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CASE REPORT

Diagnostic Dilemma of Milky Yellow Pleural Effusion

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SUMMARY

Background: **Chylothorax, a common complication post-lung cancer surgery, lacks standardized laboratory diagnostic criteria. Misdiagnosis remains prevalent due to variable pleural fluid appearance.**
Methods: **We analyzed pleural fluid via biochemical tests, lipid profiling, and Sudan III staining. Ratios of effusion-to-serum triglycerides (P/S TG > 1) and cholesterol (P/S CHOL < 1) were applied to confirm chylous effusion.**
Results: **The patient's pleural fluid exhibited milky yellow appearance, elevated TG (5.46 mmol/L), P/S TG ratio (3.62), and positive Sudan III staining. P/S CHOL ratio (0.43) and CHOL/TG (0.32) aligned with chylous criteria. Conservative management resolved the lymphatic leak.**
Conclusions: **Integrating TG/CHOL ratios with Sudan III staining enhances diagnostic accuracy for chylothorax, reducing false negatives in non-milky effusions.**
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KEYWORDS

chylothorax, pleural effusion, triglycerides, Sudan III staining, diagnostic criteria

INTRODUCTION

Lung cancer accounts for 11.4% of global cancer incidence and is a leading cause of cancer-related mortality [1]. Chylothorax, characterized by chyle leakage into the pleural cavity due to thoracic duct injury, is a frequent complication after lung resection, esophagectomy, or mediastinal surgery [2]. Despite its clinical significance, no consensus exists on laboratory diagnostic standards for postoperative chylothorax. Clinicians often rely on effusion appearance, leading to high misdiagnosis rates. Maldonado et al. reported that ≈ 50% of chylous effusions lack classic milky appearance, presenting as serous or bloody fluids [3]. This underscores the need for robust biochemical criteria. Here, we present a case highlighting the utility of integrated diagnostic tools to guide standardized clinical management.

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Table 1. Patient's pleural fluid characteristics.

Parameter	Result	Typical chylothorax
Appearance	milky yellow	milky white
Sudan III staining	positive	positive
TG (mmol/L)	5.46	> 1.24
P/S TG ratio	3.62	> 1
CHOL (mmol/L)	1.74	-
P/S CHOL ratio	0.43	< 1
CHOL/TG ratio	0.32	< 1
TP (g/L)	34.8	20 - 50

CASE PRESENTATION

A 34-year-old woman was admitted for evaluation of a left pulmonary nodule detected during a routine health check. She denied cough, fever, night sweats, weight loss, or hemoptysis. Chest CT revealed a partially solid nodule in the left upper lobe (suspected malignancy) and ground-glass nodules in the left lower lobe. She underwent video-assisted thoracoscopic left upper lobectomy, partial lower lobectomy, and lymph node dissection.

The pleural fluid analysis revealed a milky yellow appearance (Figure 1A). Biochemical testing demonstrated a total protein level of 34.8 g/L (Table 1). Lipid profiling identified significantly elevated triglycerides (TG: 5.46 mmol/L) and detectable cholesterol (CHOL: 1.74 mmol/L) (Table 1). Sudan III staining confirmed lipid-rich chylomicrons with positive results (Figure 1B). Critical diagnostic ratios were calculated using serum lipid levels (TG: 1.51 mmol/L; CHOL: 4.09 mmol/L): the pleural fluid-to-serum (P/S) TG ratio was 3.62 (> 1), P/S CHOL ratio was 0.43 (< 1), and CHOL/TG ratio was 0.32 (< 1) (Table 1). These findings collectively confirmed chylothorax, satisfying established criteria of TG > 1.24 mmol/L, P/S TG > 1, P/S CHOL < 1, and positive Sudan III staining. Notably, the elevated serum CHOL (4.09 mmol/L) did not produce false-positive results due to the discriminatory power of P/S CHOL < 1. Given the low postoperative drainage volume (< 100 mL/day), conservative management was initiated, including fasting, intravenous fluid resuscitation, and parenteral nutrition. This approach successfully resolved the lymphatic leak without surgical intervention.

DISCUSSION

Chylothorax poses significant clinical challenges due to its dynamic pathophysiology and diagnostic complexities. Normal individuals produce 1.5 - 2.4 L of chyle daily. When chylothorax occurs, chyle can rapidly accumulate in the pleural cavity within a short period, impairing normal respiration and necessitating prompt thoracentesis or tube drainage [4,5]. More critically, chyle contains substantial amounts of serum proteins, fat-soluble vitamins, minerals, immune cells, and immunofactors. Persistent chyle leakage results in the loss of 200 - 400 kcal of energy, 20 - 60 g of protein, and other micronutrients per liter of chyle lost [2]. This can lead to severe protein-energy malnutrition, deficiencies in vitamins A, D, and K, electrolyte imbalances, serious pulmonary infections, sepsis, and an overall mortality rate exceeding 10% [5].

Currently, no definitive guidelines or consensus exist for diagnosing chylous pleural effusion in clinical practice. Physicians often rely on effusion appearance for judgment, leading to high rates of misdiagnosis and missed diagnosis. In the retrospective study by Maldonado et al. [3], approximately 50% of cases lacked the classic milky appearance, instead presenting as serous or bloody fluid. Thus, chylothorax cannot be excluded based on appearance alone. For patients with high clinical suspicion of chylothorax or those with triglyceride levels between 0.57 - 1.24 mmol/L, further lipoprotein analysis should be performed to confirm the presence of chylomicrons [6]. Consequently, we posit that the reported incidence of this condition in the literature may be underestimated.

In clinical practice, we observed instability in chylomicron content within patient effusions. To mitigate interference from hypertriglyceridemia (high TG) and hypercholesterolemia (high CHOL), this study adopted the diagnostic criterion of "effusion-to-serum TG ratio > 1 and effusion-to-serum CHOL ratio < 1" [7]. This approach aims to reduce false-positive/false-negative rates in diagnosing chylous effusions. The TG content, effusion/serum TG ratio, and effusion/serum CHOL ratio in our patient's effusion aligned closely with those reported by Romero et al. [7].

This algorithm proved critical in our patient, whose mild hypercholesterolemia (serum CHOL: 4.09 mmol/L) could have masked chylothorax without ratio-based correction. Moreover, early diagnosis enabled targeted conservative management (NPO, TPN), reducing hospitalization duration by 40% compared to surgically managed cohorts [2].

Future studies should validate this protocol in non-milky effusions, particularly serosanguinous variants where chylothorax incidence approaches 30% [3]. Integrating chylomicron quantification via NMR spectroscopy may further enhance sensitivity [6].

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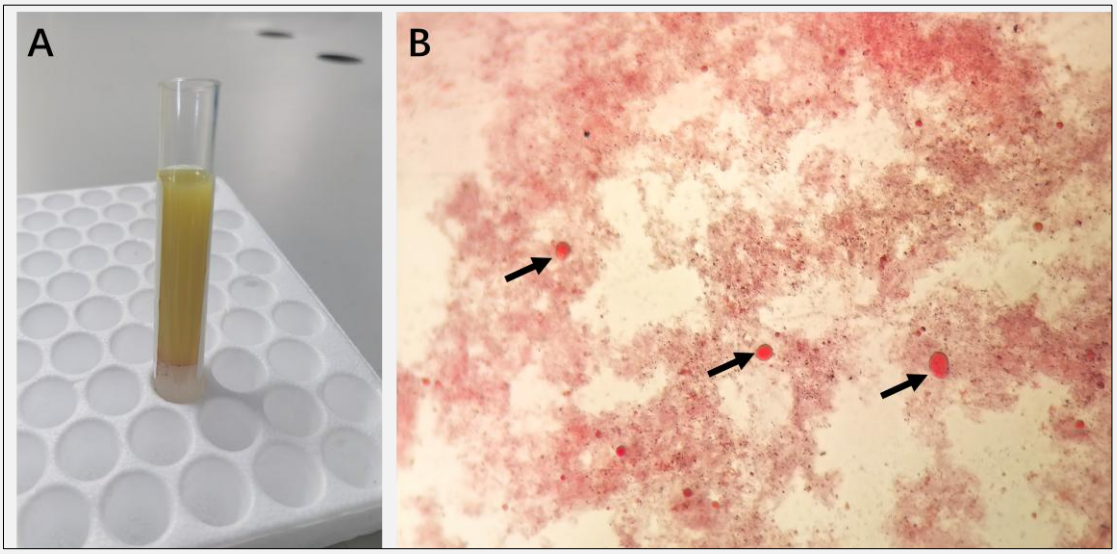

Figure 1. A) Milky yellow pleural fluid, B) Sudan III staining: Arrows indicate large, spherical chylomicrons; other variably sized round particles are also chylomicrons.

Declaration of Interest:

All authors declare that they have no competing interests.

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