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Review Article

Treatment of Recurrent Non-Malignant Pleural Effusions

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Introduction

Pleural effusion remains a major cause of respiratory distress worldwide. It is estimated that around 1.5 million people develop pleural effusion annually in the United States [1]. Pleural effusion can accumulate from pulmonary, pleural and/or extrapulmonary diseases. It can be classified as either exudative or transudative effusion by direct examination of the pleural fluid. A recent systematic review showed that Light's criteria, pleural fluid cholesterol and LDH levels, and the pleural fluid cholesterol-to-serum ratio are the most accurate diagnostic tests to differentiate exudative from transudative pleural effusion [2]. Excessive accumulation of pleural fluid develops when there is an increased pleural fluid formation and/or decreased fluid absorption [3]. Benign pleural effusion is much more common than malignant effusion [3]. The most common causes of benign transudative pleural effusion are congestive heart failure (CHF) and hepatic hydrothorax whereas parapneumonic/empyema remains the most common cause of benign exudative pleural effusion. This article discusses the management of recurrent non-malignant pleural effusion (NMPE) of CHF and hepatic hydrothorax.

Management of Recurrent NMPE in CHF

Pleural effusion in CHF is formed due to an increase in hydrostatic pressure resulting in the movement of fluid into the interstitial pulmonary space and subsequently to the pleural space. Accumulation of effusion will result when fluid reaching the pleural cavity exceeds the capacity of lymphatic drainage. Most pleural effusions are bilateral usually larger on the right, but unilateral pleural effusion (on the right more than the left) can also occur [4]. A proportion of fluid sampled from pleural effusion in patients with CHF might be classified as an exudative according to Light's criteria if patients were on diuretics. A protein gradient between serum and pleural fluid of greater than 3.1g/dl can identify such patients, who underwent diuretic therapy, where pleural fluid analysis is exudative and clinicians highly suspect that the effusion is due to CHF [3].

Initially, treatment is aimed at optimizing CHF management with dietary sodium restriction, diuretic therapy, after load reduction and inotropes if needed. Therapeutic thoracentesis can be considered in symptomatic patients awaiting treatment effect. Unfortunately, some patients will have persistent, symptomatic pleural effusion despite optimal medical management.

The treatment of recurrent effusion should be guided by patient's performance status, prognosis and preference. Table 1 summarizes the therapeutic options in patients with recurrent NMPE in CHF.

Repeated therapeutic thoracentesis might be considered in such patients who do not require frequent drainage and are not on systematic anticoagulation therapy. However, patients are at increased risk of procedure complications and require frequent hospital or clinic visits.

Thoracoscopic or chest tube pleurodesis have been considered an alternative option in patients requiring frequent drainage. Unfortunately such an approach has been associated with side effects of pleurodesis itself (pain, fever, talc embolization, empyema, adult respiratory distress syndrome, and respiratory failure) [5] as well as development of contralateral pleural effusion [6]. Several experts have recommended against using pleurodesis in patients with recurrent NMPE in CHF patients [7].

Tunneled pleural catheter (TPC) might also be considered in symptomatic patients with recurrent NMPE requiring frequent drainage. A recent study [8] retrospectively compared TPC to thoracoscopic pleurodesis (TP) in patients with recurrent, symptomatic, NMPE secondary to CHF. Although both interventions achieved similar performance score and adequate palliation, TPC showed a significantly shorter hospital stay as well as reduced readmission rate and operative morbidity. Chalhoub et al. [9] reported a series of 23 patients (13 with CHF) who received a TPC for symptomatic benign pleural effusion. TPC achieved a high rate of successful pleurodesis with a mean time of 113 ± 36 days. Srour et al. [10] recently reported 43 TPC placed in 38 patients with recurrent NMPE due to CHF. There was significant improvement in dyspnea 2 weeks after TPC insertion with successful spontaneous pleurodesis occurring in 29.0% after a median of 66 days. Pneumothorax, mostly ex vacuo, occurred in 11.6% of procedures without requiring any further intervention. Harris and coworker [11] reported that the complication rate of TPC in NMPE was around 11.2% mostly related

Table 1: Management of recurrent pleural effusion due to congestive heart failure.

Repeated therapeutic thoracentesis	-Requires frequent hospital or clinic visits -Risk of procedure complications when patients are on systemic anticoagulation -Not ideal for patients requiring frequent drainage
Thoracoscopic or chest tube pleurodesis	-Increased hospital stay -Increase probability of contralateral pleural effusion -Risk of procedural complications
Indwelling pleural catheter	-Ideal as a palliative treatment -Decrease hospital stay -Complications mainly related to chronic catheter insertion

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to empyema, cellulitis and catheter occlusion in a recent review article.

Management of Recurrent NMPE in Hepatic Hydrothorax

Hepatic hydrothorax is defined as a pleural effusion that occurs in patients with liver cirrhosis without any other causes of effusion.

Fluid is accumulated in the pleural space when negative intrathoracic pressure generated during inspiration causes transdiaphragmatic fluid shift from the peritoneal cavity through small diaphragmatic defects.

It affects about 6% of patients with cirrhosis where majority have ascites and pleural effusion predominantly occurring on the right side [12].

The initial treatment of hepatic hydrothorax is tailored toward management of portal hypertension, liver disease such as dietary sodium restriction and diuretic therapy as well as therapeutic thoracentesis. However, treating recurrent hepatic hydrothorax is challenging. Table 2 summarizes the therapeutic options in patients with recurrent hepatic hydrothorax.

Repeated therapeutic thoracentesis might be attempted for symptomatic relief in patients who do not require frequent drainage and have poor life expectancy and not candidates for other interventions. Albumin infusion post-thoracentesis is not necessary since a small volume (<2 L) will be removed during the procedure. Paracentesis should be done before thoracentesis if ascites is present to improve respiratory mechanics and reduce rapid re-accumulation of pleural effusion. However, frequent pleural drainage may cause increased protein and electrolyte depletion as well as greater infection and bleeding risks in such a frail population with liver cirrhosis and coagulopathy.

Transjugular intrahepatic portosystemic shunt (TIPS) can control hepatic hydrothorax by reducing portal pressure and is considered standard of care therapy as a bridge to liver transplantation or as a definite therapy if the latter is contraindicated [9,13]. Contraindications and complications of TIPS are listed in Table 2.

For patients requiring frequent repeated thoracentesis (drainage in less than 2 weeks), TPC is an alternative option that can decrease hospitals visits and alleviate symptoms. Although evidence to support use of TPC on hepatic hydrothorax is limited to case series or reports [9,13], experts recommend considering it as a palliative treatment or a bridge to TIPS or liver transplantation [14].

Chemical pleurodesis administered through a chest tube or thoracoscope is another option to consider. However, there is a high failure rate since ascitic fluid moves rapidly through the diaphragmatic defects into the pleural space leaving insufficient time for the pleural surfaces to maintain their apposition so that inflammatory process can result in successful pleurodesis [3,14]. Furthermore, combination of thoracoscopic repairmen of diaphragmatic defect with chemical pleurodesis and abdominal drainage have been also attempted [15].

Liver transplantation remains the definitive therapy for patients with refractory hepatic hydrothorax since median survival time is around 9 month and referral to center for transplant evaluation should be expedited [16].

Table 2: Management of recurrent pleural effusion due to hepatic hydrothorax.

Repeated therapeutic thoracentesis	-Reserved for patients who are not a candidate for TIPS, require one procedure in ≥ 2 weeks and have low life expectancy
Transjugular intrahepatic portosystemic shunt	-Definitive treatment -Contraindications (age >70 years, severe liver dysfunction, history of spontaneous hepatic encephalopathy, right-heart failure or congestive heart failure, pulmonary hypertension, complete portal vein thrombosis) -Complications (hepatic encephalopathy and shunt thrombosis)
Indwelling pleural catheter	-Reserved for patients who require frequent thoracentesis -Can be considered as palliative therapy or a bridge to other treatments such as TIPS or liver transplant
Chemical pleurodesis	-High failure rate
Liver transplantation	-Definitive therapy if patients are candidate for transplant

Conclusion

Congestive heart failure and hepatic hydrothorax are the most common causes of recurrent NMPE. Initial treatment should be directed toward the underlying disease. Further interventions for recurrent NMPE should be directed toward patient's symptomatic relief despite maximal medical therapy.

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