

## Recurrent idiopathic chylothorax

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**C**hylothorax is the presence of *chyle* (lymphatic fluid) in the pleural space. Lymphatic fluid secreted by intestinal cells, collected and transported via the thoracic duct, accumulates in the pleural space due to leakage from the thoracic duct or one of its major tributaries.<sup>1,2</sup> In childhood, chylothorax is an infrequent cause of pleural effusion and usually caused by postoperative complication, mainly occurring after cardiothoracic interventions, or by thrombosis of the left or right subclavian vein. Rarely, it is caused by malformation of the pulmonary or thoracic lymphatic system that is associated with dysmorphic syndromes.<sup>3,4</sup> The clinical manifestations are related to the presence of fluid in the thoracic cavity.<sup>2</sup> The diagnosis is established when thoracentesis demonstrates a chylous effusion (milky fluid), but chylothorax also may occur as serous and straw-colored fluid in neonates and children who are malnourished or have not received enteral feeding.<sup>2,5</sup>

The chylous drainage may lead to high morbidity and may even compromise survival because of the large amount of loss, that is, deficits in lymphocytes, protein, and immunoglobulin. The treatment of chylothorax is still debatable with different therapeutic approaches i.e., purely conservative with elemental diet or total parenteral nutrition, or surgical (early or late) with ligation of the thoracic duct, pleurodesis, or placement of pleuroperitoneal shunts.<sup>4,6</sup> The purpose of this report is to describe a case of chylothorax in a 2-year-old girl which was recurrent and difficult to manage.

### Report of the case

A 2-year-old girl was admitted twice to Hasan Sadikin Hospital. On July 10, 2003, she was first hospitalized, referred by other hospital with a diagnosis of left pleural effusion. The patient presented with progressive dyspnea of 5-day duration associated with nonproductive cough. She had a history of anorexia for 1 year and failed to gain weight. No history of tuberculosis was known from household or family members. There was neither chest surgery nor history of trauma before. She is the 7<sup>th</sup> child in her family and was born uneventfully assisted by a practice-trained traditional midwife with a birth weight of 2500 grams.

On the first admission, physical examination revealed a malnourished child with body weight of 7,900 grams (<P<sub>5</sub> NCHS) and height of 77 cm (<P<sub>5</sub> NCHS). She appeared tachypneic (respiratory rate of 48 times per minute) with blood pressure of 90/60 mmHg, pulse rate of 120 beats per minute, and temperature of 36.9°C. There was tracheal deviation to the right side. Examination revealed bulging and respiratory lag of the left chest. The left chest was dull to percussion,

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had decreased vocal fremitus, and diminished breath sounds. Heart examination revealed only distant heart sounds. Neither cyanosis nor clubbing of fingers was noted. There was no enlargement of the lymph nodes.

Laboratory findings showed hemoglobin level of 9.6 g/dl, hematocrit of 34%, platelet count of 601,000/ml, normal PT and aPTT, and WBC of  $7.6 \times 10^3/\mu\text{l}$  with normal differential count. The serum LDH, albumin, and protein total levels were 782 U/L, 4.0 g/dL, and 6.8 g/dl, respectively. Chest x-ray showed left massive pleural effusion with shift of the mediastinum to the right side (**Figure 1**). Tuberculin skin test (Mantoux test) showed 6-mm induration. Left-sided thoracentesis revealed concentrated and reddish fluid which was full of erythrocyte so differential count could not be done. The levels of fluid protein, LDH, and glucose were 4 g/dL, 440 U/L, and 110 mg/dL, respectively. Neither acid-fast bacilli (AFB) nor other bacteria were detected. Culture for *Mycobacterium tuberculosis* (MTB) of pleural fluid yielded a negative result, but polymerase chain reaction (PCR) for MTB was positive.

Histopathologic examination of the pleura showed chronic inflammation due to specific process and no malignancy. Based on such clinical and laboratory findings, the initial working diagnosis was left tuberculous exudative pleural effusion in a severe-malnourished child. She was treated with oral anti-tuberculosis, such as isoniazid, rifampicin, pyrazinamide, repeated thoracentesis, and oral prednison as well.

On the 20<sup>th</sup> day of hospitalization, due to continuing and increasing dyspnea, we repeat a thoracentesis to do several examinations suggested for investigating chylothorax, such as the examinations of triglyceride, cholesterol level, and Sudan III staining of the pleural fluid. A chest tube connected to water-

sealed drainage was placed to decompress the pleural space. The appearance of the pleural fluid was serous and straw-colored with cell count of  $1354/\text{mm}^3$  and 90% lymphocytes, protein level of 3.9 g/dL, LDH 729 U/L, and glucose 126 mg/dL. The triglyceride and cholesterol levels were 1542 mg/dL and 62 mg/dL, respectively and Sudan III test yielded positive result. She was then diagnosed as having left chylothorax. Antituberculous therapy was still continued and prednison was tapered off. She was treated with conservative treatment by giving medium chain triglyceride (MCT) milk, maintaining effective chest tube drainage, and observing drainage daily volume (**Table 1**).

Furthermore, to find out whether the chylothorax was caused by mediastinal lymphadenopathy, we did a chest computed tomographic (CT) scanning. The CT scan confirmed a left pleural effusion with collapse of the left lung but no detection of mediastinal lymphadenopathy (**Figure 2**).

A lymphoscintigraphy examination with Intradermal Sulfur Colloid Tc-99m was also performed and showed radioactivity in the left hemithorax confirming leakage of chyle as shown in **Figure 3**.

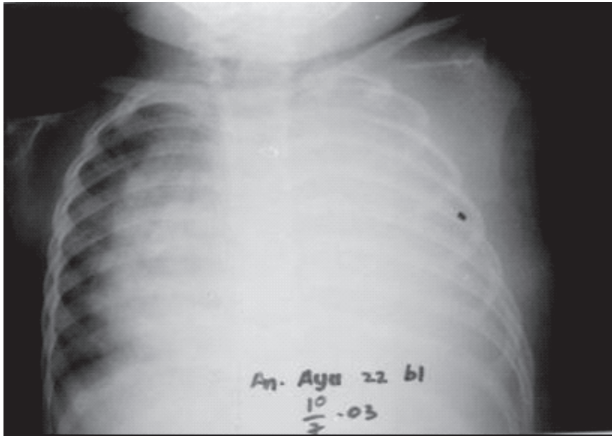
On the 39<sup>th</sup> day of hospitalization, the condition of the patient improved with no chyle production, so the chest tube was released. Chest x-ray and ultrasonography showed no pleural effusion. Antituberculous therapy and MCT diet were still continued. She was discharged from the hospital on the 50<sup>th</sup> day of hospitalization, and advised to have a follow-up visit to the pulmonology outpatient clinic.

On September 13, 2003, after 2 weeks at home, the symptoms recurred with chest x-ray showing left massive pleural effusion. We, therefore, consulted her to the Thorax Surgery Department for operative intervention. Unfortunately, her parents refused the surgery plan. She was then treated with MCT diet and a chest tube connected to water-sealed drainage was left in place to keep the lung expanded.

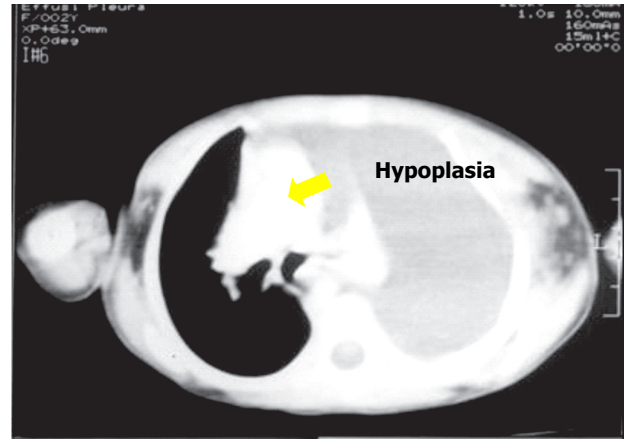
A follow-up after six months of tuberculostatic treatment showed that the patient seemed to take the drugs regularly. After that, we kept monitoring and at the last follow-up (April 17, 2004), her weight gain was still poor. No respiratory symptoms were noted, except dullness to percussion below ICS IV of left hemithorax. Chest x-ray and ultrasonography showed pleural effusion as seen in **Figure 4** and **5**.

**TABLE 1.** VOLUME OBSERVATION OF CHYLE DRAINAGE

Day	Volume (cc)	Day	Volume (cc)
1	500	11	300
2	500	12	150
3	500	13	100
4	500	14	30
5	500	15	10
6	500	16	10
7	500	17	10
8	500	18	10
9	500	19	-
10	500		



**FIGURE 1.** CHEST X-RAY SHOWED LEFT MASSIVE PLEURAL EFFUSION WITH CONTRA-LATERAL SHIFT OF MEDIASTINUM TO THE RIGHT SIDE.

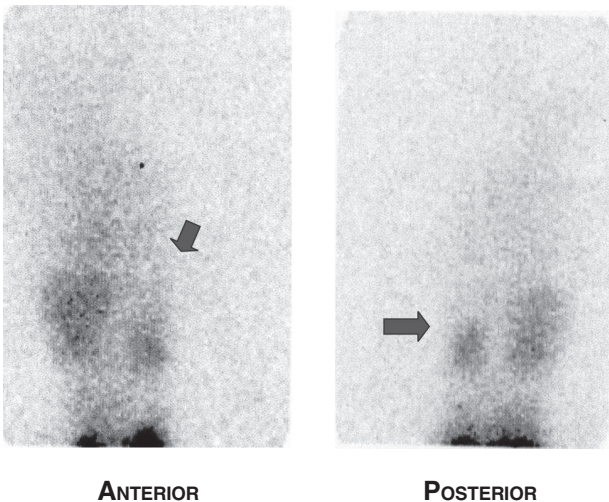


**FIGURE 2.** A COMPUTED TOMOGRAPHIC SCAN OF THE CHEST REVEALED LEFT PLEURAL EFFUSION WITH COLLAPSE OF THE LEFT LUNG AND NO MEDIASTINAL LYMPHADENOPATHY

## Discussion

Chylothorax in children may be a complication of any thoracic surgical procedure, non-iatrogenic trauma, malignant infiltration, or it may occur spontaneously.<sup>6</sup> In 1971, Bessone and colleagues suggested a classification of chylothorax into congenital, postoperative traumatic, nonsurgical traumatic, and nontraumatic chylothorax.<sup>1</sup> Spontaneous nontraumatic chylothorax is uncommon. It can be caused by multiple disorders,

of which neoplasm is by far the most frequent cause. Lymphoma is responsible for almost 75% of malignancy-associated chylothorax. Other causes include filariasis, amyloidosis, thrombosis of jugulosubclavian confluence, hepatic cirrhosis and lymphangiomyomatosis. Many studies reported that patients developed chylothorax after cardiac surgery,<sup>3,4,6</sup> whereas pulmonary tuberculosis is an extremely rare cause of chylothorax.<sup>7</sup> In children with no history of trauma or chest surgery, evidence of malignancy or tuberculosis must be sought.<sup>5</sup>



**FIGURE 3.** LYMPHOSCINTIGRAPHY WITH INTRADERMAL SULFUR COLLOID Tc-99M SHOWED RADIOACTIVITY IN THE LEFT HEMITHORAX

In our patient, diagnosis of left tuberculous pleural effusion was first based on clinical manifestations and laboratory findings including pleural fluid analysis which yielded supportive histopathologic findings and positive PCR for MTB. Study of Nagesh *et al* in India found that PCR shows a sensitivity of 70%, specificity of 100%, and positive predictive value of 100%. So far, it is concluded that a positive PCR result means that a patient definitely has tuberculosis. In tuberculous pleural effusions, which are frequently caused by a hypersensitivity reaction to tuberculous protein, bacillary load may be extremely low and thus PCR is the method of choice for detecting the organism because of its high sensitivity and specificity.<sup>8</sup> For this reason, we gave antituberculous and steroid therapy which then failed to decrease the effusion.

The straw-colored effusion made us initially not think the possibility of chylothorax. We repeat a thoracentesis to investigate the possibility of the presence of





**FIGURE 4.** CHEST X-RAY AT THE LAST FOLLOW-UP STILL SHOWED EFFUSION

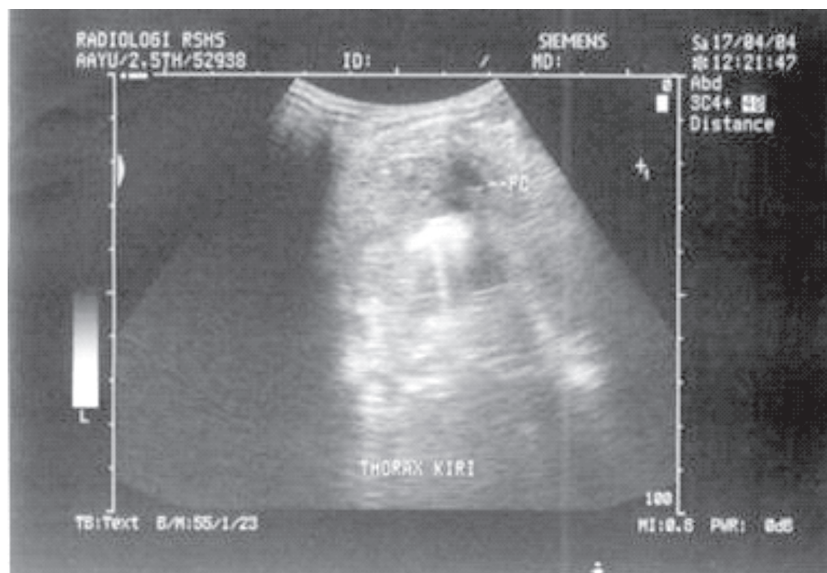
chylothorax by examining triglyceride level, cholesterol level, and Sudan III staining of the pleural fluid.

The diagnosis of chylothorax is highly suggested by the presence of a non-clotting milky fluid, which is obtained from the pleural space at thoracentesis or chest tube insertion.<sup>1</sup> Chyle appears milky because of the presence of chylomicrons<sup>5</sup>. Although Staats *et al* reported that only

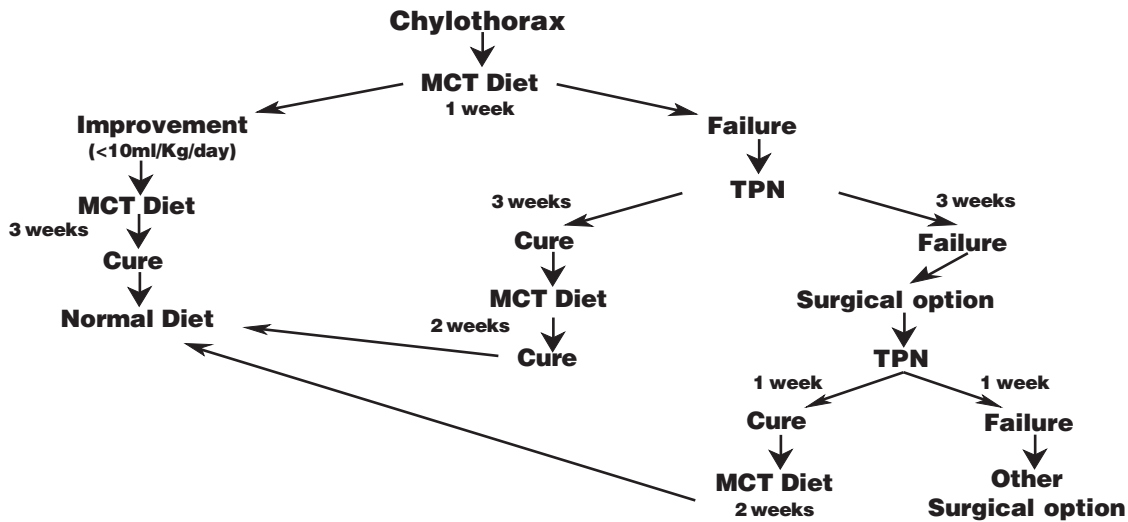
50% of chylous effusions were milky,<sup>3</sup> we initially missed the diagnosis due to the straw-color. In neonates and children who are malnourished or have not received enteral feeding, the chyle may appear as serous and straw-colored fluid.<sup>5</sup> In traumatic chylothorax, the chyle may initially appear blood-stained, and this may be misleading.<sup>1</sup>

Initially, no clear definition of chyle in children existed and very often, adult values were applied for its definition. But since 1999, several studies proposed criteria for diagnosing chylothorax in children i.e., number of cells of  $>1000$  per milliliter with more than 70% of cells presenting as lymphocytes, protein level of  $>2$  g/dL, and sterile culture.<sup>6</sup> Another criteria mentioned a triglyceride level of  $>1.1$  mmol/L and an absolute cell count of  $>1000$  cells/ $\mu$ L, with a lymphocyte fraction of  $>80\%$ .<sup>4</sup> The measurement of triglyceride level in a pleural effusion is the most accurate way to establish the diagnosis. A level of  $>110$  mg/dL reflects a 99% chance that the fluid is chyle, a level of  $<50$  mg/dL almost excludes chylothorax. If triglyceride level is between 50 and 100 mg/dL, a lipoprotein analysis should be done.<sup>3,9,10</sup> The diagnosis is confirmed by the finding of fat globules on microscopic examination with Sudan III staining test.<sup>1,6</sup>

In our patient, the diagnosis of chylothorax was based on the examination of the pleural fluid yielding cell count of  $1354/\text{mm}^3$  ( $>1000/\text{mm}^3$ ) with



**FIGURE 5.** ULTRASONOGRAPHY AT THE LAST FOLLOW-UP STILL SHOWED EFFUSION.



**FIGURE 6.** THERAPEUTIC APPROACH FOR CHYLOTHORAX<sup>6</sup>

lymphocyte fraction of 90%, protein level of 3.9 g/dL (>2 g/dL), triglyceride level of 1542 mg/dL (>110 mg/dL), positive Sudan III test, and a sterile culture. Although the appearance of pleural fluid initially revealed concentrated and reddish fluid, later it was serous and straw-colored. To distinguish from pseudochylothorax, obtaining a cholesterol/triglyceride ratio of the fluid can help because most chylous effusion have a ratio of less than 1, which was found in our patient<sup>11,12</sup> It is important to note that true chyle must be distinguished from pseudochyle that can be caused by pleural tumors or chronic infections.<sup>6</sup> Tuberculosis is the most frequent etiology of pseudochylothorax which usually requires several years to develop, but it also may cause rapid-onset pseudochylothorax.<sup>13,14</sup>

Once the diagnosis of chylothorax is confirmed, the pleural space should be drained and dietary management is begun.<sup>11,12</sup> Patients with chylothorax can be treated by conservative or surgery treatment.<sup>9,12</sup> Although opinions differ as to the ideal management, most authors agree that, at least initially, the management should be non-operative or conservative.<sup>11</sup>

Conservative treatment entails draining of the pleural space with chest tube thoracotomy or repeated thoracentesis, and reducing chyle production by giving total parenteral nutrition or a fat-restricted oral diet supplemented with medium chain triglyceride (**Figure**

6).<sup>6,9,10</sup> There is no standard of how long conservative therapy should be tried before considering operative intervention because in approximately 50% of patients, the thoracic duct leak closes spontaneously, and the other 50% require surgical intervention.<sup>1</sup> Indications for surgical intervention include the following: 1) chyle leak greater than 1 L/day for 5 days or a persistent leak for more than 2 weeks despite conservative management; 2) nutritional or metabolic complications, including electrolyte depletion and immunosuppression; 3) loculated chylothorax; and 4) postesophagectomy chylothorax.<sup>9</sup>

Our patient was initially treated with conservative management consisting of maintaining chest tube connected to water-sealed drainage, providing nutritional support with MCT in milk, and antituberculous therapy. The patient responded to conservative therapy on the 14<sup>th</sup> day (chyle production became <70 cc/day). During the maintenance of chest tube thoracotomy for 20 days, chyle collected was 5620 cc with a mean of 500 cc/day. It started to decrease on the 11<sup>th</sup> day. We released the chest tube on the 19<sup>th</sup> day when there was no more production of chyle. During the follow-up, chylothorax recurred in 3 weeks after the release of chest tube or after 1 month of MCT diet. In consequence, the patient likely required operative intervention.

Although the diagnosis of chylothorax can be confirmed, the etiology of the underlying dis-

ease could not be determined. Chest CT scan showed no mediastinal lymphadenopathy which is one of the causes of chylothorax. Initially, tuberculosis was thought to be the cause based on the clinical manifestations, positive Mantoux test in a severe-malnourished child, and positive PCR of pleural fluid, though it did not match to the pathophysiology of the disease. Yet, we still do not know whether there is malformation of the lymphatics which can spontaneously leak and close as well. Thus, we suggested that our patient had an idiopathic chylothorax even though it is mostly occur in neonates and has good prognosis.<sup>3,11</sup> In the study of Beghetti *et al*, conservative treatment was successful in 80% of the chylothorax patients.<sup>6</sup> Because in this case the etiology of chylothorax was unknown and the patient had recurrent chylothorax and severe malnutrition, the prognosis was poor.

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