Respiratory Medicine 157 (2019) 7–13

Contents lists available at ScienceDirect

Respiratory Medicine

journal homepage: www.elsevier.com/locate/rmed

Review article

Clinical approach and review of causes of a chylothorax

Leonard E. Riley, Ali Ataya*

University of Florida College of Medicine, Division of Pulmonary, Critical Care, and Sleep Medicine, Gainesville, FL, USA

ARTICLE INFO

Keywords:
Chylothorax
Chylous effusion
Pseudochylothorax
Pleural effusion

ABSTRACT

A chylothorax, also known as chylous pleural effusion, is an uncommon cause of pleural effusion with a wide differential diagnosis characterized by the accumulation of bacteriostatic chyle in the pleural space. The pleural fluid will have either or both triglycerides > 110 mg/dL and the presence of chylomicrons. It may be encountered following a surgical intervention, usually in the chest, or underlying disease process. Management of a chylothorax requires a multidisciplinary approach employing medical therapy and possibly surgical intervention for post-operative patients and patients who have failed medical therapy. In this review, we aim to discuss the anatomy, fluid characteristics, etiology, and approach to the diagnosis of a chylothorax.

1. Introduction

A chylothorax, also known as chylous pleural effusion, is an uncommon cause of pleural effusion with a wide differential diagnosis characterized by the accumulation of bacteriostatic chyle in the pleural space. In this review, we aim to discuss the anatomy, fluid characteristics, etiology, and approach to the diagnosis of a chylothorax.

2. Definitions

A chylothorax is caused by the extravasation of chyle into the pleural space due to obstruction or injury to the thoracic duct or its tributaries or transdiaphragmatic flow from the peritoneal cavity [1–3]. The pleural fluid is often milky in appearance and is characterized by elevated triglycerides > 110 mg/dL or the presence of chylomicrons [1,4]. Another cause of milky appearing pleural effusion is a pseudochylothorax, also known as a cholesterol effusion and chyliform effusion, which is a cholesterol-rich fluid associated with chronic inflammatory disorders [5,6]. The clinical definition of a pseudochylothorax is the combination of a milky pleural effusion, pleural cholesterol level greater than 200 mg/dL, pleural triglyceride level typically below 110 mg/dL, a pleural cholesterol/triglyceride ratio of greater than one, and often the presence of cholesterol crystals seen on microscopy [5,7,8].

3. Anatomy

The thoracic duct carries chyle from the chest and has a variable anatomy. Classically, the thoracic duct originates from the abdomen at the cisterna chyli at the level of the second or third lumbar vertebra [2,9]. It ascends through the posterior mediastinum on the left-side of the azygous vein, right-side of the descending thoracic aorta, and posterior to the esophagus [2,9]. The thoracic duct then crosses to the left of the esophagus at the level of the fifth or sixth thoracic vertebra [2]. It continues upward posterior to the aortic arch and ends at the junction of the left jugular vein [2,9]. This description represents the most common route, with a multitude of anatomical variations reported in the literature. Up to 40% of patients will have a multiple channels through the mediastinum, 6% do not cross vertebra and ultimately drain into the right-sided venous system, and the majority of variations occur with the lymphovenous connection with either drainage into the internal jugular vein, jugulovenous angle, subclavian vein, or multiple entry points [10]. The underlying anatomy of the thoracic duct and its tributaries not only derive clinical significance with creating a differential, but also with performing cannulation for a lymphangiogram.

4. Chylothorax characteristics

4.1. Patient characteristics

A chylothorax is suspected clinically when milky fluid (Fig. 1) is collected from the pleural space; however, this “classical” appearance is reported to occur in 22–44% of patients that ultimately met diagnostic criteria [1,11]. This highlights the importance of including a chylothorax in the differential when reviewing clinical history and associated findings. The effusion occurs in a unilateral pattern in 84% of

* Corresponding author. University of Florida, Division of Pulmonary, Critical Care and Sleep Medicine. 1600 SW Archer Rd, M452, PO Box 100225, Gainesville, FL, 32610, USA.
E-mail address: AliAtaya@gmail.com (A. Ataya).

https://doi.org/10.1016/j.rmed.2019.08.014
Received 18 December 2018; Received in revised form 12 August 2019; Accepted 20 August 2019
Available online 22 August 2019
0954-6111/

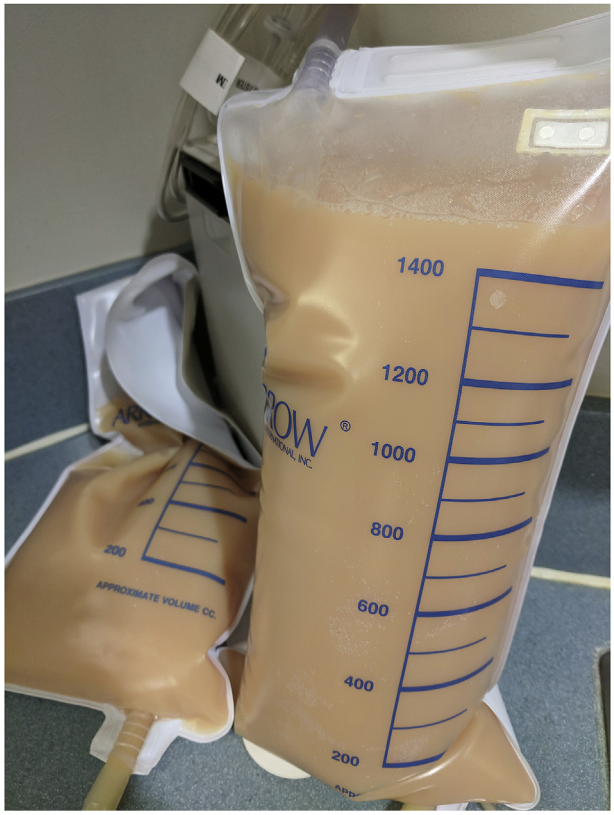

Fig. 1. Chylous pleural fluid with a milky appearance.

cases with 50–60% of all cases occurring on the right-side [1,6]. Patients may be asymptomatic or describe symptoms similar to other forms of pleural effusions, such as dyspnea and nonproductive cough. High fever and pleurisy are uncommon symptoms because chyle does not irritate the pleural surface [12,13].

4.2. Pleural fluid analysis

A chylothorax has been defined as fluid with either or both triglycerides > 110 mg/dL and the presence of chylomicrons, which are considered the gold standard for diagnosis [1,3,4,6]. Maldonado et al. found in a review of 103 adults at a single center with a chylothorax, the mean ± standard deviation triglyceride value was 728 ± 797 mg/dL and cholesterol value 66 ± 30 mg/dL [11]. Chyle is reported to have a protein concentration of 2–3 g/dL in humans [2]. It may be assumed that a chylothorax would reflect this and be either a transudative or LDH-discordant exudative effusion; however, Agrawal et al. found 22 chylothoraces with a variety of pleural fluid patterns [1]. A discordant pleural effusion is an effusion that meets exudative criteria by either LDH or protein but not both [1]. When categorized by transudative, protein-discordant exudative, LDH-discordant exudative, or concordant exudative effusion they found that lymphocyte-predominant protein-discordant exudative effusions resulted in a group where no alternative cause other than leakage of chyle into the pleural space could be found [1]. This pattern of an elevated protein concentration was attributed to water and solute reabsorption reported after analyzing the fluid properties of an excised chylous mesenteric cyst [1,14]. It was also postulated that chylous effusions do not meet exudative criteria by LDH due to its low circulating concentration in chyle and its larger molecule size, which does not readily extravasate out of the capillaries [1]. When the pleural fluid is not a lymphocyte-predominant protein-discordant exudative pattern it suggests a concomitant etiology for the effusion [1]. The milky fluid appearance occurs in 22–44% of patients, and in a review of 74 patients, the median triglyceride level was significantly higher in milky effusions (822 mg/dL) compared to nonmilky effusions (241 mg/d) [1,11]. The nonmilky appearance and lower triglyceride content are attributed to poor nutritional status or surgical trauma; nonetheless, gross appearance does not correlate with any specific cause except bloody effusions following surgery [11].

Table 1
Traumatic etiologies of chylothorax.

Surgical	Non-surgical
Esophageal surgery	Thoracic radiation
Congenital heart surgery	Seat bell
Mediastinal lymph node dissection	Childbirth
Lobectomy	Stretching
Pneumonectomy	Blunt trauma
Lung transplant	Sneezing
Tracheal resection	Vomiting
Cardiovascular surgery	Thoracolumbosacral orthosis
Aorta surgery	
Neck surgery	
Thymectomy	
Thyroidectomy	
Sympathectomy	
Laparscopic gastric banding	
Diaphragmatic hernia repair	
Spine surgery	
Simple nephrectomy	
Radical nephrectomy	
Pacemaker implantation	
Thoracic duct embolization	
Tube thoracostomy	
Endoscopic ultrasound with fine needle aspiration	
Central venous catheterization	

5. Etiology

5.1. Traumatic causes

Traumatic causes have been described for about 50% of chylous effusions and may be further narrowed into surgical and nonsurgical etiologies [15,16]. Surgical and medical interventions involving the lungs, trachea, mediastinum, cardiovascular, aorta, neck, esophagus, diaphragm, stomach, and vertebral bodies have been reported to lead to a chylothorax [17–40]. (Table 1) The two most common surgical causes associated with a chylothorax are esophagectomy and corrective procedures for congenital heart disease [15]. Non-surgical trauma to the chest or increased intra-abdominal pressures may also lead to a chylothorax, such as blunt trauma, childbirth, stretching, sneezing, vomiting, seat belts, and thoracolumbosacral orthosis [41–47] (Table 1).

5.2. Non-traumatic causes

5.2.1. Malignant

Non-traumatic causes are reported to comprise between 39% and 72% of all chylothoraces, with the majority as a result of malignant etiologies accounting for 17%–46% of all cases [11,15,48]. Lymphoproliferative malignancies, specifically lymphoma, are the bulk at approximately 61%; however, multiple other hematologic and solid tumors have been associated with it [15,48–51]. (Table 2).

5.2.2. Lymphatic disorders

Lymphatic anomalies and diseases, such as lymphangioleiomyomatosis, pulmonary lymphangiectasia, and lymphangiomas have also been associated with chylous effusions. Lymphangioleiomyomatosis (LAM) is the proliferation of abnormal smooth muscle cells “LAM cells” in association with the tuberous sclerosis complex mutations, which primarily affects women of childbearing age [52]. Computed

Table 2
Non-traumatic etiologies of chylothorax.

Malignancy	Lymphatic disorder	Miscellaneous
Lymphomatous	Lymphangioleiomyomatosis	SVC thrombosis
Leukemia	Lymphangiectasis	Fibrosing mediastinitis
Lung cancer	Lymphangioma	Yellow nail syndrome
Mediastinal	Lymphangiomatosis	Gorham-Stout syndrome
Kaposi sarcoma		Sarcoidosis
Myeloma		
Infectious		**Chylous ascites**
Tuberculosis		Cirrhosis
Filariasis		Nephrotic syndrome
		Congestive heart failure

tomography (CT) of the chest classically demonstrates diffuse thin-walled cysts surrounded by normal lung parenchyma with an estimated 10.1% of people with LAM having a chylothorax [53,54].

Pulmonary lymphangiectasia, also known as congenital pulmonary lymphangiectasia, primary pulmonary lymphangiectasia, or pulmonary cystic lymphangiectasis, is a rare disease characterized by the presence of pathologically dilated lymphatic vessels [55,56]. This may be the result of a pulmonary lymphatic developmental anomaly, generalized lymphatic abnormality, or acquired etiology from surgery, radiation, infection, tumor, or trauma [55,56].

Lymphangiomas are the focal proliferation of lymphatic tissue presenting as multicystic or sponge-like accumulations [56]. Lymphangiomatosis is the presence of multiple lymphangiomas, which are due to lymphatic developmental abnormalities and the majority of cases present by 20 years of age [56]. Lymphangiomas may present as mediastinal, pulmonary, or chest wall lesions that can lead to chylous effusions [56].

Yellow nail syndrome is a rare disease that is classically characterized by yellow nails, lymphedema, and respiratory manifestations with a median age of 60 years [57,58]. Respiratory disease includes pleural effusions (46%), bronchiectasis (44%), chronic sinusitis (41%), and recurrent pneumonias (22%) [57]. When pleural effusions are present, they are predominantly bilateral (72%) and less commonly unilateral right-sided (15.2%) or left-sided (12.8%) [58]. However, only approximately 12.1%–30% of all presenting effusions are chylous [57,58]. The exact pathophysiology of yellow nail syndrome is unclear, but is thought to be a lymphatic transport failure, which can be hereditary or acquired [58–60].

Gorham-Stout syndrome also known as Gorham's disease, phantom bone disease, and vanishing bone syndrome is a rare entity characterized by destruction and absorption of bone [61,62]. This is thought to be due to massive osteolysis with enhanced activity and number of osteoclasts, vascular malformations, and proliferation of lymphatic channels [62,63]. Several bones may be involved including, extremities, spine, pelvis, and the skull [61]. When the disease extends into the chest and most commonly thoracic duct occlusion, a chylothorax may develop, which has been reported in up to 17% of cases [64,65].

5.2.3. Chylous ascites and intraabdominal causes

The presence of concomitant chylous ascites and pleural effusion may be due to a systemic disorder or a primary abdominal process. Similar to other disorders with both pleural and peritoneal fluid collections, chylous pleural effusions are thought to accumulate secondary to transdiaphragmatic fluid migration or thoracic duct obstruction from increased portal venous pressure [1,66]. Liver cirrhosis, nephrotic syndrome, congestive heart failure, infections, surgical, malignancy, lymphatic disorders, and post-surgical scarring have all been reported to occur [1,3,56,66–70]. Pleural fluid characteristics are similar to ascitic fluid analysis [1].

5.2.4. Sarcoidosis

A pleural effusion occurs in approximately 3% of all cases of sarcoidosis, and cases of chylous effusions have been reported [71,72]. A chylothorax with sarcoidosis has been attributed to occlusion of the thoracic duct or abdominal lymphatic duct by lymphadenopathy [71–73].

5.2.5. Infections

Infections may also lead to chylous effusions with *Mycobacterium tuberculosis* described most commonly and in several cases of immune reconstitution syndrome [74,75]. A chylothorax has also been reported with hepatitis A, paragonimiasis, and paracoccidioidomycosis [76–78].

6. Diagnostic approach

6.1. Pleural fluid analysis

Clinical suspicion for a chylothorax may be presumed after identifying a milky appearing fluid on thoracentesis or if the clinical history is consistent with a possible etiology for a chylothorax (Tables 1 and 2). Initial studies should include a serum and pleural fluid triglyceride levels (Fig. 2). If the pleural fluid triglyceride level is $>$ 110 mg/dL then a chylothorax is highly suspected [1,4]. However, if triglycerides are $<$ 110 mg/dL and the clinical history or pleural effusion appearance are consistent with a possible etiology of chylothorax, then a pleural chylomicron study can be performed. The presence of pleural chylomicrons confirms the diagnosis of a chylothorax, and their absence suggests an alternative etiology. Once a chylothorax is confirmed, the pleural fluid characteristics may further elucidate the cause. Agrawal et al. reviewed analysis of 22 chylothoraces and found a chylothorax may present with a variety of pleural fluid patterns, but in the setting of a lymphocyte-predominant protein-discordant exudate, there no other underlying etiologies. (1) However, if the pleural fluid pattern was not a lymphocyte-predominant protein-discordant exudate, then further investigation into contributing effusion etiologies should be investigated (1).

6.2. Imaging

Chest radiography has limited utility identifying specific etiologies of a chylothorax, with the exception of traumatic etiologies. CT of the chest, abdomen, and pelvis may narrow the differential by identifying sites of traumatic injuries to the lymphatic system, compressive mediastinal or abdominal lymphadenopathy, ascites, or malignant lesions. Lymphangiography, lymphoscintigraphy, and magnetic resonance (MR) lymphangiography are alternative imaging techniques to visualize the lymphatic system and selection of each modality is patient individualized.

Lymphangiography, also known as lymphography, is the cornerstone of lymphatic vessel and lymph node imaging [79]. It utilizes the injection of a poppyseed based oil (e.g. Lipiodol) into the lymphatic vessel of the foot or ankle, and then the flow of contrast is followed to the thoracic duct by fluoroscopy [79]. The thoracic duct is then evaluated by conventional radiography or CT [79]. In a retrospective review, Alejandre-Lafont et al. found 79% of patients with a chylothorax, chylous ascites, lymphocele, and lymphatic fistula that underwent lymphangiography had the leak detected [80]. They also found that lymphaniograms were associated with occlusion of the leak in 70% of patients with output of $<$ 500 mL/day and 35% of patients with $>$ 500 mL/day; overall a 51% success, which did not depend on cause of duct damage or time between injury and intervention [80] Lymphangiography may be complicated by oil embolization, lipoid pneumonia, wound infection, pulmonary edema, and urticaria at the site of cannulation [81–83]. However, the incidence of complications are directly related to the amount of injected contrast, which should not exceed a total volume of 14 mL [79,84].

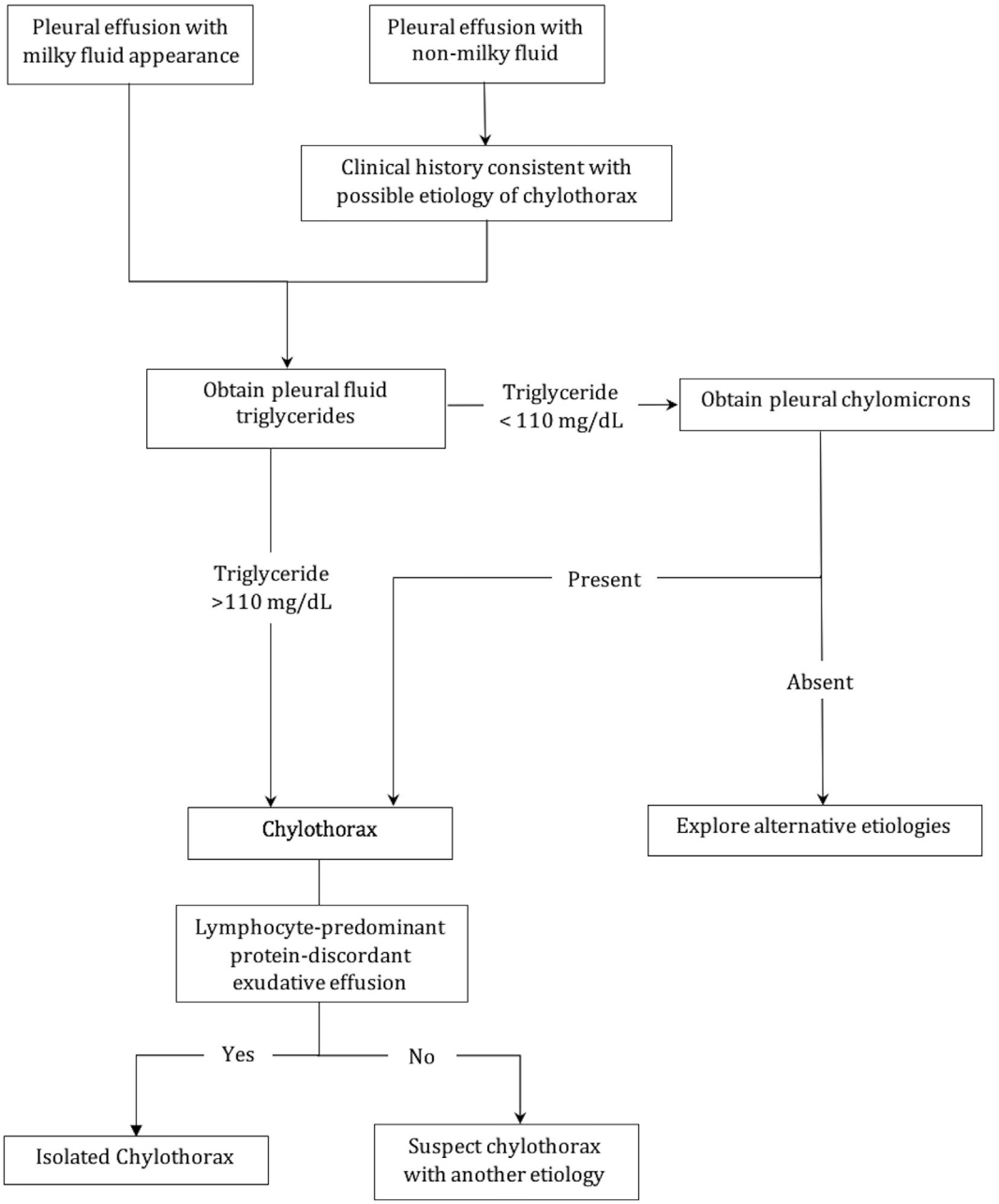

Fig. 2. Chylothorax diagnostic algorithm.

Lymphoscintigraphy uses the subcutaneous injection of water-soluble radiotracer (Technetium-99 albumin solution), which is absorbed into the lymphatic capillaries and carried throughout the lymphatic circulation [85]. The radiotracer is then imaged using CT and single-photon emission computer tomography (SPECT/CT). Lymphoscintigraphy poorly visualizes small vessel leaks, morphologic details, and leaks into free third-spaces due to the water-soluble nature of the radiotracer; however, it has been successfully employed to identify the lymphatic leak leading to a chylothorax [85–88].

Noncontrasted MR lymphangiography has also been used to identify a central lymphatic vessels and chyle leaks related to LAM, non-Hodgkin's lymphoma, trauma, and lymphangiomas [89,90]. Benefits of MR lymphangiography include high spatial resolution, production of 3D imaging, perioperative planning, and no exposure to radiation [89]. On the other hand, MR lymphangiography may be cost prohibitive or not available at some centers [79].

7. Management

Currently, there are no official, evidence-based guidelines for the management of a chylothorax. Our approach to management of a chylothorax is first delineated by chest tube output (Fig. 3). When chest tube output is ≥ 1100 mL over any 24 h, ≥1 L/day for more than five days, or ≥2 L after two days of optimal conservative therapy, operative therapy should be considered [2,91,92]. For chylothoraces with chest tube output volumes less than this, medical therapy with pleural fluid drainage, dietary modification, and initiation of a somatostatin analogue may be considered.

We recommend pleural drainage via tube thoracostomy or indwelling catheter, which provides symptom relief and a way to quantify the accumulation of pleural fluid. Intermittent thoracentesis is an alternative strategy for pleural drainage in patients not suspected to have rapid reaccumulation of fluid, patient preference, or poor prognosis.

Chyle is made up of triglycerides (e.g. neutral fat, free fatty acids,

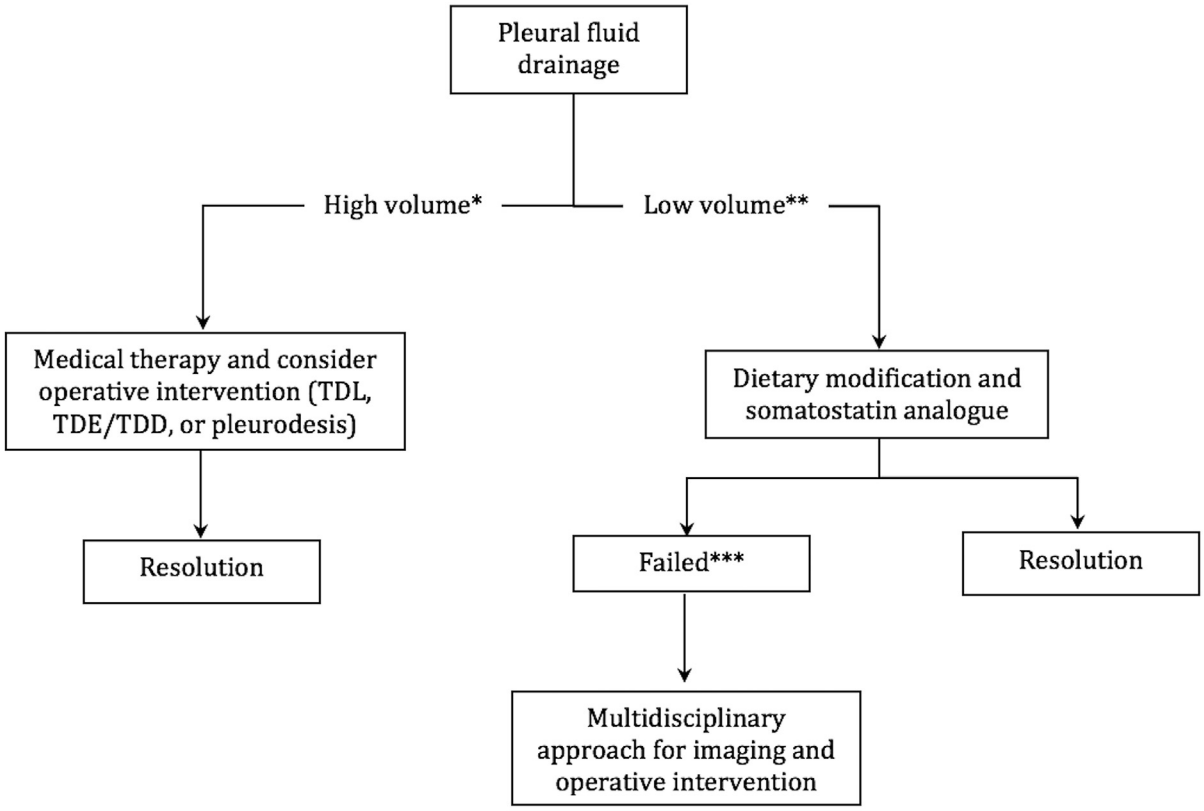

Figure 3 Legend

*High volume is defined as: chest tube output is ≥1,100 mL over any 24 hours, ≥1L/day for more than five days, or ≥2 L after two days of optimal conservative therapy

**Low volume is defined as: <1, 100mL over any 24 hours, <1L/day for more than five days, or <2 L after 48 hours

***Failure is defined as: daily loss of >10 mL/kg at day five post-operatively, >2 weeks of chest tube output, or rapidly declining nutritional status.

Fig. 3. Chylothorax management algorithm.

phospholipids, and cholesterol), protein, electrolytes, cellular elements, and micronutrients [93]. Long-chain triglycerides are taken up in the mucosal membrane of intestinal lacteals and the thoracic duct; whereas, absorption of medium-chain triglycerides occurs through the portal vein bypassing the lymphatic system [93–96]. Using medium-chain triglycerides and avoiding long-chain triglycerides, leads to decreased lymphatic flow and subsequently decreased chylous effusion accumulation [94,96,97]. Individuals with a chylothorax should receive a high-protein, low-fat diet (< 10 g fat/day). Oral feeding should be provided when possible, but total parental nutrition (TPN) is an alternative route for those who have failed oral intake or concern for inadequate oral intake [93]. A fat-free diet (< 5 kcal fat/serving) is an another option, although it is unpalatable and challenging to maintain [93,97]. If there is a concern for developing a fatty acid deficiency, then a 500 mL of 10% lipid emulsion or 250 mL of a 20% emulsion, three times per weekly can be administered [93].

Somatostatin and octreotide, a synthetic somatostatin analogue, bind to somatostatin receptors and reduces chyle production, lymph flow, and intestinal fat absorption [98,99]. It has been used effectively in conjunction with diet modification to reduce the accumulation of a chylothorax and prevent surgical intervention [100]. Continuous infusion (6 mg/day) or subcutaneous injection (50 or 100 μg every 8 h) preparations have been successfully used [101–103].

Patients who have a daily loss of > 10 mL/kg at day five post-operatively, > 2 weeks of chest tube output, or rapidly declining nutritional status are considered to have failed medical therapy, and therefore should consider interventions including thoracic duct ligation (TDL), thoracic duct embolization or disruption (TDE/TDD), and medical or surgical pleurodesis [104,105]. TDL is done by open thoracotomy or video-assisted thoracoscopy and has a 95% success rate for postoperative chylothoraces [106]. TDE is performed by injecting contrast into the thoracic duct to find the leak and sealing it with embolized coils and glue; whereas, TDD is performed by macerating the thoracic duct with multiple needle passes under fluoroscopy [107]. Pamarthi et al. had a 72% clinical success rate with TDE and 55% clinical success rate with TDD [107]. Pleurodesis has an 80%–100% success rate in both postoperative chyle leaks and nonsurgical chylothoraces [106]. The decision to employ either TDL, TDE/TDD, pleurodesis, or a combination of these therapies should be done with a multidisciplinary approach focused on the underlying pathology, patient prognosis, and patient preference.

8. Conclusion

The presence of a chylothorax is a lesser common pleural effusion with a broad differential centering around impaired lymphatic drainage generally due to trauma, malignancy, or lymphatic disorders(Tables 1 and 2). The pleural fluid will have either or both triglycerides >

110 mg/dL and the presence of chylomicrons [1,4]. Reviewing the pleural fluid pattern and those patients without a lymphocyte-predominant protein-discordant exudate, may also suggest another underlying etiology of the effusion. Management of a chylothorax requires a multidisciplinary approach employing medical therapy and possibly surgical intervention for post-operative patients and patients who have failed medical therapy.

Conflicts of interest

None.

Disclosures

None.

References

[1] V. Agrawal, P. Doelken, S.A. Sahn, Pleural fluid analysis in chylous pleural effusion, Chest 133 (6) (2008) 1436–1441.
[2] M.B. A, W.D. C, O.s.G. C, Chylothorax, BJS 84 (1) (1997) 15–20.
[3] V. Skouras, I. Kalomenidis, Chylothorax: diagnostic approach, Curr. Opin. Pulm. Med. 16 (4) (2010) 387–393.
[4] B. Staats, R. Ellefson, L. Budahn, D. Dines, U. Parkash, K. Offord, The lipoprotein profile of chylous and nonchylous pleural effusions, Mayo Clin. Proc. 55 (11) (1980) 700–704.
[5] A. Lama, L. Ferreiro, M.E. Toubes, A. Golpe, F. Gude, J.M. Álvarez-Dobaño, F.J. González-Barcala, E. San José, N. Rodríguez-Núñez, C. Rábade, C. Rodríguez-García, L. Valdés, Characteristics of patients with pseudochylothorax—a systematic review, J. Thorac. Dis. 8 (8) (2016) 2093–2101.
[6] J.T. Huggins, Chylothorax and cholesterol pleural effusion, Semin. Respir. Crit. Care Med. 31 (06) (2010) 743–750.
[7] V. Agrawal, S.A. Sahn, Lipid pleural effusions, Am. J. Med. Sci. 335 (1) (2008) 16–20.
[8] S. CS, L. RW, Chylothorax and pseudochylothorax, Clin. Chest Med. 6 (1985) 163–174.
[9] M. Kiyonaga, H. Mori, S. Matsumoto, Y. Yamada, M. Sai, F. Okada, Thoracic duct and cisterna chyli: evaluation with multidetector row CT, Br. J. Radiol. 85 (1016) (2012) 1052–1058.
[10] P. K, B. M, P. A, W. J, Review of thoracic duct anatomical variations and clinical implications, Clin. Anat. 27 (4) (2014) 637–644.
[11] F. Maldonado, F.J. Hawkins, C.E. Daniels, C.H. Doerr, P.A. Decker, J.H. Ryu, Pleural fluid characteristics of chylothorax, Mayo Clin. Proc. 84 (2) (2009) 129–133.
[12] R. Light, Y.C. Lee, Pleural Diseases, third ed., Williams and Wilkins, Baltimore, 1995.
[13] S. Romero, Nontraumatic chylothorax, Curr. Opin. Pulm. Med. 6 (4) (2000) 287–291.
[14] K.M.W. Keough, M. Hawco, S. Acharya, D.A. Malatjalian, W. Snedden, A. Kwan, J.A. Barrowman, A chylous mesenteric cyst and a study of its contents, Dig. Dis. Sci. 24 (10) (1979) 797–801.
[15] C.H. Doerr, M.S. Allen, F.C. Nichols, J.H. Ryu, Etiology of chylothorax in 203 patients, Mayo Clin. Proc. 80 (7) (2005) 867–870.
[16] C. Hooper, Y.C.G. Lee, N. Maskell, Investigation of a unilateral pleural effusion in adults: British Thoracic Society pleural disease guideline 2010, Thorax 65 (Suppl 2) (2010) ii4–ii17.
[17] H.J. Cho, D.K. Kim, G.D. Lee, H.J. Sim, S.H. Choi, H.R. Kim, Y.-H. Kim, S.-I. Park, Chylothorax complicating pulmonary resection for lung cancer: effective management and pleurodesis, Ann. Thorac. Surg. 97 (2) (2014) 408–413.
[18] S.J. Lonie, S. Ch'ng, N.Z. Alam, G.M. Wright, Minimally invasive tracheal resection: cervical approach plus video-assisted thoracoscopic surgery, Ann. Thorac. Surg. 100 (6) (2015) 2336–2339.
[19] M. Milonakis, A.C. Chatzis, N.M. Giannopoulos, C. Contrafouris, D. Bobos, G.V. Kirvassilis, G.E. Sarris, Etiology and management of chylothorax following pediatric heart surgery, J. Card. Surg. 24 (4) (2009) 369–373.
[20] K. Abdel-Galil, R. Milton, J. McCaul, High output chyle leak after neck surgery: the role of video-assisted thoracoscopic surgery, Br. J. Oral Maxillofac. Surg. 47 (6) (2009) 478–480.
[21] Y. Shen, M. Feng, M.A. Khan, H. Wang, L. Tan, Q. Wang, A simple method minimizes chylothorax after minimally invasive esophagectomy, J. Am. Coll. Surg. 218 (1) (2014) 108–112.
[22] S. Sugimoto, M. Tanaka, K. Suzawa, H. Nishikawa, S. Toyooka, T. Oto, T. Ozaki, S. Miyoshi, Pneumocephalus and chylothorax complicating vertebrectomy for lung cancer, Ann. Thorac. Surg. 99 (4) (2015) 1425–1428.
[23] C. Zerrweck, R. Caiazzo, L. Arnalsteen, G. Dezfoulian, H. Porte, F. Pattou, Chylothorax: unusual complication after laparoscopic gastric banding, Obes. Surg. 19 (5) (2009) 667–670.
[24] P.Y. Chang, T.Y. Chao, M.S. Dai, Early occurrence of chylothorax related to thoracic irradiation and concomitant chemotherapy, Clin. Oncol. 17 (4) (2005) 291.
[25] A. Limsukon, D. Yick, N. Kamangar, Chylothorax: a rare complication of tube thoracostomy, J. Emerg. Med. 40 (3) (2011) 280–282.
[26] R. Thomas, D.J. Christopher, A. Roy, A. Rose, S.T. Chandy, R.A. Cherian, J. Rima, Chylothorax following innominate vein thrombosis – a rare complication of transvenous pacemaker implantation, Respiration 74 (3) (2007) 338–340.
[27] B.M. Repko, L.B. Scorza, R.P. Mahraj, Recurrent chylothorax after neck surgery:percutaneous thoracic duct embolization as primary treatment, Otolaryngology-Head Neck Surg. (Tokyo) 141 (3) (2009) 426–427.
[28] H.D. Waikar, P. Kamalaneson, M.S. Mohamad Zamri, A.G. Jayakrishnan, Chylothorax after off-pump coronary artery bypass graft surgery: management strategy, Ann. Card Anaesth. 21 (3) (2018) 300–303.
[29] C. Wu, Y. Wang, Z. Pan, Y. Wu, Q. Wang, Y. Li, Y. An, H. Li, G. Wang, J. Dai, Analysis of the etiology and treatment of chylothorax in 119 pediatric patients in a single clinical center, J. Pediatr. Surg. 54 (7) (2018) 1293–1297.
[30] F. Mongelli, M. FitzGerald, S. Cafarotti, R. Inderbitzi, Chylothorax after endoscopic ultrasound with fine-needle aspiration causing migrating appearance of a solitary fibrous tumor of the pleura, Ann. Thorac. Med. 13 (2) (2018) 114–116.
[31] J. Odendaal, V.Y. Kong, B. Sartorius, T.Y. Liu, Y.Y. Liu, D.L. Clarke, Mechanical complications of central venous catheterisation in trauma patients, Ann. R. Coll. Surg. Engl. 99 (5) (2017) 390–393.
[32] V. Merki, J. Pichler, R. Giger, G. Mantokoudis, Chylothorax in thyroid surgery: a very rare case and systematic review of the literature, J. Otolaryngol. Head Neck Surg. 45 (2016) 52.
[33] W. Liang, B. Yu, Y. Wang, G. Qiu, J. Shen, J. Zhang, H. Zhao, Y. Zhao, Y. Tian, S. Li, Pleural effusion in spinal deformity correction surgery- a report of 28 cases in a single center, PLoS One 11 (5) (2016) e0154964.
[34] V. Prabhu, C. Passant, Left-sided neck dissection and chylothorax: a rare complication and its management, J. Laryngol. Otol. 126 (6) (2012) 648–650.
[35] A.H. Allaham, A.L. Estrera, C.C. Miller, P. Achouh, H.J. Safi, Chylothorax complicating repairs of the descending and thoracoabdominal aorta, Chest 130 (4) (2006) 1138–1142.
[36] G. Marulli, M. Schiavon, E. Perissinotto, A. Bugana, F. Di Chiara, A. Rebusso, F. Rea, Surgical and neurologic outcomes after robotic thymectomy in 100 consecutive patients with myasthenia gravis, J. Thorac. Cardiovasc. Surg. 145 (3) (2013) 730–736.
[37] K.F. Kwong, L.B. Cooper, L.A. Bennett, W. Burrows, Z. Gamliel, M.J. Krasna, Clinical experience in 397 consecutive thoracoscopic sympathectomies, Ann. Thorac. Surg. 80 (3) (2005) 1063–1066.
[38] S.C. Abreu, D.S. Sharp, A.P. Ramani, A.P. Steinberg, C.S. Ng, M.M. Desai, J.H. Kaouk, I.S. Gill, Thoracic complications during urological laparoscopy, J. Urol. 171 (4) (2004) 1451–1455.
[39] M.S. Herridge, A.L. de Hoyos, C. Chaparro, T.L. Winton, S. Kesten, J.R. Maurer, Pleural complications in lung transplant recipients, J. Thorac. Cardiovasc. Surg. 110 (1) (1995) 22–26.
[40] R.D. Cespedes, S.J. Peretsman, M.J. Harris, Chylothorax as a complication of radical nephrectomy, J. Urol. 150 (6) (1993) 1895–1897.
[41] V. Agrawal, P. Doelken, S.A. Sahn, Seat belt-induced chylothorax: a cause of idiopathic chylothorax? Chest 132 (2) (2007) 690–692.
[42] S.K. Cammarata, R.E. Brush, R.C. Hyzy, Chylothorax after childbirth, Chest 99 (6) (1991) 1539–1540.
[43] K.M. Reilly, E. Tsou, Bilateral chylothorax: a case report following episodes of stretching, J. Am. Med. Assoc. 233 (6) (1975) 536–537.
[44] E. Apostolakis, K. Akinosoglou, E. Koletsis, D. Dougenis, Traumatic chylothorax following blunt thoracic trauma: two conservatively treated cases, J. Card. Surg. 24 (2) (2009) 220–222.
[45] J. García-Tirado, H.S. Landa-Oviedo, I. Suazo-Guevara, Spontaneous Bilateral Chylothorax Caused by a Sneeze: an Unusual Entity with Good Prognosis, Arch. Bronconeumol. 53 (1) (2017) 32–33.
[46] E. Yekeler, H. Ulutas, Bilateral chylothorax after severe vomiting in a child, Ann. Thorac. Surg. 94 (1) (2012) e21–e23.
[47] M.E.M. Air, J. Friedly, Chylothorax complicating inpatient rehabilitation after thoracic spinal cord injury: a review of risk factors and anatomy for the physiatrist, Am. J. Phys. Med. Rehabil. 91 (12) (2012) 1086–1090.
[48] V.G. Valentine, T.A. Raffin, The management of chylothorax, Chest 102 (2) (1992) 586–591.
[49] C.-L. Teng, K.-W. Li, J.-T. Yu, S.-L. Hsu, R.-C. Wang, W.-L. Hwang, Malignancy-associated chylothorax: a 20-year study of 18 patients from a single institution, Eur. J. Cancer Care 21 (5) (2012) 599–605.
[50] K. Pandya, C. Lal, J. Tuchschmidt, C.T. Boylen, O.P. Sharma, Bilateral chylothorax with pulmonary kaposi's sarcoma, Chest 94 (6) (1988) 1316–1317.
[51] S.N. Davis, F. Clark, Multiple myeloma as a cause of chylothorax, J. R. Soc. Med. 79 (1) (1986) 49-49.
[52] S.R. Johnson, J.F. Cordier, R. Lazor, V. Cottin, U. Costabel, S. Harari, M. Reynaud-Gaubert, A. Boehler, M. Brauner, H. Popper, F. Bonetti, C. Kingswood, European Respiratory Society guidelines for the diagnosis and management of lymphangioleiomyomatosis, Eur. Respir. J. 35 (1) (2010) 14–26.
[53] N. Gupta, G.A. Finlay, R.M. Kotloff, C. Strange, K.C. Wilson, L.R. Young, A.M. Taveira-DaSilva, S.R. Johnson, V. Cottin, S.A. Sahn, J.H. Ryu, K. Seyama, Y. Inoue, G.P. Downey, M.K. Han, T.V. Colby, K.A. Wikenheiser-Brokamp, C.A. Meyer, K. Smith, J. Moss, F.X. McCormack, Lymphangioleiomyomatosis diagnosis and management: high-resolution chest computed tomography, transbronchial lung biopsy, and pleural disease management. An official American thoracic society/Japanese respiratory society clinical practice guideline, Am. J. Respir. Crit. Care Med. 196 (10) (2017) 1337–1348.
[54] J.H. Ryu, C.H. Doerr, S.D. Fisher, E.J. Olson, S.A. Sahn, Chylothorax in lymphangioleiomyomatosis*, Chest 123 (2) (2003) 623–627.

[55] R. Soferman, H. Mussaffi, L. Schreiber, H. Nagar, Y. Sivan, Congenital pulmonary lymphangiectasis, Clin. Pediatr. 42 (9) (2003) 831–834.
[56] J.L. Faul, G.J. Berry, T.V. Colby, S.J. Ruoss, M.B. Walter, G.D. Rosen, T.A. Raffin, Thoracic lymphangiomas, lymphangiectasis, Lymphangiomatosis, and lymphatic dysplasia syndrome, Am. J. Respir. Crit. Care Med. 161 (3) (2000) 1037–1046.
[57] F. Maldonado, H.D. Tazelaar, C.-W. Wang, J.H. Ryu, Yellow nail syndrome: analysis of 41 consecutive patients, Chest 134 (2) (2008) 375–381.
[58] L. Valdés, J.T. Huggins, F. Gude, L. Ferreiro, J.M. Álvarez-Dobaño, A. Golpe, M.E. Toubes, F.J. González-Barcala, E.S. José, S.A. Sahn, Characteristics of patients with yellow nail syndrome and pleural effusion, Respirology 19 (7) (2014) 985–992.
[59] S.R. Hoque, S. Mansour, P.S. Mortimer, Yellow nail syndrome: not a genetic disorder? Eleven new cases and a review of the literature, Br. J. Dermatol. 156 (6) (2007) 1230–1234.
[60] C. Emma, C. Viviana, V. Laurence, A.W.B. S, I. Andrew, H.S. D, M.P. S, A case-control study of the lymphatic phenotype of yellow nail syndrome, Lymphatic Res. Biol. 16 (4) (2018) 340–346.
[61] V.S. Nikolaou, D. Chytas, D. Korres, N. Efstathopoulos, Vanishing bone disease (Gorham-Stout syndrome): a review of a rare entity, World J. Orthop. 5 (5) (2014) 694–698.
[62] K. Radhakrishnan, S.G. Rockson, Gorham's disease, Ann. N. Y. Acad. Sci. 1131 (1) (2008) 203–205.
[63] R.D. Devlin, r.H.G. Bone, G.D. Roodman, Interleukin-6: a potential mediator of the massive osteolysis in patients with Gorham-Stout disease, J. Clin. Endocrinol. Metab. 81 (5) (1996) 1893–1897.
[64] M.L.H. Tie, G.A. Poland, E.C. Rosenow, Chylothorax in gorham's syndrome: a common complication of a rare disease, Chest 105 (1) (1994) 208–213.
[65] D. Bruch-Gerharz, C.-D. Gerharz, H. Stege, J. Krutmann, M. Pohl, R. Koester, T. Ruzicka, Cutaneous lymphatic malformations in disappearing bone (Gorham-Stout) disease: a novel clue to the pathogenesis of a rare syndrome, J. Am. Acad. Dermatol. 56 (2, Supplement) (2007) S21–S25.
[66] S. Romero, C. Martin, L. Hernandez, J. Verdu, C. Trigo, M. Perez-Mateo, L. Alemany, Chylothorax in cirrhosis of the liver: analysis of its frequency and clinical characteristics, Chest 114 (1) (1998) 154–159.
[67] W.-Y. Lin, G.-M. Lin, C.-C. Wu, Coexistence of non-communicated chylothorax and chylous ascites in nephrotic syndrome, Nephrology 14 (7) (2009) 700-700.
[68] H. Colak, T. Alici, H. Tekce, D. Öz, A. Erol, F. Aras, S. Kursat, Chylous ascites and chylothorax due to membranous nephropathy, Clin. Nephrol. 67 (2007) 333-333.
[69] K.J. Kim, D.W. Park, W.S. Choi, Simultaneous chylothorax and chylous ascites due to tuberculosis, Infect. Chemother. 46 (1) (2014) 50–53.
[70] V. Villena, A. de Pablo, P. Martin-Escribano, Chylothorax and chylous ascites due to heart failure, Eur. Respir. J. 8 (7) (1995) 1235–1236.
[71] B. Bhattarai, F. Schmidt, A. Devkota, G. Policard, S. Manhas, V. Oke, C.C. Agu, M.R. Basunia, D. Enriquez, J. Quist, P. Kharel, A case of chylothorax in a patient with sarcoidosis: a rare and potentially fatal complication, J. Community Hosp. Intern. Med. Perspect. 5 (4) (2015), https://doi.org/10.3402/jchimp.v5.28300.
[72] N.T. Soskel, O.P. Sharma, Pleural involvement in sarcoidosis, Curr. Opin. Pulm. Med. 6 (5) (2000) 455–468.
[73] P.R. Jarman, M.K. Whyte, I. Sabroe, J.M. Hughes, Sarcoidosis presenting with chylothorax, Thorax 50 (12) (1995) 1324–1325.
[74] S. Rajagopala, R. Kancherla, R.P. Ramanathan, Tuberculosis-associated chylothorax: case report and systematic review of the literature, Respiration 95 (4) (2018) 260–268.
[75] J.-N. Lin, C.-H. Lai, Y.-H. Chen, L.-L. Chang, S.S.-J. Lee, H.-H. Lin, Immune reconstitution inflammatory syndrome presenting as chylothorax in a patient with HIV and Mycobacterium tuberculosis coinfection: a case report, BMC Infect. Dis. 10 (2010) 321-321.
[76] K. Mehta, S. Shinde, S. Rego, A. Shet, Hepatitis a associated with chylothorax: an uncommon presentation of a common infection, J. Trop. Pediatr. 61 (6) (2015) 468–473.
[77] R.S. Wright, M. Jean, K. Rochelle, D. Fisk, Chylothorax caused by paragonimus westermani in a native californian, Chest 140 (4) (2011) 1064–1066.
[78] F.F. Fernandes, V.O. Alves, T.E.G. Sánchez, W.D.d. Paula, A.N.C. Santana, Chylothorax in Paracoccidioidomycosis vol. 58, Revista do Instituto de Medicina Tropical de Sao Paulo, 2016 57-57.
[79] A. Guermazi, P. Brice, C. Hennequin, E. Sarfati, Lymphography: an old technique retains its usefulness, RadioGraphics 23 (6) (2003) 1541–1558.
[80] E. Alejandre-Lafont, C. Krompiec, W.S. Rau, G.A. Krombach, Effectiveness of therapeutic lymphography on lymphatic leakage, Acta Radiol. 52 (3) (2011) 305–311.
[81] G.H. Sokol, M.E. Clouse, L.M. Kotner, J.B. Sewell, Complications of lymphangiography in patients of advanced age, Am. J. Roentgenol. 128 (1) (1977) 43–44.
[82] P. Richardson, E.H. Crosby, H.A. Bean, D. Dexter, Pulmonary oil deposition in patients subjected to lymphography: detection by thoracic photoscan and sputum examination, Can. Med. Assoc. J. 94 (21) (1966) 1086–1091.
[83] J.Q. Knochel, P.R. Koehler, F.J. Miller, Need for chest radiographs during and after lymphography, Am. J. Roentgenol. 132 (6) (1979) 981–982.
[84] P.A. Dolan, Lymphography: complications encountered in 522 examinations, Radiology 86 (5) (1966) 876–880.
[85] R.Y. Yoshida, S. Kariya, S. Ha-Kawa, N. Tanigawa, Lymphoscintigraphy for imaging of the lymphatic flow disorders, Tech. Vasc. Interv. Radiol. 19 (4) (2016) 273–276.
[86] T. Stavngaard, J. Mortensen, J. Brenoe, L.B. Svendsen, Lymphoscintigraphy using technetium-99m human serum albumin in chylothorax, Thorac. Cardiovasc. Surg. 50 (04) (2002) 250–252.
[87] J.M. Restrepo, V.J. Caride, Lymphoscintigraphy and radionuclide venography in chylothorax, Clin. Nucl. Med. 29 (7) (2004) 440–441.
[88] K. Suga, N. Kume, A. Hara, G. Miura, N. Matsunaga, K. Sugi, K. Esato, Abnormal lymphatic flow demonstrated by lymphoscintigraphy in chylothorax correlation with lymphography, Clin. Nucl. Med. 24 (9) (1999) 716–717.
[89] E.Y. Kim, H.S. Hwang, H.Y. Lee, J.H. Cho, H.K. Kim, K.S. Lee, Y.M. Shim, J. Zo, Anatomic and functional evaluation of central lymphatics with noninvasive magnetic resonance lymphangiography, Medicine 95 (12) (2016) e3109-e3109.
[90] D.-x. Yu, X.-x. Ma, Q. Wang, Y. Zhang, C.-f. Li, Morphological changes of the thoracic duct and accessory lymphatic channels in patients with chylothorax: detection with unenhanced magnetic resonance imaging, Eur. Radiol. 23 (3) (2013) 702–711.
[91] J.S. Reisenauer, C.A. Puig, C.J. Reisenauer, M.S. Allen, E. Bendel, S.D. Cassivi, F.C. Nichols, R.K. Shen, D.A. Wigle, S.H. Blackmon, Treatment of postsurgical chylothorax, Ann. Thorac. Surg. 105 (1) (2018) 254–262.
[92] S.M. Lagarde, J.M.T. Omloo, K. de Jong, O.R.C. Busch, H. Obertop, J.J.B. van Lanschot, Incidence and management of chyle leakage after esophagectomy, Ann. Thorac. Surg. 80 (2) (2005) 449–454.
[93] K. Sriram, R.A. Meguid, M.M. Meguid, Nutritional support in adults with chyle leaks, Nutrition 32 (2) (2016) 281–286.
[94] I. Lichter, G.L. Hill, E.R. Nye, The use of medium-chain triglycerides in the treatment of chylothorax in a child, Ann. Thorac. Surg. 5 (4) (1968) 352–355.
[95] B. Bloom, I.L. Chaikoff, W.O. Reinhardt, Intestinal lymph as pathway for transport of absorbed fatty acids of different chain lengths, Am. J. Physiol. Leg. Content 166 (2) (1951) 451–455.
[96] S.A. Hashim, H.B. Roholt, V.K. Babayan, T.B. Van Itallie, Treatment of chyluria and chylothorax with medium-chain triglyceride, N. Engl. J. Med. 270 (15) (1964) 756–761.
[97] D.C. Ruppin, W.R.J. Middleton, Clinical use of medium chain triglycerides, Drugs 20 (3) (1980) 216–224.
[98] S.A. Al-Zubairy, A.S. Al-Jazairi, Octreotide as a therapeutic option for management of chylothorax, Ann. Pharmacother. 37 (5) (2003) 679–682.
[99] I. Kalomenidis, Octreotide and chylothorax, Curr. Opin. Pulm. Med. 12 (4) (2006) 264–267.
[100] R. Yin, R. Zhang, J. Wang, L. Yuan, L. Hu, S. Jiang, C. Chen, Y. Cao, Effects of somatostatin/octreotide treatment in neonates with congenital chylothorax, Medicine 96 (29) (2017) e7594-e7594.
[101] J.-M. Collard, P.-F. Laterre, F. Boemer, M. Reynaert, R. Ponlot, Conservative treatment of postsurgical lymphatic leaks with somatostatin-14, Chest 117 (3) (2000) 902–905.
[102] R.F. Kelly, S.J. Shumway, Conservative management of postoperative chylothorax using somatostatin, Ann. Thorac. Surg. 69 (6) (2000) 1944–1945.
[103] J.J. Mafé, J.M.G. Caravajal, B. Baschwitz, J.M.R. Paniagua, Bilateral chylothorax after thymectomy via median sternotomy and resolution through conservative treatment, Eur. J. Cardiothorac. Surg. 24 (3) (2003) 466–468.
[104] J.G. Selle, W.H. Snyder 3rd, J.T. Schreiber, Chylothorax: indications for surgery, Ann. Surg. 177 (2) (1973) 245–249.
[105] L. Dugue, A. Sauvanet, O. Farges, A. Goharin, J. Le Mee, J. Belghiti, Output of chyle as an indicator of treatment for chylothorax complicating oesophagectomy, BJS 85 (8) (1998) 1147–1149.
[106] S. Paul, N.K. Altorki, J.L. Port, B.M. Stiles, P.C. Lee, Surgical management of chylothorax, Thorac. Cardiovasc. Surg. 57 (04) (2009) 226–228.
[107] V. Pamarthi, M.S. Stecker, M.P. Schenker, R.A. Baum, T.P. Killoran, A. Suzuki Han, S.K. O'Horo, D.J. Rabkin, C.-M. Fan, Thoracic duct embolization and disruption for treatment of chylous effusions: experience with 105 patients, J. Vasc. Interv. Radiol. 25 (9) (2014) 1398–1404.