A 12-year-old Girl with Pneumonia

Robert Listernick, MD

This 12-year-old girl was transferred from an outside hospital for treatment of pneumonia. She had been well until 7 days before admission, when she developed what was felt to be cellulitis of her left lower extremity. She was given intravenous clindamycin, and the swelling and erythema improved. However, the following day, she started having respiratory distress, and she was found to have an infiltrate with a pleural effusion on chest X-ray. Chest tube was placed for drainage, after which computerized tomography (CT) revealed pericardial effusion prompting transfer.

Her past medical history was remarkable. She had a similar episode of pneumonia with effusion 7 years earlier that required a chest tube on the left side. She was a 31-week fraternal twin, who had no perinatal complications. At birth, she was noted to have left lower extremity hemihypertrophy. At the time she presented to us, she was 7 inches shorter than her fraternal twin sister and had also been recently diagnosed as having growth hormone deficiency. Family history was unremarkable.

On exam, she was an alert interactive girl who was in mild respiratory distress. Temperature was 102°, pulse 120, respiratory rate 28, blood pressure 120/60. Pulse oximetry was 95% while receiving 3 liters of oxygen. Weight and height were below the 5th percentile and were in the 50th percentile for a 9.5-year-old. HEENT exam was unremarkable. She was not dysmorphic. There were crackles at her left base with good air entry bilaterally. Cardiac exam was normal. Abdomen was soft without masses or organomegaly. Left lower extremity was longer and thicker than the right lower extremity. There was no pitting edema or tenderness.

On laboratory evaluation, hemoglobin 10.3 g/dL, white blood cell count 6,000/mm³ with 86% neutrophils and 14% lymphocytes. C-reactive protein was 27 mg/dL and albumin 2.4 g/dL. Echocardiography revealed a large circumferential pericardial effusion with tamponade physiology.

Robert Listernick, MD, moderator: Can we see the radiology?

James Donaldson, MD, pediatric radiologist: The first chest X-ray showed almost complete opacification of the left lung. Most likely, there was a large pleural effusion, although it might have been a total parenchymal consolidation. Before she arrived here, the outside hospital had placed pleural and pericardial drains. It looks like a classic pneumonia with parapneumonic effusion.

Stanford T. Shulman, MD, pediatric infectious disease physician: This looks like a straightforward complicated pneumonia, except that it’s unusual for a child to have two episodes of complicated pneumonia.

Dr. Listernick: Theories?

Dr. Shulman: First thoughts would be either an immunodeficiency or a predisposing anatomic abnormality. Most likely, there would have been a history of more frequent infections if an immunodeficiency was present. Pericardial effusion is also an unusual complication of pneumonia.

Dr. Listernick: Do all pleural effusions require drainage when associated with complicated pneumonias?
The echocardiogram shows right atrial collapse during diastole, indicating tamponade physiology.

Wayne Franklin, MD, pediatric cardiologist: The echocardiogram shows right atrial collapse during diastole, indicating tamponade physiology. Cardiac output goes down, and there is greater blood pressure variability with respiration. The ejection fraction might be normal, but diastolic filling is poor. It’s important to look at the cardiac physiology when assessing these patients; the size of the effusion is not as important as the effect the fluid is having on cardiac function. Sometimes, small pericardial effusions can exert a profound effect. Careful attention should be paid to the vital signs when monitoring the patient. The heart rate may creep up slowly until the “bottom falls out” suddenly and the patient goes into cardiogenic shock.

Dr. Listernick: The first night in the hospital she had distinct episodes of respiratory distress that would resolve when the pericardial tube was unclamped and allowed to drain. The pleural fluid was straw-colored. It had 578 white blood cells/mm³, 80% lymphocytes; pH 8.4, total protein 4.5 g/dL, triglycerides 500 mg/dL. Comments?

Kim Watts, MD, pediatric pulmonologist: These findings are quite suggestive of a chylothorax. If it were chyle, I would have expected to see more lymphocytes. If she were being fed, the fluid should have been milky from the absorbed fat. Still, these are certainly clues pointing to the possibility of chyle.

Dr. Listernick: I neglected to state that there was a vague, unconfirmed history of chylothorax during her first episode of pneumonia several years ago. The actual records were unavailable. Culture of the pleural fluid here grew a few colonies of methicillin-sensitive S. aureus.

Dr. Shulman: It’s very hard to believe that she now has staphylococcal pneumonia and empyema, given the bland nature of the pleural fluid and how well she looks.

Dr. Donaldson: Another small point against this being a simple pleural effusion associated with pneumonia is the fact that the chest tube kept putting out 150 cc of pleural fluid daily. That’s highly unusual for an infectious pneumonia.

Dr. Listernick: Why would someone have a chylous effusion?

Dr. Watts: Chylothoraces may be the result of traumatic injury to the thoracic duct, obstruction of the lymphatics, or developmental abnormalities involving the lymphatic system. Congenital chylothoraces generally present at birth with re-
spiratory distress and may be associated with nonimmune hydrops fetaiis, Noonan syndrome, Turner syndrome, or primary abnormalities of the lymphatics. Traumatic injury to the thoracic duct may occur during cardiopulmonary surgery. Obstruction of the thoracic duct may occur due to constrictive pericarditis, thoracic infections, neoplasia, or superior vena cava thrombosis. Finally, we often see chylothoraces following the Fontan procedure for congenital heart disease, which lead to elevated superior vena cava pressure.

Alexander Dzakovic, MD, pediatric surgeon: We attempted a VATS procedure, but we found a thick rim of tissue and could not insert the trochar into the actual pleural space. Instead, we performed a lateral thoracotomy and cleaned out the abnormal tissue. When we peeled off the tissue, the lung underneath looked completely normal. There were no obvious lymphatic malformations, and the lung re-expanded normally. We also performed a pericardial window, so as to promote drainage of the pericardial sac, as well as a lung biopsy. In the mediastinum, we saw some apparent water density collections that made us wonder about the presence of a lymphatic malformation. Unfortunately, lymphangiograms are technically extremely difficult to perform in young children, so one wasn’t performed.

Elaine Cham, MD, pediatric pathologist: The pleural surface was quite thickened and scarred. There were multiple dilated lymphatics in the pleural and pericardial tissues consistent with the diagnosis of lymphangiectasis.

Dr. Listernick: Let’s switch gears for a minute. She was said to have unilateral hemihypertrophy of the lower extremity. What should have been the approach to this finding when she was an infant?

Joel Charrow, MD, pediatric geneticist: First, if a limb is involved, you should note whether the girth and the length of the limb are involved. In my experience, if the limb is just thicker but not longer, it is more likely that there’s an underlying vascular or lymphatic malformation. If there’s an increase in length, it’s more likely hemihypertrophy, or the popular term of the moment, hemihyperplasia. Hemihyperplasia can involve the entire half of the body or just a single limb.

Dr. Listernick: What’s the differential diagnosis of hemihyperplasia?

Dr. Charrow: It might be idioopathic without a clear definable cause. Secondary causes include Klippel-Trenaunay-Weber syndrome, which is characterized by large cutaneous capillary and cavernous hemangiomas and/or lymphedema, neurofibromatosis type-1 with an underlying plexiform neurofibroma, Russell-Silver syndrome, and Proteus syndrome, characterized by connective tissue nevi and fatty and vascular malformations. In addition, hemihyperplasia is often seen in Beckwith-Wiedemann syndrome (BWS), along with macroglossia, omphalocele, and linear creases in the ear lobes.

Dr. Listernick: What’s the genetic diagnostic approach for evaluation of hemihyperplasia?

Dr. Charrow: First, we look for evidence of a recognizable syndrome. Testing for BWS is somewhat complicated. BWS is associated with abnormal transcription of imprinted genes on the short arm of chromosome 11. Approximately 20% of BWS patients have paternal uniparental disomy of this region, eg, both areas of this chromosome come from the same parent. In a few patients, fluorescent in situ hybridization studies can identify duplications or translocations in that region. This testing is often done in a step-wise fashion. Recently, some patients who have what was thought to be isolated hemihyperplasia have been found to have BWS genetic mutations.

Dr. Listernick: Once the diagnosis of hemihyperplasia has been established, how should those children be followed?

Dr. Charrow: There is a real risk for the development of abdominal tumors, specifically Wilms’ tumor, hepatoblastoma, and adenocortical carcinoma. Although recommendations vary somewhat, in general, these children should undergo abdominal ultrasonography every 3 months until 8 years. Many physicians also perform serial alpha fetoprotein levels, although I think that the evidence of its utility is not clear.

Dr. Listernick: In examining her longer leg, I thought it more likely that she had underlying lymphedema. One diagnosis that I wondered about was Noonan syndrome.
Dr. Charrow: Noonan syndrome is associated with short stature, and there may be lymphedema and pulmonary lymphangiectasis. However, she had none of the dysmorphic facial features characteristic of Noonan syndrome: ptosis, down-sloping palpebral features, low set posteriorly rotated ears, and a webbed neck. In addition, she didn’t have the classic heart disease of Noonan syndrome, pulmonic stenosis, and the pulmonary lymphangiectasis is usually symptomatic at birth. Nonetheless, it is a reasonable diagnosis to consider.

Don Zimmerman, MD, pediatric endocrinologist: As an interesting side note, it’s well established that sex steroids promote the secretion of growth hormone. People who have delayed onset of puberty, such as children with Noonan or Turner syndrome, experience a phase of poor growth and low growth hormone levels; they’re functionally growth hormone deficient. I wonder about the validity of her diagnosis of growth hormone deficiency.

Dr. Listernick: How do you establish the diagnosis of Noonan syndrome?

Dr. Charrow: Five genes are known to cause Noonan syndrome. They are all involved in the same signaling pathway. You can order a “Noonan chip” that will sequence each of the genes involved in order of frequency. This child did not have any known Noonan mutation.

Dr. Listernick: So what can we do about the pulmonary lymphangiectasis?

Dr. Watts: Therapies that have been tried in the past have been a diet rich in medium chain triglycerides in order to decrease chyle formation and the use of either somatostatin or octreotide. Although the mechanism of action is unclear, octreotide may act on somatostatin receptors to decrease lymphatic flow. Mixed results have been found with either therapy.

Dr. Dzakovic: We hope that our mechanical pleurodesis during the VATS procedure destroyed the potential space in which the lymphatic fluid accumulated.

Dr. Listernick: Thank you, everybody.

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**Key Learning Points**

1. Chylothoraces may be the result of traumatic injury to the thoracic duct, obstruction of the lymphatics, or developmental abnormalities involving the lymphatic system. Congenital chylothoraces generally present at birth with respiratory distress and may be associated with nonimmune hydrops fetalis, Noonan syndrome, Turner syndrome, or primary abnormalities of the lymphatics.

2. Video-assisted thoracoscopic surgery (VATS) is an effective means of treating complicated pneumonias with effusions during which pleurodesis can destroy the potential space in which lymphatic fluid accumulates.

3. Hemihyperplasia may be idiopathic or associated with Klippel-Trenaunay-Weber syndrome, neurofibromatosis type-1 with an underlying plexiform neurofibroma, Russell-Silver dwarfism, Proteus syndrome, and Beckwith-Wiedemann syndrome.

4. Individuals with hemihyperplasia are at risk for the development of Wilms’ tumor, hepatoblastoma, and adrenocortical carcinoma. These children should undergo abdominal ultrasonography every 3 months until 8 years.