Changing pleural fluid triglyceride levels in cirrhotic chylothorax

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Abstract
Chylothorax is an uncommon disease entity, but it occasionally poses a diagnostic challenge to physicians. Pleural fluid triglyceride level has been advocated as a screening test to diagnose chylothorax. However, its level can be depressed if there is an additional pathology driving the process of pleural fluid production. We report a case of high-volume pleural fluid output due to dual pathologies, cirrhotic hydrothorax and chylothorax, causing an initial failure to diagnose chylothorax due to low pleural fluid triglyceride level. The fluid triglyceride levels were unmasked after the treatment for underlying portal hypertension. These findings were further substantiated by positive lipoprotein electrophoresis for chylomicron. In this patient, lipoprotein electrophoresis of his pleural fluid specimen helps distinguish chylothorax as a second pathology amidst the underlying cirrhotic hydrothorax.

KEYWORDS
chylomicrons, chylothorax, cirrhosis, transudative pleural effusion, triglyceride

INTRODUCTION
Cirrhotic chylothorax is an uncommon disease entity. In a retrospective cohort involving 1038 cirrhotic patients, 49 (4.7%) and 3 (0.3%) patients had hepatic hydrothorax and chylothorax, respectively.1 Transdiaphragmatic migration of chylous ascites into the pleural cavity can give rise to chylothorax.2 Pleural fluid triglyceride level or its ratio to plasma triglyceride level have been used as the screening criteria for chylothorax.3 However, false-negatives may occur using specific cut-offs and thus lead to a missed diagnosis. We report a case of changing pleural fluid triglyceride levels in cirrhotic hydrothorax, which masked the underlying chylothorax.

CASE REPORT
A 60-year-old man was hospitalized for massive right-sided pleural effusion and moderate ascites. He had a Child–Pugh grade C cirrhosis due to chronic hepatitis B infection. He had a history of recurrent ascites due to portal hypertension and was once controlled by oral diuretics. As the patient was distressed by the massive pleural effusion, a chest drain was inserted with a fluid output of a slightly milky appearance, which led to the resolution of respiratory symptoms and ascites. The pleural fluid analysis suggested its transudative nature (pleural fluid total protein [TP] < 10 g/L, lactate dehydrogenase [LDH] 43 U/L; plasma TP 64 g/L, LDH 171 U/L) and was presumably secondary to cirrhotic hydrothorax based on Light’s criteria. There was no evidence of pleural infection or malignancy. A component of chylothorax was initially suspected due to the slightly milky fluid appearance, but it was rejected as the pleural fluid triglyceride concentration was 0.96 mmol/L, which was lower than the diagnostic cut-off of 1.24 mmol/L.3

The daily volume of pleural fluid output remained high and up to 1500 ml. Fluid restriction and regular intravenous albumin infusion were implemented, but only mild reduction of the daily pleural fluid production, and the fluid remained slightly milky in appearance. The borderline blood pressure also precluded an up-titration of diuretics or the addition of beta-blockers to control portal hypertension. A recheck of pleural fluid triglyceride level was 1.75 mmol/L, and its ratio to plasma triglyceride (0.50 mmol/L) was greater than 1, which fell into the range of chylothorax. As this dramatic change of pleural fluid triglyceride levels led to a doubtful diagnosis of chylothorax, a gold standard test was considered necessary to establish the diagnosis. Therefore, the pleural fluid was sent to a tertiary centre for analysis.
which revealed a dense chylomicron band in the sample (Figure 1). The patient was diagnosed to have chylothorax in addition to cirrhotic hydrothorax.

After the diagnosis of chylothorax was established, the patient was put on a low-fat diet with medium-chain triglyceride supplement. There was no significant drop in the pleural fluid output but progressive regression of milky appearance upon serial pleural fluid sampling (Figure 2). Computed tomography of the thorax and abdomen did not reveal any mediastinal pathology or hepatic malignancy, and the chyle presumably originated from the ascites due to cirrhosis.

The key events are summarized below in chronological order:
- 11 December 2019 (day 1): admission
- 12 December 2019 (day 2): insertion of chest drain
- 17 December 2019 (day 7): onset of Staphylococcus aureus empyema
- 30 December 2019 (day 30): chest drain removal
- 31 December 2019 (day 31): discharge

**DISCUSSION**

The diagnosis of chylothorax in cirrhosis can be challenging. Identifying a distinct band of chylomicron on the lipoprotein electrophoresis is the gold standard test to establish the diagnosis, but this test is not widely available. Staats et al. proposed that a screening triglyceride value is a critical step in the diagnostic process, with a level greater than 1.24 mmol/L (110 mg/dl) suggestive of chylothorax. Equivalent cases with triglyceride levels between 0.57 and 1.24 mmol/L (50–110 mg/dl), as the first fluid triglyceride result in our patient, would require lipoprotein electrophoresis for definitive diagnosis. Alternative screening criteria using a fluid to plasma triglyceride ratio greater than 1 had also been adopted. Nevertheless, these studies assumed the patients were affected by a single aetiology and neglectable effects on fluid triglyceride levels if an additional pathology is present. A potential diagnostic pitfall may exist if the second pathology of pleural fluid production (cirrhotic hydrothorax in this case) ‘dilutes’ the pleural fluid triglyceride concentration, which thus limits the diagnostic use of these proposed cut-offs, leading to a ‘false-negative’ result. The use of other technology, for example, nuclear magnetic resonance-based pleural fluid lipoprotein analysis, could potentially demystify the lipid composition of the samples. During the management of a coexisting aetiology, the fluid triglyceride concentration could increase over time, allowing physicians to make the diagnosis. This strategy is particularly essential if lipoprotein electrophoresis is not readily available to test for the presence of chylomicron.

Chyle was conventionally said to be bacteriostatic and considered resistant to infection due to its abundant immunoglobulins and white blood cells. However, the occurrence of empyema in our patient challenged this belief. The patient was complicated with Staphylococcus aureus empyema 5 days after the drain insertion. The pleural fluid became turbid, together with a surge of pleural fluid LDH to 240 U/L. He was treated successfully by a course of co-amoxiclav. After the occurrence of empyema, pleural fluid output dropped significantly and allowed chest drain removal. He was then discharged with a progressive loosening of dietary restriction. In the subsequent 2 months, he was admitted twice for symptomatic ascites, which was not milky in appearance. He also had no recurrence of pleural effusion.
patient has fortunately benefited from the pleural infection by achieving pleurodesis and free from the recurrence of chylothorax. Strict precautionary measures should still be observed on pleural drain care to avoid hospital-acquired pleural infection.

In the present case, chylothorax was masked by coexisting cirrhotic hydrothorax. The successful diagnosis relied on a high level of clinical suspicion, optimization of the underlying portal hypertension and the serial sampling of pleural fluid. The change of pleural fluid triglyceride levels during the diagnostic process is a rarely reported potential pitfall, yet an essential clue to diagnosing chylothorax. Testing for the presence of chylomicron in the pleural fluid should be considered when the suspicion of chylothorax persists.

CONFLICT OF INTEREST
None declared.

DATA AVAILABILITY STATEMENT
Data sharing is not applicable to this article as no new data were created or analysed in this study.

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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