A 2-Year-Old Male with Pneumonia

A 2-year-old male was admitted to the hospital for treatment of pneumonia. Eight days before admission, he developed fever, rhinorrhea, and a cough. After 5 days, he was brought to his physician, who diagnosed otitis media and gave him cefdinir. He continued to have daily fevers with intermittent “shakes.” On the day of admission, he was noted to be breathing faster and not drinking. There was no history of vomiting, diarrhea, abdominal pain, or other symptoms, nor any significant travel history or exposure to sick contacts. The family history was unremarkable.

On exam, he was tachypneic and in mild respiratory distress. Weight and height were in the 25th percentile. Pulse was 120, respiratory rate 36, blood pressure 100/60. Examination was unremarkable except for decreased breath sounds at the right base.

Laboratory evaluation revealed hemoglobin 7.4 g/dL with MCV 64; white blood cell count 12,000/mm³ with 71% neutrophils and 24% lymphocytes; and reticulocyte count 2.2%. Respiratory syncytial virus and influenza polymerase chain reaction testing were negative. Tuberulin skin testing was negative. A chest X-ray and computerized tomography (CT) scan of the chest revealed “necrotizing pneumonia.”

He received intravenous cefuroxime and clindamycin. His anemia was believed to be caused by an iron deficiency; it was noted that he drank 40 oz of 2% milk daily. No organism was recovered as a cause of the pneumonia.

He remained in the hospital for 7 days and completed a 2-week course of intravenous antibiotics at home, followed by several weeks of oral antibiotics.

Robert Listernick, MD, moderator:
Can we please see the imaging studies?

Mary Wyers, MD, pediatric radiologist:
On the initial chest X-ray, there’s a large infiltrate at the right lung base. There are small, round lucencies within the infiltrate that appear to be necrotic cavity areas. On the CT scan, there was mediastinal adenopathy. Within the infiltrate at the right base, there are multiple low-density cystic areas filled with fluid and air. This likely represents an acute necrotizing pneumonia, although it’s certainly a possibility that there is an underlying congenital lesion, such as a sequestration or congenital cystic adenomatoid malformation (CCAM).

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CT using adult protocols is equivalent to that of 350 to 500 chest X-rays. Even using pediatric parameters, it delivers an equivalent dose of 150 chest X-rays.

Is this pneumonia clearly caused by *Streptococcus pneumoniae*?

**Dr. Katz:** Not at all. Although certain strains of *Streptococcus pneumoniae* have become major causes of necrotizing pneumonia, this child’s pathogen could easily be either *Staphylococcus aureus* or *Streptococcus pyogenes*. All three may cause clinically indistinguishable necrotizing pneumonia. The rate of positive blood cultures is low; we frequently don’t isolate an organism.

**Dr. Listernick:** Based on that, what should be the choice for initial antibiotic therapy?

**Dr. Katz:** Although we often start with cefuroxime, it doesn’t provide adequate methicillin-resistant *Staphylococcus aureus* (MRSA) coverage. If we are concerned about MRSA, we can add clindamycin. There’s also a new FDA-approved cephalosporin, ceftaroline, which covers MRSA, group A *Streptococcus*, and most cephalosporin-resistant pneumococci. We may start to use this in select circumstances when more pediatric data are available.

**Dr. Listernick:** What should the chest X-ray look like several months after the end of therapy?

**Dr. Wyers:** Most will look normal or have very minimal scarring, no matter how extensive the pneumonia.

**Dr. Listernick:** I should mention that the child had had an iron-deficient diet, and it was thought that he had classic iron-deficiency anemia. He was given therapeutic doses of iron on discharge.

Over the next 2.5 years, he was seen in the emergency room twice. The first time was for respiratory symptoms, and his chest X-ray revealed “partial consolidation of the medial aspect of the right lower lobe.” The discharge diagnosis was “viral illness with secondary pneumonia and reactive airway disease.” He was given albuterol and cefdinir.

A year later, he was seen after a 1-week history of fever and cough. Two days before admission, he had “coughed up” spots of blood twice. The mother mentioned that he was “breathing fast.” On exam, he was described as looking well, but was mildly tachypneic. Chest X-ray showed “a patchy area of opacity in the right lower lobe, which was present on comparison with previous studies.” He was diagnosed with “atypical pneumonia” and was given azithromycin.

Thirteen months later, which brings us to the present at 6 years of age, he returned with a chief complaint of “spitting up blood,” which had started 1 hour previously, and now he also had throat pain. There was no history of fever, difficulty breathing, or cough.

On exam, he was well-appearing, sitting comfortably in bed. Pulse was 160, respiratory rate 24, blood pressure 100/60. His growth parameters were still in the 25th percentile and he had been growing normally. HEENT exam was unremarkable with no obvious source of bleeding. Lungs were clear. Cardiac exam was normal. Abdomen was soft and nontender without masses or organomegaly. Initial hemoglobin was 11.3 g/dL.

**Mary Nevin, MD, pediatric pulmonologist:** It’s worth stating that children who have two or more documented pneumonias should have a thorough evaluation.

**Dr. Listernick:** Doesn’t it depend on what the X-ray actually looks like?

**Dr. Nevin:** Agreed. Often what is read as “pneumonia” is just a small area of atelectasis or even normal, right
lower lobe vasculature. Children who have those types of X-rays and repeated respiratory symptoms generally have reactive airway disease or asthma. Assuming these are real areas of consolidation, the differential diagnosis changes substantially if they are in the same segment or lobe of the lung (e.g., sequestration, congenital cystic adenomatoid malformation) or in differing areas (e.g., aspiration, immunodeficiency, etc).

Dr. Listernick: How concerned should we be right now?

Dr. Nevin: That’s difficult to say. This child is described as appearing well with normal hemoglobin; the most common reason for “spitting up blood” would be epistaxis. On the other hand, he’s had three documented “pneumonias.”

Dr. Listernick: Assuming this is persistent, how can we decide where the bleeding is coming from?

Dr. Nevin: It may be difficult. We’ve had children undergo endoscopy in the operating room sequentially by ENT physicians, pulmonary medicine, and gastroenterology when the source of the bleeding is obscure.

Dr. Listernick: The decision was made to admit the child to the hospital. An astute senior resident noted 3+ digital clubbing that no one else had noticed, making it infinitely more likely that he was having hemothysis. The ENT physician performed nasopharyngoscopy in the emergency room, and no source for the bleeding was found. Let’s talk about clubbing for a moment. What causes clubbing?

Erin Allen, MD, chief pediatric resident: There are several hypotheses. Because of the presence of intrapulmonary shunting, megakaryocytes, which are usually trapped within the pulmonary circulation, escape fragmentation and release platelet-derived growth factor in the end capillaries of the digits. Individuals with a variety of inflammatory diseases may have clubbing caused by endogenous production of other growth factors. Finally, in patients who have autosomal dominant primary hereditary osteoarthropathy, clubbing is caused by mutations in 15-hydroxyprostaglandin dehydrogenase, which leads to chronically elevated prostaglandin E2 levels.

Key Learning Points

1. The radiation dose of a chest CT using adult protocols is equivalent to that of 350 to 500 chest X-rays. Using pediatric parameters, it delivers an equivalent dose of 150 chest X-rays.
2. Necrotizing pneumonia is most commonly caused by *Streptococcus pneumoniae*, *Staphylococcus aureus*, or *Streptococcus pyogenes*.
3. One theory of the pathogenesis of clubbing suggests that, because of the presence of intrapulmonary shunting, megakaryocytes that are usually trapped within the pulmonary circulation escape fragmentation and release platelet-derived growth factor in the end capillaries of the digits.
4. The differential diagnosis of clubbing includes any of the causes of chronic hypoxia, such as longstanding parenchymal pulmonary disease; or any of the causes of right-to-left shunting, such as cyanotic heart disease or pulmonary arteriovenous malformations. In addition, there are a number of disparate causes of clubbing: inflammatory bowel disease, chronic liver disease (most likely related to hepatopulmonary syndrome and the development of intrapulmonary shunting), hyperthyroidism, and a variety of pulmonary neoplasms.

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

Dr. Allen: Any of the causes of chronic hypoxia, such as longstanding parenchymal pulmonary disease, or any of the causes of right-to-left shunting, such as cyanotic heart disease or pulmonary arteriovenous malformations. There are also a number of disparate causes of clubbing, including inflammatory bowel disease, chronic liver disease (most likely related to hepatopulmonary syndrome and the development of intrapulmonary shunting), hyperthyroidism, and a variety of pulmonary neoplasms.

Dr. Listernick: He was admitted to the pulmonary service and bronchoscopy was planned for the next morning.

Mark Haupt, MD, pediatric pulmonary fellow: The differential diagnosis on admission included diverse entities such as hereditary hemorrhagic telangiectasia, immunodeficiency syndromes, and cystic fibrosis. Even though his weight and length are normal, it has been shown that children of Hispanic descent, as this patient is, may have a normal BMI at the time of presentation of cystic fibrosis.

Dr. Listernick: The following morning, during the bronchoscopy, he developed massive life-threatening pulmonary hemorrhage.

Dr. Haupt: Initially, we noted a small trail of blood leading from an occluded bronchus intermedius to the right upper lobe before the massive hemorrhage started. The endotracheal tube filled rapidly with blood, and ventilation became difficult. The surgeons came immediately. It was difficult to say if the blood was coming from the right upper lobe or distally.

David Rothstein, MD, pediatric surgeon: One option was to blindly place an endobronchial blocker, which would effectively isolate the lung that
was bleeding from normal pulmonary parenchyma, allowing us to ventilate the normal lung. The problem was that we didn’t know from which part of the lung the bleeding was arising.

A second option was thoracotomy and clamping the hilum. Fortunately, the bleeding stopped abruptly as we were about to intervene. We could tell it was coming from the right lower lobe, and we thought the most likely source was an aberrant bronchial artery. Once he was stabilized and resuscitated with blood, he went for immediate angiography.

**Dr. Wyers:** Two abnormally large bronchial arteries were identified and thought to be possible sources of bleeding. They each underwent embolization. We did not identify an abnormal systemic arterial supply of the lung, which would be seen in a pulmonary sequestration.

**Dr. Listerick:** Although the bleeding had stopped before the embolization, it didn’t recur. What was the thought process at this point as to the etiology of the bleeding?

**Dr. Haupt:** We wondered whether he had bronchiectasis involving the right lower lobe related to his previous necrotizing pneumonia, which ultimately led to the vascular abnormalities. We see this type of bleeding and abnormal vasculature in our older patients with cystic fibrosis. He had a negative sweat test.

**Dr. Rothstein:** The bleeding didn’t recur and we decided that he needed a right lower lobe lobectomy, but that we should first give him time to recover. We wanted to perform the operation thoracoscopically because the recovery time is faster and there is probably less effect on the development of the chest wall.

**Dr. Listerick:** The removed lung had significant scarring and bronchiectasis with areas of marked inflammation. There was no evidence of either a sequestration or CCAM. His immunologic evaluation was unremarkable. Despite the presence of clubbing, it was felt that the entire process was caused by the previous necrotizing pneumonia.