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Congenital chylothorax

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Saowani Chumdermpadetsuk* Sudee Chomdej**

พิมลรัตน์ ไทยธรรมยานนท์, เสาวนีย์ จำเดิมเผด็จศึก, สudee ชมเดช. ภาวะ
น้ำเหลืองคั่งในช่องปอดแต่กำเนิด. จุฬาลงกรณ์เวชสาร 2527 ตุลาคม ; 28(10):
1171-1186

รายงานผลสำเร็จของการรักษาผู้ป่วย congenital chylothorax 1 ราย โดย
ไม่ต้องเจาะปอดซ้ำหลายครั้ง หรือใส่ท่อระบายน้ำเหลืองออกจากช่องปอด พร้อมทั้ง
รายละเอียดเกี่ยวกับผู้ป่วยรายอื่นอีก 45 ราย ที่มีรายงานไว้ในวารสารการแพทย์ภาษา
อังกฤษที่สามารถรวบรวมได้ ผู้ป่วยรายนี้เป็นทารกคลอดก่อนกำหนด มีอาการหายใจ
ลำบากตั้งแต่แรกคลอด เกิด pneumothorax ร่วมกับ chylothorax ในช่องปอด
ข้างขวา หลังจากรักษา pneumothorax หาย อาการแสดงของ chylothorax
เด่นชัดขึ้น ได้เจาะน้ำจากช่องปอด 2 ครั้ง และให้การรักษาต่อตามอาการ เลี้ยงด้วยนม
Pregestimil® และน้ำมัน medium chain triglyceride (M.C.T. oil)
chylothorax หายไปเองหมดภายใน 25 วัน

โรคนี้ในทารกอาจเป็นโรคที่หายเองได้ การเจาะปอดซ้ำหลาย ๆ ครั้ง และการ
ใส่ท่อระบายน้ำเหลืองออกจากช่องปอดอาจไม่จำเป็น ยกเว้นในกรณีที่มีอาการหายใจ
ลำบาก

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Pleural effusion is uncommon during neonatal period. It occurs occasionally in babies with Hydrop fetalis, Turner's syndrome or Pneumonia. However, chylothorax is the most common form of pleural effusion encountered within the first 2 months of life. Its etiology may either be from a congenital abnormality of the thoracic duct or a thoracic duct injury during intrathoracic surgery for congenital heart disease, the repair of esophageal atresia or diaphragmatic hernia⁽¹⁾; occlusion of the superior⁽²⁾ vena cava following placement of a central venous catheter can also cause thoracic duct obstruction resulting in chylothorax.

The incidence of congenital chylothorax is extremely low. No case was found among 88,638 deliveries at Chulalongkorn Hospital during 1978-1982. There has been about 60 cases of congenital or spontaneous chylothorax, occurring within the first 2 months of life, reported in English literature since 1926. 45 cases are available for review. Mortality rate was approximately 15.5%. The surviving infants recovered spontaneously within 3-4 weeks without the recurrence of the chylothorax. In this article a case of congenital chylothorax in a premature infant at Chulalongkorn Hospital is reported, presenting successful conservative treatment as an alternative approach that differs from other literatures reviewed.

Clinical features and Pathogenesis of chylothorax

From the review of 45 cases of congenital chylothorax reported in English literature, the infants were mostly full term with normal deliveries. The mothers of 5 infants had polyhydramnios. Boys are more affected than girls (M : F = 29 : 15). Within a varying length of time after birth to 7 weeks, the infants became dyspneic with rapid respiration and retraction. Twenty nine infants (65 percent) had onset within the first 24 hrs. of life and 37 (80 percent) were symptomatic by the end of the first week. In twenty-one cases (50 percent) the right side was involved, in 12 left-sided and 12 bilateral. (Table I)

The etiology of congenital chylothorax is uncertain⁽³⁾. Some authors feel it could be the result of a thoracic duct injury during the birth process. This is unlikely as most patients had no history of difficult delivery while no thoracic duct abnormality was found in those who had had exploratory thoracotomy. Perry RE⁽⁴⁾ et al attempted to demonstrate a rupture of the thoracic duct using the oral administration of fat soluble dyes (such as sudan III) without success. Nevertheless, an increased fetal venous pressure occurring during delivery and eventually leading to the rupture of a weak thoracic duct wall is a possible mechanism. The exact nature of the congenital defect can only be theorized

Table I Summary of 45 cases of Spontaneous chylothorax

Author	Year	Sex	Site	Age of onset	Treatment	No taps	Fluid	Result
1. Stewart and Linner	1926	M	R	4 days	Thoracenthesis	14	Milky, color of egg yolk	died
2. Hilgenberg	1929	M	L	4 days	-	-	Milky	died
3. Janet et al.	1936	M	R	1 day	Thoracenthesis	1	White, creamy	cured
4. Rohleder	1937	M	R	6 days	-	-	Yellow, creamy	-
5. Everhart & Jacobs	1939	M	R	Birth	Thoracenthesis	10-15	Milky, yellow	died
6. Forbes	1944	F	Bilateral	3 weeks	Thoracenthesis	42	Chylous	died
7. Wessel	1944	M	R	13 days	Thoracenthesis	13-15	Milky, Yellow	died
8. Watson and Foster	1946	F	R	7 weeks	Thoracenthesis	14	Milky	cured
9. Bauman	1947	M	L	6-9 weeks	Thoracenthesis	13	Chylous	cured
10. Cuzell and Scherl	1949	M	R	15 hours	Thoracenthesis	6	Turbid, orange	cured
11. Sakula	1950	M	R	2 days	Thoracenthesis	3	Opalescent, yellow	cured
12. Martinez	1950	M	L	4 days	Thoracenthesis	-	-	cured
13. Blood and Fairchild	1953	F	L	3.5 weeks	Thoracenthesis	5	Milky, white	cured
14. Stirlacci	1955	F	R	1 hour	Thoracenthesis	3	Clear, yellow to milky	cured
15. McKendrie et al.	1957	F	L	Birth	Thoracenthesis	7	Milky	cured

Table I (continue)

Author	Year	Sex	Site	Age of onset	Treatment	No taps	Fluid	Result
16. Currarino and Silverman	1957	F	R	6 hours	Thoracentesis	-	Strawcolored	died
17. Feinerman et al.	1957	M	L	5 days	Thoracentesis	1	Chylous	cured
18. Randolp and Gross	1957	M	L	1 hour	Thoracentesis, Explore thoracotomy	10	Milky	cured
19. Randolp and Gross	1957	F	L	Birth	Thoracentesis, Explore thoracotomy	7	Thick gray-yellow to milky	cured
20. Dahl and Sawyer	1959	M	L	7 days	Thoracentesis	6	creamy, orange yellow	cured
21. Boles and Izant	1960	M	R	4 weeks	Thoracentesis	27	Milky	cured
22. Boles and Izant	1960	M	R	Birth	Thoracentesis	5	Serous to milky	cured
23. Stephen and Otto	1961	M	Bilateral	Birth	Thoracentesis	1	Clear, yellow	cured
24. Represse et al.	1962	M	L	Birth	Thoracentesis	3	Transparent, yellow orange	cured
25. Breton et al.	1962	F	R	14 days	Thoracentesis	1	Lactescent, yellow	cured
26. Perry et al.	1963	M	R	58 hours	Thoracentesis, Tube thoracotomy	3	Turbid orange	cured
27. Bornhurst and Carsky	1964	F	Bilateral	1 day	Thoracentesis	2	Clear, yellow	died
28. Bornhurst and Carsky	1964	M	L	Birth	Tube thoracotomy	1	Clear, yellow	cured

32. Brodman et al.	1974	M	R	18 hours	Thoracenthesis, Tube thoracotomy	3	Clear, straw colored	cured
33. Bensoussan et al.	1975	F	Bilateral	5 hours	Thoracenthesis, Tube thoracotomy	5	Clear yellow to milky	cured
34. Peitersen and Jacobson	1977	F	R	Birth	MCT diet and Tube- thoracotomy	-	Milky	cured
35. Yoss and Lipsitz	1977	M	L	Birth	Thoracenthesis	1	Serous, clear	cured
36. Yoss and Lipsitz	1977	M	R	Birth	Thoracenthesis	2	Yellow, clear	cured
37. Koffler et al.	1978	M	Bilateral	Birth	MCT diet, Thoracenthesis, Tube thoracotomy	1	Yellow, clear to milky	cured
38. Koffler et al.	1978	M	Bilateral	Birth	MCT diet, Thoracenthesis, Tube thoracotomy	1	Yellow, clear	cured
39. Vain et al.	1980	M	R	14 days	MCT diet, Thoracenthesis, Tube thoracotomy	1	-	cured
40. Vain et al.	1980	M	Bilateral	Birth	MCT diet, Thoracenthesis, Tube thoracotomy	1	-	cured
41. Vain et al.	1980	F	Bilateral	Birth	MCT diet, Thoracenthesis, Tube thoracotomy	1	-	cured
42. Vain et al.	1980	M	Bilateral	Birth	MCT diet, Thoracenthesis, Tube thoracotomy	1	-	cured
43. Vain et al.	1980	M	Bilateral	Birth	MCT diet, Thoracenthesis, Tube thoracotomy	1	-	cured
44. Lange and Manning	1981	-	Bilateral	Birth	Thoracenthesis, Tube thoracotomy	Rt x 2 Lt x 1	Straw color to cloudy	cured
45. Petres	1982	F	Bilateral	Birth	Thoracenthesis, Tube thoracotomy	2	Clear, golden to chylous	cured

and not proved at this time, but an immaturity of the lymphatic development may be an underlying cause. Mckendry⁽⁶⁾ has recorded autopsy findings disclosing dilated peripheral lymphatics which apparently failed to communicate with the more central channels. Furthermore, many associated conditions in congenital chylothorax have been reported such as congenital lymphangiomatosis⁽⁶⁾, congenital marble skin (cutis marmorata telangiectatica) and Down's syndrome.⁽⁷⁾ Causes of chylothorax in adults or children are summarized in Table II.

Table II Causes of chylothorax

- I. Trauma**
 1. Penetrating wounds
 2. Crushing injuries to chest or spine
 3. Spinal hyperextension
 4. Precipitous rise of intrathoracic pressure
 5. Surgical mishap
- II. Neoplasm**
 1. Primary in the mediastinum
 2. Metastatic to mediastinal lymph nodes
 3. Metastatic foci in the intra-ductal lymph stream
 4. Primary tumor of the thoracic duct
- III. Infection**
 1. Tuberculous lymphadenitis
 2. Nonspecific mediastinitis
 3. Ascending lymphangitis
 4. Filariasis

IV. Venous thrombosis

1. Left subclavian, left jugular
2. Superior vena cava

V. Aortic aneurysmal erosion

VI. Congenital anomalies of the ductal system

Clinical pictures

Respiratory difficulty may be noted immediately after birth or may appear insidiously, with a subtle intermittent tachypnea or dyspnea, which may occur only when the baby cries or is fed. Cyanosis may or may not be present. Those infants with delay onset of symptoms may develop satisfactorily for many weeks before experiencing sudden collapse with a shock-like picture; dyspnea is then usually present and cyanosis develops frequently during such episodes. Nutritional depletion almost always ensues, later when the loss of chyle by repeated thoracentesis is significant. Physical examination discloses a striking absence of fever in a patient with severe respiratory distress. Respiratory rate may be 100 per minute and retraction is frequently seen. Signs on the involved side include decreased chest movement, dullness to percussion, decreased aeration, and often a shift of the apex beat away from the affected side.

Laboratory data

1. **Blood count** : anemia is not a feature of the illness. The total leukocyte count is usually normal. Lymphocytopenia can be reasonably expected as a consequence of chyle loss, although it is not always present.

2. Chest roentgenography Generally, it shows massive effusion with marked compression of the lung. Other causes of respiratory distress may be ruled out by the chest film. In the case of massive bilateral pleural effusion, the cardiac shadow may be obscured. Ultrasonography or diagnostic thoracentesis will establish the diagnosis.

3. Chemical analysis of the effusion

The diagnosis should be suspected at the initial thoracentesis; it is substantiated by an assay of the fluid as outlined in Table III. The actual nature of the effusion is apparently related to the dietary intake of the infant. Initially, the fluid is clear and straw colored, but as fats in the milk are introduced, a chylous, milky appearance is noted. Breast-fed babies with chylothorax may exhibit a bright yellow stain in the chyle.

Table III Characteristics of chyle^(s)

1. Milky appearance
2. Separates into 2 distinct layers on standing
3. Clears when fat is extracted by alkali and ether
4. Most of the fat present is neutral fat
5. Odorless
6. Sterile
7. Bacteriostatic
8. Alkaline reaction
9. Fat content 160 to 660 mg/dl
10. Specific gravity greater than 1012
11. Protein content generally between 2.4 and 6.2 mg/dl.
12. Cholesterol content 48-200 mg/dl

13. Leukocyte count and composition vary, but lymphocytes predominate

14. Stains with any lipophilic dye

Treatment

Objectives of management of chylothorax are as follow :

1. maintenance of nutrition and ventilation in the hope that spontaneous cessation of the leakage will occur. This aim can be accomplished by parenteral nutrition to replace the chyle loss and thoracentesis.

2. diminishing the chyle leak from the thoracic duct by feeding the infant with a medium chain triglyceride (MCT) diet.

3. keeping the lungs fully expanded so that the visceral and parietal pleura will approximate to obliterate the thoracic duct leakage.

There are 2 methods of management of chylothorax, non operative and operative treatment.

1. Non operative treatment

Results of medical treatment are satisfactory. Thirty eight of the 45 reported cases are cured by thoracentesis. In 13 percent of them the effusion ceases after a single thoracentesis. However, usually the fluid reaccumulates and multiple thoracentesis are required. As many as 42 thoracentesis were performed on a single patient reported by Forbes and as much as 2,000 ml of chyle was aspirated. Unfortunately, this patient died with severe inanition. The mortality rate is high being about 15 percent. The usual therapy for chylothorax consists of repeated thoracentesis and MCT oral

formula. Generally thoracentesis is instituted clinically for the diagnostic purpose or when severe uncompensated respiratory distress occurs and persists until fluid accumulation decreases. Brodman RF⁽⁹⁾ et al recommended a maximum of three thoracentesis. If fluid reaccumulated after the third thoracentesis, a chest tube drainage should be instituted on the affected side. Continuous suction on the chest tube not recommended, because the increase in negative intrapleural pressure may keep the duct fistula open. Meanwhile oral feeding should be discontinued and substituted with intravenous alimentation. Recently, there have been encouraging reports of the use of a MCT diet in patients with chylothorax,⁽¹⁰⁾ the rationale being a reduction in the chyle flow and thereby a decreased accumulation in the pleural spaces. This fat is not absorbed by the lymphatic system but enters the portal venous system.

Kurtz TW and Hsu CH reported a case of chylothorax in an adult which resolved rapidly when mechanical ventilation with positive end expiratory pressure was begun for the treatment of an acute respiratory distress syndrome. They believed that PEEP may induce elevations in the functional residual capacity and total lung volume. Therefore, approximation of the pleurae would be facilitated by the complete lung expansion, promoting a tamponade of the thoracic duct defect. Pilon RN supported this logical approach and found, in his study using anesthetized dogs, that there was a highly significant relationship between the application of PEEP and the

reduction of lymph flow. He further speculated that continuous positive airway pressure (CPAP) could also reduce the lymphatic flow.

2. Operative treatment

Surgery is usually not indicated in the treatment of chylothorax, since the site of leakage is generally not apparent by gross examination at operation. In 1946 Lampson performed the first successful intrathoracic ligation of a traumatic chylous fistula in human. This method of direct approach has subsequently been used in the treatment of many cases of chylothorax. Thoracotomy should be performed on the side of the effusion. Randolph JG and Gross RE⁽⁸⁾ in 1957 described the first two cases of congenital chylothorax treated by operation. Their aims of treatment were to ligate the leaking vessels whenever possible, or the main thoracic duct above and below the leak when the exact site of leakage cannot be determined, and poudrage to produce a pleurodesis. Curci MR and Dibbins AW performed a parietal pleurectomy in one infant with massive chylous effusion and no specific site for a chyle leak identified. The chylothorax cleared immediately following the operation. They felt that if 3-4 weeks of medical management failed, an operation was indicated. Since medical treatment yields excellent results (38 of 45 cases or 84% were cured within 3-4 weeks) and it is difficult to find the leakage during operation, most surgeons try to avoid surgery in these infants. However surgical treatment may be beneficial in treating those

infants who do not respond to 4 weeks of medical treatment or infants with other associated lymphatic anomalies such as lymphangiomatosis or congenital marble skin.

Case report

A premature 2670 gm. female infant was born spontaneously to a G₂P₁ Indian mother on October 10, 1983. Her mother had been on several medications, such as Depo-Provera, Duvadilan, for 3-4 weeks to stop the premature labor prior to delivery. Apgar scores were 5 and 7 at 1st and 5th minute respectively.

Physical examination revealed a 36 week gestation infant who had tachypnea (RR 50-60/min), grunting, coarse rales over both lungs, 3 cm. enlarged liver and edematous hands and legs. C.B.C. showed Hb. 19.4 gm/dl Hct. 58% WBC 16,800/mm³ N 30% L 56% E 12% Band 2% NRBC 8%. Urinalysis was normal. Oxygen, Penicillin G. Sodium, Gentamicin and intravenous fluid were administered. On the next day (October 11, 1983), she remained pink in the oxygen box but rather irritable and developed more tachypnea (RR 84-100/min), more grunting with subcostal retraction and diminished breath sounds over the Rt.

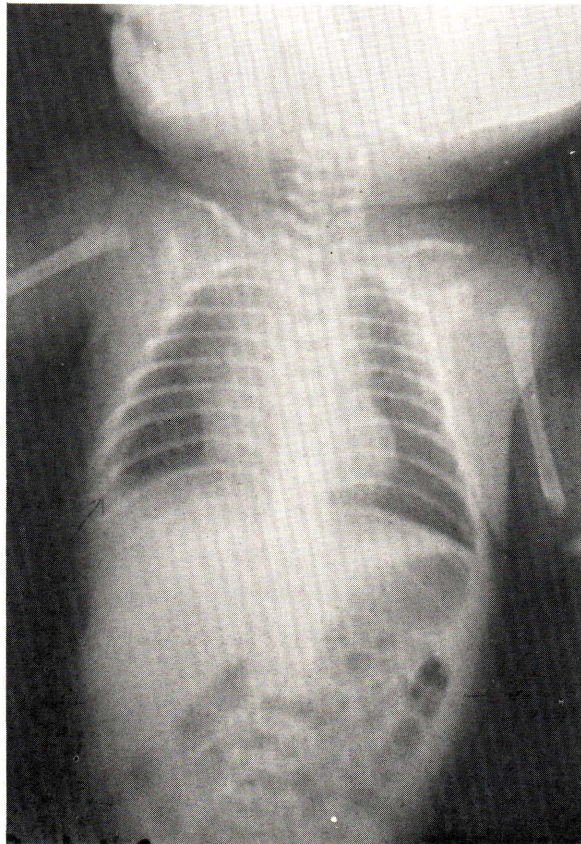


Figure 1 Chest x-ray film taken on the 2nd day of life showed hyperaeration and minimal Rt. pleural effusion (arrow).

side of the chest. Heart sounds were normal, best heard in the Lt side. Chest roentgenogram showed a suspicious Rt pneumothorax, with hyperaeration and minimal Rt. pleural effusion. (Figure 1). The infant was referred to the nursery of Chulalongkorn hospital. Needle aspiration of Rt. chest yielded continuous flow of air. Underwater drainage with No. 12 Fr. polyethylene tube was performed with continuous low-pressure suction. Respiration immediately became less labored. Chest tube was removed on

October 14, 1983. Oxygen was discontinued and feeding was begun on October 16, 1983. Repeated chest x-ray showed well expanded lungs with minimal Rt. pleural effusion. The infant was still tachypneic (RR 68-74/min) without cyanosis or retraction. The wound of Rt. chest drainage was also infected, but the culture yielded no growth. She was transferred back to the hospital where she was born. Repeated chest film on October 18, 1983, disclosed that the Rt pleural effusion has significantly

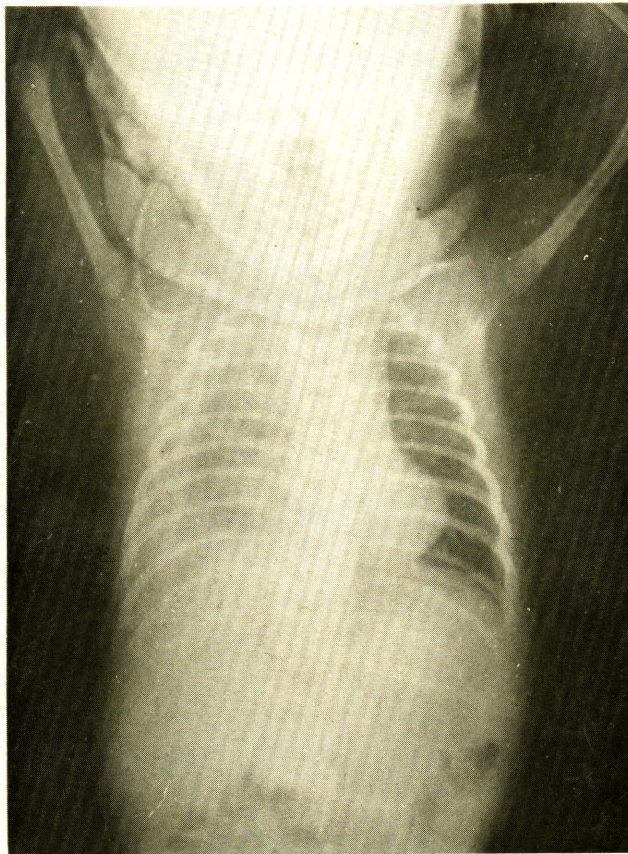


Figure 2 Chest x-ray film taken on the 9th day of life showed significant increase in Rt. pleural effusion.

increased (Figure 2). Forty-five milliliter of yellowish pus-like fluid was removed by thoracentesis. Analysis of the pleural fluid are shown in Table IV. Respiratory difficulty had diminished (RR 50-60/min). Heart and lungs were within normal limits on the roentgenogram. Antibiotics were changed to cloxacillin and amikacin. Feeding was continued with breast milk and Pregestimil.^(R) On October 24, 1983 recurrent Rt. pleural effusion was noted from the chest x-ray. The 2nd thoracentesis yielded 44 ml. of milky yellowish fluid. (Table IV) Based on these findings, the diagnosis of chylothorax was made. Feeding was continued with Pregestimil and MCT only. Despite the recollection of fluid noted on the 2 subsequent weekly chest x-ray films, she continued to be clinically stable in terms of respiratory status, (RR 68-76/min) and gradually could better tolerate bottle feeding. Chest aspiration was therefore not repeated. At the age of 33 days her breathing pattern was much less labored and slowed to 56/min. Due to the presence of diarrheal symptoms, cholestyramine (Questran)[®] ½ package x 3/day for 3 days was started on the 34th day of life. The effusion ceased completely on the 38th day. The infant breathed normally and tolerated feeding well. There was no demonstrated recurrent pleural effusion on follow up at the age of 8 months. She was changed to regular formula without difficulty.

Discussion

The diagnosis of congenital chylothorax can be made clinically and be confirmed roentgenographically. The roentgenographic diagnosis is sometimes difficult when faced with pulmonary atelectasis or pneumothorax. Our patient is different from the other reported cases because pneumothorax presented first, probably secondary to vigorous resuscitation at birth. Through retrospective evaluation, the onset of chylothorax in this infant may be assumed to have been positive from the first day of life since pleural effusion was already demonstrated in the chest roentgenogram. Thoracostomy drainage of the pneumothorax should not cause thoracic duct injury.

If a pleural effusion is noted during the neonatal period, an initial diagnostic and therapeutic tap should be performed, removing as much fluid as possible, to verify its high fat and protein content. The characters of the fluid obtained from the first thoracentesis were compatible with chyle. It consisted of a high protein content (4.5 gm/dl) and numerous mononuclear cells. Delayed diagnosis of chylothorax in this infant was caused by the presence of an infected thoracostomy wound.

The morbidity and mortality associated with chylothorax are related to the volume of chyle produced and the length of time required to correct this condition. Most authors prefer to insert a chest tube for continuous drainage, if the effusion is large in

amount and recurrent. Although tube thoracotomy may reduce the incidence of pneumothorax complicated by repeated thoracenteses and the duration of illness, it carries definite complications. Obstruction of the chest tube is frequently encountered. This is due to the high protein content of chyle and the technical limitation of insertion of the larger tube. In addition, significant losses of fats and proteins through massive chyle loss may affect the nutritional status of the infant. Adverse effects of chyle loss are listed in Table V. Infants with excessive chyle loss should be considered high risks to infection and should be aggressively treated for infection. Mc Williams⁽¹³⁾ et al examined the T-lymphocyte number in three patients who developed post-operative chylothoraces and found that all patients developed transient T-lymphocyte depression and a proportional increase in B-lymphocytes similar to that seen in long term thoracic duct drainage. Since the immunoglobulin contents in the chyle are related to the serum, hypogammaglobulinemia may occur. Berberich et al⁽⁶⁾ found that both humoral and cell-mediated immunity returned to normal when the chylous drainage stopped.

Table V Adverse effects of excessive chyle loss

1. Loss of water, salt, protein and fat
2. Metabolic acidosis⁽¹⁴⁾
3. Lymphocytopenia
4. Hypogammaglobulinemia

Prematurity in our reported case added more to these problems. Although she was tachypneic, her nutritional status could be maintained appropriately by both bottle and gavage feedings, and her condition had remained stable without severe respiratory embarrassment, so that repeated thoracentesis or tube thoracotomy were not indicated. The chylothorax gradually decreased and disappeared by the age of 38 days. Total duration of conservative treatment with MCT diet was 25 days. The patient gained weight well and has no evidence of nutritional deficit nor infection. Therefore, conservative treatment should be the suitable regimen of management of the congenital chylothorax. Oral administration of cholestyramine can diminish intestinal fat absorption. Its effect on chyle leak in our patient is not conclusive. Since the patient's respiration rate had decreased prior to the administration of cholestyramine, the ceasing of chylothorax in this patient was probably not due to this drug. However, further study of this drug on patients with chylothorax or chylous ascites should be done with precaution.

There are at least 3 brands of MCT formula, Portagen, Biosorbin and Pregestimil. Their MCT contents are 80%, 87.5% and 40% respectively, with other essential fatty acids in the form of long chain triglycerides. Infants fed with these formulae still have chyle leaks and may be cured slower than those infants receiving only parenteral nutrition. Peitersen B and Jacobson

BB⁽¹⁵⁾ studied the volume and contents of lipid and protein in the pleural fluid from a patient with spontaneous chylothorax and found that the pleural fluid production could not be correlated with the treatment neither of parenteral nonfatty nutrition nor the administration of "Biosorbin". Triglyceride and total fatty acid concentrations in the pleural fluid decreased significantly during parenteral treatment but increased during the MCT treatment to the levels seen when the child was fed with human milk. They concluded that the ceasing of the pleural effusion might have indicated a spontaneous recovery in accordance with the natural cause of the chylothorax.

Although congenital chylothorax is an uncommon occurrence in the newborn period it may create a life threatening situation either from respiratory embarrassment or from malnutrition secondary to the loss of chyle rich in proteins and lipids. Early diagnosis should be established since the prognosis is very favorable. Antepartum diagnosis is reported in several cases, by ultrasonography.^(10,17) These infants are treated in utero and immediately after birth. Without early and correct diagnosis these infants would not have survived. The physician's awareness and understanding of the disease are essential in the management of congenital chylothorax.

Table IV Analysis of the pleural fluid

No. of Thoracentesis	Age (d)	Amount (ml)	Characters of fluid	Sp. Gr.	Cell count (/ ml) and differential	Protein (gm/dl)	Sugar (mg/dl)	Cholesterol (mg/dl)	Granstain and C/S
1	7	45	Yellowish, Pus-like	1030	Mononuclear; 14,250	4.5	100	-	negative
2	13	44	Yellow, milky	1033	Mononuclear; 8,750	6.25	90	140	negative

อ้างอิง

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