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Serotype 19A bacteremic pneumococcal pneumonia after 4 doses of 13-valent conjugate vaccine: a review of pneumococcal conjugate vaccine effectiveness

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Abstract

We report a case of bacteremic pneumococcal pneumonia due to serotype 19A in a child who had received four doses of the 13-valent pneumococcal conjugate vaccine, and review the literature on effectiveness of this vaccine. Pediatricians should be alert to the fact that up-to-date immunization status with pneumococcal vaccine does not preclude illness from invasive disease caused by a vaccine serotype.

Keywords

bacteremia; bacteremic pneumonia; *Streptococcus pneumoniae*; serotype 19A; 13-valent pneumococcal conjugate vaccine; vaccine effectiveness

After the licensure of the 7-valent pneumococcal conjugate vaccine (PCV7) in 2000 an increase in replacement serotypes was observed, particularly of serotype 19A. This became the most common serotype causing invasive pneumococcal disease (IPD) in children, including those without underlying conditions.¹ Serotype 19A, along with other strains, was included in the 13-valent pneumococcal conjugate vaccine (PCV13) licensed for use in 2010 partly to combat the most common replacement serotypes now causing IPD.

Reports of vaccine failure from PCV13 have been documented most frequently for serotype 3,^{2,3} however to date this has not been described for other serotypes. We report a case of bacteremic pneumococcal pneumonia due to serotype 19A in a child who had received four doses of PCV13.

Case report

A 3 year-old previously healthy female presented to an outside hospital with a one day history of fever, cough and dyspnea. On arrival, she was febrile to 38.2 °C, with a respiratory rate of 40 breaths/minute, heart rate of 144 beats/minute, and oxygen saturations

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of 98% on room air. Her white blood count was 20.4×10^9 cells/L with 67% neutrophils, hemoglobin of 10.4 g/dL, platelet count of 264×10^9 /L, erythrocyte sedimentation rate of 15 mm/hour. Chest radiography showed a retrocardiac infiltrate (Figure 1). Due to a history of rash with amoxicillin, she was given a dose of intravenous azithromycin 10 mg/kg before transfer to our institution for inpatient care.

Six hours after arrival, she developed generalized abdominal pain, associated with tachycardia, tachypnea, increased work of breathing, and fevers to 39.3 °C. An x-ray of the chest showed the retrocardiac infiltrate, and abdominal x-ray revealed moderate stool burden. C-reactive protein and lactic acid were both elevated at 75.5 mg/L and 3.5 mmol/L, respectively. An abdominal ultrasound demonstrated right lower quadrant adenopathy. Due to increased concern for sepsis, she was started on ceftriaxone 50 mg/kg every 12 hours. A CT chest and abdomen revealed an area of non-enhancing consolidation in the left lower lobe (Figure 2), consistent with lobar pneumonia. The blood culture drawn at the referring hospital turned positive after 25 hours of incubation, growing gram-positive cocci in pairs and chains. Due to suspicion for Group A *Streptococcus*, clindamycin was added at 10 mg/kg every 6 hours. An echocardiogram to evaluate a heart murmur did not detect any vegetations or abnormalities.

The blood culture was subsequently identified as *Streptococcus pneumoniae* by Matrix-Assisted Laser Desorption Ionization Time of Flight (MALDI TOF) mass spectrometry (bioMérieux, Durham, NC). Quellung reaction (Serum Statens Institut, Copenhagen, Denmark) classified the serotype as 19A. Antimicrobial susceptibility testing using the Etest demonstrated susceptibility to vancomycin and levofloxacin, intermediate susceptibility to penicillin and ceftriaxone, and nonsusceptibility to clindamycin, azithromycin, and meropenem. Azithromycin, clindamycin and ceftriaxone were discontinued and the patient was changed to intravenous levofloxacin, 10 mg/kg every 12 hours. On hospital day 4, she was transitioned to oral levofloxacin and discharged to complete a 14-day course. She was followed up by phone a week later and was clinically improved.

Our patient had received PCV13 at 2 months of age, 4 months 1 day of age, and 6 months 17 days of age. She received her fourth dose of PCV13 at 12 months 11 days of age. Due to the development of IPD in spite of receipt of all 4 doses of PCV13, an immune deficiency evaluation was undertaken. This revealed normal IgG, IgG subclasses, IgA, and IgM levels, with protective titers to diphtheria and tetanus. Total classic complement pathway screen was within normal range. She had an adequate response to her pneumococcal vaccine with titers over 1.3 µg/mL for 50% of her tested antigens. Her pneumococcal serotype 19A IgG level was 21.01 µg/mL, drawn three days after her hospital admission.

Discussion

Pneumococcal antibody titers vary over time, even in healthy subjects. Serum antibody titers in most patients after pneumococcal polysaccharide vaccination decrease after several months to years.⁴ The conjugation to diphtheria toxoid for development of PCV is believed to lead to increased immune stimulation and subsequently greater responsiveness.⁴ Waning antibody levels can occur, and nonimmunized subjects can demonstrate protective antibody

levels to some serotypes as a result of clinical or subclinical infection. Measurements of pneumococcal serologic assays are useful in assessing for seroconversion, as well as assessing for humoral immune competence. However, while a titer of 1.3 µg/mL is considered a protective response, normal ranges can vary by serotype and by age.⁴ A two-fold increase in titers has been proposed as an appropriate response to vaccination in those 24 months to 5 years of age, with conversion of 50% or more of the serotypes tested; for subjects 6 years of age or older, a normal response is defined as conversion of 70% of the serotypes tested.⁴

Immunogenicity varies among pneumococcal capsular serotypes, with serotype 3 and 8 being immunogenic even in young children, and serotypes 6B and 23F being poor immunogens.⁵ In immunogenicity studies, PCV13 has been comparable to PCV7 in eliciting substantial opsonophagocytic assay (OPA) activity.⁶ High OPA titers were seen for 98-100% of children after immunization with PCV13. As opsonophagocytosis is the primary mechanism for clearance of pneumococci from the host, measurement of OPA appears to correlate with vaccine-induced protection. When vaccine protectiveness is trialed under controlled conditions, efficacy data is obtained.⁷ For PCV13, vaccine efficacy rates for serotype 19A have been calculated to be 70% after one or more doses, with a 95% confidence interval ranging from 10-90%.⁸

However, vaccine efficacy is based on a putative correlate of protection, and is a distinctly different entity from vaccine effectiveness which also takes into account vaccine potency and other nonvaccine-related factors.⁷ Vaccine failure has been reported in fully immunized children, most notably due to serotype 3 after PCV13,^{2, 3} but also serotype 19A after PCV10,⁹ and after receipt of one dose of PCV13.¹⁰ This is less surprising for serotype 3 based on its lower antibody titers and limited booster effect seen in PCV13 immunogenicity studies.⁶ However, serotype 19A has shown consistently high geometric mean concentrations and OPA titers after both the 3-dose series and after the toddler dose.⁶

Conclusion

This is the first documented case of pneumococcal bacteremic pneumonia caused by a vaccine serotype 19A occurring in an immunocompetent child after receipt of four doses of PCV13. Further surveillance is warranted to see how effective PCV13 is in reducing invasive pneumococcal disease caused by serotypes contained within the vaccine. Pediatricians should be alert to the fact that up-to-date immunization status with PCV13 does not preclude illness from invasive pneumococcal disease caused by a vaccine serotype.

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References

1. Kaplan SL, Barson WJ, Lin PL, Stovall SH, Bradley JS, Tan TQ, Hoffman JA, Givner LB, Mason EO Jr. Serotype 19A Is the most common serotype causing invasive pneumococcal infections in children. *Pediatrics*. 2010; 125(3):429–436. [PubMed: 20176669]
2. Antachopoulos C, Tsolia MN, Tzanakaki G, Xirogianni A, Dedousi O, Markou G, Zografou SM, Eliades A, Kirvassilis F, Kesanopoulos K, Roilides E. Parapneumonic pleural effusions caused by *Streptococcus pneumoniae* serotype 3 in children immunized with 13-valent conjugated pneumococcal vaccine. *Pediatr Infect Dis J*. 2014; 33(1):81–83. [PubMed: 24172850]
3. Madhi F, Godot C, Bidet P, Bahuaud M, Epaud R, Cohen R. Serotype 3 Pneumococcal Pleural Empyema in an Immunocompetent Child after 13-valent Pneumococcal Conjugate Vaccine. *Pediatr Infect Dis J*. 2014; 33(5):545–546. [PubMed: 24732391]
4. Orange JS, Ballow M, Stiehm ER, Ballas ZK, Chinen J, De La Morena M, Kumararatne D, Harville TO, Hesterberg P, Koleilat M, McGhee S, Perez EE, Raasch J, Scherzer R, Schroeder H, Seroogy C, Huissoon A, Sorensen RU, Katial R. Use and interpretation of diagnostic vaccination in primary immunodeficiency: a working group report of the Basic and Clinical Immunology Interest Section of the American Academy of Allergy, Asthma & Immunology. *J Allergy Clin Immunol*. 2012; 130(3 Suppl):S1–24. [PubMed: 22935624]
5. Hidalgo H, Moore C, Leiva LE, Sorensen RU. Preimmunization and postimmunization pneumococcal antibody titers in children with recurrent infections. *Annals of allergy, asthma & immunology : official publication of the American College of Allergy, Asthma, & Immunology*. 1996; 76(4):341–346.
6. Kieninger DM, Kueper K, Steul K, Juergens C, Ahlers N, Baker S, Jansen KU, Devlin C, Gruber WC, Emini EA, Scott DA. Safety, tolerability, and immunologic noninferiority of a 13-valent pneumococcal conjugate vaccine compared to a 7-valent pneumococcal conjugate vaccine given with routine pediatric vaccinations in Germany. *Vaccine*. 2010; 28(25):4192–4203. [PubMed: 20417262]
7. Weinberg GA, Szilagyi PG. Vaccine epidemiology: efficacy, effectiveness, and the translational research roadmap. *J Infect Dis*. 2010; 201(11):1607–1610. [PubMed: 20402594]
8. Miller E, Andrews NJ, Waight PA, Slack MP, George RC. Effectiveness of the new serotypes in the 13-valent pneumococcal conjugate vaccine. *Vaccine*. 2011; 29(49):9127–9131. [PubMed: 21983361]
9. Ho PL, Chan MY, Chow KH, Chiu SS. *Streptococcus pneumoniae* serotype 19A bacteremia in a child fully immunized with 10-valent pneumococcal conjugate vaccine. *Journal of microbiology, immunology, and infection = Wei mian yu gan ran za zhi*. 2014; 47(2):164–165.
10. Lu CY, Ting YT, Huang LM. Severe *Streptococcus pneumoniae* 19A pneumonia with empyema in children vaccinated with pneumococcal conjugate vaccines. *Journal of the Formosan Medical Association = Taiwan yi zhi*. 2014

Figure 1.
Chest, lateral view, demonstrating retrocardiac infiltrate

Figure 2.
Chest CT demonstrating area of non-enhancing consolidation in left lower lobe