Community-Acquired Pneumonia: Judicious Use of Antibiotics or Treatment Failure?

You admit a previously healthy, moderately ill–appearing 2-year-old boy with bilateral crackles and a density in the right middle lobe on chest radiograph. He has been coughing and febrile for 4 days. After 2 days of treatment with 90 mg/kg per day of amoxicillin, his primary care physician requests admission due to failure to improve and mild dehydration. You wonder if there are any tests that can help determine the need for continued antibiotic therapy.

Pediatric hospitalists frequently treat community-acquired pneumonia (CAP). CAP has an incidence of 33 per 100,000 children <5 years of age and 14.5 per 100,000 children <16 years of age in the developed world, and about one-half of these patients are admitted for inpatient care. Although the etiology of CAP varies by age, *Streptococcus pneumoniae* is the most common causative agent of bacterial CAP.

Recent guidelines released by the Pediatric Infectious Diseases Society and the Infectious Diseases Society of America suggest treating CAP with ampicillin or penicillin G for the fully immunized infant or school-aged child or using a third-generation parenteral cephalosporin (ceftriaxone or cefotaxime) for hospitalized infants and children who are not fully immunized, in regions where local epidemiology of invasive pneumococcal strains document high-level penicillin resistance, or for infants and children with a life-threatening infection.

In our ongoing efforts to be more judicious with the use of antibiotics for CAP, the importance of getting the diagnosis right and then narrowing the antibiotic spectrum is paramount. Diagnostic testing that distinguishes viral from bacterial respiratory disease would be a major contribution to the clinical care of children.

Procalcitonin (PCT) is a precursor molecule of calcitonin. It is also a marker of inflammation, especially inflammation resulting from bacterial infections. The value of PCT in detecting bacteremia has now been established by using numerous studies. Evidence also supports PCT as a potentially sensitive and specific tool for detecting bacterial pneumonia, with greater positive predictive value (PPV) and negative predictive value (NPV) than other markers such as C-reactive protein (CRP), interleukin 6, or white blood cell (WBC) counts.

An early study from France evaluated 72 children who met the criteria for CAP (temperature >38°C, clinical symptoms, and chest radiograph findings) and attempted to correlate inflammatory markers with bacterial etiology. The ability of PCT, CRP, interleukin 6, and WBC counts to detect bacterial versus viral pneumonias...
was studied by using various cutoffs. A PCT cutoff of 1 μg/L differentiated bacterial and viral pneumonias more effectively than CRP, WBC count, or interleukin 6, with greater sensitivity, specificity, PPV, and NPV.

Another study retrospectively evaluated the ability of PCT to predict response to antibiotic therapy in 125 children aged 1 month to 16 years who were hospitalized for CAP and empirically treated with β-lactam antibiotics (amoxicillin or ceftriaxone). The outcome studied was clinical response (with apyrexia <48 hours after treatment a “success” and ≥48 hours a “failure”). Etiologies were identified by using blood culture, fluorescent viral immunoassay, PCR, and pleural fluid analysis where relevant. The study concluded that compared with WBC count, neutrophil count, and CRP, PCT is the best marker that predicts apyrexia/treatment response to β-lactam antibiotics. The study showed that in those patients with PCT >3 ng/mL, 75% responded to therapy within the first 24 hours and 94% responded in the first 48 hours. This study, using a 3-ng/mL cutoff for PCT, reported a sensitivity of 55.7%, specificity of 78.9%, PPV of 93.7%, and NPV of 24.2%. An indirect conclusion of the study was that a PCT level of >3 ng/mL is suggestive of pneumococcal CAP, although the authors did note that the threshold may be too high for practical use.

An Italian study used PCT measurements to guide antibiotic treatment choices. The authors randomized (in a 1:1 ratio) 319 hospitalized children with CAP to receive standard treatment versus an algorithm based on PCT cutoff values. In the PCT algorithm group, children did not receive antibiotics on admission unless their PCT was >0.25 ng/mL. If they qualified to start antibiotic therapy, they were treated only until their PCT level was <0.25 ng/mL. The children in the standard treatment group were treated per protocol: antibiotic monotherapy chosen on the basis of age if mild, and combined β-lactam and macrolide therapy if severe, for 7 to 14 days depending on severity. The study found that the PCT algorithm group received significantly fewer antibiotic courses (85.8% vs 100%; \( P < .05 \)), were exposed to antibiotics for less time (5.37 vs 10.96 days; \( P < .05 \)), and experienced fewer antibiotic adverse effects (3.9% vs 25.2%; \( P < .05 \)). Using this cutoff of 0.25 ng/mL to navigate antibiotic therapy decisions, the investigators avoided the issue of whether the pneumonia was viral or bacterial in origin; rather, they suggested a cutoff value of 0.25 ng/mL that can be used to safely identify all CAP cases that do not need antibiotic therapy, as well as those that could do with shorter courses, regardless of the underlying etiology.

You order a PCT test on the 2-year-old, and the result comes back as 0.1 ng/mL. You decide to hold off on any antibiotic therapy and use supportive measures only. In 24 hours, the fever is gone, the child is feeling better, drinking well, and ready for discharge. Although PCT testing may not currently be available at many institutions, its superior ability to distinguish bacterial infection from other causes of inflammation makes it a useful tool in the evaluation of hospitalized children, and it most likely will soon augment or replace other inflammatory markers. Pediatric hospitals will need to learn the indications, cutoffs, and nuances of this new tool.

REFERENCES