leandro, D. N. Samonakis, C. K. Triantos, M. Senzolo, K. Fung, et al. 2009. TIPS for

- refractory ascites: a single centre experience. *J. Gastroenterol.* 44:1089–1095.
19. Fanelli, F., F. M. Salvatori, P. Rabuffi, E. Boatta, O. Riggio, P. Lucatelli, et al. 2009. Management of refractory hepatic encephalopathy after insertion of tips: long-term results of shunt reduction with hourglass-shaped balloon-expandable stent-graft. *AJR* 193:1696–1702.
 20. Garcia-Tsao, G., R. J. Groszmann, R. L. Fisher, H. O. Conn, C. E. Atterbury, and M. Glickman. 1985. Portal pressure, presence of gastroesophageal varices and variceal bleeding. *Hepatology* 5:419–424.