Eur J Pediatr (1986) 145:286–292

European Journal of
Pediatrics

Primary lymphatic dysplasia in children: chylothorax, chylous ascites, and generalized lymphatic dysplasia

D.M. Smeltzer, G.B. Stickler, and R.E. Fleming

Mayo Medical School and Department of Pediatrics, Mayo Clinic and Mayo Foundation, Rochester, Minnesota, USA

Abstract. Primary lymphatic "dysplasia", a congenital maldevelopment, interferes with function of the lymphatic system and causes effusion of chyle or lymph into the limbs and pleural or peritoneal cavity. Between 1955 and 1982, 38 Mayo Clinic patients were found to have a chylous effusion or dysplasia of the lymphatic system. In 22, the condition was secondary to surgery or other medical problems and in 16 it was primary. These cases were separated into three categories: chylothorax, chylous ascites, and generalized lymphatic dysplasia. Conservative therapy, such as a restricted fat diet or total parenteral nutrition with repeated thoracentesis or paracentesis, was effective in the children with isolated abnormalities of the lymphatic system (75% resolution rate, no deaths). All five children with documented generalized dysplasia reported in the literature had died; of the three reported here, one has died and two have become progressively worse.

Key words: Lymphatic diseases – Dysplasia

Introduction

Lymphatic "dysplasia" is a congenital maldevelopment of the lymphatic system interfering with its function and causing an effusion of chyle or lymph into the limbs and pleural or peritoneal cavity. There are four major presentations of primary lymphatic dysplasia in children: (1) lymphedema; (2) chylothorax, sometimes associated with lymphangiomatosis; (3) chylous ascites, occasionally with signs of intestinal lymphangiectasia; and (4) generalized lymphatic dysplasia, i.e., the presence of all three components.

This paper presents our experience with children who have chylothorax or chylous ascites, or both, but especially those with generalized lymphatic dysplasia. Since primary lymphedema in children and adolescents was reviewed recently [36], it will not be examined closely in this report.

Methods

The medical index record retrieval system at the Mayo Clinic ensured that the records of virtually all patients through 20 years of age seen between 1955 and 1982 and given a diagnosis of "chylothorax," "chylous ascites," or "lymphangiectasis" became available for review.

Further, the recorded results of 141 consecutive thoracenteses and 30 consecutive abdominal paracenteses performed between 1956 and 1982, in patients from birth through age 20 years, were examined to identify additional cases of chylous effusion.

A chylous effusion was defined as one that was "cloudy," "milky," or "resembling chyle or lymph" (since most patients were on a diet containing fat) and having a total fat content greater than 1000 mg/dl with elevated concentrations of chylomicrons and triglycerides, total protein exceeding 3 g/dl or exceeding half the plasma protein, and a specific gravity greater than 1.012 but containing no microorganisms [21, 30, 35, 40, 44, 50].

Offprint requests to: G.B. Stickler, Mayo Clinic, 200 First Street SW, Rochester, MN 55905, USA

Abbreviations: CT = computed tomography; TPN = total parenteral nutrition

Cases identified

Either a chylous effusion or a dysplasia of the lymphatic system was found in 38 cases. The problem was postoperative chylothorax in 18 – following repair of congenital heart disease in 17 and repair of a tracheoesophageal fistula in 1. Additionally, there was a case of generalized lymphangiectasis without chylothorax or chylous ascites, one of chylothorax secondary to Hodgkin disease, one secondary to nephrotic syndrome, and a fourth consisting of a single lymphangioma. These cases (22 altogether) will not be discussed further because they are considered to be secondary lymphatic dysplasia. Table 1 provides clinical data on each of the 16 cases retained for study.

Of the 141 consecutive thoracenteses reviewed, 21 (15%) demonstrated a chylous effusion; and half of these were secondary to thoracic surgery. Only one pleural effusion was due to a neoplasm, and it was chylous. None of the 30 consecutive paracenteses was chylous.

Correlation with outcome implies that the cases are best divided into categories of single abnormalities (chylothorax or chylous ascites) and multiple abnormalities representing generalized dysplasia.

Single manifestations

Of the patients with only chylothorax or chylous ascites (cases 1–12), seven were girls and five were boys. The onset of their symptoms was generally early in life, occurring at birth in two and at or before the age of 2 in six others. The signs included

Table 1. Clinical data on 16 cases of primary lymphedema

Case no.	Sex	Age at		Associated conditions and complications	Outcome[a]
		Onset	Diagnosis		
Chylothorax					
1 [33]	F	3 months	4 years	Lymphedema Osteomyelitis in recurrent hemangioma of femur	Resolution
2 [33]	F	2 months	13 months	Lymphedema Anorexia nervosa at age 18 years	Died secondary to anorexia nervosa; chylothorax resolved
3 [12,33]	F	Birth	6 days	None	Resolution with thoracentesis
4	M	2 years	7 years	Lymphedema Hemangioma of femur Hepatosplenomegaly Scrotal reflux	Stable for 3 years with conservative treatment
5	F	15 years	15 years	Febrile illness – pneumonia?	Recurrent despite repeated thoracenteses for 1 year
6	M	1 week	3 weeks	None	Resolution with thoracentesis
7	F	8 years	18 years	Hemoptysis Lymphangiomatosis?	Worse after 2 years without treatment
Chylous ascites					
8	M	3 years	9 years	Lymphedema Intestinal lymphangiectasia Steatorrhea	Resolution with MCT diet
9	F	16 months	3 years	Strawberry hemangioma Intestinal lymphangiectasia Steatorrhea	Improvement with MCT diet
10 [16]	F	5 years	5 years	Cytomegalovirus infection	Resolution with paracentesis
11	M	18 months	2 years	None	Unknown
12	M	Birth	1 month	Lymphedema Hemophilia A	Resolution with MCT diet and paracentesis
Chylous ascites and chylothorax					
13	M	Birth	1 year	None	Resolution with MCT diet
Generalized lymphatic dysplasia					
14	M	Birth	6 years	Lymphangioma of femur	Worse 6 years later
15	M	Birth	4 years	Exploratory laparotomy negative	Died secondary to respiratory insufficiency
16	M	16 years	19 years	Cellulitis of scrotum Laparotomy negative	Worse 4 years later

[a] MCT = medium-chain triglyceride

lymphedema in five patients, intestinal lymphangiectasia in two who had chylous ascites, hemangiomas in two with chylothorax, and a strawberry hemangioma in one with chylous ascites. Complications included osteomyelitis in a child with chylothorax, possible pneumonia in one with chylothorax, and a cytomegalovirus infection in one with chylous ascites (Table 1). The outcome in these 12 cases of single abnormality was generally good. Symptoms resolved or stabilized with conservative treatment in nine and worsened in only two. (One other had no follow-up.) None of the patients traced died.

Two manifestations

Case 13 seems to fall between the group with a single abnormality and that with generalized lymphatic dysplasia. The patient had chylous ascites and chylothorax; both were present at birth – yet his symptoms resolved with conservative treatment.

Generalized lymphatic dysplasia

Of the three patients with multiple abnormalities (cases 14–16), all were boys and in two the onset of symptoms was at birth. Patient 14 had a probable lymphangioma of the femur and patient 16 had recurrent cellulitis in lymphedema of the scrotum. Exploratory laparotomy to rule out a potentially treatable condition in two of these cases was not helpful. At follow-up, one patient had died and the other two had progression of symptoms at 4 and 6 years.

Case 14. A boy was 11 years old when first seen at this institution in August 1983. His sister had died at the age of 4 because of endocardial fibroelastosis, but he had two healthy brothers.

No relatives had a history of lymphatic disorders. The patient had been born by normal vaginal delivery, but was noted at birth to have respiratory distress, a right clavicle fracture, scrotal edema, and bilateral lower limb edema.

His early growth and development had been complicated by increasing swelling of the lower limbs and scrotum and by the presence of dyspnea on exertion. At 5 or 6 months, examination had identified bilateral pleural effusion, hemangioma of the forehead, and lymphedema of the legs, scrotum, and penis; lymphangiography had shown "blocked lymphatics." Pneumonia has occurred at 2 and 4.5 years, a left femur fracture at the age of 3, and a series of clavicle fractures secondary to minor falls (possibly associated with lymphangiomas).

At 5 years old, dyspnea on exertion, orthopnea, and exercise intolerance had been noted; and 8 months later (at 6 years) an examination had been performed. He was found then to be "husky," with pitted ear lobules, mild hepatosplenomegaly, ascites, and a bilateral pleural effusion. Studies included lymphangiography, which showed "retrograde flow from iliac to scrotal lymphatics and lymph flowing from periaortic nodes to intercostal nodes bilaterally." Thoracentesis of the pleural effusion produced 40 ml of chylous fluid (analysis: glucose, 91 mg/dl; protein, 6.3 g/dl; amylase, 29 units/l; lactic dehydrogenase, 340 units/l; and triglycerides, 1728 mg/dl). Spironolactone had been prescribed, and a no-added-salt diet had been recommended.

By the age of 8, the patient had discontinued all medication. A low-salt, low-fat diet was associated with subsequent improvement of the leg edema but worsening of the scrotal edema.

At the age of 11, the patient was referred to this institution for evaluation for possible scrotal debulking surgery. On examination, his height was 133 cm (5th–10th centile) and weight 36.6 kg (50th–75th centile). He was found to have pitted ear lobules, longitudinal facial shape, massive scrotal edema, ascites, an enlarged spleen (4 cm below the costal margin), and minimal lower limb swelling (left greater than right). Chest radiographs showed a large left pleural effusion. A computed tomography (CT) scan of the chest and abdomen showed pleural fluid and thickening bilaterally, with pelvic ascites. Electrocardiographic and echocardiographic findings were normal, as were values for sodium, total protein, creatinine, alkaline phosphatase, aspartate aminotransferase, cholesterol, triglycerides, and albumin. The hemoglobin value was 11.8 g/dl.

Surgical treatment for the huge scrotal swelling was postponed because of the respiratory insufficiency.

Three months after this examination, sepsis developed from streptococcal pharyngitis and caused osteomyelitis of the left ankle. Surgical drainage of the infected region was undertaken elsewhere; but under general anaesthesia a left pneumothorax and pulmonary edema led to respiratory failure, which he survived.

At the age of 11.5 years the patient returned here to be evaluated for scrotal surgery. He was moderately restricted in physical activity because of dyspnea but otherwise asymptomatic. The physical findings were unchanged. A chest radiograph showed a large left pleural effusion. Pulmonary function tests disclosed a mixed restrictive and obstructive pattern with approximately 50% reduction from predicted normal flow rates, vital capacity, and functional residual capacity. Scrotal debulking surgery was delayed again because of concern over pulmonary function during anaesthesia.

Case 15. The boy was 4 years old when seen initially at the Mayo Clinic. There was no family history of lymphatic disorders or swelling. He was the product of a normal pregnancy and delivery. At his birth, his mother had noted that he had a left groin mass, and by the age of 2 days his left thigh had become larger than the right thigh. Progressive enlargement of the left leg and left half of the penis and scrotum had continued up to the age of 6 months, and the problem was diagnosed as congenital lymphedema.

At 14 months an exploratory laparotomy, performed because of a left lower quadrant abdominal mass, showed lymphedema of the lower bowel and retroperitoneal space. However, postoperatively, the swelling remained stable and the patient was relatively healthy.

At 4 years, he had had gradual onset of swelling of the middle epigastric area. Three months before admission here, he had experienced colicky pain lasting 2 or 3 days, localized to the left flank and subcostal area. The swelling initially increased but shortly after repeated vomiting it began to diminish spontaneously.

The patient was referred to this institution because of continued ascites. On examination, his height was 102 cm (25th centile) and weight was 19.5 kg (70th–90th centile). The left lower limb was swollen to the hip, and ascites and a left pleural effusion were noted. A chest radiograph showed pleural effusion. A lower limb radiograph showed increased subcutaneous tissue, consistent with lymphedema. The hemoglobin value was 11.0 g/dl and the leukocyte count was 1700/μl. Findings from urinalysis were normal. Thoracentesis showed milky fluid (protein, 5.25 g/dl; fat, 2336 mg/dl). Abdominal exploration showed chylous fluid in the abdominal cavity but normal viscera.

Radiation treatment was given: 200 rad to the abdomen each day for 6 days.

At home, the patient continued to have recurrent chylous effusion and ascites despite repeated thoracenteses and paracenteses. After losing weight and showing signs of respiratory insufficiency, he died at the age of 7 of respiratory failure secondary to a chylous pleural effusion.

At autopsy (performed at Memorial Hospital, South Bend, IN), body size was judged to be typical of a child aged 4 years; lymphedema of the left leg and ascites were noted. The abdominal cavity contained 500 ml of chylous fluid, and the enlarged liver weighed 730 g. There was an 8 mm, firm, deep purple nodule in the spleen. The chest had a 200 ml chylous pleural effusion in the right side, and the left pleural space had been obliterated by fibrous adhesions. In the pericardial sac there was 15 ml of pink-stained chyle, and the mediastinum contained chronically edematous tissue that leaked chyle when incised. No thoracic duct was identified. The remaining viscera and vessels were grossly normal.

Microscopic examination showed increased and dilated lymphatics in the pericardium, liver, spleen, and tissues of the leg. The liver was normal otherwise, but several angiomas (probably lymphangiomas) were found in the spleen, including the 8 mm nodule. Lymphangiectasia was seen in the tissues of the mediastinum.

Case 16. A 19-year-old youth was seen at the Mayo Clinic because of episodes of scrotal swelling and groin pain associated with shaking chills and fever. Over 3 years, he had experienced four such episodes; all resolved after treatment with penicillin. On physical examination, he was 180 cm tall and

weighed 70 kg. The review of systems was positive only for hematuria after vigorous exercise. He had no sexual or urologic difficulties and had had no previous swelling. All laboratory results were normal.

The patient returned 1 week later during his fifth episode of scrotal swelling and cellulitis. He looked well. The only abnormal finding was enlargement of the spleen by 2 cm. Bone-marrow studies showed only reactive marrow. A repeat chest radiograph showed left pleural effusion, which thoracentesis proved to be chylous. A lymphangiogram showed no vessels on the left side and small vessels on the right, with backflow of dye to the dermis. Laparatomy disclosed chylous fluid in the abdomen but otherwise normal findings. Subsequently the patient was dismissed with final diagnoses of scrotal lymphedema with recurrent cellulitis, chylous ascites, and chylothorax.

Four years later, correspondence with the patient indicated that he still was having recurrent episodes of scrotal cellulitis and the he had mild dyspnea on exertion.

Discussion

Chylothorax

Among our cases of primary lymphatic dysplasia, chylothorax was the most common manifestation. Among newborn infants, chylothorax generally is the most common type of pleural effusion; and in chylothorax series composed largely of newborn infants, males outnumber females (23 to 10 in one report [3], 2:1 ratios in two others [32, 49]). No report has provided a distribution of age and sex in children with chylothorax.

Neonatal chylothorax, defined as a chylous pleural effusion diagnosed by the age of 2 months, is considered to be a result of congenital maldevelopment of the lymphatic system [3, 23, 28, 32, 43]. However, in childhood (and adulthood), chylothorax usually is caused by trauma or infection [23].

Infants and children often present with respiratory insufficiency as the chief complaint: of those with congenital chylothorax, 75% have respiratory difficulty within the first week of life [3, 6, 32, 49]. Cyanosis, absence of fever, increased respiratory rate, dullness to percussion of the lungs, decreased breath sounds, and a pleural effusion by chest radiograph are typical findings at the time of diagnosis; signs of nutritional depletion are seen occasionally although not often with use of a medium-chain-triglyceride diet and parenteral nutrition [3, 23, 32].

There may be a history of trauma, as from a complicated delivery, a hypertension injury of the spine (in seizures, automobile accidents, falls) or a surgical insult. Surgical repair of congenital heart lesions [45] and other mediastinal and thoracic surgery such as repair of tracheoesophageal fistula and operations on the lung and diaphragm [4, 31, 45] are frequent causes of chylothorax in children. Interestingly, ligature of the thoracic duct has not been shown to cause either chylothorax or chylous ascites [7, 26, 50]; rather, thrombosis of the superior vena cava is thought to cause the effusion [41]. Central venous lines and catheters also have been suspected of producing chylothorax by thrombosis [10, 41]. The possibility of minute undetected trauma probably is overemphasized; more likely is a congenital maldevelopment whose effect appears later in childhood [3, 13, 33].

Always, the diagnosis of chylothorax in children rests on demonstration of chyle in pleural fluid obtained by thoracentesis.

In some children a syndrome of chylothorax and lymphangiomatosis may be found. This association is very rare; but if the lymphangiomatosis is generalized it is nearly always fatal [2]. Lymphangiomatosis is a systemic involvement by lymphangiomas, usually in the long bones, predisposing the patient to frequent pathologic fractures. On skeletal radiographs, these lesions are seen as osteolytic. Generalized lymphangiomatosis may be difficult to distinguish from primary lymphatic dysplasia, unless an autopsy shows involvement of other organs and tissues. The absence of chylous ascites or lymphedema favors the diagnosis of generalized lymphangiomatosis and chylothorax, a probable variant of generalized lymphatic dysplasia. Chylothorax with a single associated lymphangioma is a benign condition that can be treated as if the child had chylothorax alone.

Children with lymphangiomatosis and chylothorax present either with respiratory insufficiency and the signs of chylothorax mentioned above or with a pathologic fracture. Biopsy shows that these lytic lesions are lymphangiomas containing a chylous effusion [18]. In the seven cases of this combined syndrome reported in the literature [2, 11, 18, 24, 29, 38, 39], findings have included multiple lesions of the thoracic duct not responsive to ligation, dilated lymphatic channels, and lymphangiomas throughout the bones and organs of the body. These are similar to the findings in generalized lymphatic dysplasia.

Although lymphangiography is useful in adults to rule out the presence of a mediastinal tumor, it is rarely required for diagnosis of chylothorax and lymphangiomatosis in infants and children. Obstruction of the thoracic duct is a rare cause of chylothorax in children; and in our series, only 1 patient among 38 had a neoplasm. Thus, in the absence of systemic signs and symptoms of malignancy, lymphangiography is contraindicated. ^{131}I-labeled triolein has been used to demonstrate a leak of chyle from the thoracic duct; and it may be a helpful procedure, less invasive than lymphangiography [48].

Treatment. The treatment of chylothorax in infancy and childhood had become fairly standardized [25]. After the initial thoracentesis, one or two more therapeutic taps should be done to eliminate the effusion [3, 12, 23]. A high-protein, medium-chain-triglyceride diet with fat-soluble vitamin supplements should lessen the flow of chyle from the intestinal tract [14]. If the chylothorax remains after 2 weeks, a chest tube with slight negative pressure [9] should be inserted and nothing be given by mouth. Total parenteral nutrition (TPN) should be started if needed, and should be continued for at least 2 more weeks. Thus, surgery is delayed for at least 1 month from the time of diagnosis. At operation, the thoracic duct should be identified and any leaks sutured. If none is found, ligation of the thoracic duct or pleural decortication, or both, should be performed. Servelle and Noguès [35] recommended finding the leak and suturing it, because ligation and pleurodesis will only worsen the chylothorax and may even cause chylous ascites by destroying important collaterals. This conservative policy should be followed in cases of postoperative chylothorax also, because it often makes a second thoracotomy unnecessary [45].

Chylous ascites. Another manifestation of lymphatic dysplasia in children is chylous ascites [19] which results from an effusion,

or leak, of lymphatic fluid from the mesentery, cisterna chyli, or lower thoracic duct into the peritoneum. Intestinal lymphangiectasia is a variant [19], in which proteins, lymphocytes, and immunoglobulins are lost into the gastrointestinal tract and fat is malabsorbed because lymphatics are incompetent. Children with intestinal lymphangiectasia are predisposed to infections, protein malnutrition, and generalized edema [15, 35, 42].

Chylous ascites is extremely rare in children: only 58 pediatric cases were reported in the literature from 1951 through 1980 [40]. The male/female ratio is approximately 2:1, as in chylothorax [21, 40, 44]; and the disorder is found more frequently in children before the age of 2 than after [4, 17, 21].

Of children with chylous ascites, up to 50% have a congenital malformation predisposing to lymphatic leakage [21, 34, 37]. Lymphangiograms have demonstrated obstruction of the cisterna chyli and chylous reflux into the peritoneal space in some cases of congenital chylous ascites [8]. (In adults, neoplastic obstruction is seen in one-half of the cases [21, 40].)

Treatment. Diagnosis and treatment differ between children and adults. Children often give a history of increasing respiratory distress caused by abdominal distention [47]. A careful physical examination revealing ascites and a diagnostic paracentesis showing chylous effusion will confirm the diagnosis. Such studied as CT scanning and lymphangiography should be restricted to cases with systemic signs of malignancy or an obvious abdominal mass, because less than 3% of chylous ascites in infants and children is due to neoplasms [40, 44].

The treatment should begin with several therapeutic paracenteses and a high-protein, medium-chain-triglyceride diet. After 2 weeks, a drain should be inserted and maintained with slight negative pressure. This conservative plan should be continued for at least 1 month [1, 19, 21, 27, 34, 37]. Two recent studies [1, 40] have suggested using total parenteral nutrition and nothing by mouth as early as 1 week after diagnosis to help resolve the ascites. If after 1 month of conservative treatment the ascites remains or the patient's condition has worsened, an exploratory laparotomy is the next step [40, 44]. If no obvious cause for the ascites is ascertained, all the major lacteals should be examined for evidence of leaks requiring suturing. If a specific cause is found, the surgical cure rate can reach 85% [40]. Peritoneo-venous shunting, attempted in a few cases, has had mixed results [19]. Also proposed is resection of the intestine in the region of leaky lymphatics [22], but other investigators have reported unsatisfactory results from this technique [19] (B. Kaufman: personal communication).

Generalized lymphatic dysplasia

The three cases described above are examples of the third major manifestation of lymphatic dysplasia in children. The diagnosis of generalized lymphatic dysplasia requires the pres-

Table 2. Clinical data from eight cases of generalized lymphatic dysplasia

Source	Sex	Age at		Clinical manifestations	Outcome
		Onset	Diagnosis		
Chang et al. [5]	M	7 years	7 years	Chylothorax Splenomegaly Thrombocytopenia Afibrinogenemia	Died, age 7 years
Chang et al. [5]	M	9 years	9 years	Chylothorax Hemangioma	Died, age 9 years
Heimpel et al. [20]	M	2 years	20 years	Chylothorax Lymphedema Generalized lymphangiectasis	Died, age 20 years
McKendry et al. [28]	F	Birth	Newborn	Chylothorax Chylous ascites Lymphedema	Died, age 15 months
Warwick et al. [46]	F	Birth	Newborn	Chylous ascites Lymphedema Hemangioma	Died, age 5 years
Present report					
Case 14	M	Birth	6 years	Chylothorax Lymphedema Probable lymphangioma Ascites	Worse 6 years later
Case 15	M	Birth	4 years	Chylothorax Chylous ascites Lymphedema	Died, age 7 years
Case 16	M	16 years	19 years	Chylothorax Chylous ascites Lymphedema	Worse 4 years later

ence of chylothorax, chylous ascites, and lymphedema. Forms of generalized lymphatic dysplasia include lymphangiomatosis, intestinal lymphangiectasia, and generalized lymphangiectasis. The prognosis generally is much worse than in cases that include only one or two of the individual problems. Indeed, the outcome is a major difference between generalized dysplasia and the individual problems. There are few reports of documented generalized lymphatic dysplasia in the literature: only five in addition to the three in this paper (Table 2). Of the eight patients, six died; and the condition of the other two has worsened since the initial diagnosis.

Chang et al. [5] have made a significant distinction between the terms "lymphangioma" and "lymphangiectasis." Lymphangioma is defined as a primary, truly dysplastic process, whereas lymphangiectasis is a secondary dilatation of preexisting normally developed lymphatic vessels. Their proposed pathogenesis of generalized lymphatic dysplasia is that a combination of venous and lymphatic dysplasia exists at birth, and later stress causes leakage of chyle. The distinction is difficult to make clinically. Our case 14, for example, seems to have evidence of a lymphangioma (the fractures of the femur), chylothorax, lymphedema, and probably chylous ascites. One must assume that chylous effusions beginning after the age of 2 probably are caused by lymphangiectasis and secondary leaks, rather than by lymphangioma.

McKendry et al. [28], who published the first report of generalized lymphatic dysplasia, thought that the peripheral lymphatic vessels failed to connect to the main channels. This hypothesis was based on the surgical finding that their patient had a normal, patent thoracic duct and on the autopsy findings of many dilated peripheral lymphatics. Heimpel et al. [20] proposed that obstruction of the thoracic duct causes chyle to leak into various cavities and organs of the body. Servelle and Noguès [35] offered an entirely different explanation, relating all the lymphatic disorders to a malformation of the chyliferous vessels: the cisterna chyli is functionally obstructed, causing collateral vessels on the diaphragm to enlarge – a type of lymphangiectasis; these vessels frequently rupture, causing chylothorax or chylous ascites, or both; and the obstruction also can force reflux into the limbs, causing lymphedema, and into the intestinal tract, causing protein-losing enteropathy. Servelle and Noguès [35] stressed that the mediastinal lymphangiectatic vessels are important collaterals, whose transection can worsen the chylous effusions.

Heimpel and co-workers [20] found multiple foam cells in spleen, liver, and bone marrow, findings suggestive of a lipid storage disease.

Perhaps, the "irregularly shaped large cells with foamy cytoplasm and dense nuclei" which had replaced some of the fat tissue noted at laparotomy in the patient reported by Warwick and co-workers [46] were similar to those seen by Heimpel et. al. [20].

The enlargement of the spleen and liver noted by Heimpel et al. was associated with the presence of these foam cells. However, Chang and associates [5] attributed the splenomegaly to the enlarged lymphatic channels which were lined with endothelial cells.

Putting these interpretations together, the pathogenesis of these manifestations may be considered as a series of events. First, there is a congenital malformation of either the thoracic duct of the cisterna chyli or the connection between normally developing peripheral lymphatic vessels and these central vessels. This malformation reduces the normal flow of lymph from the limbs. Then the peripheral lymphatics, having an increasing load, dilate, from collaterals, and often rupture to leak chyle into the pleural or peritoneal cavities or the limbs. Once the effusion begins, the pressure gradients rarely allow it to stop spontaneously; and often it persists until the patient dies from respiratory insufficiency.

Several statements about generalized lymphatic dysplasia can be derived from our reported cases and the other five in the literature. Lymphedema was present at birth in four of the eight and developed later in a fifth. The presenting symptom was shortness of breath in three cases, abdominal distension in two, lymphedema in two, and scrotal cellulitis in one. Autopsies on the six children who died revealed dilatation of lymphatics throughout the body in all and hemangiomas of the spleen in two. The thoracic duct was normal in two patients, obstructed in two, atrophied in one, and not seen in one. The immediate cause of death was pulmonary failure in five cases and infection in the sixth.

Treatment. The consistency of findings, both during the patient's life and at autopsy, allows us to suggest the following treatment plan. The diagnosis should be made on the basis of history and physical examination, with thoracenteses or paracenteses to document the chylous nature of the effusion. Conservative treatment should be used first, consisting of a high-protein, medium-chain-triglyceride diet [14] with vitamin supplements, and several taps during the first 2 weeks [3, 12, 23]. If that brings no improvement, one then should proceed to total parenteral nutrition [1, 40] and no oral feedings (to decrease the flow of chyle from the intestinal tract), accompanied by repeated aspirations of the effusions for the next 2 weeks. After that, if the dyspnea is worsening, surgery must be considered [40, 44]. At thoracotomy, identification and suturing of the leak in the thoracic duct or diaphragmatic collaterals are advised [20]. Blind ligation of the duct with pleural decortication should be done only as a last resort [35].

References

1. Asch MJ, Sherman NJ (1979) Management of refractory chylous ascites by total parenteral nutrition. J Pediatr 94:260–262
2. Berberich FR, Ochs HD, Schaller RT (1975) Lymphangiomatosis with chylothorax. J Pediatr 87:941–943
3. Brodman RF (1975) Congenital chylothorax: recommendations for treatment. NY State J Med 75:553–557
4. Cevese PG, Vecchioni R, D'Amico DF, Cordiano C, Biasiato R, Favia G, Farello GA (1975) Postoperative chylothorax: six cases in 2,500 operations, with a survey of the world literature. J Thorac Cardiovasc Surg 69:966–971
5. Chang C-K, Viseskul C, Opitz JM, Herrmann J, Pellett JR, Baker JW, Gutenberger JE, Gilbert EF (1974) Generalized lymphangiectasis associated with chylothorax; a possible dysplasia of the lymphatic system. Z Kinderheilkd 118:9–24
6. Chernick V, Reed MH (1970) Pneumothorax and chylothorax in the neonatal period. J Pediatr 76:624–632
7. Crandall LA Jr, Barker SB, Graham DG (1943) A study of the lymph flow from a patient with thoracic duct fistula. Gastroenterology 1:1040–1048
8. Cráven CE, Goldman AS, Larson DL, Patterson M, Hendrick CK (1967) Congenital chylous ascites: lymphangiography demonstration of obstruction of the cisterna chyli and chylous reflux into the peritoneal space and small intestine. J Pediatr 70:340–345
9. DeCancq HG (1965) The treatment of chylothorax in children. Surg Gynecol Obstet 121:509–512
10. Dhande V, Kattwinkel J, Alford B (1983) Recurrent bilateral pleural effusions secondary to superior vena caval obstruction as a

complication of central venous catheterization. Pediatrics 72:109–113
11. Ducharme J-C, Bélanger R, Simard P, Bazinet H-P (1982) Chylothorax, chylopericardium with multiple lymphangioma of bone. J Pediatr Surg 17:365–367
12. Feinerman B, Burke EC, Olsen AM (1957) Chylothorax in infancy. Proc Staff Meet Mayo Clin 32:314–319
13. Freundlich IM (1975) The role of lymphangiography in chylothorax: a report of six nontraumatic cases. Am J Roentgenol 125: 617–627
14. Gershanik JJ, Jonsson HT Jr, Riopel DA, Packer RM (1974) Dietary management of neonatal chylothorax. Pediatrics 53:400–403
15. Gleason WA Jr, Roodman ST, Laks H (1979) Protein-losing enteropathy and intestinal lymphangiectasia after superior vena cava-right pulmonary artery (Glenn) shunt. J Thorac Cardiovasc Surg 77:843–846
16. Greydanus DE, Smith TF, Stickler GB (1977) Acute encephalopathy with liver dysfunction, chylous ascites and cytomegalovirus infection. Infection 5:255–258
17. Gribetz D, Kanof A (1951) Chylous ascites in infancy: with report of a case with vitamin A absorption studies. Pediatrics 7:632–641
18. Gutierrez RM, Spjut HG (1972) Skeletal angiomatosis: report of three cases and review of the literature. Clin Orthop 85:82–97
19. Guttman FM, Montupet P, Bloss RS (1982) Experience with peritoneo-venous shunting for congenital chylous ascites in infants and children. J Pediatr Surg 17:368–372
20. Heimpel H, Bierich JR, Herrmann JM, Meister H, Vollmar J (1979) Dysplasia of the lymphatics with lymphoedema, generalized lymphangiectasis, chylothorax and 'pseudostorage disease'. Lymphology 12:228–240
21. Kelley ML Jr, Butt HR (1960) Chylous ascites: an analysis of its etiology. Gastroenterology 39:161–170
22. Kinmonth JB (1976) Disorders of the circulation of chyle. J Cardiovasc Surg 17:329–339
23. Kirkland I (1965) Chylothorax in infancy and childhood: a method of treatment. Arch Dis Child 40:186–191
24. Koblenzer PJ, Bukowski MJ (1961) Angiomatosis (hamartomatous hem-lymphangiomatosis): report of a case with diffuse involvement. Pediatrics 28:65–76
25. Kosloske AM, Martin LW, Schubert WK (1974) Management of chylothorax in children by thoracentesis and medium-chain triglyceride feedings. J Pediatr Surg 9:365–371
26. Lee FC (1922) The establishment of collateral circulation following ligation of the thoracic duct. Johns Hopkins Hosp Bull 33:21–31
27. Lesser GT, Bruno MS, Enselberg K (1970) Chylous ascites: newer insights and many remaining enigmas. Arch Intern Med 125: 1073–1077
28. McKendry JBJ, Lindsay WK, Gerstein MC (1957) Congenital defects of the lymphatics in infancy. Pediatrics 19:21–34
29. Morphis LG, Arcinue EL, Krause JR (1970) Generalized lymphangioma in infancy with chylothorax. Pediatrics 46:566–575
30. Nix JT, Albert M, Dugas JE, Wendt DL (1957) Chylothorax and chylous ascites: a study of 302 selected cases. Am J Gastroenterol 28:40–53
31. Oshio T, Matsumura C (1983) Chylothorax following Bochdalek herniorrhaphy in an infant. J Pediatr Surg 18:298–299
32. Randolph JG, Gross RE (1957) Congenital chylothorax. Arch Surg 74:405–419
33. Roy PH, Carr DT, Payne WS (1967) The problem of chylothorax. Mayo Clin Proc 42:457–467
34. Sanchez RE, Mahour GH, Brennan LP, Woolley NN (1971) Chylous ascites in children. Surgery 69:183–188
35. Servelle M, Noguès C (1981) The chyliferous vessels. Expansion Scientifique Française, Paris
36. Smeltzer DM, Stickler GB, Schirger A (1985) Primary lymphedema in children and adolescents: a follow-up study and review. Pediatrics 76:206–218
37. Sturmer FC Jr (1965) Infantile chylous ascites: review of literature and case report. Am Surg 31:281–284
38. Takamoto RM, Armstrong RG, Stanford W, Fontenelle LJ, Troxler G (1971) Chylothorax with multiple lymphangiomata of the bone. Chest 59:687–689
39. Tucker SM (1967) Bilateral chylothorax with multiple osteolitic lesions? generalized abnormality of lymphatic system? Proc R Soc Med 60:17–19
40. Unger SW, Chandler JG (1983) Chylous ascites in infants and children. Surgery 93:455–461
41. Vain NE, Swarmer OW, Cha CC (1980) Neonatal chylothorax: a report and discussion of nine consecutive cases. J Pediatr Surg 15: 261–265
42. Vallet HL, Holtzapple PG, Eberlein WR (1972) Noonan syndrome with intestinal lymphangiectasis: a metabolic and anatomic study. J Pediatr 80:269–274
43. Van Aerde J, Campbell AN, Smyth JA, Lloyd D, Bryan MH (1984) Spontaneous chylothorax in newborns. Am J Dis Child 138:961–964
44. Vasko JS, Tapper RI (1967) The surgical significance of chylous ascites. Arch Surg 95:355–367
45. Verunelli F, Giorgini V, Luisi VS, Eufrate S, Cornali N, Reginato E (1983) Chylothorax following cardiac surgery in children. J Cardiovasc Surg 24:227–230
46. Warwick WJ, Holman RT, Quie PG, Good RA (1959) Chylous ascites and lymphedema. Am J Dis Child 98:317–329
47. Whittlesey RH, Ingram PR, Riker WL (1955) Chylous ascites in childhood: report of five cases. Ann Surg 142:1013–1020
48. Woolfenden J, Struse TB (1977) Diagnosis of chylothorax with ^{131}I-triolein: case report. J Nucl Med 18:128–129
49. Yancy WS, Spock A (1967) Spontaneous neonatal pleural effusion. J Pediatr Surg 2:313–319
50. Yater WM (1935) Non-traumatic chylothorax and chylopericardium; review and report of a case due to carcinomatous thromboangiitis obliterans of the thoracic duct and upper great veins. Ann Intern Med 9:600–616

Received August 20, 1985 / Accepted September 30, 1985