WHAT IS YOUR CALL?

An unusual cause of empyema in a teenage boy

Jonathan H. Rayment MDCM MSc, Michael Weinstein MD

A previously healthy 17-year-old boy presented to his family physician with an increasingly productive cough and fever of 5 days' duration. Based on a clinical diagnosis of atypical pneumonia, he was prescribed azithromycin. Five days later, his symptoms had not resolved, and left-sided chest pain had developed. His family physician ordered a chest radiograph, which showed consolidation in the lower left lobe. Bacterial pneumonia was diagnosed, and the patient was prescribed high-dose amoxicillin (1g taken orally twice daily).

The patient's symptoms did not improve with amoxicillin therapy, and 2 days after initiation, his cough and chest pain worsened, and he began to experience marked anorexia and malaise. Five days later, he presented to a local hospital with fever, tachypnea and severe respiratory distress. A chest radiograph showed a large left-sided pleural effusion (Figure 1). Although lobar consolidation could not be ruled out based on this chest radiograph, we felt that the radiographic appearance was most likely consistent with reaccumulation of the patient's pleural effusion, especially given his recent history. Broad-spectrum intravenous antibiotics were initiated in the emergency department, and a chest tube was inserted, which drained 400 mL of turbid fluid. He was transferred to a pediatric hospital with a diagnosis of empyema.

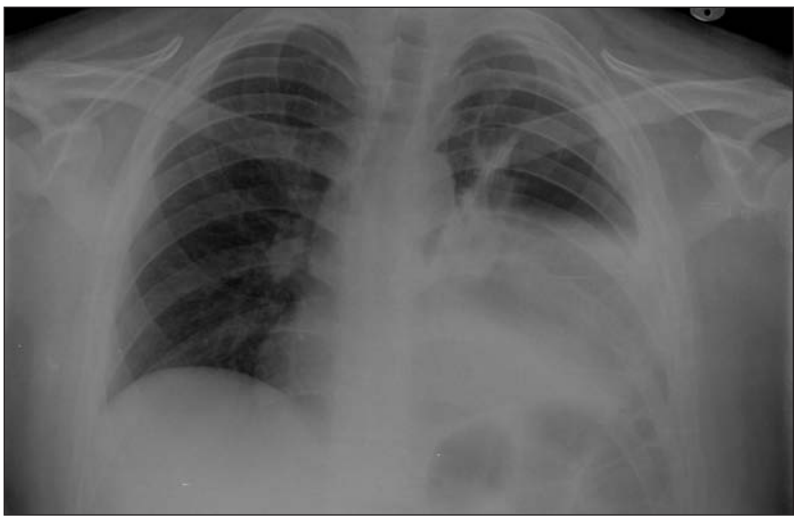

Figure 1: A portable chest radiograph showing a large, left-sided pleural effusion.

What is the most likely pathogenic agent in this case?

a. *Streptococcus pneumoniae*
b. *Mycoplasma pneumoniae*
c. Influenza A
d. *Staphylococcus aureus*

The most likely pathogen in this case is *S. pneumonia* (a). Given the unilateral findings on the chest radiograph, *M. pneumoniae* or Influenza A are unlikely to be the cause, because these agents typically result in diffuse, bilateral changes visible on a radiograph. In addition, these agents are infrequently associated with a large parapneumonic effusion. *Staphylococcus aureus* is a less common cause of typical bacterial pneumonia.

Our patient had been previously well, was born in Canada, had no relevant travel history and had no known sick contacts or animal exposures. He did not have epidemiologic risk factors for tuberculosis, and he had received all appropriate vaccinations. He mentioned being briefly submerged in his backyard hot tub 3 weeks earlier. He recalled some coughing at that time, but he did not lose consciousness. Given the history of hot tub submersion, we also considered infection with *Pseudomonas aeruginosa*.

Which antibiotics would you prescribe?

a. Ampicillin and gentamicin
b. Meropenem, vancomycin and metronidazole
c. No antibiotics; chest tube drainage is sufficient
d. Cefotaxime, vancomycin and ciprofloxacin

We started intravenous cefotaxime and vancomycin, adding ciprofloxacin for coverage of *P. aeruginosa* (d). Ultrasonography of his chest showed a free-flowing parapneumonic effusion; thus, we decided to proceed with drainage via a chest tube rather than

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Correspondence to: Jonathan Rayment, jonathan.rayment@sickkids.ca

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intervene with fibrinolytic or surgical (video-assisted thoracoscopic surgical) therapy.

Aerobic and anaerobic cultures of the blood and pleural fluid showed no growth at 5 days. The results of an acid-fast stain for *Mycobacteria*, polymerase chain reaction for *Mycoplasma*, and culture of the pleural fluid for *Legionella* were negative. A tuberculin skin test was nonreactive. On the eighth day of his stay in hospital, anaerobic Gram-negative bacilli were isolated from the pleural fluid, but these were thought unlikely to be pathogenic.

Over the subsequent 10 days, our patient improved at a rate typical of patients with stage 1 empyema (i.e., exudative).[1] Intermittent fever persisted up to the time of discharge. Given his clinical condition and laboratory results, intravenous ciprofloxacin was discontinued after a total of 5 days, and vancomycin and cefotaxime were changed to levofloxacin taken orally at 7 days to cover multidrug-resistant *S. pneumoniae*. The patient's chest tube was removed on day 11, and he was discharged home on day 12 with a 4-week prescription for oral levofloxacin therapy.

After discharge, high fever and a worsening cough developed. On day 6 after discharge, the patient returned to the pediatric emergency department in substantial respiratory distress. A chest radiograph showed reaccumulation of the left-sided pleural effusion. A chest tube was inserted emergently, and 750 mL of grossly purulent fluid containing Gram-negative bacilli were drained. Cefotaxime, vancomycin and metronidazole were administered intravenously.

On day 3 of his readmission, anaerobic Gram-negative bacilli were again isolated from the pleural fluid. This isolate and the isolate from the previous admission were analyzed by sequencing of 16S ribosomal RNA. In both cases, the results showed sequence homology with *Prevotella* species.

The patient's clinical status improved rapidly in hospital. His chest tube was removed on day 9, and he was discharged on day 10 with a 1-month prescription for metronidazole to be taken orally. The patient was well at his 2-week and 1-month follow-up visits, with no signs of recurrence.

Discussion

In this report, we describe the failed treatment of pneumonia and empyema in a teenage boy who had received timely, guideline-informed empirical treatment. The cause of this treatment failure was *Prevotella*, an uncommon anaerobic pathogen.

Empyema is defined as the presence of intrapleural pus. The pathophysiology involves several stages. The first stage is a free-flowing parapneumonic effusion (exudative, stage 1). This may progress to a purulent effusion with loculations, which is known as empyema (fibropurulent, stage 2), and, eventually, a fibrinous peel may form (organizational, stage 3).[2]

Small pleural effusions can be managed with empiric antibiotic therapy alone.[2,3] Larger effusions may require surgical intervention as well as antibiotic therapy. In the case of large free-flowing parapneumonic effusions (stage 1), simple percutaneous drainage with an indwelling catheter can, in addition to antibiotic therapy, be sufficient to achieve disease control.[2–4] In the case of loculated or fibrosed effusions (stage 2 or 3), guidelines recommend drainage plus intrapleural fibrinolytics (e.g., tissue plasminogen activator), and management using video-assisted thoracoscopic surgery should be considered.[2–4] Absolute indications for surgical management are generally thought to be persistent respiratory distress or signs of sepsis despite appropriate antibiotic therapy.[2–4] Relative indications are less clearly defined, and the most effective intervention modality remains controversial in the literature.[2–5] The decision to treat should, therefore, take into consideration the patient's clinical status, radiographic findings, local surgical expertise and patient and parent preferences.[3,5]

The empiric selection of antibiotics in the treatment of uncomplicated pneumonia in children is

Table 1: Microbiology, empiric antibiotic therapy and surgical therapy of empyema in children

Bacterial causes of empyema[6–8]	Empiric antibiotic therapy[3,5,9]	Surgical therapy*[2–5]
• *Streptococcus pneumoniae* • *Staphylococcus aureus* • Group A *Streptococcus*	• Third-generation cephalosporin (intravenous)	• Chest tube drainage, and/or fibrinolytics and/or video-assisted thoracic surgery
• Methicillin-resistant *S. aureus* (in some geographic regions)	• Third-generation cephalosporin (intravenous) plus vancomycin or clindamycin	
• Anaerobic bacteria (mostly in children with impaired airway defenses)	• Third-generation cephalosporin (intravenous) plus clindamycin	

*Need for and choice of surgical therapy should take into account the patient's clinical status, radiographic findings, local surgical expertise and patient and parent preferences. See text for details.

based on decades of observational microbiological studies.[6–8] The most common pathogen in pneumonia in preschool-age children is *S. pneumoniae,* and the empiric treatment of childhood bacterial pneumonia is high-dose amoxicillin.[3,9] In school-age children and adolescents, atypical organisms (*M. pneumoniae* or *Chlamydia pneumoniae*) are seen with increasing frequency. As such, older children with clinical signs of atypical pneumonia (indolent presentation, bilateral clinical and radiographic findings) should be given a macrolide,[3,9] as was done in this patient's case.

Empyema develops in the context of treatment failure of uncomplicated pneumonia. Treatment failure can be related to a delay in initial treatment or the presence of resistant or unusually virulent organisms. The microbiology of empyema mirrors those of childhood uncomplicated pneumonia, with *S. pneumoniae*, *S. aureus* and Group A *Streptococcus* being the most common agents.[7,8] There is evidence that pneumococcal serotypes not covered by the 7-valent pneumococcal vaccine (especially 1, 3, 7F and 19A) are more likely to cause empyema, which could account for the observed rise in empyema rates over the past decade.[10]

Empiric administration of a third-generation cephalosporin is the first-line antibacterial management of empyema (Table 1).[2-9] Vancomycin or clindamycin should be considered in regions where methicillin-resistant *S. aureus* is prevalent.[3,5] Cefuroxime axetil or amoxicillin-clavulanate are suggested in national guidelines and position statements as oral stepdown antibiotic agents.[3,5] Levofloxacin is also commonly used for older teenagers and adults in the stepdown management of suspected multidrug-resistant *S. pneumoniae* disease.[11] The total duration of antibiotic therapy required in cases of empyema is not known, but most experts recommend at least 4 weeks.[3,9]

This case demonstrates that the presence of an unusual pathogenic organism can lead to treatment failure of uncomplicated pneumonia, even when guidelines are followed (Table 2).[1-5] Anaerobic organisms are very unusual causes of pneumonia and empyema in neurologically normal, otherwise healthy children.[6-8] Those with impaired mechanical airway defenses (neurologic injury or tracheostomy) or those who have overgrowth of their normal oral flora are at a higher risk of anaerobic pleuropulmonary infections. Clindamycin, metronidazole, aminoglycosides or quinolones are the agents of choice for expanded coverage for cases in which anaerobic agents are suspected.[12]

Table 2: Causes, interventions and signs of treatment failure in empyema

Cause	Intervention[2–5]
• Resistant or atypical organism	• Augmentation of antibiotic therapy
• Complicated parapneumonic effusion	• Fibrinolytics and/or video-assisted thoracic surgery
• Necrotizing pneumonia	• Computed tomography and surgical consultation
Signs of treatment failure	
• Persistent high fever* and other signs of sepsis • Persistent respiratory distress • Persistent chest pain	

*Intermittent low-grade fevers are expected during the normal course of recovery from empyema and do not necessarily indicate treatment failure.[1,5]

Conclusion

This case underscores the need for clinicians to maintain a high index of suspicion for unusual causes of pneumonia and empyema, particularly when the course of illness is protracted and the response to standard treatment is atypical.

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Affiliation: The Department of Paediatrics, the Hospital for Sick Children, Toronto, Ont.

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