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CASE REPORT

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Superimposed pleural infection in cirrhotic chylothorax

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Abstract

Chylothorax contains an abundant amount of immunoglobulins and white blood cells, leading to the belief that superimposed pleural infection is unlikely. We report two cases of biochemically confirmed chylothorax due to cirrhosis, complicated by superimposed pleural infection following repeated pleural interventions. These findings highlight the potential for superimposed infection in chylothorax and challenge the belief in the bacteriostatic effect of chyle. Clinical vigilance is essential to consider this possibility if features of infection arise during the management of chylothorax.

KEYWORDS

chylomicrons, chylothorax, cirrhosis, pleural infection, triglyceride

INTRODUCTION

Chylothorax is characterized by the presence of chyle in the pleural space, which contains a significant amount of immunoglobulins and white blood cells (WBCs) from the lymphatic system. Due to these immune components, it has been conventionally believed that chyle is bacteriostatic and superimposed infection is unlikely in preexisting chylothorax. However, we report two cases of superimposed bacterial pleural infection in patients with chylothorax due to cirrhosis, both of which were successfully treated with antibiotics.

CASE REPORT

Patient 1

A 60-year-old man with underlying Child-Pugh grade C viral hepatitis B cirrhosis was hospitalized 1 month prior for the first episode of right pleural effusion and recurrent ascites. A chest drain was inserted during that admission, which evacuated slightly milky pleural effusion and resolved his respiratory symptoms. The ascites also improved with the drainage of the pleural effusion. Pleural fluid analysis suggested dual pathologies: cirrhotic hydrothorax, evidenced by its transudative nature based on Light's criteria; and chylothorax, indicated by the slightly milky appearance and presence of chylomicrons in the pleural fluid. The challenging diagnostic process of establishing the diagnosis of chylothorax for this patient was described elsewhere.[1] There was no clinical evidence of pleural infection or malignancy on whole-body computed tomography. Therefore, the chyle was presumed to originate from the ascites due to cirrhosis.

Upon this admission, the patient presented again with recurrent pleural effusion and ascites. His respiratory symptoms and ascites improved after chest drain insertion, which also yielded milky pleural fluid. However, the daily pleural fluid output remained high, necessitating continuous chest drain placement. Multiple medical interventions targeting the dual pathologies were attempted, including fluid restriction, intravenous albumin infusion, and a low-fat diet with medium-chain triglyceride (MCT) replacement, but the high fluid output persisted. Up-titration of diuretics and the addition of beta-blockers were limited by borderline blood pressure.

On the sixth day of pleural fluid drainage, the patient developed a methicillin-sensitive *Staphylococcus aureus* (MSSA) pleural infection presumably due to the prolonged chest drain placement. The pleural fluid became turbid, with a rise in pleural fluid lactate dehydrogenase (LDH) level

TABLE 1 Serial laboratory parameters and treatment for patients 1 (A) and 2 (B).

A

Patient 1	Day 1 (current admission)	Day 6	Day 7	Day 8	Day 11	Day 15	Day 18
Blood results							
WBC ($\times 10^9$/L)	3.9	13.4	17.5	8.0	6.1		6.1
CRP (mg/L)			160.5	126.1	52.7		13.9
Pleural fluid results							
Total WBC (count/L)	78	9560				195	
Neutrophil (%)	1	96				30	
Lymphocyte (%)	29	1				63	
Monocyte (%)	70	2				7	
Total protein (g/L)	<10	21				12	
LDH (U/L)	38	240				100	
Culture	Negative			MSSA (culture sent on day 6)			
Pleural fluid appearance	Slightly milky	Slightly milky	Slightly milky	Turbid	Turbid	Slightly turbid	Clear, straw colour
Remarks		Commencement of co-amoxiclav					

B

Patient 2	1st admission	2nd admission	3rd admission	4th (current) admission Day 1	4th (current) admission Day 3	4th (current) admission Day 6	4th (current) admission Day 8
Blood results							
WBC ($\times 10^9$/L)	3.9	3.6	11.6	9.7		17.0	12.8
CRP (mg/L)	2.9	1.8	76.3	96.3		194.2	191.6
Pleural fluid results							
Total WBC (count/L)	215		3410	1050			
Neutrophil (%)	5		84	60			
Lymphocyte (%)	30		5	5			
Monocyte (%)	60		11	35			
Total protein (g/L)	26	24	30	18			
LDH (U/L)	62	70	169	73			
Culture	Negative	Negative	Negative		MRSA (culture sent on day 1)		
Pleural fluid appearance	Clear, straw colour	Clear, straw colour	Slightly turbid	Milky	Milky	Milky and turbid	Turbid
Treatment	Prophylactic ciprofloxacin	Prophylactic ciprofloxacin	Full dose levofloxacin	Prophylactic ciprofloxacin	Prophylactic ciprofloxacin	Commencement of vancomycin	Commencement of intrapleural urokinase for 3 days

Abbreviations: CRP, C-reactive protein; LDH, lactate dehydrogenase; MRSA, methicillin-resistant *Staphylococcus aureus*; MSSA, methicillin-sensitive *Staphylococcus aureus*; WBC, white blood cells.

from baseline 38 U/L to 240 U/L and an increase in blood WBC and C-reactive protein (CRP) levels (Table 1). Culture of pleural fluid aspirated from the indwelling drain (inserted on day 1 of this admission) yielded MSSA. The drain wound was clear, and no other infective source was identified. The MSSA was considered the causative microorganism as there was a feature of active sepsis and a lack of an alternative infective focus, including peritonitis. The patient was

successfully treated with a course of co-amoxiclav. Following empyema, pleural fluid output dropped significantly, allowing chest drain removal. He was then discharged and resumed a normal diet. Since then, the patient has had monthly hospitalizations for ascites drainage, but there has been no recurrence of pleural effusion.

Patient 2

A 71-year-old man was hospitalized for recurrent right-sided pleural effusion. He had Child-Pugh grade C cirrhosis due to chronic hepatitis B infection and recurrent ascites requiring regular paracentesis. He also had a history of oesophageal varices, portal vein thrombosis, and spontaneous bacterial peritonitis, for which he was on lifelong ciprofloxacin prophylaxis (250 mg daily).

The patient began developing right pleural effusion 2 months before the current admission. The initial right pleural drainage yielded straw-coloured pleural fluid, which was transudative and monocytic in nature. Both pleural fluid bacterial culture and cytological examination were negative. A diagnosis of hepatic hydrothorax was established, and the dose of diuretics was increased to optimize fluid status.

The patient experienced symptomatic recurrence of right pleural effusion 3 weeks later (1 month before the current admission), necessitating another drainage episode. The pleural fluid analysis showed similar results, consistent with those for hepatic hydrothorax and negative bacterial culture.

One week later (2 weeks before the current admission), the patient presented with fever and right-sided chest pain, and a chest x-ray (CXR) showed a recurrence of right pleural effusion. Pleural drainage was performed, yielding slightly turbid fluid. The pleural fluid was exudative (total protein [TP] 30 g/L, LDH 169 U/L) and neutrophilic (84%) in nature, but with a negative bacterial culture. A full septic workup was negative, and the fever resolved after switching from ciprofloxacin to full-dose levofloxacin. With pleural drainage and intravenous albumin infusion, his pleural effusion subsided before discharge. Serial laboratory parameters are shown in Table 1.

In this admission, he presented again with a moderate right-sided pleural effusion (Figure 1A). He was afebrile upon admission. His WBC level was within the normal range (9.7×10^9/L), but the CRP level was elevated to 96.3 mg/L. A chest drain was inserted, yielding pleural fluid with a milky appearance without a foul smell. Pleural fluid analysis revealed a transudative (TP 18 g/L, LDH 73 U/L) and neutrophilic (60%) nature. The pleural fluid bacterial culture was negative. The fluid triglyceride (TG) level was elevated to 1.94 mmol/L and the pleural fluid/serum TG ratio was 2.77 (1.94/0.7), confirming the diagnosis of chylothorax (Table 1B). Given that both values were higher than the diagnostic cutoff, we did not check the pleural fluid chylomicron level as it was more expensive and not readily available. Pleural fluid TG level was not checked before this admission because of a lack of characteristic milky appearance. A recent whole-body CT did not reveal any suspicious thoracic or abdominal malignancy. Therefore, the source of chylothorax was presumably due to cirrhosis. The patient was placed on a low-fat diet with MCT replacement and received intravenous albumin infusion.

The patient remained afebrile initially and was continued with the usual prophylactic ciprofloxacin, but the pleural fluid culture sent upon admission grew methicillin-resistant *Staphylococcus aureus* (MRSA). The current and old chest drain wounds were clear, and the systemic workup revealed no alternative infectious focus. Vancomycin was commenced once the pleural fluid culture result was available, in addition to ciprofloxacin prophylaxis. Despite the above

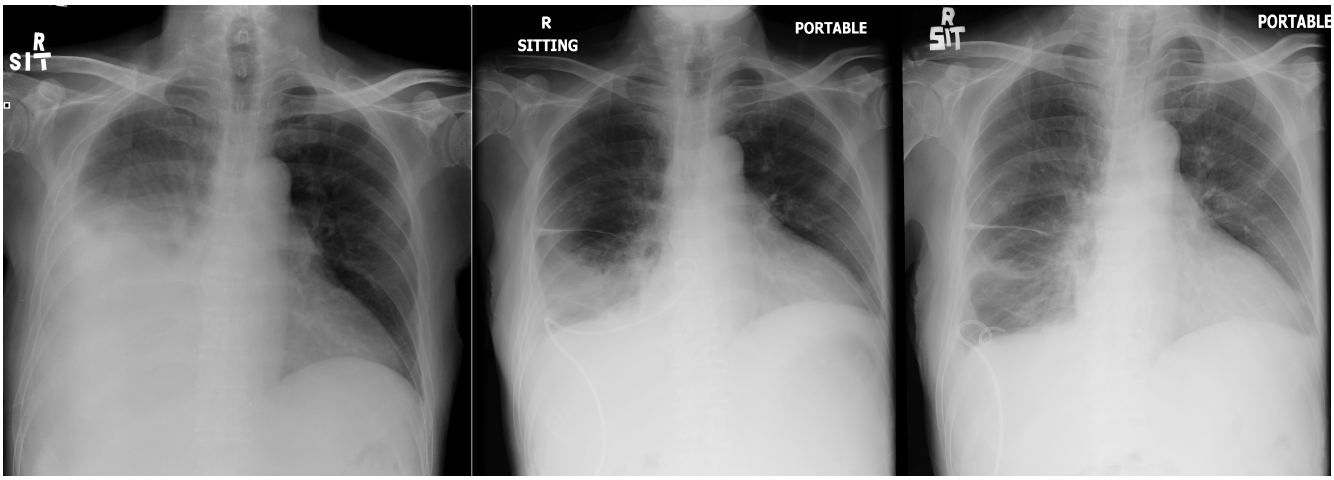

FIGURE 1 Serial chest x-ray images of patient 2. (A, left) Presence of right pleural effusion on admission, (B, middle) persistence of loculated right pleural effusion despite drainage and before the administration of intrapleural urokinase, and (C, right) near complete resolution of right pleural effusion after the 3 days daily administration of intrapleural urokinase.

management, the CXR only showed partial drainage of pleural effusion, with the remaining effusion becoming loculated (Figure 1B). The patient developed a high fever on the sixth day of admission. Repeated blood tests showed a rising trend of WBC (17.0×10^9/L) and CRP (194.2 mg/L) levels. Thoracic ultrasound confirmed dense septations in the right pleural space. As the patient only had a small bore (Fr 8) pleural drain in place, the patient was not eligible for intrapleural tissue plasminogen activator and deoxyribonuclease. Consequently, intrapleural urokinase was administered daily for three consecutive days. The drain output improved, the fever subsided, and there were improving trends in WBC and CRP levels afterwards. The pleural space was drained dry, and pleural fluid output slowly ceased (Figure 1C). He then remained afebrile, and vancomycin was continued to complete a 4-week course. The patient has not had recurrent right-sided pleural effusion since then.

DISCUSSION

Traditionally, chyle has been considered bacteriostatic and resistant to infection due to its high levels of white blood cells (WBCs) and immunoglobulins. However, this assumption has not been formally assessed. The two cases discussed here prove that infection can occur in chylothorax, supporting the few previously reported cases of infected chylothorax.[2,3]

Two risk factors contributed to the occurrence of infection in these cases. First, repeated pleural interventions and prolonged chest drain placement for high-output chylothorax are significant risk factors for hospital-acquired pleural infection. This finding was also suggested by a recent multicenter retrospective study across three continents that identified 77 patients with chylothorax. Infection was the main complication in the cohort, with 4 patients having pleural infections were all secondary to either recent chest tubes or indwelling pleural catheter (IPC) replacement.[3] Second, both patients were immunocompromised due to advanced cirrhosis. Similar to the care of patients with chest drains, regular monitoring of pleural fluid output is mandatory. Strict precautionary measures should be observed in pleural drain care to avoid hospital-acquired pleural infection, even in cases of chylothorax. When signs of infection appear in patients with chylothorax, especially those with chest drains and an immunocompromised state, the pleural fluid should be examined for any changes in its gross appearance, presence of sediments in the drainage conduit after overnight settlement and sent for microbiological investigations. Treating physicians should be vigilant about this possibility as the occasional milky appearance of pleural infection may mimic that of chylothorax. On the other hand, as the pleural fluid of chylothorax can appear serous during the fasting state, a persistent milky or cloudy appearance of the fluid in a fasting patient should also raise the suspicion of pleural infection.

Various treatments for chylothorax have been described, including dietary manipulation, medical pleurodesis, and surgical ligation of the thoracic duct and its tributaries or percutaneous lymphatic intervention. The success rates of these treatments vary and depend on the underlying cause. The presence of high-output hepatic hydrothorax, as seen in the two cases discussed, further complicates the condition. The success rate of thoracoscopic talc pleurodesis in hepatic hydrothorax is often low, with an immediate efficacy of 47.6% in a small cohort.[4] However, patients who survive a superimposed infection have a high success rate of pleurodesis and cessation of pleural fluid production, even if the underlying pathology persists. Post-infectious pleurodesis has been reported in patients with IPC-related infections, particularly those caused by staphylococci, with a 79% pleurodesis rate.[5] Fortunately, both patients in this report benefited from the post-infectious pleurodesis and remained free from the recurrence of chylothorax.

In conclusion, we discussed two cases of cirrhotic chylothorax with subsequent superimposed pleural infection following prolonged chest drain placement. Treatment of superimposed infection should follow the usual antibiotic regimen for pleural infection and pleural fluid culture results. Patients who survived pleural infection may benefit from successful pleurodesis.

AUTHOR CONTRIBUTIONS

All authors listed have equal contribution on conceptualization, text drafting, and manuscript review.

CONFLICT OF INTEREST STATEMENT

None declared.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

ETHICS STATEMENT

The authors declare that appropriate written informed consent was obtained for the publication of this manuscript and accompanying images.

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