A Large Non-Traumatic Chylothorax Leading to Acute Respiratory Failure
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Citation

Abstract
Pleural effusions causing respiratory failure are largely due to malignancy and infectious etiology. Chylothorax causing large pleural effusion and respiratory failure is rare. We present a patient admitted for acute respiratory failure due to a large right side non-traumatic chylothorax. Investigation revealed chylous effusion secondary to non-Hodgkin lymphoma of the follicular type. The use of octreotide together with dietary modifications successfully resolved the effusion.

INTRODUCTION
Pleural effusions can be found in up to 60% of the patients admitted to the intensive care unit (ICU); most of the effusions are transudates, small and with two-thirds due to noninfectious causes, namely heart failure (35%) and atelectasis (23%) (1, 2). In general, large or massive effusions are due to malignancy followed by parapneumonic or infectious processes. Chylothorax is a rare cause of a large pleural effusion and acute respiratory failure. We present a patient with acute respiratory failure due to massive unilateral pleural effusion. A non-traumatic chylothorax secondary to follicular lymphoma was found and the effusion resolved with infusion of octreotide.

CASE
An 82 year-old man was transferred from a skilled nursing facility for worsening shortness of breath of several days duration. He was found to be in hypoxic acute respiratory failure and required intubation and mechanical ventilation. There was no history of fever, hemoptysis, weight loss or other constitutional symptoms. His past medical history was remarkable for diabetes mellitus, hypertension, cardiac pacemaker, hypothyroidism, dementia and chronic kidney disease. He was a nonsmoker and had no recent surgery or trauma. He was born in New York and there was no history of travel. His PPD status was negative. He was ambulatory with assistance at the SNF. On examination in the ICU, the patient was orally intubated and sedated. He was afebrile with normal vital signs. Blood pressure ranged from 110/60 mmHg to 130/80 mmHg. There was no clubbing or lymphadenopathy. Lung exam revealed decreased breath sounds on the right side of the chest. Cardiac exam revealed a regular rate and rhythm with a soft systolic murmur Grade II/VI at the apex. No hepatomegaly or ascites was identified. Lower extremity 1+ pitting edema was present. The rest of the exam was unremarkable. Laboratory findings included a hemoglobin level of 14.4 g/dl, white cell count 8 k/ul, mildly elevated creatinine of 1.8 mg/dl. (Reference level 0.6-1.1 mg/dl), ProBNP-768pg/ml., PaO2 was 85 mm Hg on FiO2 of 40%. Thyroid function test, serum lactate dehydrogenase (LDH), amylase, angiotensin converting enzyme levels and cardiac markers were all normal. The chest roentgenogram (CXR) on admission revealed a large right pleural effusion.
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Figure 1
The chest roentgenogram (CXR) on admission revealed a large right pleural effusion.

Thoracocentesis showed a milky white-yellowish fluid as seen in figure 2 below.

Figure 2
Thoracocentesis showed a milky white-yellowish fluid

Biochemical analysis revealed triglyceride of 1915 mg/dl, cholesterol of 101 mg/dl, 83% lymphocyte, Ph 7.50, protein fluid/serum ratio of 0.76, glucose 144 mg/dl, LDH fluid/serum ratio of 0.67. All septic work-up including stain, cultures and AFBs of pleural effusion were negative. Pleural fluid cytology was negative for malignant cells. The pleural fluid was consistent with an exudative chylothorax.

A chest and abdominal contrast tomogram (CT) was performed as shown below in figure 3.
A chest and abdominal contrast tomogram (CT) was performed.

The CT revealed a large right pleural effusion with compression atelectasis and paratracheal, AP window, subcarinal, azygo-esophageal recess and pericardial phrenic lymphadenopathy. Minimal ascites was also visible. Two-dimensional echocardiogram showed a normal ejection fraction of 60% and moderate pulmonary hypertension with RVSP of 45 mmHg. An inspection bronchoscopy was negative.

A bone marrow biopsy revealed a non-Hodgkins lymphoma (follicular lymphoma).

The patient failed several trials of weaning, a pig tail was inserted in the right pleural cavity for fluid drainage. Additionally, he was started on medium-chain triglyceride diet; however after 3-4 days the pleural fluid drainage remained between 1-1.5 L/day. On day 5 of admission, octreotide was started with a steady decrease in PE drainage. Prednisone was started on day 7 of admission for treatment of the NHL. The pleural drainage was removed on day 9 after 24 hours of less than 50 ml of drainage, chest roentgenogram on day 11 of admission shows almost complete resolution of right pleural effusion as seen below in figure 4.

Subsequently, his clinical course was complicated with sepsis and pneumonia and as per family request he was transferred to hospice care where he died.

DISCUSSION

Chylothorax is usually classified as traumatic or non-traumatic (3) Traumatic cases are sub-classified as iatrogenic or non-iatrogenic (20% of traumatic cases) etiologies causing damage of the thoracic duct.

The incidence of non-traumatic chylothorax ranges from 50% to 60%. Non-traumatic etiologies include malignancy, sarcoidosis, retrosternal goiter, amyloidosis, superior vena cava thrombosis, benign tumors, congenital duct abnormalities and diseases of the lymph vessels such as yellow nail syndrome, lymphangioleiomyomatosis and haemangiomatosis. Thoracic duct obstruction due to malignancy is the commonest cause of non-traumatic chylothorax with lymphoma found in up to 75% of cases (non-Hodgkin’s>>Hodgkin’s).

Other disorders associated with chylothorax include infections such as tuberculosis, histoplasmosis and filariasis. Rarely, congestive heart failure and mediastinal radiation have been associated with chylothorax (6, 7, 8).

In three large case series, the most common causes of a transudative, chylous effusion were CHF, hepatic cirrhosis, and nephrotic syndrome (7, 8, 9).

The clinical features of chylothorax depend on the rate of chyle accumulation in the pleural space as well as the concomitant effect of the etiology. The presentation of non-
Hodgkin’s lymphoma (NHL) depends upon the type of lymphoma and the areas of involvement. Some NHLs behave indolently while others are very aggressive. Aggressive lymphomas present acutely or subacutely with a rapidly growing mass, systemic B symptoms (ie, fever, night sweats, weight loss), and/or elevated serum LDH and uric acid. Lymphomas with aggressive presentation include diffuse large B cell lymphoma, Burkitt lymphoma, adult T cell leukemia-lymphoma, and precursor B and T lymphoblastic leukemia/lymphoma. Indolent lymphomas, like in our patient, are often insidious, presenting with slow growing lymphadenopathy, hepato-splenomegaly, or cytopenias. Lymphomas with indolent presentation include follicular lymphoma, chronic lymphocytic leukemia/small lymphocytic lymphoma, and splenic marginal zone lymphoma (10).

Peripheral lymphadenopathy can be found in more than two third of the patients with NHL and approximately 20% present with mediastinal adenopathy. Mediastinal involvement can be the sole presentation in primary NHL or as part of systemic disease. Other associated thoracic findings include pleural and rarely pericardial effusion.

Pleural disease is seen in up to 10% of patients at the time of diagnosis (11). Three mechanisms have been postulated in the pathogenesis of pleural effusions in NHL: a) obstruction of the thoracic duct by lymphadenopathy mainly mediastinal and retroperitoneal, b) direct lymphomatous infiltration of the pleura and c) obstruction of pleural lymphatic by mediastinal lymphadenopathy (8). Obstruction of the thoracic duct by lymphadenopathy is believed to be the major cause of chylothorax in lymphoma although lymphomatous infiltration of the pleura can also be found (8, 9).

Twenty to 30% of patients with NHL and Hodgkin disease develop pleural effusions; most of the effusions in Hodgkin disease are paraneoplastic and result from thoracic duct obstruction. Most patients with effusions due to NHL have T-cell–type lymphomas and direct pleural infiltration (12). Investigation of suspected chylothorax begins with the confirmation of the diagnosis by fluid analysis, followed by the identification of the leakage point where possible.

The finding of a pleural fluid triglyceride levels >1.24 mmol/l (110 mg/dl) with a cholesterol <5.18 mmol/l (200 mg/dl) is diagnostic of chylothorax (13). Unlike other exudative effusions, the diagnosis of the underlying cause of chylothorax cannot usually be established from thoracoscopy or pleural biopsies. In non-surgical cases, a chest CT to exclude mediastinal pathology (especially lymphoma) is mandatory. The site of leak may be demonstrated by lymphangiography. The investigation should continue until the etiology is discovered (14).

The diagnosis of NHL is usually made by lymph node biopsy. Pleural fluid evaluation can be diagnostic in some cases. Bone marrow (BM) aspiration with biopsy is recommended in all patients as this may help to determine the diagnosis and staging. BM involvement is seen in 18% to 36% of patients with aggressive and highly aggressive NHL and in 40% to 90% in patients with indolent NHLs, making the yield of marrow biopsy quite high in the latter setting (15, 16).

In general, the management of non-traumatic chylothorax is directed toward systemic treatment against the causative agent with interventions to maintain adequate nutritional status and decrease chyle production (5). Chyle is produced at a rate of 2-4 liters/day and can increase up to 5 liters/day on a high fat diet. Chyle drains into the venous system via the thoracic duct at the junction of the internal jugular and subclavian veins. The flow of chyle can be decreased with medical and surgical management. The medical management of chylosus effusions comprises of maintenance of nutrition, the reduction of flow in thoracic duct lymph, and the maintenance of full expansion of the affected lung. Treatment aimed at minimizing chyle formation includes bed rest and either total parenteral nutrition or a high protein diet with dietary fat replaced by medium chain triglycerides, or both. Medium chain triglycerides are directly absorbed across the gastrointestinal mucosa into the portal circulation.

The successful use of somatostatin and octreotide has been reported in a few cases mainly involving postoperative and pediatric patients. (17, 18, 19) . It is known that somatostatin reduces intestinal absorption of fats and intestinal blood flow and motility. Thus, administration of somatostatin, simultaneously with TPN, is a therapeutic option for treatment of chylothorax and could reduce the need for surgical intervention. However, data regarding the administration of octreotide instead of somatostatin is mixed (19, 20, 21).

Chemotherapy, and occasionally radiation, are used for pleural effusion in patients with lymphoma. In many instances, specific treatment will have good effect on the underlying disease, but the chylothorax can remain, and therefore further measures will be necessary (22). Older studies reported up to 68% resolution of chylothorax in patients with lymphoma treated with radiation therapy.
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(23). Talc pleurodesis is an option for those patients who fail chemo-radiation; a study documented a success rate of 100% in the prevention of recurrence of PE at 30, 60, and 90 days following the procedure (24). Other management options for recurrent chylothorax in patients with cancer poorly responsive to treatment of malignancy includes placement of an indwelling pleural catheter. Insertion of catheter is simple and is generally done on an outpatient basis. In one retrospective study, placement of indwelling pleural catheter was associated with decreased risk of requiring second pleural intervention. Indwelling pleural catheter is mainly used in the palliative relief of symptomatic chylothorax (25).

In non-traumatic chylothorax managed with prolonged conservative treatment, there are risk for considerable losses of fluid (up to 2.5 liters daily), protein, fat and lymphocytes, resulting in thirst, weakness, hypoproteinemia, and immunological abnormalities. Secondary infection and possible late complications, such as loculation of the effusion and the development of fibrothorax are other complications (26, 27, 3).

Surgical management should be considered if daily chyle leak exceeds 1.5 liter in adult (28) or chyle drainage rate is more than 1 liter/day for more than 5 days (29). The prognosis in non-traumatic chylothorax is dependent on the underlying disease process and is worse in malignancy related chylothorax. In the 18 patients with chylothorax reported by Fairfax et al, five of the seven with a non-traumatic etiology (3 malignancies) died within two years of the occurrence (30).

CONCLUSION

Patient with chylothorax can represent a diagnostic and management challenge for the clinician. The finding of a non-traumatic exudative chylothorax should prompt the aggressive search for the cause in order to exclude the possibility of an underlying malignant lymphoma. Other malignancies can cause blockage of the thoracic duct by metastatic spread, but this is actually a fairly rare occurrence. Bone marrow biopsy should be performed in unexplained cases as can lead to an early diagnosis without the need for a more invasive procedure, especially in the critically ill patient. An initial trial of octreotide and dietary management is advisable prior to more aggressive interventions.

References

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