Bilateral chylothorax complicating a case of chronic lymphocytic leukemia: a case report

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Abstract

Chylothorax occurs when lymphatic fluid leaks from the thoracic duct and accumulates in the pleural space. Bilateral chylothorax caused by chronic lymphocytic leukemia (CLL) has been rarely reported in the literature. Sludging of lymph might be the underlying cause. We present a case of bilateral chylothorax in a patient with CLL.We also briefly discuss etiology, possible pathogenesis in our case along with diagnostic options and treatment modalities.

Introduction

Chylothorax occurs when lymphatic fluid leaks from the thoracic duct and accumulates in the pleural space. Common causes of chylothorax are trauma, malignancies and surgery of the thoracic duct. Bilateral chylothorax caused by chronic lymphocytic leukemia (CLL) has been rarely reported in the literature.[1] Lymphoma accounts for around 70% of cases due to malignancy.[2] Bilateral chylothorax caused by CLL has been rarely reported in the literature.[1] Treatment of the underlying cause, measures to decrease chyle production, drainage and obliteration of the pleural space, appropriate fluid and nutritional replacement, and providing necessary respiratory care remain the mainstay of management.

Case Report

A 63-year-old female, diagnosed with CLL 2 years prior to this hospitalization, presented with a gradually worsening cough and shortness of breath for the past 2 months along with dry cough and symptoms of malaise and myalgia. According to the Rai staging system, patient had high-risk stage III CLL. On examination, the patient had vocal fremitus on palpation and decreased breath sounds on auscultation in the left hemithorax. Complete blood count revealed white blood count of $87.9x10^3$ cells/microliter with 97% lymphocytes, 2% neutrophils and 1% monocyte. Her Hemoglobin was 9.7 gm/dl and platelet count was $107x10^3$ cells/microliter. Computed Tomography (CT) scan of the chest revealed a large left-sided pleural effusion causing near complete atelectasis of left lung with rightward mediastinal shift (Figures 1 and 2). No mediastinal or hilar lymphadenopathy was seen on chest CT. Bilateral axillary and upper abdominal lymph nodes compatible with history of CLL were seen. Her right lung was clear. She was started on intravenous ceftriaxone and azithromycin empirically for possible community acquired pneumonia. A thoracentesis was performed with ultrasound guidance and 2400 mL of milky yellow fluid was removed. Pleural fluid analysis revealed 3.7 g/dl of protein (serum protein: 6.9 g/dl), 101 unit/L of LDH and 104 mg/dl of glucose consistent with exudative pleural effusion. Triglyceride (TG) level in the fluid was extremely high at 553 mg/dl. White cell count was elevated at 900 with 99% lymphocytes. Gram stain, pleural fluid culture, AFB stain and Lowenstein culture were negative. Given the high lymphocyte count in the pleural fluid and history of CLL, antibiotics were discontinued. High TG level in the fluid and milky appearance confirmed the presence of chylothorax. Flow cytometry of the pleural fluid showed 73% monotypic B-cells consistent with CLL. Lack of CD 38 expression in the lymphocytes from pleural fluid was predicted to have a favorable clinical outcome (Figure 3). Since the initial diagnosis, multiple thoracocentesis had to be performed due to recurrent chylothorax, so insertion or a pleurex catheter was decided. In the interim, she developed pleural effusion on the right side as well, and 500 ml of milky chylous pleural fluid was drained. Since her CLL had never been treated chemotherapy was proposed and accepted by the patient. Currently, she has completed the first round of chemotherapy and bilateral chylothorax persists. She is being treated with pleurex catheter on the left side and intermittent thoracentesis on the right side every 4-6 weeks.

Discussion

Chylothorax is defined as an accumulation of lymphatic fluid from the thoracic duct or its tributaries in the pleural space. Etiologies of Chylothorax can be broadly divided into traumatic, malignancy, miscellaneous and idiopathic.[1,3] The thoracic duct typically arises from the cisterna chyli and enters the chest cavity through the aortic hiatus. It ascends through the chest to the right of the vertebral column and crosses to the left at the level of the carina and then drains in the left jugulo-subclavian vein junction. The course of the thoracic duct varies greatly in the population, and the described path is only present in half the population. Chyle can accumulate in either the left or right pleural space, depending on where the thoracic duct is disrupted. If the disruption occurs below the fifth thoracic vertebra, the thoracic duct is on the right side of the vertebral column and right-sided chylothorax occurs. However, if the thoracic duct is disrupted above the fifth thoracic vertebra, the chylothorax occurs in the left pleural space. Traumatic injury disrupts the thoracic duct, leading to chyle leakage into the pleural space, it includes surgery such as mediastinoscopy, lung resection and lymphadenectomy and direct injury via straining, coughing or vomiting. Malignancy typically involves infiltration or lymphatic obstruction. Other miscellaneous conditions that result in chylothorax include congenital lymphatic disorders including Down syndrome and tuberous sclerosis, lymphatic obstruction due to sarcoidosis, pulmonary tuberculosis, or increased venous pressure from congestive heart failure. Idiopathic causes of chylothorax such as congenital chylothorax, minor unrecognized trauma and miscellaneous causes including cirrhosis, sarcoidosis and congestive heart failure account for other infrequent causes of chylothorax.[3-5] Half of the cases of chylothorax are due to trauma to the large supra-diaphargmatic lymphatics, while the second most common cause is

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malignancy accounting for 25% of cases, amongst the latter 75% are reported as lymphoma. CLL is a rare cause of chylothorax, and has only been reported in a few other instances.[6-8] Bilateral chylothorax is even rare and has not been frequently reported so far.[9] Usually, the patient with chylothorax remains asymptomatic until a large amount of chyle accumulates in the pleural space. Symptoms are generally nonspecific, including dyspnea, nonproductive cough and chest discomfort. Pleuritic chest pain and fever are uncommon because chyle is not irritating to the pleural surfaces.[10] Rarely, patients may experience a rapid accumulation of fluid in the pleural space, causing a tension chylothorax. Physical examination findings are nonspecific and mainly include decreased breath sound on the affected side. The pleural fluid is typically described as a white milky color, as was seen in our case, but other studies have found that the fluid may appear serous, yellow or bloody. Milky fluid is suggestive of chylothorax, but other considerations include pseudochylothorax and empyema. In order to make the diagnosis of chylothorax, the pleural fluid triglyceride levels should be greater than 110 mg/dl. If triglyceride levels are indeterminate (between 50-110 mg/dl) and differential diagnosis of pseudochylothorax is lingering, the gold standard for diagnosis of chylothorax is lipoprotein analysis showing chylomicrons in the pleural fluid.[11]

Typically, chylothorax occurs in malignancy due to mediastinal lymphadenopathy. In paucity of mediastinal lymphadenopathy, pathogenesis of chylothorax in CLL is not well understood. In our case also, there was no obvious mediastinal mass effect, which could have disrupted or compressed the thoracic duct.[12] In this particular case, we hypothesized that the chylothorax could have been due to the presence of an extremely large number of abnormal lymphocytes in lymphatic fluid due to CLL, which might have caused sludging in the lymphatic system, resulting in the pseudo-obstruction of the lymphatics draining the pleura and subsequent chylothorax. Similar mechanism has been described by *Rice et al*.[3] We cannot rule out subtle lymphadenopathy, which may have been missed on the chest CT due to the massive chylothorax.

Regarding management of chylothorax, treatment of the underlying cause, measures to decrease chyle production, drainage and obliteration of the pleural space, appropriate fluid and nutritional replacement, and providing necessary respiratory care remain the mainstay of management. Low fat diet comprising of medium chain triglycerides and total parenteral nutrition are two options that have shown variable success.[12] In conditions such as sarcoidosis and congestive heart failure, treating the primary condition resolves the chylothorax. In contrast, treatment of CLL with chemotherapy resulted in resolution of the malignancy, but continuation of the chylothorax.[13] Other reports showed that pleurodesis was an effective treatment for chylothorax in CLL.[14] Pleurodesis allows for adhesion of the pleural surfaces, preventing chyle from accumulating in the pleural space. Surgical intervention involves ligation of the thoracic duct at the leak site via thoracotomy or video assisted thoracoscopy is helpful for cure, especially if chylothorax was caused by trauma and disruption of duct. Repeated thoracocentesis or chest tube drainage is a practical management strategy to relieve the symptoms for patients waiting for surgery or chemotherapy. In another case, the chylothorax was successfully treated with mediastinal irradiation.[6] For our patient, we opted for initial treatment with chemotherapy with the intention to reduce the number of tumor cells and relieve the pseudo obstruction of pleural lymphatics. Currently the patient continues with chest tube drainage on right side and intermittent thoracentesis on left side. If chylothorax persists, surgical pleurodesis as definite treatment will be planned.

Conclusions

In patients with CLL who present with a new pleural effusion, chylothorax should be suspected and pleural fluid TG levels should be checked. Bilateral chylothorax in CLL is extremely rare presentation. If chylothorax is bilateral, traumatic rupture is a less likely cause for it. Sludging of lymph is more likely etiology in such cases.

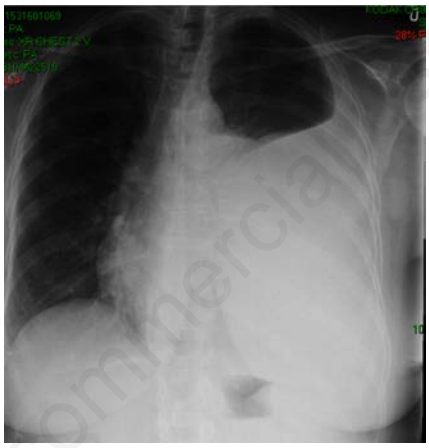

Figure 1. Large left pleural effusion with aeration of only the lung apex. Shift of the mediastinum seen to the right.

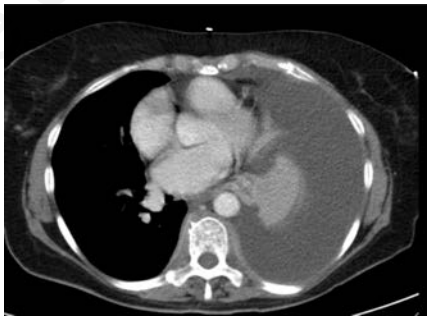

Figure 2. Large left pleural effusion causing near complete atelectasis of left lung with rightward heart deviation seen in CT Chest.

Clinical History

Indication For Study
Evaluation for chronic lymphocytic leukemia

Specimen
Pleural Effusion, Left

Viability
97% (7AAD exclusion)

Interpretation
Pleural Effusion, Left:
- 73% monotypic B-cells consistent with chronic lymphocytic leukemia/small lymphocytic lymphoma, negative for CD38.

Comments
Lack of CD38 expression in CLL/SLL is associated with a more favorable clinical outcome. Clinical and morphologic correlation is recommended for full interpretation.

Populations Analyzed		
Lymphocytes:	94%	There is a mixed population of B- lymphocytes (73% of total cells), T-lymphocytes (21% of total cells), and NK-cells (0.1% of total cells). No pan-T-cell antigen is detected. CD4:CD8 ratio is normal at 3.2:1. Analysis of the B-cells shows a monotypic (dim lambda) B-cell population (73% of total cells) expressing CD5, CD19, CD20 (dim), CD45, CD43, and CD23. They are negative for CD38, FMC7, and CD10.
CD45 Negative Events/Debris:	6%	No significant reactivity with the markers tested (may represent degenerated cells, unlysed red blood cells, debris, etc.)

Figure 3. Flow cytometry report of pleural effusion fluid.

Management of chylothorax is based on the treatment of the underlying condition, pleural drainage, pleurodesis and surgical ligation of the thoracic duct.

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