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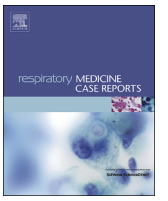

Case Report

Medical thoracoscopy with talc pleurodesis for refractory hepatic hydrothorax: A case series of three successes

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ABSTRACT

Medical thoracoscopy with chemical pleurodesis is a last resort for managing patients who suffer. from recurrent hepatic hydrothorax. However, despite pleurodesis, the rapid fluid build-up can hinder the successful apposition of the pleural surfaces. To improve the chances of success, we investigated the effectiveness of abdominal paracentesis before chemical pleurodesis via medical thoracoscopy to reduce significant fluid shifts from the peritoneal to the pleural cavity.

We present a series of three patients with liver cirrhosis complicated by hepatic hydrothorax who underwent medical thoracoscopy with talc pleurodesis. Before the procedure, we optimised medical treatment, and if needed, we performed large-volume paracentesis to prevent rapid reaccumulation of pleural fluid. All study subjects achieved treatment success, defined as relief of breathlessness and absence of pleural effusion at 12 months.

Complications related to the treatment included hepatic encephalopathy and acute kidney injury, which were managed conservatively. To manage symptomatic and recurrent hepatic hydrothorax, medical thoracoscopy with talc pleurodesis, preceded by the evacuation of ascites, can be considered as a treatment option. This procedure should be considered early for those who do not respond to medical management and are not suitable candidates for TIPS or liver transplantation.

1. Introduction

Hepatic hydrothorax is the presence of more than 500 ml of pleural fluid in a patient with cirrhosis without cardiopulmonary or pleural disease [1–3]. It can complicate the disease course of 5 %–15 % of patients with cirrhosis. These patients are at increased risk of hepatic encephalopathy, ascites, acute kidney injury, and mortality. Hepatic Hydrothorax mainly results from the passage of ascitic fluid into the pleural space via minor diaphragmatic defects [4–9]. These defects are more common in the right hemidiaphragm, partly explaining why hepatic hydrothorax is right-sided in 73–85 % of the patients [10–12]. The management of hepatic hydrothorax needs a team of specialists, including hepatologists, pulmonologists, interventional radiologists, and surgeons.

Refractory hepatic hydrothorax, resistant to conventional treatments, namely sodium restriction and high-dose diuretics, complicates the disease course of 20–25 % of patients [13,14]; such cases are often challenging to treat due to rapid fluid migration from the abdomen to the pleural space [15]. According to the data, patients suffering from Hepatic hydrothorax have a high mortality rate of up to 51 % [16]. Typically, they are treated with serial thoracentesis and transjugular intrahepatic portosystemic shunt (TIPS) placement. In cases where TIPS fails or cannot be performed, other options, such as IPC insertion, pleurodesis, or thoracoscopic surgery to

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repair diaphragmatic defects, may be considered. However, the only definitive therapy for Hepatic hydrothorax is liver transplantation.

Chemical pleurodesis can have varying outcomes in cases of refractory hepatic hydrothorax. The procedure is challenging as keeping the pleural surfaces opposed for a sufficient time makes it difficult to allow the inflammatory process to result in pleural symphysis [15]. As a result, chemical pleurodesis is rarely performed and is usually reserved for cases where no other options are available. None of the published studies have emphasised the importance of ascitic fluid management in the treatment protocol before chemical pleurodesis. This series describes the successful treatment of refractory hepatic hydrothorax in three patients through chemical pleurodesis via medical thoracoscopy, achieving positive outcomes where the existing literature had previously shown poor results. The procedure followed our institutional protocol, which involved using lidocaine with 1:200,000 adrenaline for local anaesthesia and alfentanil and midazolam for procedural sedation. A Richard Wolf rigid thoracoscope was inserted through a 7mm port to visualise the pleural surfaces after the pleural space was aspirated entirely. Pleurodesis was performed using 4-g talc, and a 24-F chest was left in place with a negative 2.5kPa pressure until the drainage dropped to less than 100 ml in 24 hours, and the lung had re-expanded on chest X-ray and ultrasound. Procedure-related morbidity and mortality were defined as the occurrence of any complication and death within a month of the procedure. Successful pleurodesis was defined as the resolution of breathlessness and the absence of pleural effusion on chest X-ray at 12 months post-intervention; this constituted our overall follow-up period.

2. Case presentations case 1

A 71-year-old male with cirrhosis secondary to non-alcoholic steatohepatitis (NASH) was electively admitted for medical thoracoscopy and talc pleurodesis. He had noticed worsening breathlessness for 5–6 weeks.

Previous medical issues included portal hypertension with esophageal varices, portal vein thrombosis, and ascites. Due to the previous history of portal vein thrombosis, TIPS was not considered. He was assessed for liver transplantation in the past but was not considered a suitable candidate due to frailty. He had previously required repeated large-volume paracentesis, with the latest instance occurring a week before admission. He had also required recurrent therapeutic aspiration for a right-sided transudative pleural effusion. A previous attempt at talc pleurodesis via tube thoracostomy was unsuccessful. Other medical issues included type 2 diabetes mellitus and COPD. His medication list included amiloride, carvedilol, spironolactone, and furosemide, which were optimised before admission.

His examination was remarkable for a respiratory rate of 25/min with an oxygen saturation of 93 % on air. He had no evidence of clinically detectable ascites, which was confirmed by an abdominal ultrasound.

Tables 1 and 2 summarise routine blood results, pleural fluid studies, abdominal ultrasound, echocardiogram, and CT chest, abdomen, and pelvis results. The pre-procedure chest X-ray is shown in Fig. 1a.

Thoracoscopy was performed on the admission day, including routine pleural biopsies and talc pleurodesis. The biopsy results showed fibrofatty tissue, and post-procedure blood tests showed leucocytosis and elevated CRP. During his hospital stay, he developed hepatic encephalopathy and acute kidney injury, which were treated conservatively. Unfortunately, the first attempt at pleurodesis was unsuccessful, and a repeat procedure was performed on the tenth day. The chest drain was removed on the fifteenth day.

Table 1
Summary of routine blood results, abdominal ultrasound, echocardiogram, and CT chest, abdomen, and pelvis results.

	Case 1	Case 2	Case 3
CBC			
WBC, 109/L	14.9	6	8.6
Hb, g/L	100	96	102
Plt, 109/L	219	205	308
INR, range	1.2	1.4	1.1
ALT, IU/L [5–31]	25	18	12
AP U/L (30–130)	95	75	450
Total Bilirubin umol/L (0–21)	18	7	18
Albumin, g/dl (35–50)	30	32	26
Creatinine, umol/L (60–120)	95	93	157
Na, mmol/l (133–146)	128	136	136
MELD score	9	9	14
CTP class	B	B	B
Etiology of Liver disease	NASH	HCV-CLD	Alcohol-related
Echocardiogram	Normal Biventricular function	EF 84 %, right atrial dilatation, mild tricuspid, and trivial aortic and pulmonary regurgitation	Limited study due to massive pleural effusion distorting cardiac images. EF > 60 %
CT-Chest, Abdomen, and Pelvis	Liver cirrhosis with portosystemic collaterals. Large right-sided pleural effusion with mild free fluid in the abdomen and pelvis.	Coarse liver echotexture with small volume ascites	Coarse liver echotexture with moderate to large ascites and a large left sided pleural effusion

CTP: Child-Turcotte-Pugh, NASH: Non-alcoholic steatohepatitis, HCV-CLD: Hepatitis C-induced liver disease.

Table 2
Summary of Pleural fluid studies.

Findings	Case 1	Case 2	Case 3
Pleural fluid			
Pleural/serum protein (ratio)	<0.5	<0.5	<0.5
SPAG	>1	>1	>1
Pleural LDH	77	63	84
Cytology	Negative	Negative	Negative
Culture	Negative	Negative	Negative
Pleural drainage			
At thoracoscopy, ml	1300	2600	2400
Talc dose (gram)	4	4	4
Pleural drain dwell time, days	15 days	7 days	3 days

SPAG: Serum to pleural fluid albumin gradient.

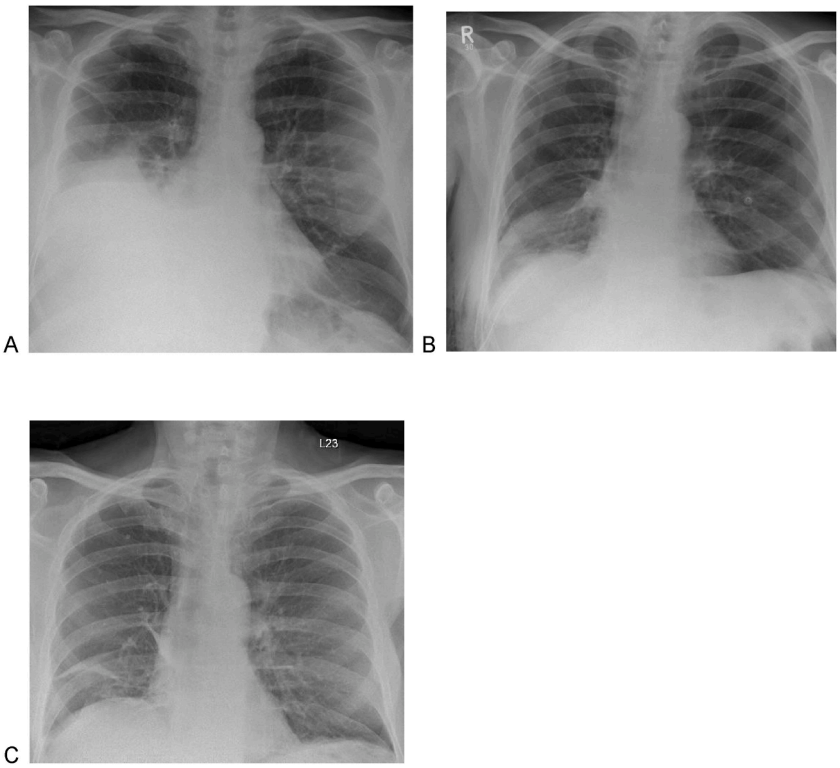

Fig. 1. Chest X-ray- case 1
A) Initial Chest X-ray before treatment; large, right-sided pleural effusion
B) 1-day post pleurodesis
C) 1-year post pleurodesis.

The patient remained asymptomatic and free of hydrothorax for up to one year. The outcomes of the procedure are summarised in Table 3, and the post-procedure and 1-year chest X-rays can be seen in Fig. 1b and c.

3. Case 2

A 78-year-old lady presented to the emergency room with worsening breathlessness. A Chest X-ray on admission (Fig. 2a) showed a large right-sided pleural effusion; hence, she was admitted for further work-up.

She was known to have Hepatitis C-related liver cirrhosis and had achieved seroconversion with anti-viral therapy in the past. Cirrhosis-related complications included portal hypertension with grade I oesophagal varices, mild ascites, and a recurrent right-sided transudative pleural effusion that required therapeutic aspiration on multiple occasions. Due to frailty, she was not eligible for liver transplantation or TIPS, as per the referring team. Other health problems included hypertension, chronic kidney disease, ischemic heart disease, and diabetes mellitus. Her medications included bumetanide, spironolactone, amlodipine, atenolol, aspirin, atorvastatin, metformin, telmisartan, and a proton pump inhibitor.

On examination, she appeared pale with an oxygen saturation of 94 % on air.

Table 3
Treatment outcomes of chemical pleurodesis via medical thoracoscopy in patients with hepatic hydrothorax.

No.	Age /Gender	Pleurodesis attempts	Success (yes/No)	CTP Class	Recurrence (yes/No)	Deceased (yes/No)	Survival (days)	Complications
1	71/M	2	Yes	B	No	Yes	Two years	Fever/leucocytosis/Hepatic encephalopathy/Acute kidney injury
2	78/F	1	Yes	B	No	Yes	Four years	Leucocytosis/Acute Kidney Injury
3	62/M	1	Yes	B	No	No	Still alive	Fever/leucocytosis

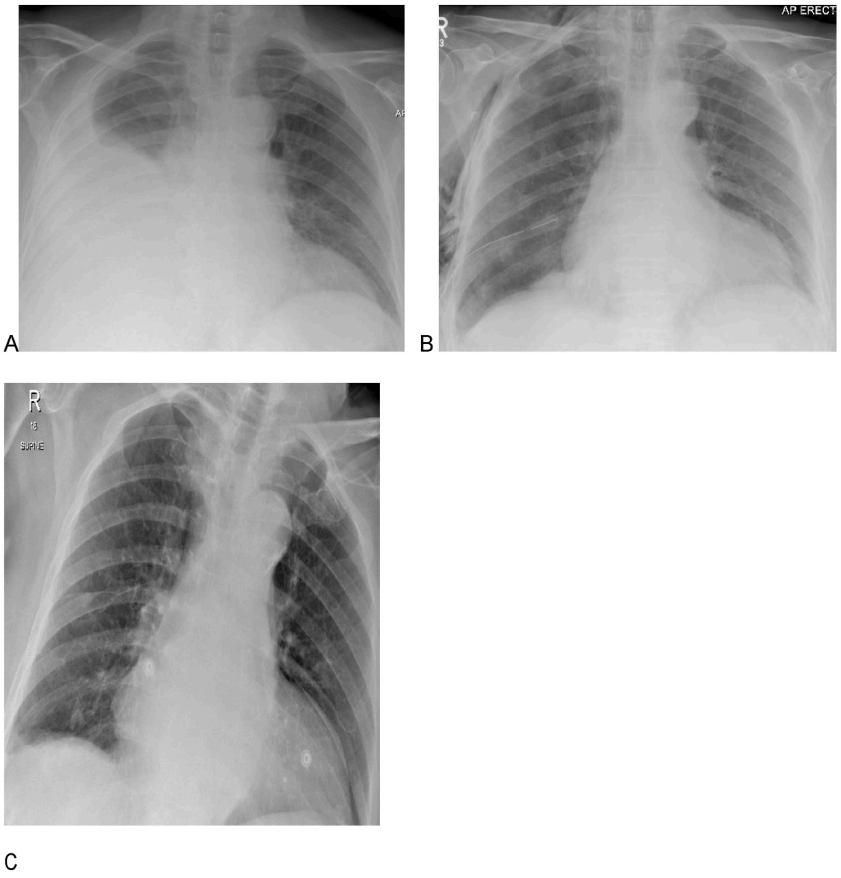

Fig. 2. Chest X-ray- case 2
A) Initial chest X-ray before treatment: massive right-sided pleural effusion
B) 1-day post pleurodesis
C) 1-year post pleurodesis.

Tables 1 and 2 summarise the blood workup results, pleural fluid analysis, abdominal ultrasound, echocardiogram, and CT chest, abdomen, and pelvis findings.

During her hospital stay, she was kept on a low-sodium diet, her diuretic therapy was optimised, and a repeat pre-procedure abdominal ultrasound showed no evidence of ascites.

After being in the hospital for a week, she had a thoracoscopy with talc pleurodesis. However, after the procedure, she suffered from acute kidney injury, which was treated with hydration. Post-procedure complications are listed in Table 3. The chest drain was kept in place for seven days, and she was discharged the day after it was removed. Chest X-rays taken one day and one year after the procedure are shown in Fig. 2b and c.

4. Case 3

A 62-year-old male was admitted with breathlessness and abdominal distension for the last three months. He had also experienced fatigue, loss of appetite and weight loss in the recent months.

His past medical history was significant for hypertension, diabetes, and alcohol abuse.

On examination, he had a respiratory rate of 22/min and oxygen saturation of 94 % on air. Other examination findings included pallor, bilateral leg oedema, and absent breath sounds along the right hemithorax. He had moderate ascites on examination.

A provisional diagnosis of chronic liver disease due to previous alcohol abuse was made after ruling out other causes.

Tables 1 and 2 list the blood work-up, pleural fluid results, abdominal ultrasound, echocardiogram, and CT chest, abdomen, and pelvis reports. The chest X-ray noted complete opacification of the left hemithorax (Fig. 3a).

During his hospital stay, he remained under the care of the gastroenterology team. To achieve adequate diuresis, he was started on a furosemide infusion, which was later replaced by oral spironolactone and furosemide. Large-volume paracentesis was performed three times during his stay, with sequential drainage of 790 ml, 2.5 L, and 9.5 L of ascitic fluid. Our team also aspirated 1.5 and 1.3 L of pleural fluid to ease his breathlessness. The primary team concluded that given his poor performance status and frailty, he would not be suitable for interventions, namely TIPS or liver transplantation.

After being hospitalised for four weeks and experiencing continuous shortness of breath and low oxygen levels, our medical team was consulted to perform a medical thoracoscopy with talc pleurodesis. Before the procedure, an abdominal ultrasound was conducted to ensure that there was no significant accumulation of fluid in the abdomen. The chest drain was removed three days after the procedure, and the patient was discharged shortly after. Post-procedure events are listed in Table 3. The chest X-ray taken one day and one year later showed successful resolution of the hepatic hydrothorax (as seen in Fig. 3 b and c).

5. Discussion

In 2014, we introduced medical thoracoscopy in our institution and have performed 419 thoracoscopies to date. Out of these, three were conducted on patients with refractory hepatic hydrothorax. Pleurodesis is often challenging in such cases due to fluid migration from the abdomen into the pleural space. To improve the success rate of pleurodesis, we examined the impact of draining ascitic fluid before conducting medical thoracoscopy with chemical pleurodesis. Our meticulous attention to controlling ascitic fluid

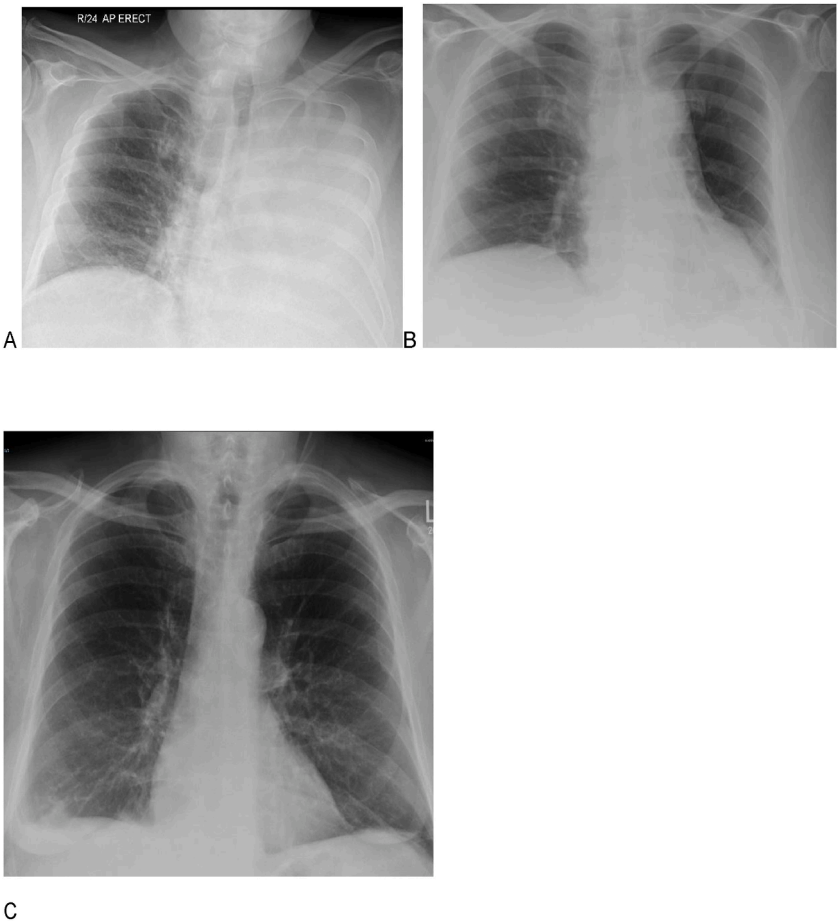

Fig. 3. Chest X-ray -case 3
A) Initial chest Xray before treatment: massive left-sided effusion
B) 1-day post pleurodesis
C) 1-year post pleurodesis.

immediately before the procedure led to a higher success rate than the previously published case series [17,18]. One patient required a repeat of chemical pleurodesis during the same admission.

Severely symptomatic patients with hepatic hydrothorax, despite sodium-restricted diets and diuretic therapy, often require more invasive measures such as repeated thoracentesis, chemical pleurodesis, surgical repair of diaphragmatic defects, TIPS, and liver transplantation [8,19–21]. While Liver transplantation remains the definitive treatment for hepatic hydrothorax, most patients are unsuitable candidates. Therapeutic thoracentesis can decrease large effusions successfully. However, it is associated with potential risks, such as pneumothorax, hemothorax, vasovagal episodes, laceration of the liver or spleen, and empyema. If someone requires frequent aspirations, it may be beneficial to consider other treatment options [22].

Tube thoracostomy for refractory hepatic hydrothorax may increase the risk of infection, electrolyte imbalance, protein deficiency, acute renal failure, and bleeding [23–25].

Furthermore, due to the continuous accumulation of pleural fluid, it may become impossible to remove the chest tube [25]. A study of 1981 patients managed with chest drains for recurrent hepatic hydrothorax noted a significantly higher mortality risk (odds ratio [OR] 2.1, 95 % CI 1.4–3.1) [26].

Although chemical pleurodesis with tube thoracostomy alone has been attempted to treat hepatic hydrothorax [27], it has had low success rates due to the rapid fluid build-up, which prevents approximation of the pleural surfaces [28].

Indwelling pleural catheters are an effective treatment for malignant pleural effusions. However, when compared to repeated thoracentesis in the treatment of refractory transudative pleural effusions, a higher adverse event risk was noted, with no significant difference in breathlessness at 12 weeks [29]. Another retrospective study examined their role in 62 patients with refractory hepatic hydrothorax. The results indicated a high rate of adverse events at 36 %, with a success rate of only 16 % [30]. Further research is thus required to understand the role of indwelling pleural catheters in hepatic hydrothorax.

TIPS can be a viable treatment option in patients requiring frequent pleural drainage with response rates of up to 70–80 % [31–37]. However, potential risks include portosystemic encephalopathy, TIPS stenosis, and technical complications seen in 25–30 % of cases [32]. Furthermore, poor outcomes are more likely for older patients, those with severe liver disease (Child-Pugh score >10, MELD score >15–17), and those with deranged renal function [37,38], making it unsuitable for most patients. As our patients were not eligible for TIPS, we had to explore alternative strategies.

Physicians have recently resorted to utilising VATS to identify defects in the diaphragms of patients suffering from refractory hepatic hydrothorax. These defects are subsequently sealed using biological glue or sutures [7]. Nevertheless, it is worth noting that using VATS necessitates administering general anaesthesia, which could pose a risk to individuals with advanced liver disease.

A study investigating the clinical usefulness of chemical pleurodesis with or without video-assisted thoracoscopic surgery for patients with refractory hepatic hydrothorax showed a success rate of 72.7 %, with 62.5 % of patients remaining hydrothorax-free for a median follow-up of 16 weeks (range: 2–52 weeks) [17]. Similarly, a meta-analysis of 20 case reports and 13 case series, which included 180 patients, looked at the effectiveness and safety of pleurodesis via conventional thoracoscopy or video-assisted thoracic surgery for hepatic hydrothorax. The study found that 72 % of patients showed a complete response, with a very high complication rate of 82 % [18]. We believe that the high success rate in our patients was due to effective pre-procedure ascites management and complete pleural cavity drainage during the procedure while maintaining patients on adequate diuretic doses. In our patient series, all enrolled patients experienced mild complications such as fever and leucocytosis. Two patients developed acute kidney injury, and one patient experienced hepatic encephalopathy. However, all complications responded rapidly to medical therapy.

6. Conclusion

This case series suggests that refractory hepatic hydrothorax can be successfully managed with medical thoracoscopy and chemical pleurodesis if preceded by meticulous attention to the control of ascitic fluid. This approach can alleviate symptoms and effectively handle pulmonary complications in these individuals and can be considered where all other alternative options are exhausted.

CRediT authorship contribution statement

Y. Rahim: Writing – review & editing, Writing – original draft, Resources, Data curation. **R.V. Reddy:** Writing – review & editing, Supervision, Conceptualization. **M. Naeem:** Supervision, Investigation. **G. Tsaknis:** Investigation.

Declaration of Competing interest

No conflicts of interest.

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