Infective Endocarditis in a Pediatric Patient

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CASE DESCRIPTION

A previously healthy 11-year-old boy presented to the emergency department (ED)4 at Children’s Hospital Los Angeles (CHLA) with a 3-week history of intermittent fever. Two weeks before admission, he was seen at an outside hospital for his bouts of fever. At the outside hospital, chest x-rays and urine workup were within reference intervals and he was discharged with a 5-day oral azithromycin prescription for presumed bacterial infection.

In the ED at CHLA, the patient appeared to be well and in no distress. His initial vitals included the following: temperature, 37.4 °C; heart rate, 133 beats/min; blood pressure, 108/77 mm Hg; and respiratory rate, 20 breaths/min. On physical examination, small lymph nodes at the posterior neck were identified, but the rest of his examination parameters were within reference intervals. Laboratory investigations revealed mild leukocytosis [white blood cell count, 16.16 K/uL (4.31–11.00 K/uL); neutrophils, 88.4%], increased erythrocyte sedimentation rate [ESR; 102 mm/h (1–10 mm/h)] and high C-reactive protein (CRP) level [3.7 mg/dL (0.0–0.9 mg/dL)]. Urinalysis and chest x-ray were normal. After 2 sets of blood cultures were obtained, the patient was started on empiric antibiotics—vancomycin, 500 mg intravenous (IV), and ceftriaxone, 2000 mg IV, and he was admitted to the hospital for further evaluation.

One set of blood cultures (aerobic and anaerobic) obtained at the time of presentation in the ED grew gram-positive cocci 12 h after receipt in the microbiology laboratory. An additional aerobic blood culture collected on day 2 of admission was also positive for the same organism. A nasopharyngeal swab was negative for influenza A/B and respiratory syncytial virus by molecular testing. All subsequent blood cultures were negative by day 3 of hospital stay. Echocardiography performed on day 3 of admission revealed a 15- × 15-mm spherical mass on the septal leaflet of the tricuspid valve, confirming a diagnosis of infective endocarditis. Computed tomography (CT) angiogram was negative for pulmonary embolism, but he was started on enoxaparin sodium for anticoagulation therapy as a precaution. Furthermore, antimicrobial therapy was optimized upon availability of susceptibility results.

On hospital day 10, a repeat echocardiogram revealed a 17- × 12-mm homogenous mass attached to the septal leaflet of the tricuspid valve. Moderate tricuspid valve insufficiency was noted around the mass. The patient was afebrile, and inflammatory marker levels showed improvement [ESR 63 mm/h (1–10 mm/h) and CRP 0.8 mg/dL (0.0–0.09 mg/dL)], and he was subsequently

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4Nonstandard abbreviations: ED, emergency department; CHLA, Children’s Hospital Los Angeles; ESR, erythrocyte sedimentation rate; CRP, C-reactive protein; IV, intravenous; CT, computed tomography; PCV7, heptavalent pneumococcal conjugate vaccine; PCV13, 13-valent pneumococcal conjugate vaccine; PPSV23, 23-valent pneumococcal vaccine.
discharged on day 11 to complete a 6-week course of IV antibiotics as an outpatient.

One week after discharge, the patient returned to the CHLA Cardiology clinic for follow up. Review of systems was negative for fevers, excessive bleeding or bruising, chest pain, palpitations, dizziness, swelling, changes in vision, or syncope. Repeat echocardiogram showed that the vegetation had not increased in size.

Two days later (week 3 since diagnosis and initiation of antibiotics), he developed fever to 40.1 °C, cough, and rigors. He was brought back to the CHLA ED, blood cultures were redrawn, antibiotics were continued, and he was readmitted. Repeat echocardiogram at that time again showed the 17- × 12-mm mobile mass on his tricuspid valve with new worsening tricuspid insufficiency. A repeat CT angiogram further showed evidence of pulmonary emboli with wedge-shaped opacities. The patient underwent urgent surgical resection of the tricuspid valve mass and repair. Histopathology was consistent with endocardial vegetation in the setting of bacterial endocarditis. The endocardial/valvular tissue had granulation tissue formation, fibrin deposition, dystrophic calcification, and scattered neutrophils, eosinophils, macrophages, and fibroblast (Fig. 1). Both blood and tissue cultures were negative.

After surgical resection, the patient was given an additional 6-week course of appropriate antibiotics. His postoperative course was uneventful, and the patient continued to do well clinically off of antibiotics at his most recent cardiology follow-up visit.

**DISCUSSION**

The gram-positive cocci recovered from blood culture at the time of his presentation were identified as *Streptococcus pneumoniae*. Histopathology of the tricuspid valve further confirmed the diagnosis of pneumococcal endocarditis. The patient had received 4 doses of heptavalent pneumococcal conjugate vaccine (PCV7) but had not received his supplemental dose of the 13-valent pneumococcal conjugate vaccine (PCV13). Serotyping PCR performed on the initial blood isolate by the Minnesota Department of Public Health confirmed *S. pneumoniae* serotype 23A.

*Streptococcus pneumoniae* is an encapsulated gram-positive bacterium that is the most common cause of bacteremia and lower respiratory tract infections in children. It is a common colonizer of the respiratory tract and breakdown of the normal mucosal barrier is believed to play a major role in the development of pneumococcal bacteremia (1). Pediatric IPD (invasive pneumococcal disease) generally afflicts patients younger than 2 years of age or patients with an immunodeficiency, diabetes mellitus, malignancy, and chronic liver, heart, or lung disease (2). Endocardial seeding is rare and thought to be rare due to early treatment of respiratory tract infections and bacteremia.

The epidemiology of pneumococcal endocarditis has evolved extensively during the past century. Before antibiotics, *S. pneumoniae* comprised approximately 15% of endocarditis cases and was almost uniformly fatal (3). Today, *S. pneumoniae* is a rare cause of endocarditis, accounting for 3%–7%
of cases in children (4). However, even with the advent of antibiotics, pneumococcal endocarditis mortality remains high with case-fatality rates ranging from 28% to 60% (5).

First described in 1912, children diagnosed with pneumococcal endocarditis often were found to have preexisting structural heart disease (4). In the postantibiotic era, congenital heart disease, cardiac surgery, central venous access device, or immunodeficiency are the predisposing conditions in 80% to 90% of cases (6). In a case series documenting 10 years of endocarditis cases in 8 hospitals (1993–2003), 10/11 (91%) children with pneumococcal endocarditis had preexisting structural heart disease (4). A unique aspect of our patient’s case was the absence of any predisposing factors commonly associated with pneumococcal endocarditis. He was also much older than the reported mean age of 4.1 years (6).

Compared to adults, children with pneumococcal endocarditis are less likely to present with typical vascular and immunologic manifestations of infective endocarditis. This is attributed to the acute onset of the disease before diagnosis. Therefore, a high index of suspicion for endocarditis is warranted in a child with confirmed pneumococcal bacteremia, particularly if the patient’s clinical presentation fails to improve after 48–72 h of antimicrobial therapy (4, 6). Signs of endocardial seeding often present as a new or changing heart murmur; yet, some patients may not show this (4, 6). In children with pneumococcal endocarditis, vegetation in the heart is most commonly seen on the mitral valve or aortic valve (6). TTE (transsthoracic echocardiogram) revealed vegetation on the tricuspid valve in our patient, which is a rare occurrence in cases of pneumococcal endocarditis. In the pediatric population, tricuspid valve vegetation has been documented in only 6 pneumococcal endocarditis cases with 50% involving preexisting congenital heart disease (4, 6).

Our patient had received the PCV7 vaccine, which does not include \textit{S. pneumoniae} serotype 23A. PCV7, licensed in February 2000, covers \textit{S. pneumoniae} serotypes 4, 6B, 9V, 14, 18C, 19F, and 23F. In 2010, the 13-valent pneumococcal conjugate vaccine (PCV13) became available that covers PCV7 serotypes and additional serotypes 1, 3, 5, 6A, 7F, and 19A. Structural differences in capsular polysaccharides between serotype 23A and 23F explain the lack of 23A coverage by PCV7 and PCV13 (7). The 23-valent pneumococcal vaccine (PPSV23) contains 12 of the serotypes covered by PCV13 (exclude 6a) with an additional 11 serotypes to include 2, 8, 9N, 10A, 12F, 15B, 17F, 20, 22F, and 33F. The Centers for Disease Controls and Prevention recommends PCV13 vaccination for all children under 2 years of age and recommends PCV13 or PPS2V23 for children >2 years of age with certain medical conditions such as immunocompromised, diabetes, nephrotic syndrome, or chronic heart, lung, kidney, or liver disease. The rate of invasive pneumococcal disease has declined since widespread introduction of PCVs in the US beginning in 2000 (8). A 15-year (2000–2014) study characterizing \textit{S. pneumoniae} carriage after PCV vaccination in children found that non-PCV serotypes dominated. By 2014, non-PCV

**TAKEAWAYS**

- Although PCV7 and PCV13 provide protection against \textit{S. pneumoniae} serotype 23F, it does not cover serotype 23A.
- Previously healthy children with up-to-date pneumococcal vaccination can develop endocarditis from pneumococcal bacteremia.
- Suspicion for endocarditis is warranted in a child with confirmed pneumococcal bacteremia, particularly if the patient’s clinical presentation fails to improve after 48–72 h of antimicrobial therapy.
serotypes 11A, 23B, 35B, and 23A were the most common identified strains (9).

In the pediatric population, only a single instance of serotype 23A pneumococcal endocarditis was documented (4) in a 14-month-old female that had a ventricular septal defect with vegetation found on the tricuspid valve (4). To date, our patient is the first child diagnosed with 23A pneumococcal endocarditis with no preexisting congenital heart defect or predisposing factors. A case series by Givner et al. monitored pediatric pneumococcal endocarditis in 8 pediatric hospitals and found serotypes 14 and 18 accounted for 60% of the pneumococcal isolates (4). A 1998 review of the English literature on pneumococcal endocarditis in adults noted serotypes 1, 8, and 12 were most commonly detected (5). For invasive pneumococcal disease in children, surveillance of 2399 isolates between 1993 and 1999 by the US Pediatric Multicenter Pneumococcal Surveillance group reported 10% prevalence of serotype 23A, and only a single patient was diagnosed with pneumococcal endocarditis (10).

In summary, we report a rare case of pediatric endocarditis caused by S. pneumoniae 23A in a vaccinated child with no previous congenital heart defect. This highlights the importance of screening for endocarditis even in previously healthy, vaccinated children.

**REFERENCES**