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Congenital chylothorax

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A B S T R A C T

Congenital chylothorax (CC) results from multiple lymphatic vessel anomalies or thoracic cavity defects and may accompany other congenital anomalies. Fetal chylothorax may increase the risk of death and complications from pleural space lymphatic fluid accumulation, which compromises lung development, pulmonary, and cardiovascular function and from complications arising from the loss of drained lymphatic contents. Prenatal interventions might improve survival in severe cases of fetal chylothorax. The neonatal treatment strategy is generally supportive with interventions that include thoracostomy drainage and attempts to decrease chyle flow using a stepwise approach that begins with the least invasive means. Evidence-based treatment choices are lacking and are much needed. Most cases of CC resolve with time even without specific lymphatic system studies to identify the exact pathology. Expertise in performing lymphatic studies is not universally available. Data on both efficacy and safety of the various therapeutic options are needed to determine the best approach to the treatment of CC.

1. Anatomy and function of the lymphatic system

Lymph is generated in the interstitium and carried in lymphatic vessels in a unidirectional flow, joining the venous system near the junction of the left internal jugular and the left subclavian veins. There is variation in the thoracic lymphatic duct anatomy; most often (about 60%) there is a single right lymphatic duct along the right posterior mediastinum between the aorta and azygos vein that crosses to the mediastinum left of the esophagus and behind the aortic arch at the level of the fourth to sixth thoracic vertebrae [1,2].

Lymph contains cellular components (mainly lymphocytes), protein, coagulation factors, and chylomicra. Lymphatic flow per unit of weight in the fetus is about five times that of the adult. The total volume of lymphatic fluid is about 1 mL/kg; the flow through the thoracic duct in the adult is about 100 mL/h with two-thirds of the fluid generated by the liver and intestine [3]. Lymphatic flow rate is affected by diet, medications, and other factors, and may increase 2–10-fold for a few hours following ingestion of dietary fat [2]. Long-chain fatty acids are emulsified by bile acids to form fat globules, converted to chylomicra in the enterocytes, and absorbed by lymphatic capillaries called lacteals. Short- and medium-chain fatty acids are absorbed directly into the portal venous circulation without micelle formation [4]. Conditions associated with impaired lymphatic flow include space-occupying congenital pulmonary malformation (CPAM) or increased central venous/superior vena cava pressure, leading to lymphatic leakage into spaces along the route of the lymphatic vessels (the pleural and pericardial spaces) [2].

1.1. Congenital chylothorax

Fetal chylothorax, the most prevalent form of fetal hydrothorax (about 65%), occurs in 1:15,000 pregnancies, has a male:female ratio of 2:1, and occurs more frequently on the right side [5]. Congenital chylothorax (CC) is an accumulation of chyle (lymphatic fluid) within the pleural space, and may be detected prenatally or within the neonatal period. It is estimated to occur in about one per 10,000 live births and is the most frequent cause of pleural effusions in the neonatal period [6]. An epidemiologic study in Germany suggested that the prevalence of congenital chylothorax (non-post-surgical) be less frequent (1:24,000) [7].

Fetal chylothorax may compromise the space available for fetal lung growth and lead to pulmonary hypoplasia. This space occupation may also compromise vascular flow, causing heart failure and even hydrops fetalis [4]. Accumulation of a large fluid volume in the pleural space or drainage of the effusion leads to the loss of

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lymphocytes [8], antibodies, complement, and coagulation factors as well as nutrients and fluid, resulting in malnutrition and dehydration (Fig. 1) [4]. This may also increase the risk of nosocomial infections (Box 1) [8].

The prognosis for a fetus with CC depends upon the etiology (Box 2) and the presence of other anomalies, gestational age, and on the degree of pulmonary hypoplasia, with overall survival ranging from 30% to 70% [5].

1.2. Lymphatic developmental anomalies

Lymphatic developmental anomalies associated with chylothorax may be limited to the lungs or involve other organ systems. Chylothorax is usually caused by sluggish lymphatic drainage and/or by mass formation that impedes drainage. Thoracic lymphatic disorders were classified by Faul et al. [5], who modified the Hilliard classification [9].

Lymphangiomas are focal proliferations of lymphatic capillaries [2,5]. They may be present at birth as sponge-like or cystic. They grow slowly and rarely resolve spontaneously. There are several forms of lymphangiomas. The cavernous form consists of microcystic vessels. The macrocystic form is known as cystic hygroma, mostly (75%) occurring in the head and neck region. Cystic hygroma may impinge on the airways and may resolve prenatally (neonatal treatment is excision and the use of a sclerosing agent) [10]. Neonatal treatment of cavernous lymphangioma is accomplished with laser therapy. Lymphangiomas in the mediastinal and pericardial areas may cause pericardial and pleural effusions [4].

Lymphangiomatosis is characterized by the presence of multiple lymphangiomas that infiltrate different tissues, including the lungs and other thoracic tissues [5,11]. It is extremely unusual to diagnose this condition in the neonatal period.

Lymphangiectasia is characterized by dilation along the course of lymphatic vessels, but the number of vessels is normal (Fig. 2). It may be a primary developmental defect or secondary to obstruction of lymphatic flow [3]. Pulmonary lymphangiectasia may radiographically resemble pulmonary interstitial emphysema [3]. Although pulmonary lymphangiectasia is reputed to be fatal [3], there are reports of infants born with CC who later had histologic diagnosis of pulmonary lymphangiectasia and survived [12–14].

Box 1
Complications associated with congenital chylothorax.

- Mass effect
  - Hypoplastic lungs
  - Compromised pulmonary function
  - Compromised venous flow and heart failure
- Loss of lymphatic fluid components
  - Dehydration
  - Malnutrition
  - Vascular clotting
  - Infections

Box 2
Etiologies of congenital chylothorax.

- Thoracic anomalies
  - Congenital pulmonary malformations
  - Congenital diaphragmatic hernia
  - Pleural effusions
- Lymphatic anomalies
  - Lymphangioma
  - Lymphangiomatosis
  - Lymphangiectasia
  - Congenital lymphatic dysplasia syndrome

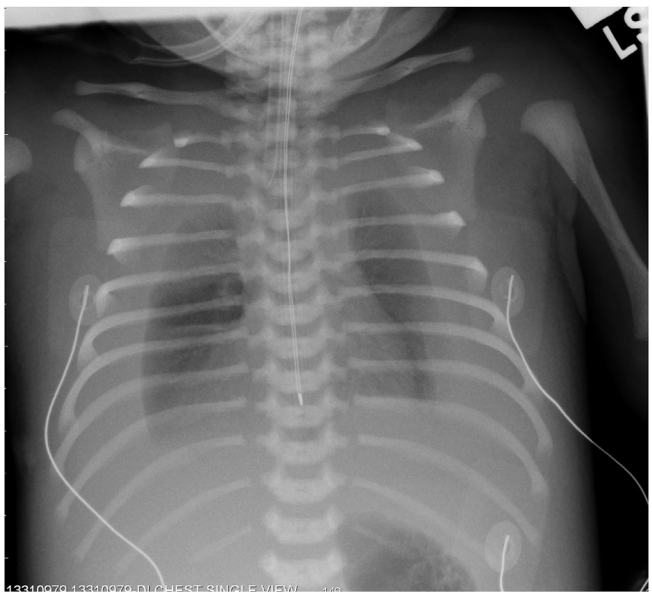

Fig. 1. Chest radiograph showing severe pleural effusions. Lungs were better expanded following bilateral thoracostomy tube placement. Infant was born at $35^{4/7}$ weeks by cesarean section at a community hospital for non-reassuring fetal heart rate, had delayed transition, complicated by anasarca, pleural effusions, respiratory failure, multi-organ dysfunction, and encephalopathy. Chylothorax was diagnosed. Chromosomal tests showed no abnormalities. Mechanical ventilation, pleural drainage, and feeding with medium-chain triglyceride-containing formula led to resolution. Brain magnetic resonance image at one week of life was structurally unremarkable. At 33 months the child had appropriate development.

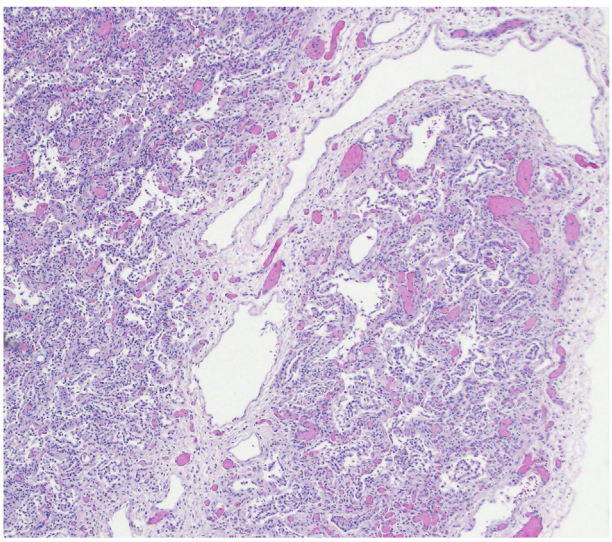

Fig. 2. Light microscopy of lung tissue shows dilated pleural and interstitial lymphatics. The lung parenchyma shows chronic changes and acute bronchopneumonia. The infant was born at 32 weeks with hydrops fetalis, had multi-organ failure, and died following severe pneumonia. Autopsy revealed congenital lymphangiectasia affecting lungs and soft tissue and associated pulmonary hypoplasia with multifocal acute bronchopneumonia, chronic lung disease, pulmonary hypertensive vascular changes, and small peripheral pulmonary thromboemboli. (Image courtesy of Raja Rabah-Hammad, MD, Departments of Pediatrics and Perinatal Pathology, Michigan Medicine.)

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