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Case report

A breathless teenager

A 14-year-old girl presented to hospital with breathlessness and fatigue. On admission she was hypoxaemic with oxygen saturations of 90%, tachycardic with a heart rate of 120 beats·min^{-1} and tachypnoeic with a respiratory rate of 40–50 breaths·min^{-1}.

2 weeks before presentation she had a blanching rash, vomiting and low-grade fevers and initially was felt to have a viral illness. She had no other significant medical history of note.

Her bloods showed a mildly elevated C-reactive protein 63 mg·L^{-1}, white cell count 9.1×10^9 cells·L^{-1}, neutrophils 7.5×10^9 cells·L^{-1}, platelets 544×10^9 cells·L^{-1} and normal albumin 42 g·L^{-1}.

A chest radiograph was performed and showed bilateral pleural effusions (figure 1).

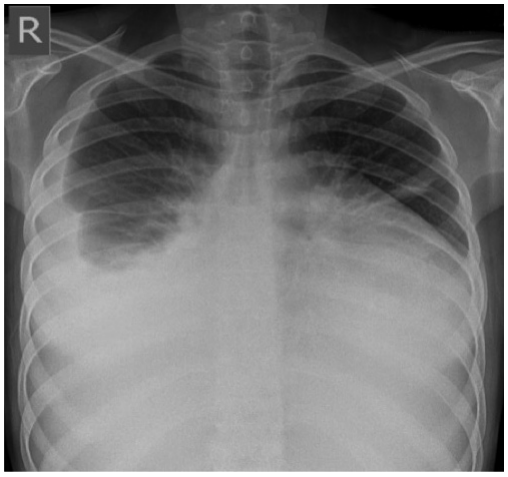

Figure 1 *Chest radiograph taken on admission.*

Task 1
What would you do first?

a) Further imaging of the thorax
b) Start antibiotics
c) Insert bilateral chest drains
d) Echocardiogram

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@ERSpublications
In children with persistent chylothoraces of unknown origin, intranodal lymphangiography can be used to help identify the source of a leak. This may enable embolisation with glue and coils to enable resolution of the chylothoraces. https://bit.ly/3gskhgJ

Answer 1
b) Start antibiotics

Intravenous cefuroxime and oral clarithromycin were given to cover for possible bacterial infection. She subsequently had an echocardiogram which showed a 2 cm pericardial effusion; following this, bilateral chest drains were inserted. The drain output appeared milky and chylothoraces were suspected. She drained 5 L from the chest drains within 2 days.

Task 2
Which of the following tests on the pleural fluid would help diagnose chylothorax?

a) Triglycerides, lymphocyte count and viral PCR
b) Lymphocyte count, bacterial culture and viral PCR
c) Triglycerides and lymphocyte count
d) Triglycerides, lymphocyte count and bacterial culture
e) Viral PCR and bacterial culture

Answer 2
c) Triglycerides and lymphocyte count

Chylothoraces in children have been described as "pleural effusions with triglycerides >1.1 mmol·L^{-1} and cell counts >1000 cells·μL^{-1} with a predominance of lymphocytes" [1]. Initial pleural sampling suggested chyle, with elevated triglycerides (6.8 mmol·L^{-1}), with no bacterial or fungal growth and no acid-fast bacilli. Subsequent sampling confirmed chyle with high lymphocyte counts and persistently elevated triglycerides.

She was commenced on a low long-chain fatty acid diet. Her left drain output decreased after 3 days and on day 5 her left drain was removed, but the right continued to drain chyle. An echocardiogram was repeated and showed a structurally normal heart with good biventricular function and no evidence of pericardial effusion. Magnetic resonance imaging (MRI) of her thorax on day 3 following admission (figure 2) confirmed bilateral pleural effusions, with a large complex 6-cm subpulmonic effusion on the right and a smaller left subpulmonic effusion. There were no soft tissue changes in the pleural cavity or chest wall and the lungs appeared normal other than compressive atelectasis from the effusions. There were nonspecific lymph nodes in the mediastinum, but no obvious mediastinal mass and no bone changes were seen.

Right drain output continued up to daily outputs of approximately 2 L. A computed tomography (CT) scan of the thorax was performed on day 9 and this showed bilateral hydropneumothoraces and areas of thickened interlobular septa and appearances were nonspecific. Chyle output continued on the right and MRI of the thorax on day 13 was requested to specifically view the thoracic duct. It showed a normal calibre thoracic duct, with no evidence of obstruction to drainage, and the bilateral pleural effusions had increased in size compared to the previous image. Right drain output continued, reducing in volume for a few days and then increased again to up to 1.5 L on day 15. A repeat chest radiograph also demonstrated evidence of re-accumulation on the left.

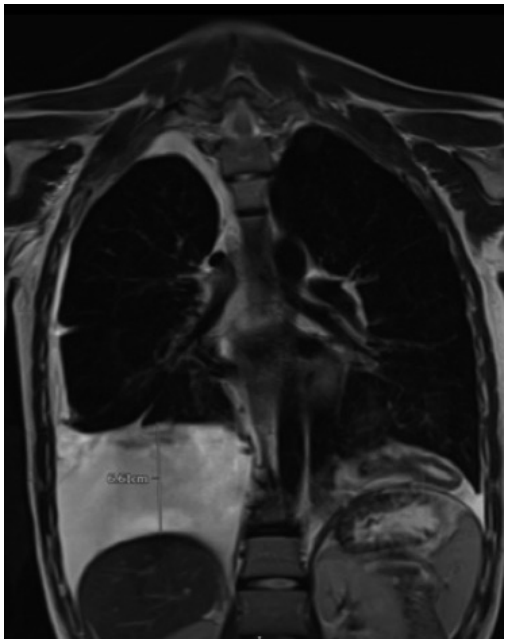

Figure 2 *MRI of the thorax on day 3 following admission.*

Task 3
What is the most likely cause of her chylothoraces?

a) Cardiac related
b) Trauma
c) Infection
d) Malignancy
e) Congenital

Answer 3

d) Malignancy and infection need excluding. Chylothorax in children is uncommon with reports in the UK previously showing 1.4 cases per 100000 children, with almost 75% of children aged <1 year [2]. The cause can be from disruption or damage to the thoracic duct, most commonly related to cardiothoracic surgery [1, 2]. Our patient had no history of thoracic trauma or cardiac surgery. If trauma had occurred you would expect to see a pathological connection between the lymphatics and the pleural space on imaging.

Infection was initially felt to be a likely cause, but blood, throat and pleural bacterial cultures were negative, making this less likely. Congenital lymphatic abnormalities are rare, especially presenting in teenage years and our patient had no dysmorphic features suggesting a chromosomal related condition. If she had a pulmonary lymphangiectasia, CT may show interstitial infiltrates and interlobular septal thickening, so this could be a possibility. Lymphangioma seemed less likely as you would expect cystic change on imaging. Malignancy still seemed the most likely cause at this stage, with a lack of evidence for another cause. The pleural fluid showed no evidence of malignant cells, but a bone marrow aspirate and pleural biopsy were arranged.

On day 17 she went to theatre and had bilateral PleurX tunnelled chest drains and a peripheral central line for total parental nutrition inserted, and underwent bone marrow aspirate and pleural biopsy.

After 5 days the right drain output declined and her right drain was clamped; however, over the next week she had ongoing high output from the left drain, of between 700 mL and 3400 mL a day. Pleural biopsy and bone marrow aspirate showed no evidence of malignancy.

We had no further indication of the aetiology of her chylothoraces. *Mycoplasma pneumoniae* and viral respiratory titres were negative and the only evidence of infection was raised *Chlamydia psittaci* and *Chlamydia pneumoniae* serological titres, which were treated with a second course of clarithromycin in her third week of admission.

She had normal immunoglobulins and auto-immune profile testing was unremarkable; there were no clinical findings in keeping with tuberous sclerosis and genetic testing ruled out Turner syndrome and Noonan syndrome.

Task 4

What is the best next step in management?

a) Give octreotide
b) Give sirolimus
c) Surgical ligation of the thoracic duct
d) Further imaging

Answer 4
a) Octreotide, a somatostatin analogue, has been shown in case reports to have a treatment effect on reducing chylous drainage [3]. On day 24 she was commenced on 2 weeks of octreotide, but despite this she continued to drain approximately 2 L of chyle per day.

A CT scan of the thorax with contrast on day 34 was organised to identify the most abnormal area of lung to help guide a biopsy. It showed a small right hydropneumothorax, with the left hydropneumothorax having almost resolved. There was bilateral interstitial thickening, with little change from previously. There was a poorly enhancing structure in the left lingula region, where an apparent fluid collection had been seen previously and the nature of this was unclear. It did not help guide our next steps and she still had significant chest drain output (figure 3).

After consultation with adult respiratory physicians, lymphangioleiomyomatosis, a rare cystic lung disease was suggested as a possible diagnosis. Sirolimus was proposed as a treatment for this; sirolimus has been reported to stabilise pulmonary function [4, 5] and reduce the size of chylous effusions and lymphangioleiomyomas [5]. We asked a national lymphangioleiomyomatosis specialist to review her case. With no cystic changes seen on CT, they concluded that lymphangioleiomyomatosis was an unlikely diagnosis and that a primary lymphatic abnormality was more likely. After this consultation and awareness of an unfavourable side-effect profile for sirolimus we decided not to pursue this treatment option.

Surgical management was considered. Ligation of the thoracic duct or cisterna chyli were options, but these would be irreversible. Without identifying the source of the leak, the procedures could risk lymphatic fluid building up in the lower limbs and abdomen.

The cause remained unclear. We were aware that the possibilities included reflux from an obstructed or pressure-overloaded thoracic duct, but MRI had demonstrated a normal calibre thoracic duct. There might have been a pathological connection in her lymphatics, which we were yet to find. A primary lymphatic anomaly may have been entirely restricted to her thoracic cavity, but this is rare [6].

Task 5
Which investigation should be performed next to help identify the origin of her lymphatic leak?

a) Repeat CT
b) Repeat MRI
c) Lymphoscintogram
d) Other

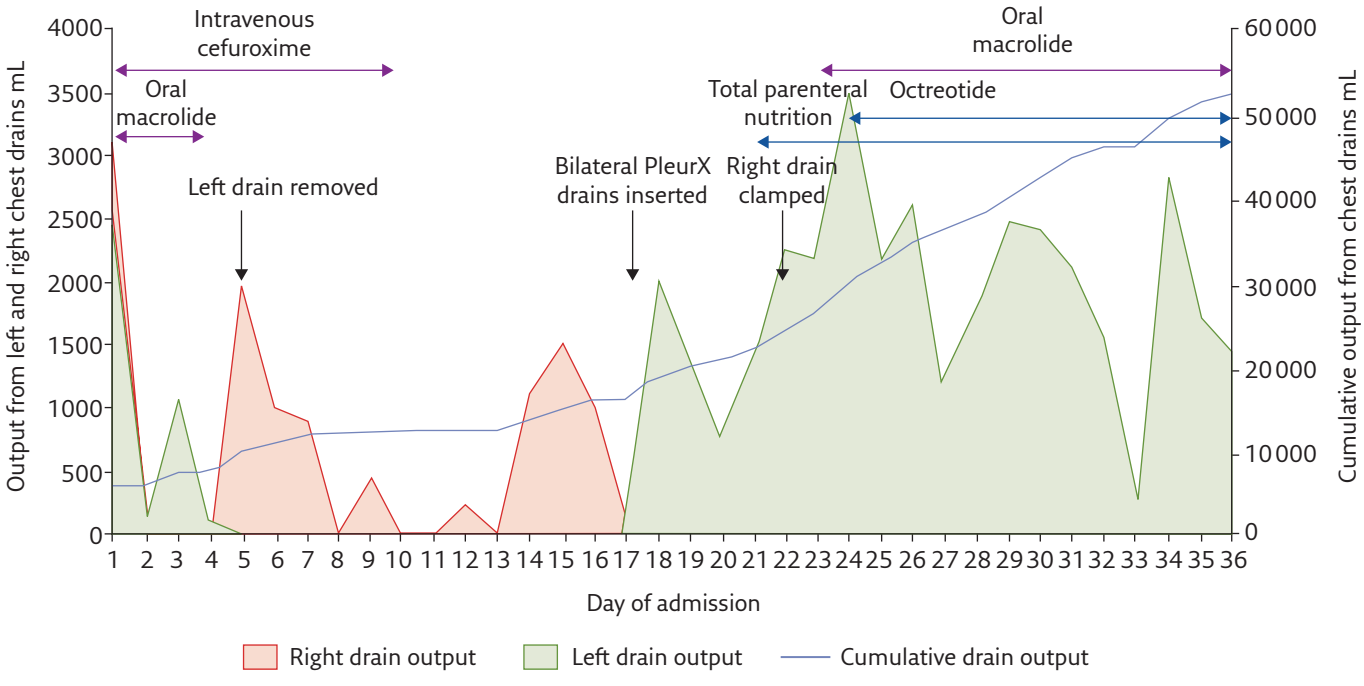

Figure 3 *Output from chest drains and cumulative output over the first 36 days.*

Answer 5
d) CT and MRI had not identified a source of the chylous leak and we had imaging demonstrating a normal calibre thoracic duct, so did not feel repeating CT or MRI would aid management. A lymphoscintogram was arranged. Radioactive tracer is injected subdermally in the web space between the toes on both feet, and transit is followed with serial imaging on a gamma camera. This is a useful test to assess lower limb lymphatic drainage speed, but is rarely useful to demonstrate lymphatic leaks (although this is a common misconception). It demonstrated normal drainage to the inguinal regions and the iliac chains. Tracer was seen in the mid abdomen, but there was no tracer or lymphatic opacification within the chest. We were no further forward (figure 4). Thus, the answer to task 5 is d): another investigation was needed.

After international consultation intranodal lymphangiography with the potential for thoracic duct embolisation was suggested. Intranodal lymphangiography is the most sensitive test to identify lymphatic leak and, if found, thoracic duct cannulation and catheter embolisation can potentially seal a leak.

Intranodal lymphangiography has been used in children [7] and the feasibility of using this technique to subsequently embolise the thoracic duct in adults dates back to 2011 [8]. There is still only a small amount of literature in children as, even in adults, case reports and case series [9] are limited to a small number of centres, as ongoing lymphatic leak despite medical management is a relatively rare condition.

After 7 weeks in hospital she underwent intranodal lymphangiography under general anaesthetic. Contrast agent was injected into lymph nodes in her groins under ultrasound guidance. The agent used was lipiodol, which is an oil-based iodine contrast that is viscous and radiodense, so it travels well through lymphatics and can be seen on fluoroscopy. To avoid extravasation and provide sufficient contrast to identify a leak, the injection of contrast is slow, over 1–2 h. It suggested a leak from a refluxing duct on the left pulmonary hilum. Fluoroscopic guidance was used for a transabdominal puncture to the cisterna chyli. This involved passing a 20-gauge needle through the mid abdomen into a lymphatic duct in the para-aortic retroperitoneum, followed by a guidewire for a Seldinger technique to pass a 2.7 French micro-catheter. Through the catheter, water-soluble contrast was injected, in larger volumes. It identified reflux into and leak from the left hilar ducts. Coils were inserted at the upper end of the duct followed by cyanoacrylate glue and lipiodol to enable the glue to be visible on chest radiography (figure 5).

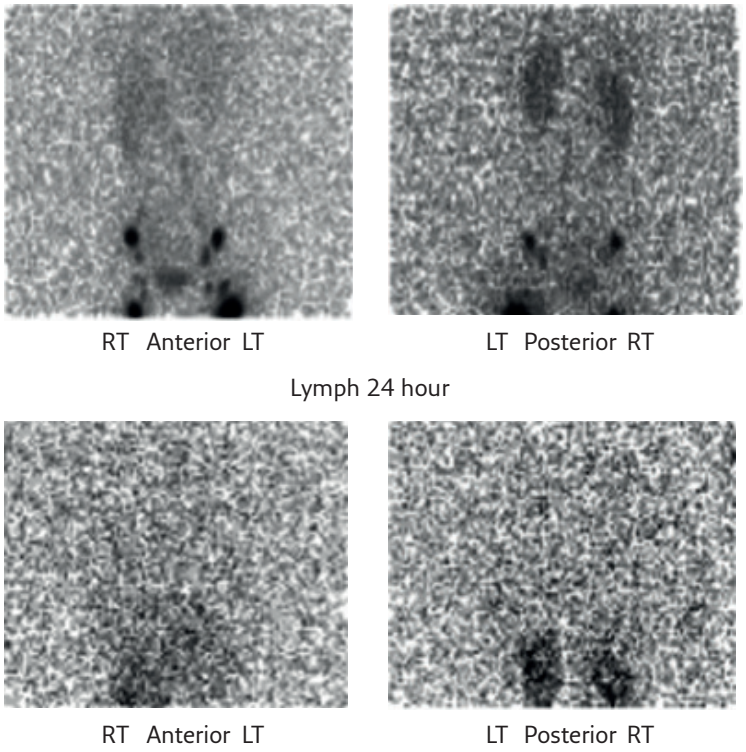

Figure 4 *Lymphoscintogram demonstrating lymphatic drainage. RT: right; LT: left.*

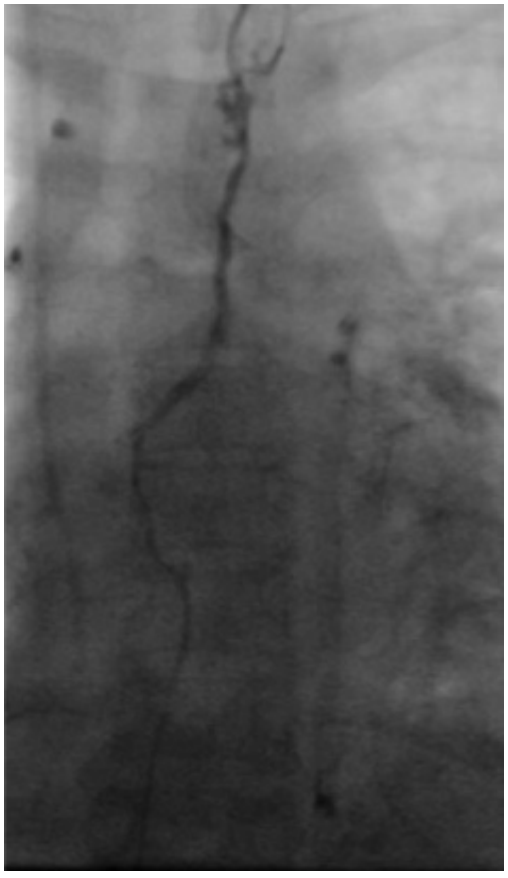

Figure 5 *Lymphangiogram demonstrating glue and lipiodol contrast in the thoracic duct.*

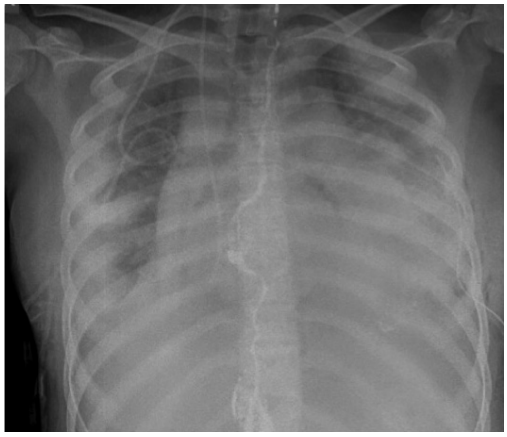

Figure 6 *Chest radiograph taken 3 days post lymphangiogram.*

The procedure risks infection, as the fine entry needle may transit through bowel loops, which is reduced by prophylactic antibiotics. There is a small risk of symptomatic bowel perforation, but the needles and catheters used are small and this is very rare. Bleeding is possible and care is needed whilst puncturing near large vessels.

The left chest drainage decreased from over 2 L per day to <1 L per day, but then gradually increased, complicated by drain blockage and requiring a new left drain, with removal of her right drain at the same time.

Most cases need two embolisation treatments to effectively seal a leak. There should be a minimum of 2 weeks conservative management between procedures to assess the result. On day 87 she underwent repeat intranodal lymphangiography. The lower part of the thoracic duct remained patent, there was some filling of abnormal lymphatic channels in the lower chest, pointing towards the left lung hilum, but no definite leak was identified. More glue was inserted, which filled and set in the thoracic duct. The glue with contrast and coils remained visible on chest radiography post procedure (figure 6).

The day after her second embolisation she developed a fever. She was treated for sepsis, with blood cultures growing *Enterococcus*, likely introduced by the transabdominal puncture. She completed 8 days of intravenous antibiotics.

After two thoracic duct embolisations her chylous leak resolved and on day 93 her drain was removed. Our patient had drained 118 L of chyle during her hospital admission (figure 7).

Follow-up

After discharge she had line sepsis, which was successfully treated with antibiotics and line removal. Having been hypoalbuminaemic, albumin normalised within 1 month. Her energy levels

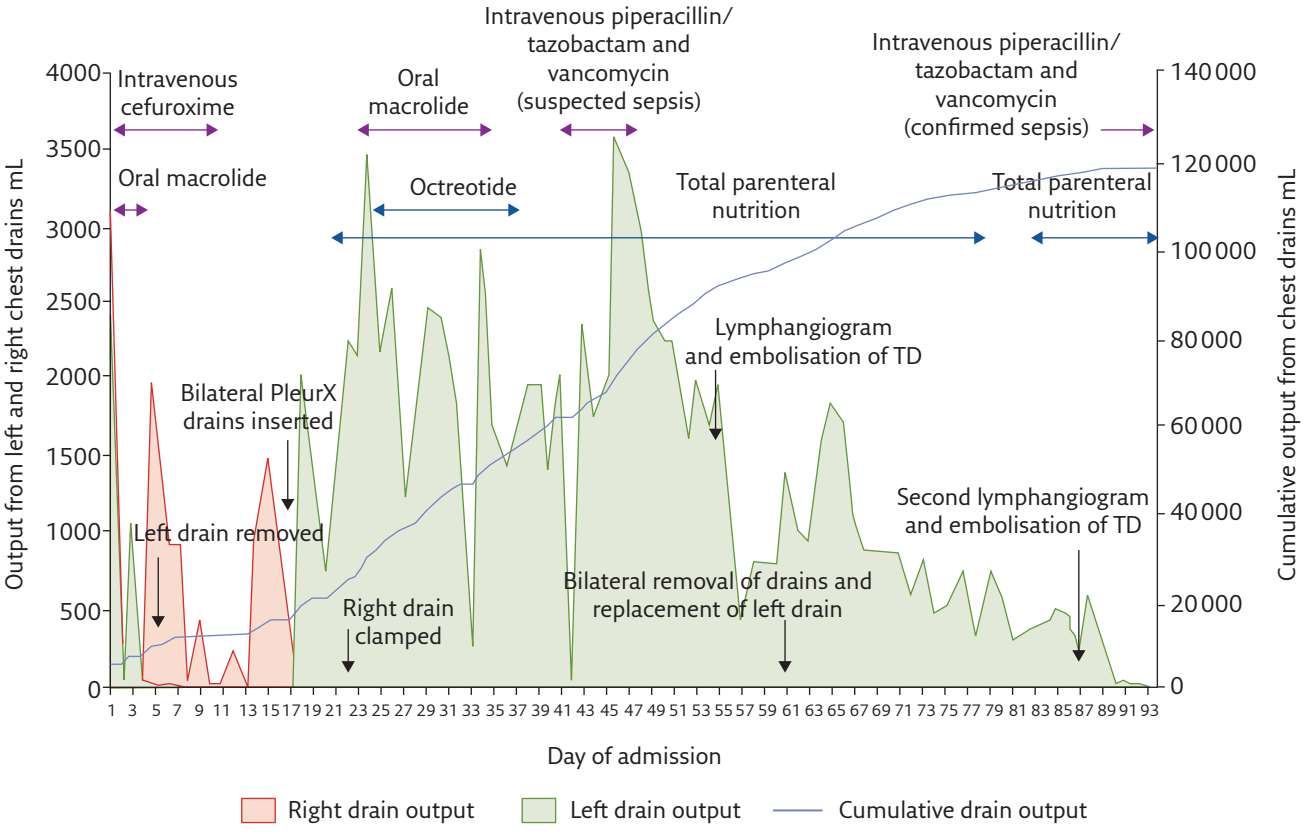

Figure 7 *Output from left and right chest drains and cumulative output over 93 days. TD: thoracic duct.*

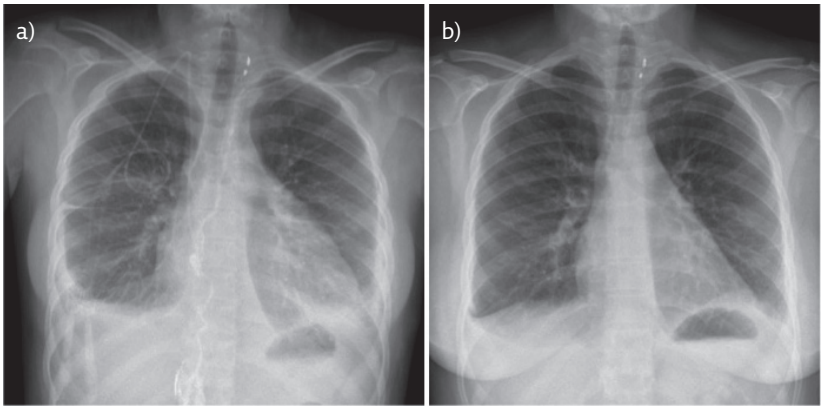

Figure 8 *Follow-up chest radiographs. a) On day 100 prior to discharge home and b) at follow-up in the clinic over 1 year later.*

improved, she started to exercise and returned to school.

2 years later she had resumed normal physical activity without breathlessness and had minimal re-accumulation of fluid on chest radiography (figure 8). Her lung function and lymphocyte count were improved.

There were no abnormal findings in the 15 genes that were analysed for lymphatic disorders.

Discussion

We have not identified the cause of her hilar leak and we assume she had a congenital lymphatic abnormality. Why this presented in her teenage years is unclear. We have not found literature linking *C. psittaci* and *C. pneumoniae* to lymphatic abnormalities, although we wonder whether infection could have triggered growth of a congenital abnormality.

We have shown that chylothoraces in a teenage girl can be successfully treated with glue and coil embolisation. Intranodal lymphangiography and embolisation should be considered with persistent chyle leak.

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Conflict of interest

C.N. Cochrane has nothing to disclose. N. Collin has nothing to disclose. S.C. Langton Hewer has nothing to disclose.

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