Hepatic hydrothorax – How would you manage it?

Hassan Al-sharif MD FRCP, Sat Sharma MD FRCP

A 53-year-old woman with a history of chronic alcoholism presented with symptomatic large right-sided pleural effusion with no evidence of ascites. After a diagnosis of hepatic hydrothorax was established, her symptoms improved with therapeutic thoracentesis. She required multiple emergency department visits for recurrent right-sided pleural effusion treated with urgent therapeutic taps. Hepatic hydrothorax is a relatively infrequent but potentially serious complication of liver cirrhosis. The management of hepatic hydrothorax, usually required in symptomatic patients, is controversial and contradictory. The case summary is followed by a question regarding available management options. The pathophysiology of hepatic hydrothorax, the role of various therapeutic options and the current favoured therapy for this not so uncommon disorder are reviewed.

Key Words: Hepatic hydrothorax; Liver failure; Transudative pleural effusions

Hydrothorax hépatique : Quelle serait votre approche?

Une femme de 53 ans ayant des antécédents d'alcoolisme chronique s’est présentée avec un épanchement pleural droit volumineux symptomatique, sans signe d’ascite. Après un diagnostic d’hydrothorax hépatique, ses symptômes se sont améliorés grâce à une thoracocentèse thérapeutique. Par la suite, elle a dû consulter plusieurs fois aux urgences pour épanchement pleural droit récurrent, traité au moyen de drains thérapeutiques ponctuels. L’hydrothorax hépatique est une complication relativement peu courante mais potentiellement grave de la cirrhose hépatique. Habituellement inévitable chez les patients symptomatiques, le traitement de l’hydrothorax hépatique ne fait toutefois pas l’unanimité. Le présent rapport de cas est suivi d’une interrogation quant aux options thérapeutiques offertes. On y passe en outre en revue la pathophysiologie de l’hydrothorax hépatique, le rôle des diverses options thérapeutiques et la conduite actuellement privilégiée en présence de cette complication qui n’est pas exceptionnelle.

HOSPITAL COURSE

Diagnostic and therapeutic thoracenteses were performed. Approximately 2 L of straw-coloured fluid was removed with symptomatic relief, and a chest radiograph showed nearly complete resolution of the pleural effusion. Three days later, the patient developed recurrent dyspnea and recurrence of the right-sided pleural effusion. A diagnosis of hepatic hydrothorax was considered after repeat therapeutic thoracenteses. She was readmitted five days later with progressive dyspnea requiring an urgent tap. A repeat ultrasound of the abdomen showed findings consistent with cirrhosis of the liver but no evidence of ascites.

Laboratory tests showed the following, including elevated liver enzymes caused by hepatic synthetic dysfunction: aspartate aminotransferase 166 U/L (normal less than 30 U/L), gamma-glutamyltransferase 719 U/L (normal 5 U/L to 38 U/L), alkaline phosphatase 204 U/L (normal 30 U/L to 120 U/L), international normalized ratio 1.3 (normal 0.9 to 1.1), albumin 26 g/L (normal 33 g/L to 45 g/L), total bilirubin 155 µmol/L (normal 2 µmol/L to 20 µmol/L), direct bilirubin 155 µmol/L (normal less than 7 µmol/L) and lactate dehydrogenase 301 U/L (normal 120 U/L to 320 U/L), as well as a normal complete blood count and negative serological markers for autoimmune diseases and vasculitis. Pleural fluid analysis revealed a transudate; pleural fluid microbiology and cytology were negative. A chest radiograph showed massive right-sided pleural effusion (Figure 1). An upper abdominal ultrasound revealed a large right-sided pleural effusion, hepatomegaly, cirrhosis, portal venous hypertension and an absence of ascites. Computed tomography of the chest and abdomen showed a macronodular liver (consistent with alcoholic cirrhosis) and a large right-sided pleural effusion; no ascites was observed. An echocardiogram showed normal left and right ventricular function without pulmonary arterial hypertension.
QUESTION
Which of the following treatment options would you employ in the management of this patient’s recurrent, symptomatic hepatic hydrothorax?

a) Prolonged tube thoracostomy;
b) Talc pleurodesis;
c) Repeated thoracenteses;
d) Diuretic therapy;
e) Transjugular intrahepatic portosystemic shunt (TIPS).

The correct answers are listed after the discussion.

DISCUSSION
The patient was treated with a salt-restricted diet, a diuretic (40 mg furosemide four times daily) and spironolactone (100 mg four times daily). The patient was then discharged and, during outpatient follow-up, she required two further therapeutic pleural taps over the next two weeks. Thereafter, she was free of pleural effusion and related symptoms for a total follow-up period of 24 months. She continues diuretic therapy and has been successful in maintaining abstinence from alcohol.

Although ascites is generally present clinically, massive symptomatic hydrothorax can develop in the absence of clinically evident ascites in liver disease. Hepatic hydrothorax is defined as a significant pleural effusion (usually greater than 500 mL) in a patient with cirrhosis of the liver but no evidence of primary cardiac or pulmonary disease (1,2). Its development is not associated with any particular etiology of cirrhosis, although many patients have alcoholic cirrhosis (3). The incidence of hepatic hydrothorax is estimated to be approximately 5% in all patients with liver cirrhosis (4) and 12% in patients with decompensated cirrhosis (5).

Pathophysiology of hepatic hydrothorax
The proposed mechanisms for the development of hepatic hydrothorax include hypoalbuminemia and the transdiaphragmatic shift of ascitic fluid through a direct communication between the peritoneal cavity and pleural space. The transfer of large volumes of fluid from the abdomen to the pleural space through defects in the diaphragm appears to be the most important mechanism (3,6). The defects are thought to result from thinning and separation of collagenous fibres in the tendinous region of the diaphragm. When intra-abdominal pressure rises as a result of ascites, coughing or straining, gaps develop between the muscle fibres, leading to small herniations of peritoneum into the pleural space. These herniations, called pleuroperitoneal blebs, may rupture or leak ascitic fluid (7). The diaphragmatic defects are small, measuring approximately 1 mm in diameter. Once the diaphragmatic communications begin to leak fluid, the combination of subatmospheric intrathoracic pressure and positive intra-abdominal pressure produces a ‘ball-valve’ mechanism of unidirectional flow of ascitic fluid into the pleural space (3). Ascitic fluid may also leak directly from the liver into the pleural space; this occurs when the bare areas of the liver are in apposition to the diaphragmatic defects. Once accumulation of the fluid of peritoneal origin into the pleural cavity exceeds the absorptive capacity of the pleural space, hepatic hydrothorax develops (8).

As in our case, there are two possible explanations for the occurrence of hepatic hydrothorax in the absence of ascites. If the diaphragmatic defect is large (as a result of the pressure gradient between the thorax and abdomen), the ascitic fluid is drawn into the pleural space and is not able to accumulate in the peritoneal cavity. It is also possible that after formation of the pleural effusion, the remaining fluid in the peritoneum is efficiently drained by the dilated abdominal lymphatics (7,8).

Diagnosis
A detailed medical history, physical examination, pleural fluid analysis and radiological imaging are the first steps in the diagnosis of hepatic hydrothorax. A transudative pleural effusion with findings of liver cirrhosis should raise suspicion of hepatic hydrothorax. Intra-abdominal injection of radiolabelled technetium provides a simple and safe method to confirm the transdiaphragmatic passage of ascites from the abdomen into the pleural space. Another method of diagnosis is thoracoscopic visualization of the diaphragmatic defects (8,9). These investigations are generally not necessary because recurrent transudative pleural effusion in the presence of liver failure without another cause is indicative of hepatic hydrothorax.

Management
The treatment of hepatic hydrothorax encompasses a reduction in the rate of ascites formation and symptomatic treatment of pleural effusion. Aggressive medical treatment consisting of salt and water restriction, as well as diuretic therapy, will diminish the production of ascites and, hence, reduce the pleural effusion. A therapeutic thoracentesis alone is generally not sufficient because pleural effusion almost always recurs (7,10). Cessation of alcohol intake is a requisite; the liver has a tremendous capacity to regenerate unless advanced cirrhosis has developed.

Figure 1) A posterolateral chest radiograph showing a massive right-sided pleural effusion
Al-sharif and Sharma

Prolonged drainage through a chest tube is not recommended because of the many adverse effects, including electrolyte and protein depletion, renal failure, impaired immunological function and iatrogenic infection of the pleural space. Cases of increased mortality secondary to prolonged chest tube drainage have been reported (11,12).

Although deemed an effective therapy for malignant pleural effusions, pleurodesis is not recommended in the treatment of hepatic hydrothorax. Success rates of pleurodesis are extremely low because the rapid accumulation of pleural fluid prevents sufficient apposition of the pleural surfaces (7). In two series, surgical repair of the diaphragmatic defects with biological glue was sufficient apposition of the pleural surfaces (7). In two series, surgical repair of the diaphragmatic defects with biological glue was sufficient (7). In two series, surgical repair of the diaphragmatic defects with biological glue was sufficient (7). In two series, surgical repair of the diaphragmatic defects with biological glue was sufficient (7). In two series, surgical repair of the diaphragmatic defects with biological glue was sufficient (7).

Drainage through the chest or sutures, if feasible, with subsequent talc poudrage was successful in 40% and 75% (7,8). Success rates were higher if the diaphragmatic defect could be visualized but lower if the only intervention was talc insufflation. Drainage through the chest tube needed to be maintained after thoracoscopic surgical repair for an average of nearly two weeks.

Currently, chest tube drainage in conjunction with continuous positive airways pressure or octreotide therapy must be considered experimental because only a few case reports exist in the literature. A widely cited abstract (13) reported successful pleurodesis with tetracycline and continuous positive airways pressure in six patients with hepatic hydrothorax; however, one of the patients died of infection of the pleural space.

TIPS has been effective in relieving symptomatic hydrothorax in 60% to 80% of patients in four case series that included a total of 81 patients (11). More recently, in another case series (14), 14 of 24 patients with symptomatic hepatic hydrothorax had complete relief of symptoms and required no additional thoracocentesis after shunt placement. An additional five patients required less frequent thoracocentesis following the TIPS procedure (14). Of the 12 patients with more than two months of follow-up, the serum albumin concentration increased in eight (mean 12 g/L) and the Childs-Pugh score improved in seven patients; however, hepatic encephalopathy developed in nine patients, and liver function deteriorated in five patients who subsequently died within six weeks of shunt placement (14). In another study of 26 patients with refractory hepatic hydrothorax (15), TIPS controlled pleural effusions in more than 90% of patients, resulting in less frequent therapeutic thoracocenteses and lower doses of diuretics. However, eight patients went on to develop hepatic encephalopathy, and six experienced shunt dysfunction (15). The overall prognosis in that study was also poor: 50% of the patients died or underwent orthotopic liver transplantation within seven months. Indeed, TIPS is not without complications; progression to hepatic encephalopathy and acute worsening of pulmonary hypertension may be encountered (16). However, if medical treatment with diuretics fails, TIPS appears to be the procedure of choice for symptomatic hepatic hydrothorax (8). This procedure should ideally be performed in a centre where liver transplantation is available. Because hepatic hydrothorax usually indicates advanced cirrhosis of the liver, liver transplantation should be a consideration in patients with progressive liver failure.

Hepatic hydrothorax is not uncommon. Internists and pulmonologists are expected to encounter this problem sporadically. This is a frustrating disorder because recurrence is the rule rather than the exception. Repeated thoracocenteses and diuretic therapy (as opposed to tube thoracocentosis and pleurodesis) is the recommended initial therapy. Failure of this therapy should lead to the consideration of TIPS and liver transplantation. The development of hepatic hydrothorax is a marker of poor prognosis; treatment is directed toward symptom control, and recovery of liver function will determine outcome.

The answers to the question on page 441 are c, d and e. Please see discussion.

REFERENCES