

Transudative Chylothorax: Report of Two Cases and Review of the Literature

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Abstract. Transudative chylothorax is a rare entity that has been associated with a limited range of clinical settings. To date, transudative chylothoraces have been described in only 13 patients, most commonly as a result of hepatic cirrhosis. Recognition of the transudative nature of these effusions is important to avoid unnecessary diagnostic testing and inappropriate management strategies. This report describes the presentation, diagnosis and management of two patients with transudative chylothoraces, and provides a brief review of the relevant literature.

Key words: Pleural effusion—Chylothorax—Transudate—Liver cirrhosis—Cardiomyopathy.

Introduction

Chylothorax is an infrequent cause of pleural effusion that is most commonly caused by obstruction or disruption of the thoracic duct. While there are many recognized etiologies of chylothorax, malignancies and trauma related to surgical procedures account for most cases.

Chylous effusions are typically alkaline exudates rich in triglycerides and chylomicrons. Nevertheless, in a small minority of patients, the chylothorax may

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be transudative in nature. In the sparse available literature regarding transudative chylothorax, the reported etiologies are fewer and include cirrhosis, amyloidosis, nephrotic syndrome, superior vena caval thrombosis, and congestive heart failure. In the context that a transudative chylothorax is uncommon and that its recognition should prompt clinicians to consider these specific etiologies, the current report presents two patients with transudative chylothorax of different etiologies and summarizes the available literature regarding 13 patients reported to date.

Case Reports

Patient 1

A 46-year-old woman was referred to our clinic for outpatient pulmonary consultation in October 2000 for a 6-month history of dyspnea on exertion, non-productive cough and a 10-pound non-volitional weight loss. Her past medical history was significant for monoclonal gammopathy of unknown significance (IgA lambda type) and systemic amyloidosis diagnosed 4 years earlier (1996) by bone marrow biopsy. Echocardiographic and renal function studies at that time suggested amyloid infiltration of the heart and kidneys. She developed end-stage renal disease and received hemodialysis treatments prior to undergoing an allogenic kidney transplant 3 years earlier (in November 1997). She had an indwelling tunneled dialysis catheter in her right internal jugular vein for 4 months around the time of the transplant. No complications were recognized at the time. Bilateral pleural effusions were first noted on a chest x-ray 2 days prior to her transplant.

Review of serial chest radiographs from 1996 through 2000 revealed little interval change, with mild-to-moderate bilateral pleural effusions, greater on the left than the right. Echocardiographic findings were also unchanged, again demonstrating restrictive physiology consistent with diastolic dysfunction. Laboratory studies, including complete blood count, renal function and thyroid studies were normal. Spirometry was consistent with pulmonary restriction: FVC 1.05 liters (30% predicted), FEV1 0.98 liters (34%), and FEV1/FVC ratio 97.5%.

Fluid obtained by thoracentesis showed a lymphocytic chylous transudate with chylomicrons present (Table 1), which was felt to be due to her amyloidosis and cardiomyopathy. The patient was treated with bilateral insertion of pleural drainage catheters and pleurodesis; candidacy for heart transplantation was considered but she died of congestive heart failure in October 2002.

Patient 2

A 61-year-old female presented to the emergency department with progressive shortness of breath, dyspnea on exertion and orthopnea of one month's duration. She had been diagnosed with hepatic cirrhosis, with evidence of chronic hepatitis B and hepatitis C, as well as significant alcohol abuse 2 years previously.

Table 1: Laboratory features of the chylothoraces in the two patients

	Patient 1		Patient 2					
	Pleural	Serum	1 st thoracentesis		2 nd thoracentesis		3 rd thoracentesis	
			Pleural	Serum	Pleural	Serum	Pleural	Serum
Color	Yellow		Yellow		Yellow		Yellow	
pH			7.5		NA		7.64	
RBC	1425 µ/L		2710		4020		995	
WBC	125 µ/L		320		480		175	
Protein	1.2 g/dL	6.5 g/dL	2.2	6.7	2.4		1.2	6.2
LDH	43 U/L	246 U/L	94	211	109	397	64	193
Glucose	112mg/dL		171	104	154	102	207	192
Albumin	1.0 g/dL	3.8 g/dL	NA	3.1	NA		< 1.0	3.1
Amylase	9 U/L		NA	NA	NA		NA	
Chylomicron screen	Positive		NA		NA		NA	
Triglyceride	104 mg/dL		NA		146	97	217	
Cholesterol	13 mg/dL		NA		NA	181	NA	
Routine culture	Negative		Negative		Negative		Negative	
AFB Culture	Negative		Negative		Negative		Negative	

NA = Not available

Screening investigations at that time revealed the presence of esophageal varices, but no overt symptoms had ever occurred. Child's-Pugh classification was graded as Stage B; there was no history of spontaneous bacterial peritonitis or overt ascites. In addition, antiphospholipid antibody syndrome had been diagnosed in 1993 after evaluation for multiple abortions and thrombocytopenia. There was no history of deep venous thrombosis or venous thromboembolism.

Evaluation in the emergency department revealed right pleural effusion of moderate size. A ventilation/perfusion scan was indeterminate. Cardiac enzymes and electrocardiogram were normal. A dobutamine echocardiogram revealed no evidence of cardiac ischemia, with a left ventricular ejection fraction of 60%. Computed tomography (CT) with contrast confirmed the presence of a free-flowing right pleural effusion and showed no evidence of thromboembolic disease within the proximal branches of the pulmonary arteries; the CT was otherwise unremarkable.

Initial thoracentesis revealed a lymphocytic transudate (36% lymphocytes) with negative microbiologic studies (Table 1). Repeat thoracentesis was again compatible with a transudative effusion, and, prompted by the lymphocytosis, measurement of triglycerides was performed and suggested chylothorax. The putative cause of the transudative chylothorax was cirrhosis. Abdominal CT showed a small amount of ascites and a pelvic fluid collection without evidence of lymphadenopathy. The patient improved symptomatically after the second thoracentesis and was discharged from the hospital. Repeat chest radiograph showed partial re-accumulation of the fluid 2 weeks later, which responded well to aggressive diuresis. Duplex ultrasonography revealed no evidence of upper extremity venous obstruction. Over the ensuing 8 months, one thoracentesis was

required for therapeutic purposes; aggressive diuresis and sodium restriction were otherwise sufficient to control the effusion.

Discussion

Transudative chylothoraces are uncommon and, in the few available reports have been associated with only a limited number of conditions, including the nephrotic syndrome, hepatic cirrhosis, heart failure, amyloidosis, and superior vena cava obstruction. Indeed, our review of the literature using Medline from 1966 to 2003 using search terms “*chylothorax AND: transudate, cirrhosis, amyloid, nephrotic, congestive heart failure, thrombosis, and superior vena cava*” has identified only 9 prior reports describing transudative chylothorax in 13 patients (Table 2). Including the 2 patients presented here, most (11/15) of the reported instances of transudative chylothorax have been ascribed to cirrhosis and to the nephrotic syndrome.

How the transudative effusion in these settings becomes chylous has been the subject of ample speculation and some specific investigation. Certainly, the conventional notion that chylothorax develops when the thoracic duct is obstructed fails to explain events in the 2 patients presented here. Alternately, several case reports and one series have suggested that translocation of chylous ascitic fluid across the diaphragm is the likely cause of chylothorax in the nephrotic syndrome and in cirrhosis [1, 2]. In each of these reports, radiolabeled tracers were injected into the abdominal cavity and subsequent migration to the thoracic cavity was detected. The mechanism for chylous ascites is unknown but possible explanations are malabsorption and bowel edema in the nephrotic syndrome [3] and elevated portal pressures along with degenerative changes in the lymphatics in cirrhosis.

With the 2 current patients included, cirrhosis is the most commonly reported etiology of transudative chylothorax, accounting for 40% (6/15) of reported cases. As with 20% of the 24 patients with chylothorax reported by Romero et al., our second patient had ascites. Though the ascites was not confirmed to also be chylous in this patient, chylous ascites frequently accompanies chylothorax, as in the series of 302 patients with both reported by Nix et al. [4]. Of note, Kinney et al. recently reported successful treatment of a chylous transudative pleural effusion with transjugular intrahepatic portosystemic shunt placement [5].

With our first patient included, heart failure has been implicated as the cause of 20% (3/15) of transudative chylothoraces. Postulated mechanisms of chylothorax in heart failure include increased lymph production due to high pulmonary venous pressures, decreased thoracic duct inflow due to elevated central venous pressure, and formation of lymphatic venous collaterals leaking into the pleural space and peritoneum [6–8]. Transudative chylothorax may respond to medical management of cardiomyopathy and congestive heart failure.

As in our first patient, amyloidosis may also be associated with transudative chylothorax. Baim et al. [9] have described a patient with rheumatoid arthritis, amyloidosis, and pleural effusions in which amyloid infiltration of the lymphatics

Table 2. Summary of available reports of transudative chylothorax

Reference/Year	Gender/Age	Diagnosis	Associated Diseases	Fluid Characteristics					Treatment	Outcome	
				Prot P/S	LDH P/S	TGP/S	CholP/S	Chylo			
Romero et al. 1998 (1)	M/64	Cirrhosis	None	0.47	0.42	15.4	0.56	+	NA	Death (hepatorenal syndrome)	
	F/70	Cirrhosis	Hepatocarcinoma	0.32	0.35	3.6	0.34	+	NA	Death (hepatorenal syndrome)	
	F/73	Cirrhosis	Atrial fibrillation	0.18	0.21	2.5	0.12	+	NA	Death (liver failure)	
	F/54	Cirrhosis	None	0.27	0.29	4.1	0.23	NA	NA	Death (upper GI bleed)	
Kinney et al. 2004 (5)	M/69	Cirrhosis	None	0.22	0.19	2.7	0.18	+	NA	Death (liver failure)	
	M/46	Cirrhosis	Hepatitis C	0.19	NA	fluid 585	NA	NA	TIPS	4.5 months follow-up successful	
Villena et al. 1995 (6)	F/84	CHF	Ischemic cardiomyopathy	0.38	fluid 89	fluid 262	fluid 52	NA	Diuretics, thoracen-tesis	Death (heart failure)	
Baim et al. 1979 (9)	M/59	Systemic amyloidosis	Rheumatoid arthritis, CHF	0.35	NA	fluid 300	fluid 54	NA	Diuretics, digitalis	Death (CHF?)	
Hanna et al. 1997 (15)	M/40mo	SVC thrombosis	Nephrotic syndrome	0	0.11	0.58	NA	NA	Anticoagulation	Resolution	
Moss et al. 1989 (2)	M/50	Nephrotic syndrome	None	0.42	0.8	Fluid 125	0.97	0.17	+	Thoracentesis	Resolved after 6 months, no follow-up available
Lindenbaum, 1968 (3)	F/61	Nephrotic syndrome	None	Fluid 0.06	NA	Fluid 127	Fluid 12	+	Diuresis, steroids	Death, renal vein thrombosis	
Shih-Hua et al. 2001 (16)	M/67	Nephrotic syndrome	None	Fluid 0.8	Fluid 150	Fluid 154	NA	+	Hemodialysis	Effusions resolved at 2 weeks	
Voudiclarì et al. 1994 (17)	F/37	Nephrotic syndrome	None	0.30	0.18	1.3	0.19	+	NA	NA	

CHF = congestive heart failure, NA = not available or not mentioned, GI = gastrointestinal, TIPS = transjugular, intrahepatic percutaneous shunt, SVC = superior vena cava, P/S = pleural/serum ratio.

was documented and implicated as the cause of chylothorax. Possible mechanisms of fluid accumulation within the pleural space include direct leakage out of intrathoracic lymphatics or movement of chylous ascites across the diaphragm.

Another recognized cause of chylothorax is superior vena caval thrombosis. Critical thrombosis at the confluence of the superior vena cava, brachiocephalic, and subclavian veins presumably leads to back pressure along the thoracic duct and its tributaries [10–14]. In the one reported case in which transudative chylothorax occurred in a patient with superior vena caval thrombosis and nephrotic syndrome, the chylothorax resolved following therapeutic anticoagulation [15].

In summary, the current report presents 2 patients with transudative chylothorax, which extends to 15 the number of cases described with this unusual type of pleural effusion. In the context that transudative chylothorax has been associated with only a few causes and that treatment may differ from that for exudative chylothoraces as well as for non-chylous transudates, clinicians' familiarity with this uncommon entity should enhance diagnostic acumen.

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