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A Case Series of Pleural Effusions of Extra-vascular Origin (PEEVO)

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Abstract

Pleural effusions are commonly encountered in clinical practice and are most frequently caused by cardiopulmonary, malignant, or inflammatory conditions. These effusions typically result from alterations in hydrostatic or oncotic pressures, pleural permeability, or lymphatic drainage. In contrast, pleural effusions of extra-vascular origin (PEEVO) arise from direct migration of non-vascular fluids into the pleural space through anatomical disruptions or fistulous connections and represent a rare but important diagnostic entity. PEEVO includes chylothorax, urinothorax, biliothorax, and pancreatic pleural effusion, each associated with characteristic pleural fluid biochemical profiles and distinct management strategies.

We present a case series of four patients with PEEVO encountered at a tertiary academic medical center, illustrating the diverse clinical contexts in which these effusions occur. The cases highlight key diagnostic features, including elevated pleural fluid triglycerides in chylothorax, pleural fluid-to-serum creatinine ratios greater than one in urinothorax, pleural fluid bilirubin exceeding serum levels in biliothorax, and markedly elevated pleural fluid amylase or lipase in pancreatic pleural effusions. Diagnostic imaging modalities such as lymphangiography, computed tomography, magnetic resonance cholangiopancreatography, endoscopic retrograde cholangiopancreatography, and renal scintigraphy played critical roles in identifying the underlying sources of fluid leakage.

This case series emphasizes the importance of maintaining a high index of suspicion for PEEVO in patients with recurrent or atypical pleural effusions. Early recognition through targeted pleural fluid analysis and focused imaging, combined with multidisciplinary, etiology-directed management, can reduce diagnostic delay, prevent recurrence, and improve clinical outcomes.

Categories: Pulmonology
Keywords: atypical pleural effusion, non-resolving pleural effusion, pleural effusion etiology, rare cause of massive pleural effusion, rare cause of pleural effusion

Introduction

Pleural effusion affects approximately 1.5 million individuals annually in the United States and is most often caused by cardiopulmonary, malignant, or inflammatory conditions [1]. These effusions typically arise from alterations in hydrostatic or oncotic pressures, pleural permeability, or lymphatic drainage [1,2].

Pleural effusions of extra-vascular origin (PEEVO) are uncommon and result from direct communication between the pleural space and non-vascular compartments, including the lymphatic, genitourinary, hepatobiliary, and pancreatic systems [3,4]. Although rare, these effusions have distinct pleural fluid biochemical signatures and require management directed at the underlying source in addition to pleural drainage [2,5]. Diagnosis of these conditions remains challenging in current medical practice given the wide breadth of pleural effusion etiologies. We present four illustrative cases of PEEVO to highlight diagnostic strategies and management principles.

Case Presentation

Case 1: chylothorax

A 78-year-old woman with multiple comorbidities presented with progressive dyspnea and a recurrent right-sided pleural effusion. Thoracentesis revealed milky-appearing fluid with triglyceride levels >700 mg/dL and lymphocyte predominance, consistent with chylothorax [6,7]. There was no history of trauma noted in the presenting history.

Initial management included dietary modification, octreotide therapy, and chest tube drainage; however, the effusion persisted. Subsequent lymphangiography identified a focal thoracic duct leak as seen in Figure *1*, and the patient underwent percutaneous thoracic duct embolization. After repeated embolization and continued nutritional support, the pleural effusion resolved completely on follow-up chest radiography.

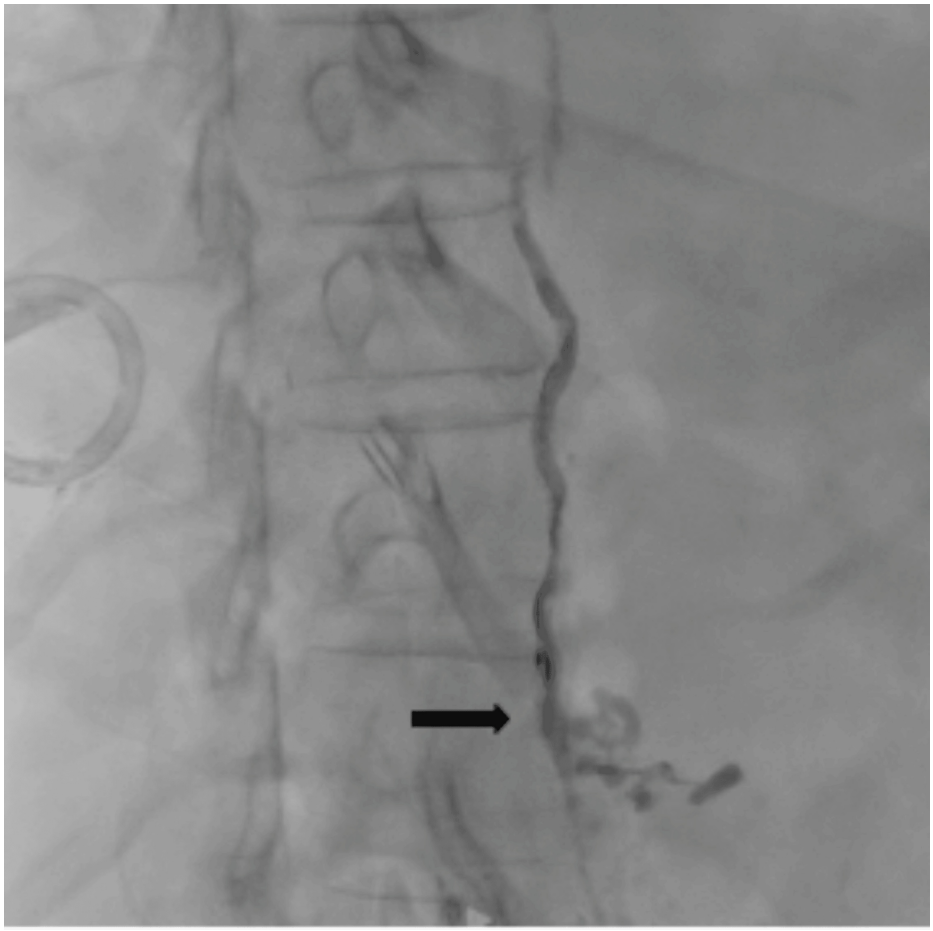


FIGURE 1: Lymphangiography shows focal thoracic duct leak

The patient underwent a transnodal lymphangiogram showing focal leakage of the thoracic duct content, as seen by the arrow, into the pleural cavity, leading to the development of chylothorax.

Case 2: urinothorax

A 62-year-old woman with a history of treated Hodgkin lymphoma presented with acute hypoxemic respiratory failure and bilateral pleural effusions. Thoracentesis demonstrated a transudative effusion. Ongoing high-output chest tube drainage, in conjunction with imaging findings of obstructive uropathy as seen in Figure *2*, raised suspicion for urinothorax. Diagnostic confirmation was supported by a pleural fluid-to-serum creatinine ratio of 1.1, with a pleural fluid creatinine of 0.34 and a serum creatinine of 0.31 [8,9]. This is due to leakage of urine into the abdominal cavity and translocation of the fluid through pores in the diaphragm and into the pleural space. Management consisted of urinary decompression and continued pleural drainage, resulting in resolution of the effusions on follow-up chest radiography and overall clinical improvement.

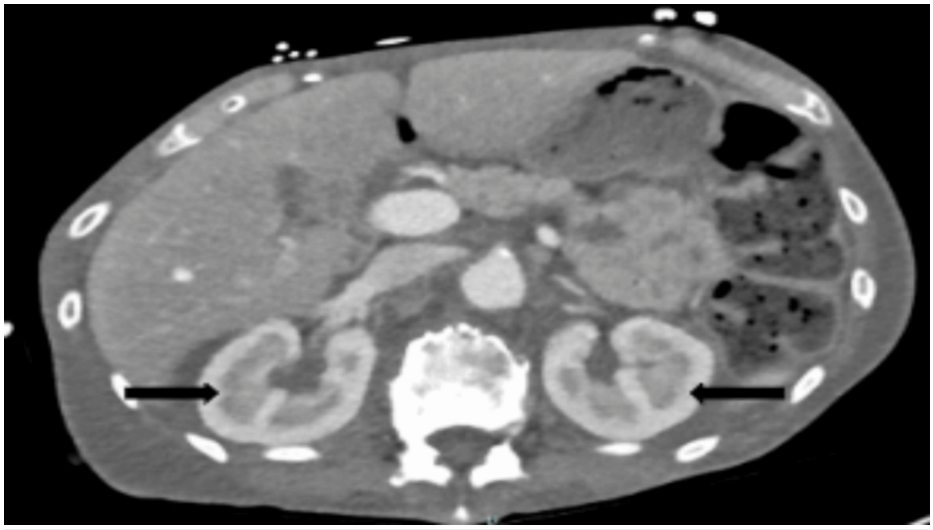


FIGURE 2: CT of the abdomen and pelvis shows evidence of renal calyx dilation due to obstructive uropathy

CT of the abdomen and pelvis shows evidence of renal calyx dilation due to obstructive uropathy (see the arrows), in the setting of high pleural fluid output leading to suspicion of urinothorax.

Case 3: biliothorax

A 68-year-old man with a history of orthotopic liver transplantation presented with a right-sided pleural effusion complicated by empyema in the setting of a biliary anastomotic leak. Thoracentesis yielded bile-stained pleural fluid with a pleural total bilirubin of 1.8 and a serum total bilirubin of 1.2. The pleural fluid-to-serum bilirubin ratio was calculated at 1.5, confirming the diagnosis of biliothorax [10,11].

Management included endoscopic retrograde cholangiopancreatography (ERCP) with biliary drainage, as seen in Figure *3*, chest tube placement with intrapleural fibrinolytics, and targeted antimicrobial therapy. Serial imaging demonstrated progressive resolution of the pleural collections.

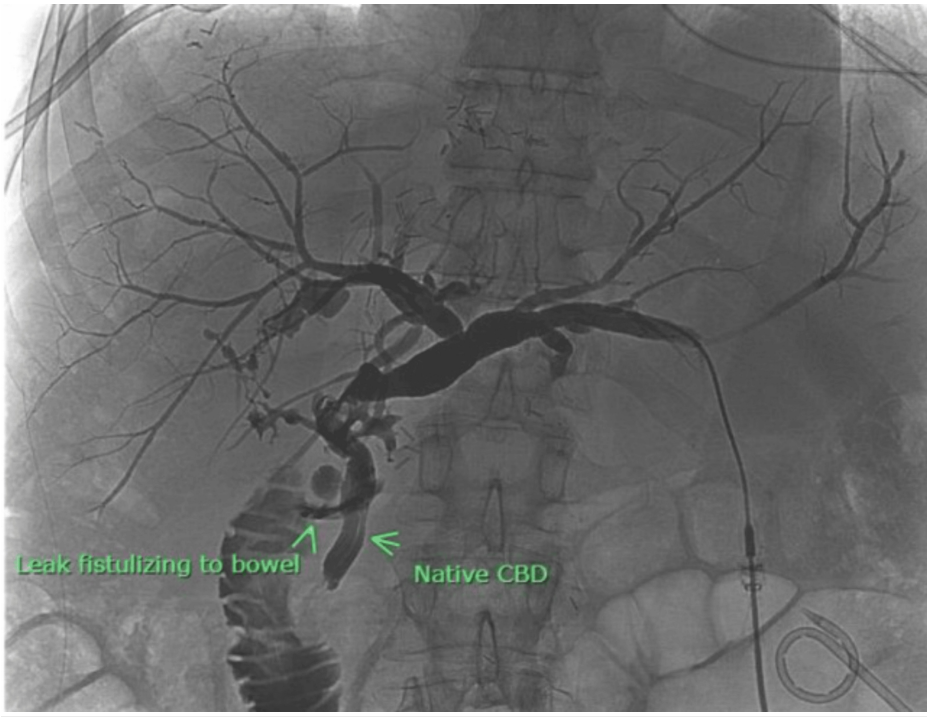


FIGURE 3: ERCP shows biliary leak fistulizing into the bowel and abdomen

ERCP shows a biliary leak fistulizing into the bowel and abdomen, as seen by the arrows, in addition to pleural fluid bilirubin elevation, confirming the development of a biliothorax through diaphragmatic translocation.

ERCP - endoscopic retrograde cholangiopancreatography; CBD - common bile duct

Case 4: pancreatic pleural effusion

A 31-year-old man with a history of alcohol use disorder and recurrent pancreatitis presented with dyspnea and large bilateral pleural effusions. CT of the abdomen showed pancreatic pseudocysts without large-volume ascites. Pleural fluid analysis demonstrated markedly elevated lipase levels, suggestive of pancreatic pleural effusion. Amylase was not checked as this test is non-specific and can also be elevated in conditions such as esophageal pleural fistulas. ERCP identified a pancreatic duct leak as seen in Figure *4*, and pancreatic duct stenting was performed [12-14]. Following endoscopic intervention and supportive care, pleural fluid output decreased significantly from an initial output of 540 cc to 80 cc, with subsequent symptomatic improvement and resolution of effusions on chest radiography.

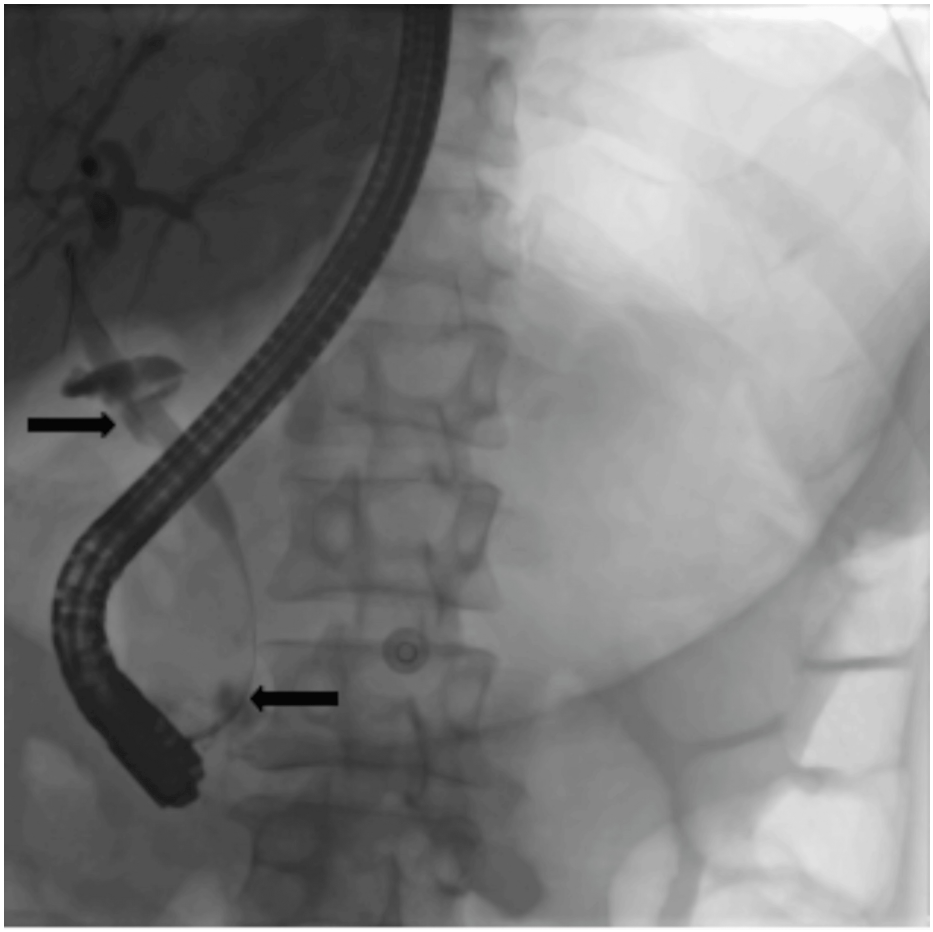


FIGURE 4: ERCP shows pancreatic duct leak into the abdominal cavity

ERCP shows pancreatic duct leak into the abdominal cavity, as seen by the arrows, along with elevated pleural fluid lipase, confirming the diagnosis of pancreatic pleural effusion through diaphragmatic translocation into the pleural cavity.

ERCP - endoscopic retrograde cholangiopancreatography

Discussion

Pleural effusions of extra-vascular origin represent a diagnostically distinct and clinically important subset of pleural disease. Unlike the majority of pleural effusions, which arise from alterations in Starling forces at the pleural microvasculature, PEEVO result from direct translocation of fluid from non-vascular compartments into the pleural space through anatomical disruptions, fistulas, or pressure gradients [3,4]. Because these effusions are uncommon and often occur in complex clinical contexts, diagnosis is frequently delayed, leading to recurrent effusions, unnecessary testing, and prolonged hospitalizations.

A key challenge in diagnosing PEEVO is that initial pleural fluid analysis may appear deceptively nonspecific. Although Light's criteria remain the first step in classifying pleural effusions, reliance on transudative versus exudative categorization alone can be misleading in PEEVO [2,6]. For example, urinothorax often presents as a transudative effusion, whereas biliothorax and pancreatic pleural effusions are typically exudative; however, overlap can occur due to secondary inflammation, infection, or chronicity [9-11].

Each PEEVO subtype has characteristic biochemical markers that are central to diagnosis. In chylothorax, elevated pleural fluid triglycerides, particularly levels exceeding 110 mg/dL, along with lymphocyte predominance strongly support the diagnosis, even in the absence of classic milky appearance [6,7]. Urinothorax is best identified by a pleural fluid-to-serum creatinine ratio greater than one, a simple and highly sensitive metric that should be considered in patients with obstructive uropathy or recent urologic intervention [8,9]. Biliothorax is suggested by bile-stained pleural fluid and confirmed by pleural fluid bilirubin concentrations exceeding serum levels, while pancreatic pleural effusions are distinguished by markedly elevated pleural fluid amylase or lipase, often significantly exceeding serum values [10-14].

Imaging plays a complementary role in confirming the diagnosis and identifying the source of leakage. Cross-sectional imaging, such as CT, can reveal associated pathology-hydronephrosis, pancreatic inflammation, pseudocysts, or postoperative changes-while more specialized modalities are often required to demonstrate the underlying communication. Lymphangiography has emerged as a valuable diagnostic and therapeutic tool in chylothorax, allowing precise localization of thoracic duct leaks and enabling percutaneous embolization [15,16]. In suspected pancreatic pleural effusion, magnetic resonance cholangiopancreatography (MRCP) provides a noninvasive means of delineating pancreatic duct anatomy and fistulous tracts, with ERCP reserved for therapeutic intervention [13-15]. Similarly, ERCP is central to both diagnosis and management of biliary leaks leading to biliothorax, while renal scintigraphy can help confirm urinothorax when conventional imaging is inconclusive [9-11].

Figure *5* summarizes the diagnostic criteria with pertinent diagnostic pleural studies, relevant imaging findings, and appropriate interventions for the various cases of PEEVO.

Case	Demographics	Pertinent Pleural Fluid Studies	Relevant Diagnostic Imaging	Interventions	Outcomes
Chylothorax	78 y/o Female with multiple comorbidities	**Fluid Analysis** Cholesterol 42 mg/dL Triglycerides 700 mg/dL	Transnodal lymphangiogram with thoracic duct leak	• Chest tube placement • Parenteral nutrition • Octreotide • Thoracic duct coil embolization *Dietary changes (low-fat diet +/- TPN)*	Serial imaging showed resolution of chylothorax
Urinthorax	62 y/o Female with hx of possible obstructive uropathy	**Fluid Analysis** Pleural Fluid-to-Serum Creatinine Ratio 1.1 Pleural Creatinine 0.34 mg/dL Serum Creatinine 0.31 mg/dL	CT Abdomen and Pelvis with evidence of renal calyx dilation	• Chest tube placement • Serial imaging studies • Urinary decompression	Serial imaging showed resolution of urinothorax
Bilothorax	68 y/o Male with hx of orthotopic liver transplant	**Fluid Analysis** Total Bilirubin 1.8 mg/dL Serum Total Bilirubin 1.2 mg/dL → **Pleural fluid-to-serum ratio: 1.5**	ERCP with biliary leak fistulizing into the bowel and abdomen	• Chest tube placement • ERCP guided placement of internal-external biliary drain • Intrapleural fibrinolytics • Serial imaging studies • Antibiotics	Serial imaging showed resolution of bilothorax
Pancreatic Pleural Effusion	31 y/o Male with hx of alcohol use disorder and recurrent pancreatitis	**Fluid Analysis** Pleural Lipase > 6000 mg/dL	ERCP with pancreatic duct leak into abdominal cavity	• Chest tube placement • Hepatobiliary surgery evaluation • Serial imaging studies • Pancreatic duct stent	Serial imaging showed resolution of pleural effusion

FIGURE 5: Summary of pleural effusion diagnostics, interventions and outcomes of studied cases

ERCP - endoscopic retrograde cholangiopancreatography

Conclusions

Pleural effusions of extra-vascular origin represent an uncommon but important diagnostic category that should be considered when pleural effusions are recurrent, atypical, or inadequately explained by cardiopulmonary or oncologic disease. Recognition relies on maintaining a high index of suspicion and integrating clinical context with targeted analysis of pleural fluid.

Management of PEEVO focuses on definitive correction of the underlying source of fluid leakage in addition to symptomatic pleural drainage. While thoracentesis and chest tube placement are important for symptomatic relief and prevention of respiratory compromise, definitive resolution is unlikely without addressing the primary pathology. This principle is illustrated across all cases in this series: thoracic duct embolization for chylothorax, urinary decompression for urinothorax, biliary drainage for biliothorax, and pancreatic duct stenting for pancreatic pleural effusion. Advances in endoscopic and percutaneous techniques have significantly reduced the need for open surgical intervention and are now considered first-line therapies in many cases.

Additional Information

Author Contributions

All authors have reviewed the final version to be published and agreed to be accountable for all aspects of the work.

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Drafting of the manuscript: Jayen Sum, Nicholas DeLuca, Samuel Erb

Critical review of the manuscript for important intellectual content: Jayen Sum, Nicholas DeLuca, Armeen Mehrabani, Mouhanned Eliliwi

Supervision: Armeen Mehrabani, Mouhanned Eliliwi

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