Official Case Reports Journal of the Asian Pacific Society of Respirology
Respirology Case Reports
OPEN ACCESS

Chylothorax and central vein thrombosis, an under-recognized association: a case series

Sze Shyang Kho[1], Siew Teck Tie[1], Swee Kim Chan[1], Mei Ching Yong[1], Sing Ling Chai[2] & Pei Jye Voon[3]

[1]Respiratory Medicine Unit, Department of Medicine, Sarawak General Hospital, Kuching, Malaysia.
[2]Department of Diagnostic Imaging, Sarawak General Hospital, Kuching, Malaysia.
[3]Department of Radiotherapy and Oncology Unit, Sarawak General Hospital, Kuching, Malaysia.

Keywords
Anticoagulation, chylothorax, malignancy, thrombosis, tuberculosis.

Correspondence
Dr. Kho Sze Shyang, Respiratory Care Unit (RCU), Sarawak General Hospital, Jalan Hospital 93586, Kuching, Sarawak 93586, Malaysia.
E-mail: bzk99@hotmail.com

Received: 16 December 2016; Revised: 14 January 2017; Accepted: 24 January 2017; Associate Editor: Wai-Cho Yu.

***Respirology Case Reports*, 5 (3), 2017, e00221**

doi: 10.1002/rcr2.221

Abstract

Chylothorax is defined as the presence of chyle in the pleural cavity. Central vein thrombosis is an under-recognized cause of chylothorax in the adult population and is commonly related to central venous catheterization. Case 1 illustrates a patient with AIDS and disseminated tuberculosis with left chylothorax and central vein thrombosis after a month of antituberculosis therapy. Case 2 was a patient with advanced seminoma who presented with left chylothorax and central vein thrombosis while on chemotherapy. Chylothorax resolved with anticoagulation for both cases. Case 3 was a lymphoma patient with central vein thrombosis who developed chylothorax during chemotherapy. Chylothorax resolved with the continuation of anticoagulation and did not recur despite his progressive underlying lymphoma. There was no central venous catheterization in any of these three cases. These cases illustrate the unique association of central vein thrombosis and chylothorax and the importance of anticoagulation in its management.

Introduction

Chylothorax is defined as the presence of chyle in the pleural cavity. It is commonly caused by direct injury to the thoracic duct after surgery or the infiltration of the lymphatic system secondary to malignant diseases. Central vein thrombosis causes backpressure in the thoracic duct return, and chyle subsequently leaks into the pleural cavity. Central vein thrombosis as a cause of chylothorax is uncommon in the adult population. Most reported adult cases in the literature were related to thrombotic complications of central venous catheterization. However, malignancies and chronic infections such as tuberculosis are pro-thrombotic in nature and thus commonly lead to thrombosis even without the added provocation. Hence, a high index of suspicion is required to look for thrombosis when encountering chylothorax in patients with malignancy or chronic infection. We report three cases of unilateral chylothorax that were associated with central vein thrombosis, and interestingly, none of our patients had undergone any central venous line placement during the course of their disease.

Case Series

Case 1

A 27-year-old man was diagnosed with AIDS after he presented with smear-positive pulmonary tuberculosis. Antituberculosis and highly active antiretroviral therapy (HAART) had been started. However, he was readmitted a month later for progressive breathlessness and left upper limb swelling. Besides upper limb swelling, there were no other clinical features suggestive of central vein thrombosis. A chest X-ray showed massive left pleural effusion. Thoracocentesis drained milky pleural fluid, and Light's criteria were transudative, with pleural fluid to serum (PF/S) protein ratio of 0.33 and PF/S LDH ratio of 0.33. The pleural fluid triglyceride level was 7.06 mmol/L. No acid-fast bacilli was detected. Computed tomography (CT) of the thorax showed extensive thoracic and

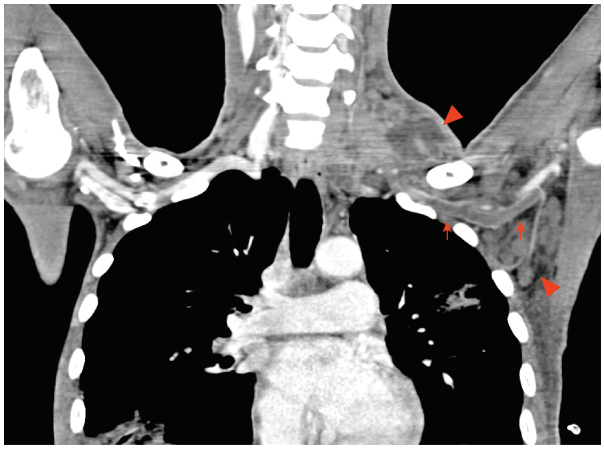

Figure 1. Coronal post-contrast computed tomography image shows long-segment thrombus in left axillary and left subclavian vein (red arrow), with left axillary and supraclavicular (red arrow head) lymphadenopathy.

abdominal lymphadenopathy with venous thrombosis from the left brachiocephalic vein to the left axillary vein (Fig. 1). A chest tube was inserted, and anticoagulation was initiated along with a fat-free diet. After two weeks of anticoagulation therapy, his chylothorax and left upper limb swelling resolved.

Case 2

A 41-year-old man initially presented with left supraclavicular lymphadenopathy, which yielded seminoma from biopsy. Subsequent CT showed a large left neck mass with mediastinal and intra-abdominal lymphadenopathy and thrombosed left internal jugular vein. The patient had responded clinically to the initial cycles of curative-intent chemotherapy. However, he subsequently presented with progressive breathlessness prior to the third cycle of his chemotherapy. There was no overt sign and symptom of central vein thrombosis. A chest X-ray revealed a massive left pleural effusion. Milky protein-discordant exudative fluid was drained, with PF/S protein ratio of 0.60 and a PF/S LDH ratio of 0.39. The triglyceride level was 5.69 mmol/L. CT assessment then showed smaller lymphadenopathy, but with new findings of left subclavian and axillary venous thrombosis with multiple collaterals and inferior vena cava thrombus (Fig. 2). The patient was started on anticoagulation and a fat-free diet. His chylothorax resolved after two weeks. Surveillance CT assessment upon completion of chemotherapy demonstrated treatment response with resolved pleural effusion, resolution of venous thrombosis, and resolved lymphadenopathy.

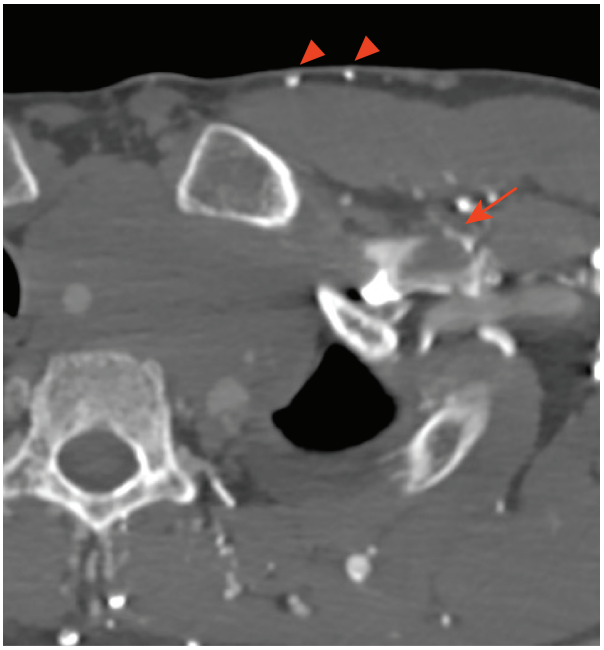

Figure 2. Axial computed tomography scan shows thrombus (red arrow) in left axillary vein, with multiple collaterals (red arrow head). Mild pleural effusion.

Case 3

A 28-year-old man initially presented with a right non-chylous exudative pleural effusion and a huge anterior mediastinal mass. Bilateral subclavian veins and the left internal jugular vein were thrombosed. A mediastinal mass biopsy confirmed the diagnosis of peripheral T-cell lymphoma. Curative chemotherapy regimen and anticoagulation were initiated. However, during the course of chemotherapy, he presented with a contralateral left massive pleural effusion. He had no clinical features of central vein thrombosis. Milky exudative effusion was drained, with a PF/S protein ratio of 0.57 and a PF/S LDH ratio of 0.81. The pleural fluid triglyceride level was 12.32 mmol/L. The patient was initiated on a with fat-free diet, and his anticoagulation was continued. Chylothorax resolved after drainage with the continuation of anticoagulation. Chylothorax did not recur even though his underlying disease continued to progress despite escalation of his chemotherapy regimen. Unfortunately, the patient succumbed to progressive lymphoma four months later.

Discussion

Chylothorax is defined by the presence of chylomicrons or a triglyceride level of over 1.24 mmol/L in the pleural fluid. Direct trauma and malignancy remain the most common

causes of chylothorax in adults, with reported rates of 50 and 30%, respectively [1]. Central vein thrombosis as a cause of chylothorax in adults is uncommon, with only a few cases reported in the literature, which were mainly related to central venous catheterization [2–4]. However, central vein thrombosis-related chylothorax is more common in the paediatric population [5–8]. Hence, a high index of suspicion for central vein thrombosis is essential in adults experiencing chylothorax, even in the absence of a central venous catheter. To the best of our knowledge, this is the first reported case series of chylothorax and central vein thrombosis in adults that were not related to central venous catheterization.

A thorough understanding of the anatomy of lymphatic drainage is fundamental in exploring the association of central vein thrombosis and chylothorax. The thoracic duct empties into the left great veins of the neck in 92–95%. Nevertheless, the final termination patterns vary greatly, with the final drainage site either in the left subclavian or the internal and external jugular veins [9]. Thrombosis of these central veins causes backpressure in the thoracic duct return, and this leads to chyle leakage into the pleural cavity. The causal effect of central vein thrombosis and chylothorax was demonstrated in animal models whereby 60% of subjects developed chylothorax after the ligation of the superior vena cava distal to the entrance of the azygous vein [10].

The association between malignancy and tuberculosis with thrombosis is well established [11,12]. The onset and resolution of chylothorax and upper limb swelling in Case 1 correlates well with the onset and resolution of thrombosis. This temporal relationship and therapeutic response suggest that thrombosis is likely the cause of the chylothorax. A similar temporal relationship was also witnessed in Case 2. In Case 3, chylothorax occurred while undergoing chemotherapy, and it resolved with the continuation of anticoagulation despite the progressive nature of his underlying lymphoma. This establishes that thrombosis plays an important role in the pathogenesis of chylothorax for Case 3 as well.

Central vein thrombosis involving the axillary or subclavian vein may occasionally be completely asymptomatic [13]. Among our three cases, only Case 1 had an overt clinical symptom of central vein thrombosis with left upper limb swelling. Hence, clinical suspicion of central vein thrombosis should remain high in a chylothorax patient with elevated thrombotic risk even if the patient is asymptomatic.

Anticoagulation is the cornerstone of therapy in central vein thrombosis, and successful recanalization of thrombosis plays an important role in the treatment of thrombosis-related chylothorax. Cases 1 and 2 show good therapeutic response with anticoagulation over a period of two weeks. Besides, both cases also highlight the fact that the control of underlying diseases remains pertinent in the treatment of chylothorax. Interestingly, in Case 3, chylothorax resolved with the continuation of anticoagulation and did not recur despite the progressive nature of his underlying lymphoma. This underscores the crucial role of anticoagulation in central vein thrombosis-associated chylothorax even if the underlying disease is not well controlled. This is in line with recommendations that anticoagulation should be continued when there is still evidence of active malignancy [14].

Generally, evidence suggests that the surgical option should only be considered if chyle flow has not diminished within two weeks [15]. Preoperative lymphangiogram is helpful in localizing the site of the lymphatic leakage before thoracic duct ligation but should only be included in the diagnostic approach if thoracic duct ligation is deemed necessary [1]. In any case, lymphangiogram is not widely available, especially in developing countries where medical resources are scarce. All of our three cases were treated successfully with anticoagulation in the span of about two weeks and were spared from any surgical intervention. Hence, rigorous efforts to seek evidence of central vein thrombosis as a cause of chylothorax is essential as such conditions can be treated effectively with anticoagulation and may spare the patients from unnecessary invasive procedures and radiation exposure.

In conclusion, malignant and inflammatory diseases are pro-thrombotic in nature, which can lead to central vein thrombosis. Central vein thrombosis is a condition that is reversible with effective anticoagulation. These three cases illustrate the unique association of central vein thrombosis and chylothorax and the role of anticoagulation in its management.

Disclosure Statement

No conflict of interest declared.
Appropriate written informed consent was obtained for publication of this case series and accompanying images.

References

1. Skouras V, and Kalomenidis I 2010. Chylothorax: diagnostic approach. Curr. Opin. Pulm. Med. 16:387–393.
2. Isik Y, Goktas U, Binici O, et al. 2013. Chylothorax developing due to thrombosis in the subclavian vein. Eur. J. Gen. Med. 10(4):243–245.
3. Warren WH, Altman JS, and Gregory SA 1990. Chylothorax secondary to obstruction of the superior vena cava: a complication of the LeVeen shunt. Thorax 45:978–979.

4. Van Veldhuizen PJ, and Taylor S 1996. Chylothorax: a complication of a left subclavian vein thrombosis. Am. J. Clin. Oncol. 19:99–101.
5. Kramer SS, Taylor GA, Garfinkel DJ, et al. 1981. Lethal chylothoraces due to superior vena caval thrombosis in infants. AJR Am. J. Roentgenol. 137:559–563.
6. Siu SLY, Yang JYK, Hui JPK, et al. 2012. Chylothorax secondary to catheter related thrombosis successfully treated with heparin. J. Paediatr. Child Health 48(3):E105–E107.
7. Kurekci E, Kaye R, and Koehler M 1998. Chylothorax and chylopericardium: a complication of a central venous catheter. J. Pediatr. 132:1064–1066.
8. Berman W, Fripp RR, Yabek SM, et al. 1991. Great vein and right atrial thrombosis in critically ill infants and children with central venous lines. Chest 99:963–967.
9. Hematti H, and Mehran RJ 2011. Anatomy of the thoracic duct. Thorac. Surg. Clin. 21(2):229–238.
10. Blalock A, Cunningham RS, and Robinson CS 1936. Experimental production of chylothorax by occlusion of the superior vena cava. Ann. Surg. 104:359–364.
11. Lee AYY, and Levine MN 2003. Venous thromboembolism and cancer: risks and outcomes. Circulation 107:I-17–I-21.
12. Robson SC, White NW, et al. 1996. Acute-phase response and the hypercoagulable state in pulmonary tuberculosis. Br. J. Haematol. 93:943–949.
13. Joffe HV, and Goldhaber SZ 2002. Upper-extremity deep vein thrombosis. Circulation 106:1874–1880.
14. Brose KMJ, and Lee AYY 2008. Cancer-associated thrombosis: prevention and treatment. Curr. Oncol. 15(suppl 1): S58–S67.
15. Selle JG, Snyder WH III, and Schreiber JT 1973. Chylothorax: indication for surgery. Ann. Surg. 177: 245–249.