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SYSTEMATIC REVIEW Open Access

Mediastinal lymphangioma and intestinal lymphangiomatosis presenting with chylothorax: a systematic review of therapeutic modalities

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Abstract

Introduction Chylothorax is defined by the accumulation of chyle in the pleural space, characterized by triglyceride levels exceeding 110 milligrams per deciliter. The clinical presentation of chylothorax varies depending on its acuity and underlying etiology. Mediastinal lymphangiomas are extremely rare and benign lesions that can affect both infants and adults. They may occur independently or in association with other lymphatic disorders and can lead to complications such as chylothorax.

Case report A 60-year-old male patient presented with shortness of breath and was diagnosed with left-sided chylothorax secondary to mediastinal lymphangioma, accompanied by intestinal lymphangiomatosis. Conservative approach was unsuccessful, and surgical therapy was needed.

Materials and methods We conducted a thorough search of the PubMed/MEDLINE, PubMed Central, and Google Scholar databases. The search parameters we used included the following Boolean terms: [("lymphangioma" OR "mediastinal lymphangioma" OR "cavernous lymphangiomas" OR "cystic hygromas" OR "capillary lymphangioma" OR "lymphangioma simplex") AND ("chylothorax" OR "chylous pleural effusion" OR "chylous effusion" OR "chylous lung")]. Our search yielded 166 articles in total, out of which we selected 17 articles for inclusion. We included patients who presented to the hospital with chylothorax secondary to mediastinal lymphangioma and those who developed chylothorax after the removal of mediastinal lymphangioma. The primary outcome was the total number of reported cases of chylothorax secondary to mediastinal lymphangioma. The secondary outcomes included patient characteristics, fluid characteristics, clinical manifestations, and therapeutic modalities.

Results The systematic review encompassed seventeen case reports. Most patients were male, spanning ages from six weeks to 82 years, with an average age of 28.35 years. Most pleural effusions were on the left side. Few cases were asymptomatic, while the most reported symptom was shortness of breath. The mean pleural triglyceride level was

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708 mg/dl, with cystic hygroma being the most common subtype. The anterior mediastinum was the most frequent location. The primary treatment involved surgical removal of the lymphangioma along with thoracic duct ligation.

Conclusion Mediastinal lymphangioma is an infrequent etiology of chylothorax and is scarcely documented in the literature. It may be present in isolation or may be associated with extra mediastinal lymphatic anomalies. The management of chylothorax in such cases is challenging with conservative measures often being ineffective, necessitating surgical intervention. The rarity of these conditions complicates the study of potential risk factors and genetic predispositions. Furthermore, there is no established consensus on the therapeutic modalities for patients with similar diagnoses which vary based on patient characteristics.

Keywords Lymphangioma, Chylothorax, Chylous effusion, Cystic hygroma, Cavernous lymphangioma, Intestinal lymphangiomatosis

Introduction

Chylothorax is defined by the presence of chyle in the pleural space. Chyle represents the lymphatic fluid mainly absorbed by the digestive tract, which is rich in fat and white blood cells, and normally transported back to the circulation by the thoracic duct [1]. Chylothorax has a characteristic milky appearance with lymphocytic predominance. It is further defined by triglyceride levels above 110 milligrams per deciliter (mg/dl) and low cholesterol levels. The expected pleural to serum triglyceride ratio is above 1 and that of cholesterol is inferior to 1 [1]. A pleural triglyceride level below 50 mg/dl excludes chylous effusion [1, 2]. Although this entity is quite rare, it can cause serious mortality and morbidity [2]. Most chylous effusions are exudative in nature, but in rare instances they can be transudative [3]. The majority are right sided (up to 50%), with a minority presenting bilaterally [1].

The presentation of chylothorax varies based on its acuity and underlying etiology. However respiratory symptoms are common such as dyspnea, cough, and chest discomfort [1, 4]. Malnutrition can occur [1, 4], secondary to fluid and nutrient loss, and manifestations can include electrolytes and metabolic abnormalities, vitamin deficiencies, weight loss and in advanced cases muscle wasting [1]. Immunosuppression is also a known complication due to losing abundant immunoglobulins and lymphocytes into the pleural space [1]. Diagnostic approach towards chylothorax includes but is not limited to: thoracentesis with fluid analysis, chest X-ray (CXR), computed tomography (CT), magnetic resonance imaging (MRI), and if needed lymphangiogram [4].

Etiologies behind chylous effusion can be categorized into two entities: traumatic and non-traumatic, traumatic being the most common. Among traumatic, the majority are iatrogenic (80%) occuring after thoracic surgery involving the mediastinum, 4% of which account for esophageal surgeries. Another example of iatrogenic chylothorax is central venous catheter related thrombosis. Traumatic non iatrogenic chylothorax account for 20% of cases and can result from blunt trauma to the chest [1, 4]. Non-traumatic causes are numerous, malignancy is the most prevalent with lymphoma being responsible for 70% of the cases [1, 4]. Other etiologies include infections (such as tuberculosis, filariasis) [2, 4], sarcoidosis, retrosternal goiter, benign tumors, and lymphangioma [4]. Another example of non-traumatic chylous effusion is chylous ascites, also known as hepatic chylothorax, which happens in cirrhotic patients, when chylous ascitic fluid crosses through diaphragmatic porosity into the chest cavity [1, 4]. In this case the effusion is a transudate. Other rare causes of transudative chylous effusion are nephrotic syndrome, amyloidosis, and superior vena cava (SVC) thrombosis [3, 4].

Chylothorax can also present in some congenital diseases such as Down Syndrome, Noonan Syndrome, and Yellow Nail Syndrome [1, 4]. Other known entities are Gorham's disease, diffuse pulmonary lymphangiomatosis and lymphangioleiomyomatosis [1, 4]. Primary lymphatic disease such as mediastinal lymphangioma is an unusual cause [1].

Mediastinal lymphangiomas can be present in infants as well as in adults, are benign, extremely rare, and account for 4.5% of mediastinal tumors [5]. There are three histological subtypes: capillary, cystic and cavernous [5, 6]. Lymphangiomas occur solely or in conjunction with systemic lymphatic disorders such as lymphangiomatosis. Lymphangiomatosis, which is a congenital benign malformation of the lymphatic system [5, 6], is believed to be secondary to a miscommunication between the main lymphatic and the peri lymphatic vessels. It can affect multiple organs including mediastinum, pleura, lung, bones, mesentery, peritoneum and retroperitoneum [6]. Mediastinal lymphangiomas can cause infections, SVC syndrome, and airway compromise [5]. Chylothorax and chylopericardium can also develop [5, 7] with subsequent signs of tamponade and heart failure [7]. We present herein a case of intestinal lymphangiomatosis associated with mediastinal lymphangioma presenting with a left sided chylothorax.

Case presentation

A 60-year-old male patient arrives to the hospital due to worsening shortness of breath. He has a history of mediastinal lymphangioma, confirmed by biopsy, diagnosed five years prior (see Fig. 1). The patient is a non-smoker and has no family history of pulmonary diseases or cancer. He also has a past incident of blunt chest trauma that did not lead to complications or require surgery.

Approximately four weeks prior to this visit, he began experiencing shortness of breath that failed to improve with albuterol or nebulizer treatments. Additional symptoms include a productive cough with clear phlegm, melena without abdominal pain or weight loss.

Upon admission, the patient presented afebrile, with tachycardia and tachypnea, but did not require supplemental oxygen. A physical examination revealed decreased breath sounds on the left side of the chest and bilateral lower extremity pitting edema. Notably, there were no palpable lymph nodes, digital clubbing, or wheezing. Initial investigations indicated a non-ischemic electrocardiogram, new onset anemia with a hemoglobin level of 8.3 g per deciliter (g/dl), and an alkaline phosphatase level of 134 Units per Liter (U/L). Blood tests also showed hypoalbuminemia (2.6 g/dl) and hypoproteinemia (4.3 g/dl). Chest imaging revealed new dense opacification of the left hemithorax, consistent with a large pleural effusion, and extensive mediastinal

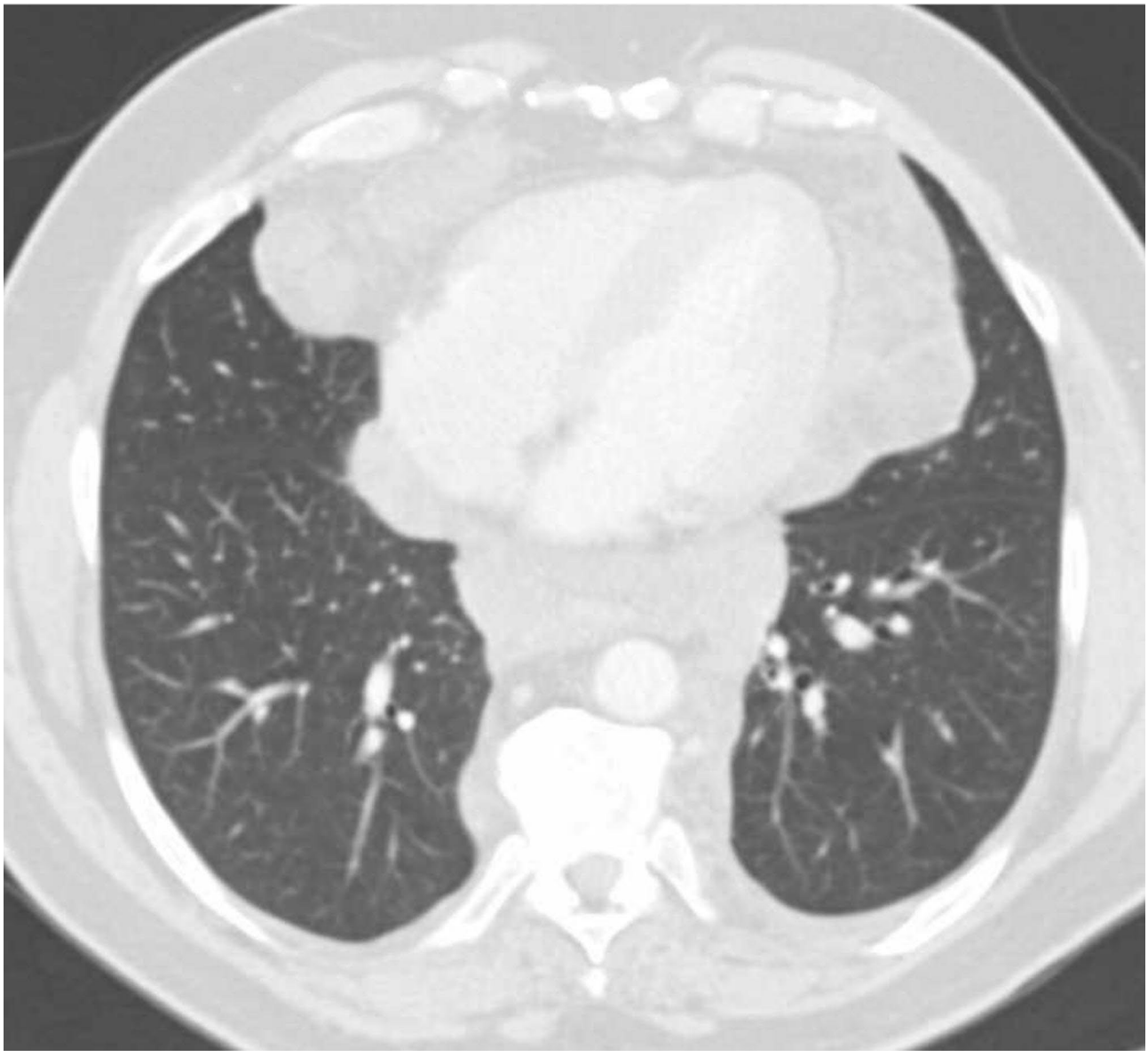

Fig. 1 Computed Tomography of the chest in 2018 showing: Mediastinal fat with abnormal fat stranding and chronic mediastinal fat nodularity and mild mediastinal and right hilar lymphadenopathy. Normal heart size

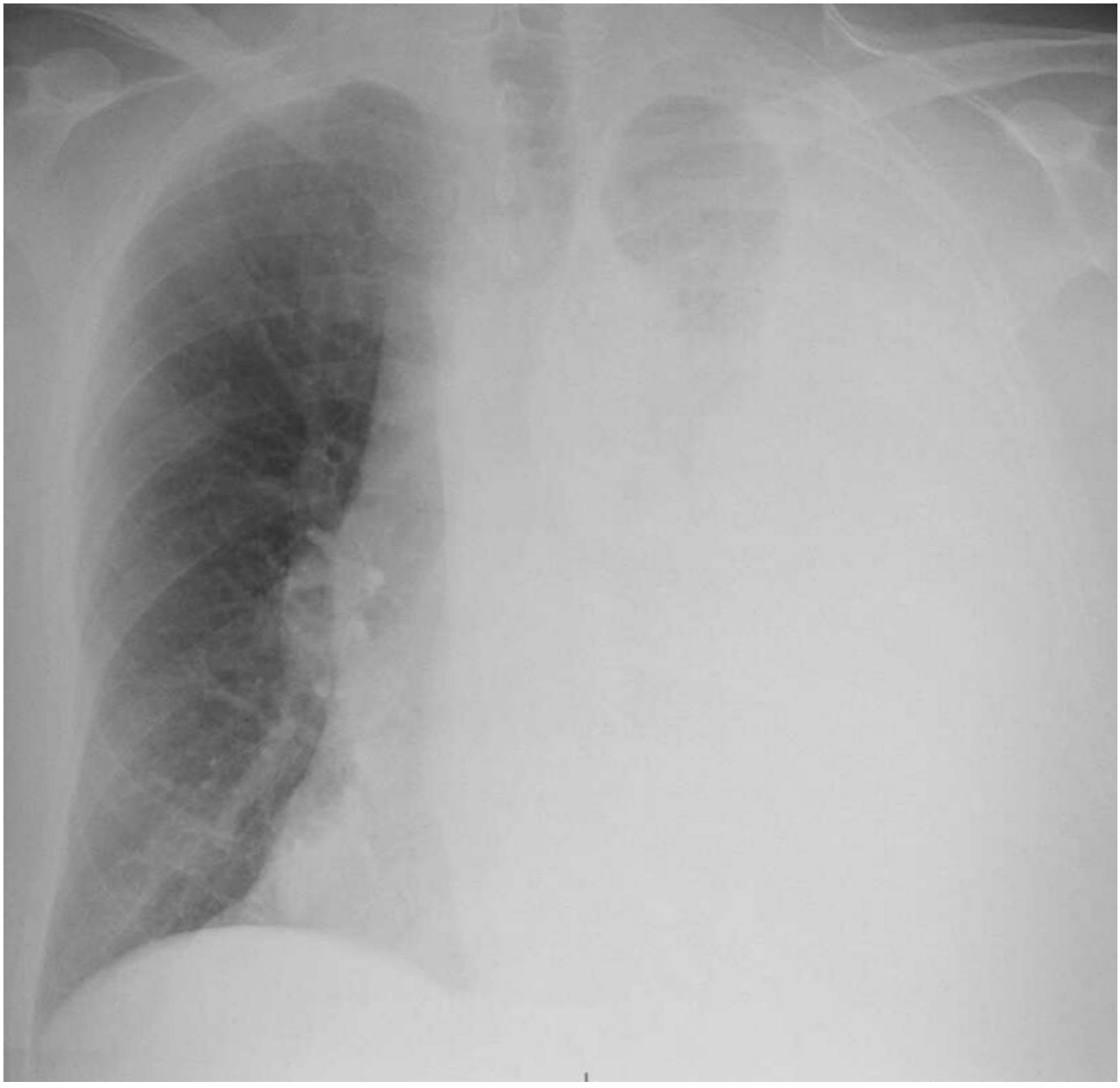

Fig. 2 Chest X-ray showing opacification of left hemithorax with large left pleural effusion, mediastinal and hilar lymphadenopathy. There is minimal aeration of the left lung apex

Table 1 Laboratory findings

Serum		Pleural fluid	
Hemoglobin	8.3 g/dl	**White blood cells**	275
Alkaline phosphatase	134 U/L	**Lymphocyte %**	45
Albumin	2.6 g/dl	**Triglyceride**	408 mg/dl
Protein	4.3 g/dl	**Cholesterol**	35 mg/dl

and hilar lymphadenopathy similar to previous imaging (Fig. 2). A 14 French pleural catheter was placed on the left side, successfully draining 1.6 L (L) milky pleural fluid. Analysis of the pleural fluid indicated an exudative effusion with a white blood cell count (WBC) of 275, of which 45% were lymphocytes, a pleural triglyceride level of 408 mg/dl, and cholesterol level of 35 mg/dl, consistent with a chylous effusion. Both the pleural fluid gram stain and culture were negative (Table 1). A CT scan of the chest following the chest tube insertion showed improved expansion of the left hemithorax with multilocular collections, a trace right pleural effusion, and again noted mediastinal lymphangioma (Fig. 3).

The patient was evaluated by gastroenterology team who deemed esophagogastroscopy (EGD), colonoscopy and capsule endoscopy necessary to evaluate patient's anemia. EGD was relevant for duodenal bulb

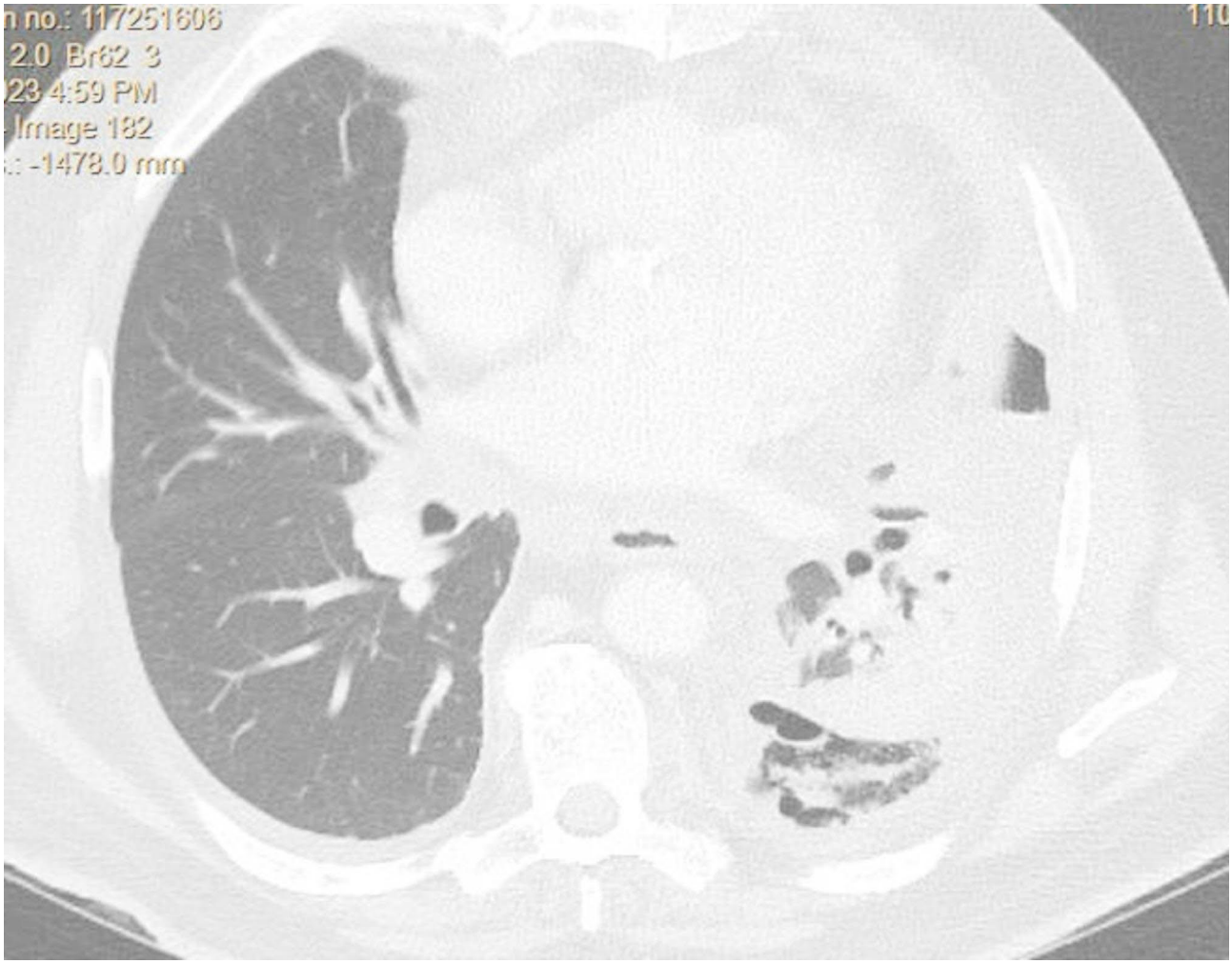

Fig. 3 Computed tomography of the chest showing left multilocular effusions with pericardiac mediastinal mass corresponding to biopsy proven lymphangioma

lymphangiectasis, colonoscopy was nonrevealing and capsule endoscopy showed diffuse lymphangiectasia in the small bowel with superficial erosions (Fig. 4). Duodenal biopsy showed minimal active duodenitis with foveolar surface metaplasia and focally dilated lacteals.

The MRI of the chest was performed which demonstrated the presence of mediastinal lymphatic malformation with moderate compression on the superior vena cava without compression upon the aortic arch or heart (Fig. 5). After ten days of hospitalization, there was persistent significant drainage from the chest tube despite low fat diet. The patient underwent a lymphangiogram by interventional radiology for possible embolization of the thoracic duct or of the leaking site. There was no visualization of the thoracic duct or definitive leakage, thus catheterization of the lymphatics was unsuccessful.

View the persistence of chest tube drainage, the patient underwent an intrapleural catheter placement (PleurX) as a bridge therapy as he was referred to another institution for surgical resection.

Materials and methods

Search strategy

The systematic review was conducted according to the Preferred Reporting Items for Systematic Review and Metanalysis reporting guidelines [8]. We explored the PubMed/MEDLINE, the PubMed central and google scholar database. The Boolean parameters that were used in our search were [(“*lymphangioma*” OR “*mediastinal lymphangioma*” OR “*cavernous lymphangiomas*” OR “*cystic hygromas*” OR “capillary lymphangioma” OR *“lymphangioma simplex”)* AND (“*chylothorax*” OR “*chylous pleural effusion*” OR *“chylous effusion”* OR “*chylous lung*”)]. Literature search included studies published before August 2024. Most of these articles were from PubMed database.

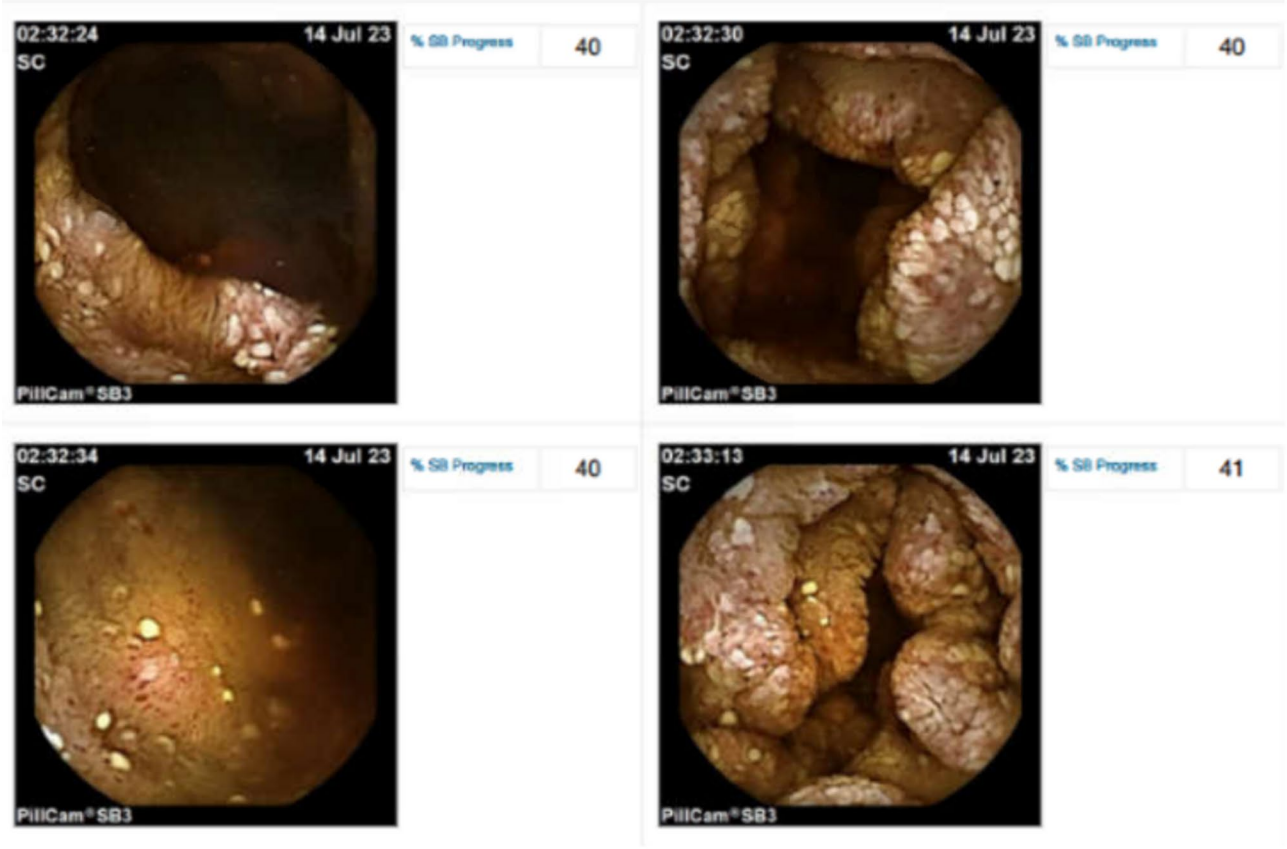

Fig. 4 Capsule endoscopy showing diffuse lymphangiectasis in the small bowels with superficial erosions

Eligibility criteria and outcomes

Studies such as case reports or series were included. Meta-analysis and systematic literature were excluded. Patients presenting to the hospital with chylothorax secondary to mediastinal lymphangioma or those who developed chylothorax post mediastinal lymphangioma removal were eligible for this analysis. We have excluded patients with the following underlying diseases: diffuse pulmonary lymphangiomatosis (DPL), neonatal/congenital lymphangiectasia, Gorham-Stout syndrome (GSS), lymphangioleiomyomatosis (LAM), Noonan or Down Syndrome and thoracic duct malformation/dysplasia/tumors. Intrauterine fetal presentations were also excluded.

Data extraction

Studies were screened and identified independently by two authors based on inclusion criteria. Mendeley Software was used to maintain the records of selected articles and to avoid duplications.

Outcomes measures

The primary outcome was the total number of reported cases of chylothorax secondary to mediastinal lymphangioma. The secondary outcomes were patients' characteristics, fluid characteristics, clinical manifestations, and therapeutic modalities. Mean pleural triglyceride level was calculated.

Results

Literature search

A total of 166 articles were identified with no additional papers from other sources. These articles were screened with title and abstract, of which seventeen articles qualified for full-text review. All of them were case reports. Our analysis includes articles from 1946 till 2019 (Fig. 6).

Study characteristics

Most of the reported patients were male [9] and only 5 of them were females with almost 3:1 ratio. The age group ranged from six weeks old to 82 years old with a mean age of 28.35. Eight out of 17 (47%) patients belonged to the pediatric group (< 21 years-old) and only four patients belonged to the age group > 50 years-old (23%). Only two patients presented with bilateral pleural effusion and the remaining majority [8] had left pleural effusion (47%). Five patients developed iatrogenic post operative chylothorax while the remaining twelve patients (70%) had chylothorax on presentation.

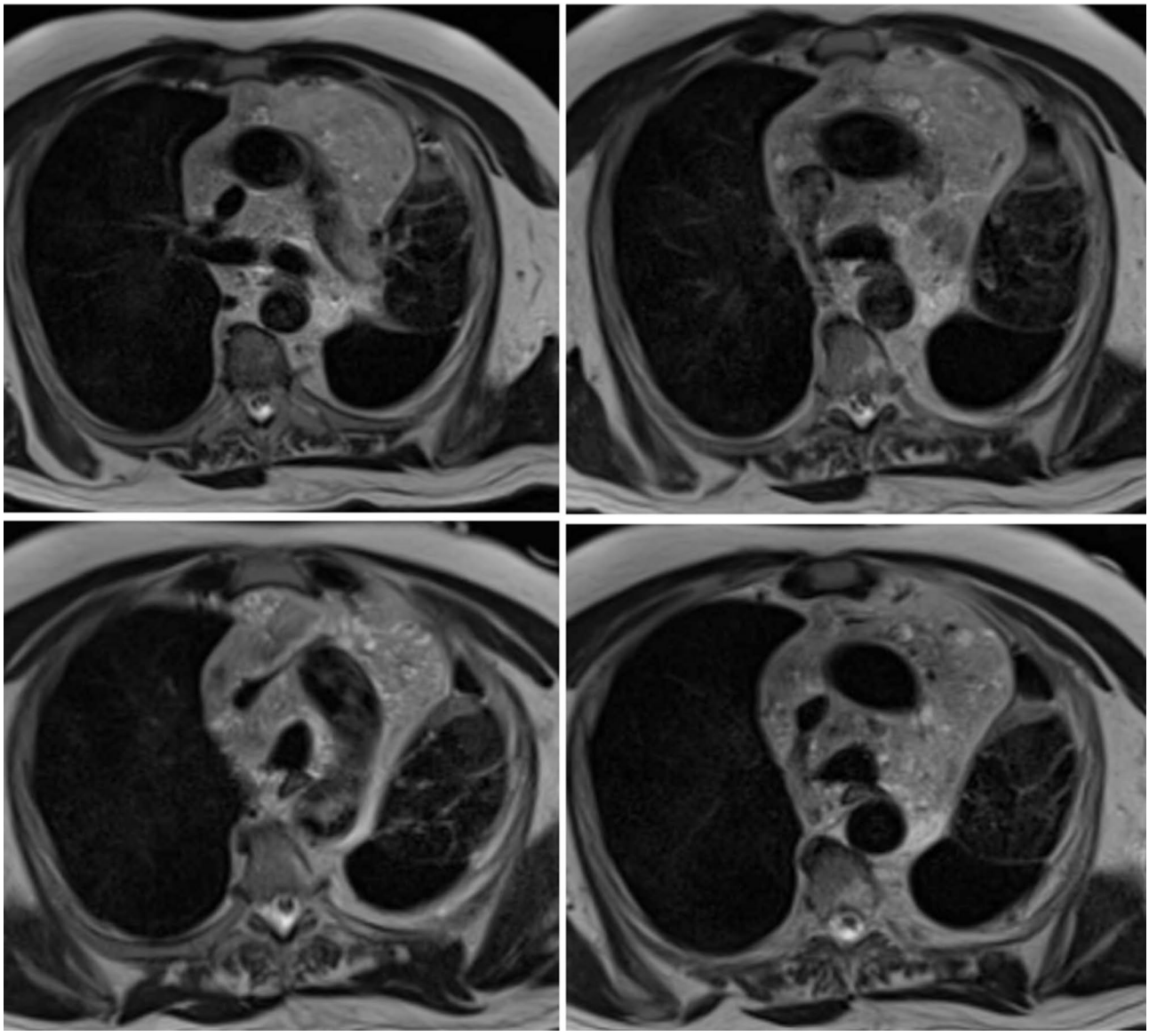

Fig. 5 MRI of the Chest showing mediastinal lymphatic malformation with moderate compression on the superior vena cava

The main presenting symptoms were cough and shortness of breath, while associated chylopericardium is only reported in two cases. Three patients were completely asymptomatic. The lowest reported triglyceride level was 149 mg/dl while the highest was 2260 mg/dl with a mean value of 708 mg/dl. Two cases of cavernous lymphangioma were noted and the remaining cases were cystic hygroma. Anterior mediastinum was the most common location of lymphangioma and three cases of lymphangioma were reported to be in the posterior mediastinum, four in the superior mediastinum and only one case in the inferior mediastinum.

Low fat diet and conservative measures failed in most cases due to persistently elevated chylous output. The main therapeutic approach consisted of surgical excision of the lymphangioma along with thoracic duct ligation. Pleurodesis has failed to improve the chylous output, however other therapeutic modalities such as pleuroperitoneal shunt, radiation therapy (2000 centi-gray divided into 10 doses delivered over 12 days) and CT guided percutaneous sclero-embolization of the thoracic duct have been successful in few instances. Results are illustrated in Table 2.

Discussion

As compared to the reported literature, our patients belong to the minority of patients who were above 50 years old. The pleural effusion in our case was on the left similar to the reported cases, with a triglyceride level of 408 mg/dl. Our patient shared same symptomatology

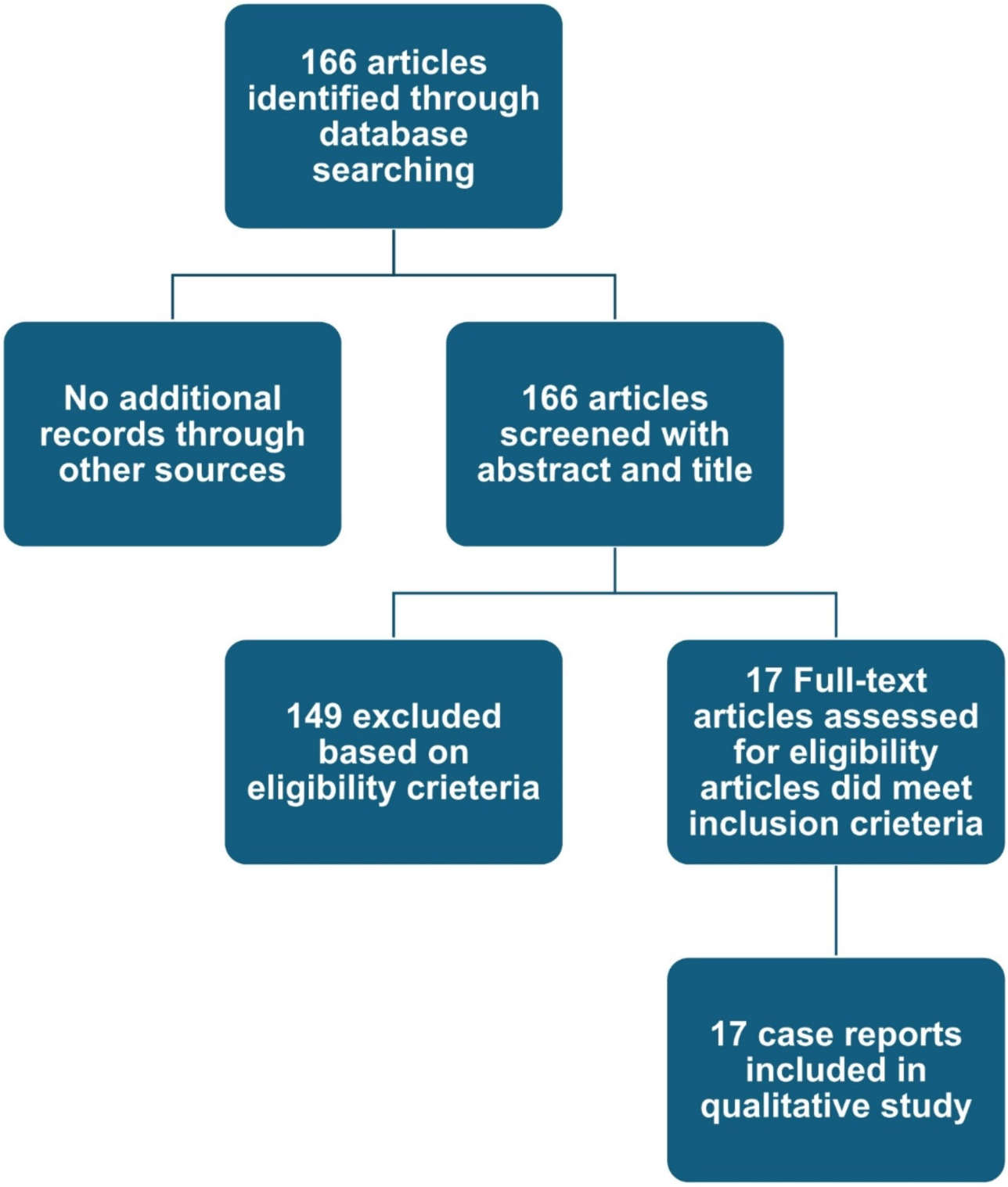

Fig. 6 PRISMA Diagram of Eligible Studies

which were mainly shortness of breath and productive cough. Our reported case was male which adds more to the gender predilection found in our review, however Park et al. reported 25 patients with mediastinal lymphangioma, where the female to male ratio was reversed with 3 to1 female predilection [9]. These cases did not have chylothorax which might suggest a more severe pathology in males. Our patient has failed

Table 2 Results of systemic review

Author	Date	Age	Gender	Symptoms	Effusions	Triglyceride mg/dl	Type	Site	Therapeutic Modality	Post-Operative
Article1. [10]	1946	32	Male	Cough (productive)	Left	-	Cystic	-	Low fat diet	No
Article2. [11]	1953	3	Male	Fever Dyspnea Developmental delay	Left	-	Cystic	-	Pleurodesis (lipiodol and penicillin 20,000 Units)	No
Article3. [12]	1968	6 weeks	Male	Respiratory distress	Left	-	-	Posterior	-	No
Article4. [13]	1968	27	Female	Asymptomatic	Right	-	-	-	Thoracic duct ligation	Yes
Article5. [14]	1980	40	Male	Fever Cough (productive) Hemoptysis	Right	-	Cystic	Superior & Anterior	Surgical removal	No
Article6. [15]	1983	19	Female	Chest discomfort Malaise Dyspnea Chylopericardium	Left	800	Cystic	Anterior	-	No
Article7. [16]	1985	21 months	Male	Fever Cough Respiratory distress	Left	-	Cystic	Anterior	Surgical removal	Yes
Article8. [17]	1986	11	Male	Cough (non-productive)	Right	-	Cystic	Posterior	Surgical removal Thoracic duct ligation Radiotherapy (20 Gy)	No
Article9. [18]	1993	55	Male	Fever Dyspnea Chest tightness	Bilateral Right > Left	149	-	-	Thoracic duct ligation corticotherapy	No
Article10. [9]	1995	20	Male	Asymptomatic	-	-	-	Anterior	Thoracic duct ligation	Yes
Article11. [19]	2005	60	Male	Dyspnea Chylopericardium	Left	-	Cystic	Anterior	Surgical removal Thoracic duct ligation	No
Article12. [20]	2007	50	Male	Asymptomatic	Right	494	-	Inferior (diaphragm)	Pleurodesis (bleomycin 1 mg/kg and interferon 3mlU/d) Octreotide (10 ug/kg) Sclerotherapy to the lymphangioma	Yes
Article13. [21]	2013	26	Female	Cough(productive) Respiratory failure	Bilateral. Right > left	251	Cavernous	Superior	Thoracic duct ligation Surgical removal	No
Article14. [22]	2014	21 months	Male	Fever Cough	Right	296	Cavernous	Superior & Anterior	Octreotide (3 ug/kg) Sclerotherapy (minocycline 2 mg/kg/day) Excision of tumor Pleuroperitoneal shunt	No

Table 2 (continued)

Author	Date	Age	Gender	Symptoms	Effusions	Triglyceride mg/dl	Type	Site	Therapeutic Modality	Post-Operative
Article15. [23]	2016	35	Female	Chest pain	-	-	-	Posterior	Partial Pleurectomy Thoracic duct sealing Pleurodesis (talc, tetracycline) Radiotherapy CT guided percutaneous thoracic duct sclero embolization	Yes
Article16. [24]	2018	82	Male	Shortness of breath	Left	2,260	Cystic	Superior & Anterior	Surgical removal	No
Article17. [5]	2019	18	Female	Chest pain Shortness of breath	Left	-	Cystic	-	Surgical Removal Pleurodesis (talc)	No

conservative approach with low fat diet as well as embolization techniques, and surgical approach was planned.

As mentioned earlier, mediastinal lymphangioma are benign tumors that compromise 4.5% of mediastinal tumors [5, 10]. They were first described clinically in 1828 [9] by Redenbacher and pathologically by Wernher in 1843 [11]. Lymphangiomas occur mostly in the neck (75%) followed by axillary region (20%) and rarely are confined to the mediastinum (1%) [9, 25]. They present mainly during infancy and in the pediatric population [26, 27] and while cervical location is the most common location, when they present in the adulthood the location tends to be mediastinal [26].

Although lymphangioma can be secondary to another underlying process (infection, surgery or radiation), they are considered usually primary malformation occurring during embryogenesis, resulting from a misconnection between the primary lymphatic cavity and the central lymphatic system [27]. Other advocate that mediastinal lymphangiomas result from the migration of an initially cervical mass, while 10% of the neck lesions have concurrent mediastinal extension [25]. The most common presenting symptom is dyspnea [26] while chyloptysis remains an uncommon finding [27].

Brown et al. have listed 14 patients with intrathoracic lymphangioma, 4 had anterior mediastinal lymphangioma, 5 had superior and 4 had posterior mediastinal lesion. It was reported that 34% of intrathoracic lymphangioma are located in the anterior mediastinum and occur in middle aged people while superior location is mainly seen in younger group and is often associated with tracheal deviation. Posterior lymphangiomas tend to extend to the retroperitoneal compartment and are often associated with bony involvement [25].

Diffuse lymphangiomatosis (DL) can involve one organ or can occur in multiple organs simultaneously such as liver, bone, spleen, kidneys, genitals gastrointestinal tract, pleura, and lungs. When occurring in the lungs it is called diffuse pulmonary lymphangiomatosis (DPL) which can cause reduced lung function, pulmonary infections and chylothorax [28]. Our patient does not have DPL however he has DL with intestinal involvement with associated mediastinal lymphangioma. Commonly, primary intestinal lymphangiectasia can be complicated by abnormal lymphatics in different locations, similar to what we have found in this patient [29]. Barrett et al. have described a similar case of intestinal lymphangiectasia presenting as protein losing enteropathy along with bilateral chylothorax in a 39-year-old female. The patient was treated with pleurectomy in addition to thoracic duct ligation. The surgical biopsy of the pleura showed abnormally dilated lymphatics. It was debatable whether this dilation is abnormal or it was a resultant accommodation of the lymphatic system to compensate the accumulated chyle and improve the pleural drainage [29]. On the other hand, Olivares et al. described a patient with chylothorax and chylous ascites associated with dilated lymphatic tissue of 15 cm in the parietal pleura as a primary anomaly [30].

There is a wide variety of therapeutic approaches outlined in the literature. However, the most successful modality was by far surgical resection [21]. Complete excision or removal of the tumor is somehow challenging rendering the recurrence rate as high as 30% [21, 26]. Although lymphangiomas are benign in nature, early surgical removal is recommended because of their growth potential [26]. It is suggested that in low output chylothorax (less than 1000 ml per day) conservative management with low-fat diet or total parenteral nutrition with or without pleurodesis might be beneficial. However, when the drainage output is more than 1000 ml per day (in most cases), conservative measures utility declines

and surgical treatment along with thoracic duct ligation are the preferred method [23].

Octreotide has been used in some reported cases without resolution of chylothorax [20, 22]. Pleurodesis with different agents such as talc, bleomycin, penicillin, lipiodol, interferon and tetracycline has also been unsuccessful [5, 11, 20, 23]. Sclerotherapy, sealing of the thoracic duct with corticosteroids or minocycline and partial pleurectomy have also failed [18, 22, 23].

Certain therapeutic techniques were successful in specific situations such as CT guided percutaneous thoracic duct sclero-embolization noted by Garcia [23], pleuroperitoneal shunt reported by Shiraga [22] or even sclerotherapy of the lymphangioma itself [20]. Despite the unsatisfactory results of radiotherapy reported by Park et al. [26], Johnson presented a similar case treated successfully with high dose radiation (20 Gy) delivered to the tumor [17].

While the treatment of mediastinal lymphangiomas remains surgical by far, it has been suggested to use Interferon alfa or chemotherapeutic agents such as cyclophosphamide [26]. Interferon alfa has anti angiogenic properties making its use effective in cases of GSS, thus the suggestion of its potential benefit in lymphangiomatosis without osteolysis [31]. In agreement with the abovementioned, vascular endothelial growth factors inhibitors such as bevacizumab, sirolimus and propranolol may also play a role in the treatment of lymphangioma, decreasing the lymphatic production and subsequently chylothorax output [28].

Conclusion

Mediastinal lymphangioma is an uncommon source of chylothorax and is infrequently mentioned in the medical literature. Its presence may or may not coexist with other mediastinal lymphatic abnormalities and genetic disorders. Managing chylothorax in these cases can be challenging through conservative methods, often necessitating surgical intervention. It is still unclear whether patients with isolated mediastinal lymphangioma would benefit from lymphoscintigraphy to identify other lymphatic abnormalities or if genetic counseling would be appropriate. The rarity of such cases complicates the study of the potential risk factors and the environmental exposures associated with these abnormalities. Furthermore, there is no established consensus on therapeutic modalities for patients with this diagnosis, leading to a highly individualized treatment.

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12890-025-03664-3.

Supplementary Material 1

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Author contributions
All authors have made contributions to writing the manuscript and interpreting the data. Maria Del Mar Cirino-Marcano and Mahtab Foroozesh are responsible for the conceptualization, supervision and editing. Marc Assaad, Roshan Acharya, Wasif Shamsi, and Elspeth Springsted are responsible for drafting the manuscript, editing and data collection.

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Data availability
Data is provided within the manuscript or supplementary information files.

Declarations

Competing interests
The authors declare no competing interests.

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References

1. Nair SK, Petko M, Hayward MP. Aetiology and management of chylothorax in adults. Eur J Cardio-thoracic Surg. 2007;32(2):362–9.
2. Gibbons SM, Ahmed F. Chylothorax diagnosis: can the clinical chemistry laboratory do more? Ann Clin Biochem. 2015;52(1):173–6.
3. Maldonado F, Hawkins FJ, Daniels CE, Doerr CH, Decker PA, Ryu JH. Pleural fluid characteristics of chylothorax. Mayo Clin Proc. 2009;84(2):129–33.
4. McGrath EE, Blades Z, Anderson PB. Chylothorax: Aetiology, diagnosis and therapeutic options. Respir Med [Internet]. 2010;104(1):1–8. Available from: https://doi.org/10.1016/j.rmed.2009.08.010
5. Salehi F, Landis M, Inculet R, Wiseman D. Case report of a rare cystic mediastinal lymphangioma mimicking recurrent pleural effusion. Case Rep Radiol. 2019;2019:1–3.
6. Uribe R, Isaza S, Prada V, Cadavid L, Quiceno W. Lymphangiomatosis in a 14-year-old female presenting with chylothorax and multiple cystic lesions. Radiol Case Reports [Internet]. 2018;13(4):782–7. Available from: https://doi.org/10.1016/j.radcr.2018.05.002
7. Bhatti MAK, Ferrante JW, Gielchinsky I, Norman JC. Pleuropulmonary and Skeletal Lymphangiomatosis with Chylothorax and Chylopericardium. Ann Thorac Surg [Internet]. 1985;40(4):398–401. Available from: https://doi.org/10.1016/S0003-4975(10)60078-1
8. Moher D, Liberati A, Tetzlaff J, Altman DG. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. J Clin Epidemiol. 2009;62(10):1006–12.
9. Matsuzoe D, Iwasaki A, Hideshima T, Yoshinaga Y, Okabayashi K, Shirakusa T. Postoperative chylothorax following partial resection of mediastinal lymphangioma: report of a case. Surg Today. 1995;25(9):827–9.
10. SWIFT EA, NEUHOF H. Cervicomediastinal lymphangioma with chylothorax. J Thorac Surg [Internet]. 1946;15(3):173–81. Available from: https://doi.org/10.1016/S0096-5588(20)31420-3
11. TOUROFF AS, SELEY GP. Chronic chylothorax associated with hygroma of the mediastinum. J Thorac Surg [Internet]. 1953;26(3):318–20. Available from: https://doi.org/10.1016/S0096-5588(20)30817-5
12. Dische MR. Mediastinal lymphangioma with chylothorax in infancy. Report of a case and review of the literature. Am J Clin Pathol. 1968;49(3):392–7.
13. Römer KH, Römer C, Schilling W. [Bilateral spontaneous chylothorax in mediastinal lymphangioma]. Zentralbl Chir. 1968;93(3):116–22.

14. Pedicelli G, Daddi G, Cumbo S, Alessi G, Ingianna O. [Cystic lymphangioma of the mediastinum. A case complicated by chylothorax and diagnosed by lymphography (author's transl)]. Ann Radiol (Paris). 1980;23(7):594–6.
15. Schurtz C, Lesbre JP, Kalisa A, Jarry G, Fardellone P, Funck F, et al. [Chylopericardium, chylothorax and cystic lymphangioma. Review of the literature Apropos of a case]. Poumon Coeur. 1983;39(4):209–13.
16. Moore TC, Cobo JC. Massive symptomatic cystic hygroma confined to the thorax in early childhood. J Thorac Cardiovasc Surg [Internet]. 1985;89(3):459–68. Available from: https://doi.org/10.1016/S0022-5223(19)38798-7
17. Johnson DW, Klazynski PT, Gordon WH, Russell DA. Mediastinal Lymphangioma and Chylothorax: The Role of Radiotherapy. Ann Thorac Surg [Internet]. 1986;41(3):325–8. Available from: https://doi.org/10.1016/S0003-4975(10)62780-4
18. Wittmann M, Schneider P, Präuer HW, Emslander HP. [Chylous lung and chyloptysis in mediastinal lymphangioma]. Internist (Berl). 1993;34(5):466–71.
19. Pop D, Benizri EI, Venissac N, Leo F, Padovani B, Mouroux J. Mediastinal cystic lymphangioma: is resection always necessary? Thorac Cardiovasc Surg. 2005;53(4):243–4.
20. Ming YC, Wong KS, Wang CJ, Lai JY. Successful management of a bilateral diaphragmatic lymphangioma. Pediatr Surg Int. 2007;23(6):591–3.
21. Ferguson R, Hodges J, Harness-Brumley C, Girod C, Bartolome S, DiMaio JM. Thoracic cavernous lymphangioma provoking massive chyloptysis. J Investig Med High Impact Case Rep. 2013;1(3):232470961350331.
22. Shiraga K, Terui K, Ishihara K, Shibuya K, Saito E, Ito K, et al. Pleuroperitoneal shunt for refractory chylothorax accompanied with a mediastinal lymphangioma: a case report. Ann Thorac Cardiovasc Surg. 2014;20:654–8.
23. Garcia RG, Rocha RD, Franceschini J, Ghefter MC, Affonso BB, Rahal A, et al. Computed tomography-guided percutaneous thoracic duct sclero-embolization for persistent chylothorax. Innov Technol Tech Cardiothorac Vasc Surg. 2016;11(4):291–4.
24. Bougioukas I, Seipelt R, Huwer H, Abteilung T, Abteilung T, Saar L. Linksseitiger chylothorax und tumor des rechten Vorderen mediastinums Left-sided chylothorax and tumor of the right anterior mediastinum fallbeschreibung diskussion. Pneumologie. 2018;851–4.
25. BROWN LR, REIMAN HM, ROSENOW EC, GLOVICZKI PM. DIVERTIE MB. Intrathoracic Lymphangioma. Mayo Clin Proc [Internet]. 1986;61(11):882–92. Available from: https://doi.org/10.1016/S0025-6196(12)62609-3
26. Park JG, Aubry MC, Godfrey JA, Midthun DE. Mediastinal lymphangioma: Mayo clinic experience of 25 cases. Mayo Clin Proc. 2006;81(9):1197–203.
27. Tregunna R, Belcher E, Cane P, Lang-Lazdunski L. An unusual case of chyloptysis. J Thorac Cardiovasc Surg [Internet]. 2011;142(1):e2–3. Available from: https://doi.org/10.1016/j.jtcvs.2011.03.012
28. Spier AB, Kurtz J, Sears D. A novel case of lymphangiomatosis in HIV. Exp Mol Pathol [Internet]. 2017;102(2):251–4. Available from: https://doi.org/10.1016/j.yexmp.2017.02.003
29. Weissberg D. Pleurectomy for chylothorax associated with intestinal lymphangiectasia. Thorax. 1987;42(11):911.
30. Olivares O, Perales J, Carrasco R. [Chylothorax and chylous ascites. A case due to lymphangiomas]. Rev Med Chil. 1965;93(9):574–7.
31. Takahashi A, Ogawa C, Kanazawa T, Watanabe H, Suzuki M, Suzuki N, et al. Remission induced by interferon Alfa in a patient with massive osteolysis and extension of lymph-hemangiomatosis: A severe case of Gorham-Stout syndrome. J Pediatr Surg. 2005;40(3):47–50.

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