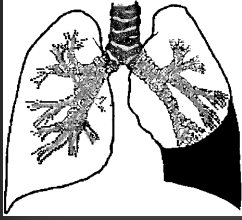


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Chylothorax

Etiology of Chylothorax

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Chylothorax represents an uncommon type of pleural effusion with distinctive features¹. It is defined by the presence of chyle in the pleural cavity, which is a type of lymphatic fluid enriched in lymphocytes (particularly T-lymphocytes), immunoglobulins, and lipids that are absorbed by the digestive tract. The thoracic duct transports the chyle from the *cisterna chyli* into the circulatory system, usually via the right jugular or subclavian veins². Between the *cisterna chyli* and the central venous system, the thoracic duct runs in close proximity to various anatomical structures including the esophagus, lungs, aorta, vertebrae and lymph nodes. Disease processes or mechanical injuries involving these structures may result in disruption and/or obstruction of the thoracic duct and/or its tributaries, resulting in leakage and accumulation of chylous fluid in the pleural cavity.

A recent retrospective observational study from the Mayo Clinic (203 patients over a 21-year period) suggests a change in the spectrum of causes for chylothorax compared to previous studies³. Traumatic injuries to the thoracic duct represented 50% of all causes of chylothorax compared to 25% in older studies²⁻⁴. Thoracic surgical procedures, particularly esophagectomy, represent the vast majority of these traumatic cases, although neck surgeries and complications associated with

percutaneous procedures, such as placement of central venous indwelling catheters or other devices (e.g. pacemaker), have also been described. By contrast, lymphomas, previously the most common cause, only account for 10% to 12% of all chylothoraces in recent studies^{3,4}. This may be due, in part, to earlier diagnosis of lymphoma and the availability of effective chemotherapy regimens that decrease the rate of complicating features, such as chylothorax. There are many unusual causes of chylothorax including cirrhosis, fungal infections, tuberculosis, sarcoidosis, congenital or acquired lymphatic malformations (lymphangiomas, lymphangiectasias, lymphangiomyomatosis, Noonan syndrome, yellow nail syndrome and Down syndrome), central venous thrombosis, chest radiotherapy, goiters, heart failure and constrictive pericarditis. Anecdotal cases of chylothorax have been described after seat-belt injuries from motor vehicle crashes, movements of neck hyperextension or even forceful sneezing and childbirth delivery. In approximately 5% of cases, a specific cause cannot be determined and the chylothorax is then labeled as idiopathic.

It should be emphasized that the diagnosis of chylothorax may not always be straightforward. The classical milky appearance of chylous effusions is only present in less than one-half of cases and is typically not seen when the patient is fasting or malnourished. In a recent study, the pleural fluid triglyceride level was <110 mg/dL in 15% of patients with chylothorax, and even <50 mg/dL in some cases⁴. Likewise, chylothorax can be transudative, as in cases associated with portal hypertension^{4,5}. Lipoprotein electrophoresis should be pursued when chylothorax is still suspected in the presence of atypical features. An accurate diagnosis will lead to more effective management strategies⁶.

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4. Maldonado F, et al. *Mayo Clin Proc* 2009; 84:129-133.
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Pleural Fluid Analysis in Chylothorax

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A chylothorax develops when the thoracic duct or one of its large tributaries ruptures allowing chyle to flow into the surrounding tissues. The thoracic duct travels from its origin in the *cisterna chyli* through the aortic hiatus of the diaphragm, at the level of the tenth thoracic vertebrae, to the right of the aorta. At the level of the fifth or sixth thoracic vertebrae, the duct enters the left posterior mediastinum and eventually joins the venous circulation at the juncture of the left subclavian and internal jugular veins. Therefore, rupture of the thoracic duct below T5 to T6 results in a right-sided chylothorax, whereas injury to the duct above this level results in a left chylothorax.

Chylothorax is an uncommon (~2% incidence) cause of pleural effusion. On pleural fluid analysis, the fluid is white and opaque if fat is present; however, the fluid can be clear yellow in the neonate who has not yet ingested milk, serous in the adult who has not eaten for 12 hours, or hemorrhagic if trauma is involved. The supernatant of a chylothorax fails to clear following centrifugation. T lymphocytes are the primary cells in chyle, typically representing >80% of the cellular population¹. The total nucleated cell count ranges from 400 to 6,800 cells/ μ L. Chyle is typically a protein discordant exudate (i.e., an effusion with a pleural fluid to serum protein ratio >0.5 and pleural LDH concentration less than two-thirds of the upper limit of the normal serum LDH value) with pleural fluid protein ranging from 2.2 to 5.9 g/dL^{1,2}. Since chyle is non-inflammatory, the LDH is in the normal range, virtually always <268 IU/L. The electrolytes in chyle are similar to plasma. Chylous fluid has been reported to have a pH ranging from 7.40 to 7.80 and a glucose concentration of 78-200 mg/dL^{1,2}. Measurement of the pleural fluid to serum glucose ratio assists in differentiating a chylous effusion (ratio <1.0) from pleural fluid attributable to the extra-vascular migration of a central venous catheter in patients receiving total

parenteral nutrition, which contains lipids and glucose (ratio >1.0)³.

The diagnosis of a chylothorax is suspected when the fluid is milky. However, this appearance can also be observed with a cholesterol effusion. Cholesterol effusions have a different pathogenesis, clinical presentation, and pleural fluid characteristics. They represent a form of lung entrapment with an active pleural process, and are neutrophilic, concordant exudates with a cholesterol level of >250 mg/dL (range 300-1500 mg/dL) and a cholesterol/triglyceride ratio >1.0². In addition to chylothorax the two other protein discordant exudates are sarcoidosis and yellow-nail syndrome.

The diagnosis of chylothorax is highly likely if the triglyceride level in the pleural fluid is >110 mg/dL and highly unlikely if the pleural fluid triglyceride level is <50 mg/dL¹. The presence of chylomicrons confirms the diagnosis. However, the patient who is fasting may have low triglyceride levels and chylomicrons may not be detected.

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Imaging of Chylothorax

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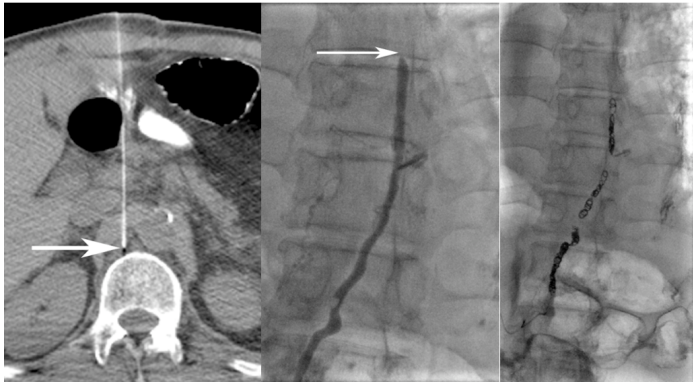
Traditionally, two imaging techniques for visualization of the lymphatic vessels have been applied: conventional lymphangiography and lymphangioscintigraphy. Injection of an oil-based contrast iodine agent directly into a lymphatic vessel at a distal extremity enables visualization of the lymph ducts after 24 hours using radiography (conventional lymphangiography). Injection of ^{99m}Tc labeled sulfur colloid or albumin intradermally at a distal extremity leads to clearance of the tracer into the lymphatic vessels and enables visualization of the

lymph ducts using a Gamma camera with serial images taken at 5 min intervals post-injection for 45–60 min (lymphangioscintigraphy). The disadvantages of conventional lymphangiography and lymphoscintigraphy, namely invasiveness and patient discomfort, combined with advances in imaging technology and contrast media development, has prompted a search for better lymphatic imaging using CT, PET, US, and MRI. However, these newer techniques are focused on lymph node detection and evaluation rather than on anatomical imaging of the thoracic duct. In analogy to indirect lymphoscintigraphy, indirect MR lymphangiography can be performed by injecting gadolinium based contrast agents intradermally or subcutaneously at a distal extremity, but experience is limited to animal studies and this technique has not yet been used routinely. Fluid-sensitive sequences such as half-Fourier single-shot turbo spin-echo (HASTE) sequences may also be used for visualization of the *cisterna chyli* and the thoracic duct without need for gadolinium based contrast agents. However, spatial resolution of these techniques is limited compared to conventional lymphangiography.

Treatment of chylothorax due to thoracic duct injuries can be performed with chest tube drainage and maintenance of a low-fat diet. However, high output chylothorax may not respond to conservative management and may require intervention. Traditionally, surgical thoracic duct ligation has been performed. More recently, percutaneous imaging guided access to the thoracic duct allows for less invasive treatment modalities. Thus, access to the *cisterna chyli* may be obtained under fluoroscopy after bilateral pedal conventional lymphangiography to opacify the thoracic duct or under CT guidance without need for conventional lymphangiography¹⁻⁴. CT guided percutaneous transabdominal puncture, catheterization of the *cisterna chyli* and injection of water-soluble iodine contrast allows for diagnosis and treatment of thoracic duct injuries. If catheterization and embolization fails, needle disruption of the *cisterna chyli* can be performed to create a controlled leak which may divert lymph flow from the damaged thoracic duct to collaterals. However, disruption may be less successful than embolization^{5,6}.

An illustrative case is that of a 68-year-old male patient with persistent chylothorax after an esophagectomy due to esophageal cancer. A

percutaneous CT guided access to the *cisterna chyli* with a 21-gauge needle was performed (*left, arrow*).



Fluoroscopy, after injection of water-soluble iodine contrast agent into the *cisterna chyli*, showed the thoracic duct abruptly ending at the T8-T9 level (*middle, arrow*). Utilizing the Seldinger technique, a microcatheter was advanced over a hydrophilic guidewire into the thoracic duct, which was embolized with multiple radiopaque micro coils (*right*).

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4. van Goor A, et al. Head Neck 2007; 29:1017-1023.
5. Cope C, et al. J Vasc Interv Radiol 2002; 13:1139-1148.
6. Boffa D, et al. Eur J Cardiothorac Surg 2008; 33:435-439.



Surgical Management of Chylothorax

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Regardless of its etiology, chylothorax represents a difficult problem that is potentially life-threatening if not dealt with promptly. A persistent high output drainage of chyle is associated with malnutrition and immunosuppression and consequent poor long-term outcomes.

The management of chylothorax is dependent upon both the etiology as well as its duration and degree. Conservative management with dietary restriction of fat and intravenous hyperalimentation may be appropriate for low output chylothoraces (<1L/day). The administration of octreotide may also be of some benefit. On the other hand, persistent high output chylothoraces typically cannot be managed with conservative measures and may require some form of intervention, each being tailored to the particular clinical situation at hand. Interventions may include surgical pleurodesis/pleurectomy, operative thoracic duct ligation and/or percutaneous access to the thoracic duct to either fenestrate or embolize it¹.

Primary thoracic duct ligation, with or without pleurodesis, is the ideal intervention for postoperative patients who have iatrogenic thoracic duct injury. Operative intervention for chylothorax should be contemplated when persistent chest tube output is greater than 1L/day². Further delay will only worsen the metabolic and immunologic derangements from persistent chyle leak and may delay recovery. In centers where percutaneous embolization of the thoracic duct is routinely performed, radiological techniques may supplant initial operative intervention.

Surgical ligation of the thoracic duct requires knowledge of its anatomy. The duct originates at the *cisterna chyli* in the abdomen and enters the chest at the aortic hiatus anterior to the vertebral bodies and posterior to the aorta. It then ascends in the right chest along the anterior surface of the vertebral bodies between the aorta and azygous vein. It finally crosses over to the left side at the carina and drains into the junction of the left jugular and subclavian veins. However, numerous variants exist. Injury of the thoracic duct at any location along its course can lead to chylothorax. Since successful surgical ligation requires identification of the proximal thoracic duct in the right chest, orally administering cream 24 hours prior to surgical exploration often aids in this procedure². If identification is not possible, then mass ligation of all tissues anterior to the esophagus and between the aorta and azygous vein should be performed. Thoracic duct or mass ligation, using sutures or clips, can be performed through a low right thoracotomy (7th interspace), as well as by video-assisted techniques (VATS).

Additionally, chemical pleurodesis with talc or pleurectomy can be performed to facilitate pleural symphysis. Our practice has been to use these measures as adjuncts to thoracic duct ligation for high output chylothoraces in the post-surgical setting². Primary chemical pleurodesis, performed either at the bedside through a chest tube or via VATS, can be effective in sealing persistently low output chylothoraces, such as those caused by lymphoma or other malignancies, in combination with conservative measures as previously outlined.

In summary, chylothorax arises from a variety of etiologies. Prompt diagnosis and treatment is required to prevent life threatening malnutrition and immunosuppression. Low output chylothorax can often be managed with conservative measures, whereas high output chylothorax requires either surgical intervention or radiological techniques.

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PLEURAL IMAGES

Chylothorax due to Retrosternal Goiter

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Pilar Vicente de Vera MD

Adela Saco MD

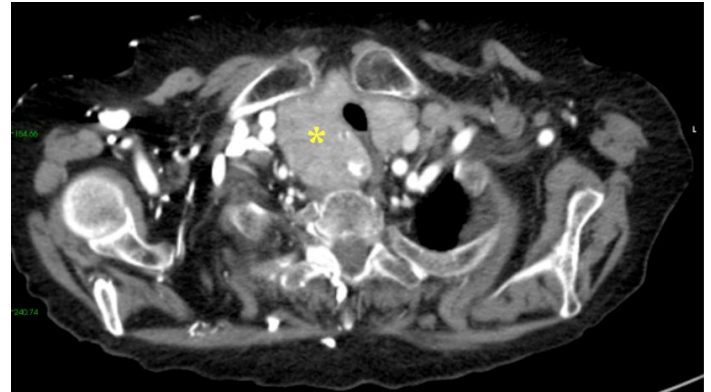
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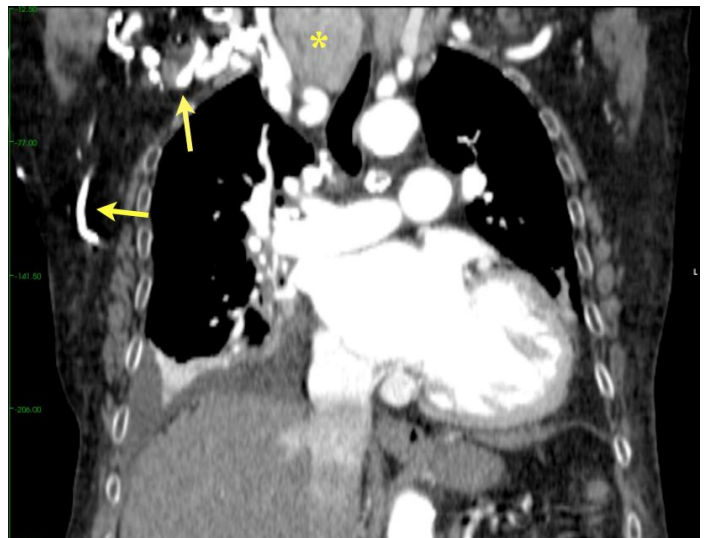
An 86-year-old woman was evaluated for progressive dyspnea. Upon examination she was found to have decreased breath sounds at the right lung base and mild pedal edema. A chest radiograph disclosed an enlarged cardiac silhouette and a right-sided pleural effusion. An echocardiogram demonstrated an ejection fraction of 35%.

Since the pleural effusion did not disappear with diuretics within a few days, a diagnostic thoracentesis was performed. The pleural fluid was milky and its analysis showed: erythrocytes 2,000/ μ L, leukocytes

250/ μ L with 92% lymphocytes, total protein 2.5 g/dL (serum 6.3 g/dL), lactate dehydrogenase 106 IU/L (serum 325 U/L), pH 7.53, adenosine deaminase 13.8 IU/L, triglycerides 340 mg/dL, cholesterol 20 mg/dL, negative cultures and no malignant cells on the cytological smear. The thyroid-stimulating hormone level was lower than 0.01 μ U/mL and the free thyroxine (T₄) level was 57 ng/dL.



The chest CT showed a large retrosternal multinodular goiter (*Figures, asterisk*) with mass effect on large vessels (e.g., brachiocephalic veins) and thoracic lymphatics as noted by the presence of right-sided venous distension on the chest wall (*Figure below, arrows*) and pleural effusion.



The symptoms were partially relieved by a therapeutic thoracentesis of 500 mL. Due to the patient's age and comorbidities, goiter surgery was not a consideration. The patient passed away two weeks after hospital discharge.