Case report

Spontaneous chylothorax complicating small cell lung cancer – Review of aetiology and diagnosis

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Keywords:
Chylothorax
Small cell lung carcinoma

A B S T R A C T

We report the first case of spontaneous chylothorax complicating small cell lung cancer. A 52 year old female presented with exertional dyspnoea, left-sided chest and neck pain, and dysphagia. The chest X-ray on admission revealed a large left-sided pleural effusion. A subsequent CT chest showed a large anterior mediastinal mass with a left brachiocephalic and jugular vein thrombosis. The patient underwent medical thoracoscopy with chest drain insertion, which drained pleural fluid high in triglycerides, consistent with a chylothorax. Due to its uncommon nature, the management of chylothorax is not well defined. Alongside the case report, we provide a review of aetiology, mechanism and diagnosis with a brief summary of treatment options.

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Introduction

A chylothorax is a rare condition in which damage or obstruction to the thoracic duct results in chyle leakage into the pleural space, often right-sided. Chyle is composed of lymph (of which immunoglobulins and T-lymphocytes are the main constituents) and fats absorbed from the digestive tract. Chylothorax can occur secondary to damage or obstruction of the thoracic duct and its tributaries. Common causes include trauma and malignancy. The incidence of spontaneous chylothorax associated with primary lung cancer is rare.

Dyspnoea, chest pain and tachycardia are common presentations [1]. Pleuritic pain and fever, however, are not features as chyle is not irritant to the pleura. Definitive diagnosis requires pleural fluid analysis to measure the proportions of different lipids. We present here a case of left-sided chylothorax in a patient undergoing chemotherapy for a primary small cell lung cancer.

Case presentation

A 52 year old non-smoker female, solicitor by profession, presented with worsening breathlessness and pain (intensity 7/10) on the left side of the neck, chest and left scapular region sometimes radiating to the head causing headaches. She also described dysphagia for fluids but not solids and worsening breathlessness on exertion. Initial observations were in normal limits. There was reduced air entry in the left lung base. Bloods were unremarkable except for a raised CRP of 36 (normal range 0–6). Chest X-ray showed a large left pleural effusion (Fig. 1). A CT chest confirmed an irregular mass in the superior mediastinum associated with left brachiocephalic and jugular vein thrombosis (Fig. 2). The patient underwent local anaesthetic thoracoscopy, drainage of pleural fluid and intercostal chest drain insertion. 1300 ml of orange coloured fluid was drained (Fig. 3). Biochemical analysis identified high levels of triglycerides, suggesting a chylothorax. Subsequent CT guided biopsy and histological analysis showed features consistent with small cell lung cancer (Supplementary Table 1).

Table 1
Pleural fluid analysis.

| Pleural fluid | pH 7.57 |
|---------------|---------|
| Microscopy    | No organisms seen. No Acid Fast Bacilli |
| Cell count    | Not performed as blood mixed Polymorphs 80% |
| Biochemistry  | Albumin 35 LDH 3934 Cholesterol 2.3 mmol/L Triglyceride 4.8 mmol/L |
| Cytology      | Lymphocyte rich effusion. No malignant cells |

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The patient was treated with 5 cycles of radiotherapy and carboplatin and etoposide but continued to deteriorate and passed away.

**Discussion: aetiology, mechanism, discussion & differential diagnosis**

**Aetiology**

Chylothorax represents 2% of all pleural effusions [2]. Trauma, both iatrogenic and non-iatrogenic, is the main cause of chylothorax. Of iatrogenic trauma, thoracic surgery is a common precipitant with esophagectomy being a frequent offender (3% of operations) [3]. Non-iatrogenic causes include penetrating trauma, fractures and childbirth [4]. Of non-traumatic cases, 70% are due to lymphoma [4]. Other reported associations are sarcoidosis, amyloidosis, congenital duct abnormalities, SVC thrombosis and yellow nail syndrome.

**Mechanism**

The mechanism of chyle formation involves damage to the thoracic duct, which is the main conduit for lymphatic drainage, or obstruction of lymphatic tributaries, leading to extravasation of chyle [5]. Leakage leads to formation of a chyloma, which can present as a supraclavicular swelling. Eventually the pleura ruptures and chyle accumulates forming a chylothorax, usually on the right side. There is large variation in the anatomy of the lymphatic system, likely due to embryological bilateral thoracic ducts [5]. In 65% of the population [4], the thoracic duct starts from the level of the second lumbar vertebra, travels alongside the aorta, and ascends to the neck to drain into the left subclavian vein [4,5]. Ducts within the system and the pressure changes from breathing help maintain the flow of chyle. Fats absorbed from the digestive tract and lymph from the lower half of the body combine to form chyle. 2–4 L/day of chyle is transported via the thoracic duct [3], thus large collections can quickly form if the system is damaged or obstructed.

**Discussion**

Our patient’s presentation of a chylothorax complicating small cell lung cancer is likely secondary to jugular vein thrombosis and compression from the anterior mediastinal mass. In cases lacking a significant background, chylothorax should raise the suspicion of malignancy and patients should be investigated for this. In patients with associated trauma, the common approach is pleural fluid analysis along with assessment for a leakage site with CT or lymphangiography [4]. Further interventions depend upon the cause, with medical and surgical options available. Our patient was managed with therapeutic thoracocentesis. She then went on to have radiotherapy for the lung cancer. Consideration should be given to consequences of chylothorax. Depletion of chyle results in loss of fats, fat-soluble vitamins, protein and therefore weight loss and malnutrition. Loss of immunoglobulins and T-lymphocytes can impair the immune system in severe cases. Chyle itself is bacteriostatic so the risk from infection here is low. However, there is 50% mortality in untreated chylothorax from the associated complications [3]. Initial management of these patients should include aggressive treatment to correct hypovolaemia, electrolyte imbalances and immunosuppression.

**Differential diagnosis**

Chylothorax, pseudochylothorax and empyema can be distinguished by the following criteria. Firstly, by physical appearance: the classical appearance of a chylothorax is of a milky, opalescent
fluid in 50% of cases [6]. However, this is sometimes unreliable since if the patient has been fasting this may be clear, and in traumatic cases it may be bloody [3]. Secondly, by biochemical criteria: a triglyceride level >110 mg/dL, cholesterol level <200 mg/dL 50% of cases [3] are exudative i.e. high protein and low lactate dehydrogenase. If the effusion is transudative this may indicate an underlying hepatic or cardiac cause, for example, cirrhosis [5]. Lastly, by fluid analysis, which is the definitive test. Presence of chylomicrons, small particles made up of long chains of triglycerides, is diagnostic as these are absorbed directly into and transported by the lymphatic system. These lipids can be detected with Sudan staining but this technique should be supported with fluid analysis as it has a low specificity [4]. Currently there are no quantitative criteria for diagnosis. If chylomicron testing is not available, triglycerides quantification can be used to aid identification. A pseudochylothorax is an effusion that may appear similar to chylothorax but does not fulfil the biochemical criteria. It is the result of a chronic effusion that may develop over months to years, which can be distinguished by its high cholesterol content. The defining criteria is a cholesterol >200 mg/dL with triglyceride <50 mg/dL but it can be > 1000 mg/dL [5]. The origin of the cholesterol is thought to be through the continued breakdown of inflammatory cells in a chronic effusion. 54% are caused by tuberculous effusions [5]. Other causes include rheumatoid pleurisy, trapped lung syndrome and partially drained empyemas. The milky appearance of pseudochyle will also disappear on addition of ethyl ether—another method of distinguishing from chyle [4]. In addition to clinical history and examination, chylothorax can be differentiated from empyema with centrifugation. Chyle will remain uniform after being processed whereas empyema will form a supernatant [4].

Conclusion

The circumstances of this patient's case are of interest as the background upon which her chylothorax developed is rare. It highlights the issues to consider in diagnosis and initial management. Currently there is not enough evidence to suggest the optimal management of these patients but the general consensus is to manage nutrition aggressively and to, where possible, manage conservatively unless surgical intervention is indicated. Ultimately, the treatment of a chylothorax in such circumstances should be directed to treat the primary tumour. It is important to consider a chylothorax early when faced with a pleural effusion in order to avoid complications such as hypotension, malnutrition and immunosuppression.

Learning points

- Importance of CXR as a screening tool
- Diagnosis of a chylothorax
- Mechanisms of chylothorax
- Differential diagnosis of a pseudochylothorax

Appendix A. Supplementary data

Supplementary data related to this article can be found at http://dx.doi.org/10.1016/j.rmcr.2015.02.005.

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