Case Report

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Case Report

Serotype 15B/15C Pneumococcal Meningitis in a Vaccinated Toddler: Advocating PCV20 Boosters for Enhanced Pediatric Protection

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Abstract: *Streptococcus pneumoniae* remains a leading cause of bacterial pneumonia and meningitis in children globally, despite pneumococcal conjugate vaccine (PCV) implementation. We report a case of fatal pneumococcal meningitis in a fully vaccinated 2-year-old male. Despite prior PCV13 vaccination, the patient developed meningitis caused by *S. pneumoniae* serotype 15B in the cerebrospinal fluid and 15C in the blood. Genomic sequencing revealed nearly identical isolates differing by a capsular switch mutation. This case highlights the limitations of PCV13 against emerging serotypes like 15B and 15C. The recent approval of PCV20, which includes serotype 15B, represents a significant advancement. We propose a PCV20 booster dose for children under five previously vaccinated with PCV13 to enhance protection against the evolving landscape of pneumococcal serotypes and reduce invasive disease. Continued surveillance and adaptive vaccination strategies are crucial, as *S. pneumoniae* continues to pose a significant threat to young children worldwide.

Keywords: Vaccine Coverage; Pediatric Vaccine; meningitis; PCV20; PCV13; invasive pneumococcal disease; *Streptococcus pneumoniae*

Introduction

Streptococcus pneumoniae is the leading cause of bacterial pneumonia and global mortality in children, and its clinical manifestations encompass a range of pneumococcal diseases, including otitis media, pneumonia, and meningitis [1,2]. According to the WHO, pneumonia (caused by various pathogens, including bacteria) and bacterial meningitis killed 740,000 and 112,000 children under 5 globally in 2019.

S. pneumoniae's prominence as a cause of bacterial meningitis in young children stems from its ability to exploit immature immunity and employ virulence factors like the polysaccharide capsule [3,4]. Its pathogenesis, from colonization to blood-brain barrier breach, underscores the importance of early intervention [1]. Pneumococcal vaccination is a crucial tool in preventing pediatric bacterial meningitis, a serious and potentially life-threatening infection caused by *S. pneumoniae*. The introduction of pneumococcal conjugate vaccines (PCVs) has significantly reduced the incidence of invasive pneumococcal disease, including bacterial meningitis, in children [5,6]. However, despite the availability of effective vaccines, pneumococcal disease remains a significant public health concern, particularly in areas with low vaccination coverage or in children with underlying medical conditions. This case report aims to highlight the importance of pneumococcal vaccination in preventing pediatric bacterial meningitis and to discuss the clinical presentation, diagnosis, and

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management of a case of pneumococcal meningitis in a child, with a focus on the role of vaccination in preventing such cases.

Case Presentation

The patient is a previously healthy 2-year-old male who presented to the emergency department with altered mental status following approximately 2 weeks of intermittent fever, vomiting and malaise. Two weeks prior, the patient's parents and sibling were ill with a suspected viral gastrointestinal infection which resolved over the course of a few days; however, the patients symptoms continued. He was seen on day 2 of symptoms and diagnosed with suspected viral gastroenteritis and treated with antiemetic medication. On day 7 of symptoms, he was seen in an Emergency Department (ED) where laboratory tests revealed normal blood counts and serum electrolytes. He was presumptively diagnosed with a bacterial gastrointestinal infection and started on oral cefixime. This was discontinued two days later at a follow up ED visit due to the symptoms believed to be more consistent with a viral illness. His symptoms continued and progressed to include altered mental status over the next 4 days.

Subsequently, he presented to the ED, the patient was noted to be febrile to 40C, tachycardic, with altered mental status (responsive only to painful stimuli). Physical examination revealed neck rigidity, extensor posturing and bilateral eye deviation suggestive of seizure activity, which was treated with benzodiazepines. Suspecting meningitis, a lumbar puncture was obtained. The cerebrospinal fluid (CSF) was cloudy, with analysis showing elevated WBC count of 2,500 x 10^6 /L, with a differential of 81% neutrophils, 15% lymphocytes, and 4% monocytes; glucose was critically low at 10 mg/dL; protein was elevated at 200 mg/dL; and the Gram stain was positive for numerous Gram-positive cocci in pairs and chains. Blood work at the time showed no leukocytosis (WBC 10.8 × 10^9/L), hypokalemia (potassium 3.0 mmol/L, and elevated lactic acid (4.5 mmol/L). CSF and blood cultures were positive for *Streptococcus pneumoniae* with susceptibility to all tested antibiotics. He was started on IV antibiotics and due to poor responsiveness, he was intubated and underwent a brain MRI for further evaluation.

Due to clinical instability, the patient was transferred to a local facility with a pediatric intensive care unit. Despite aggressive treatment, he remained comatose with minimal response. Echocardiography at that time showed a new vegetation on the mitral valve. Over the course of a few days, he developed dramatic lability in his vital signs, and emergent MRI showed impending brainstem herniation. A brain death exam was performed, confirming brain death, and care was withdrawn in order to pursue organ donation.

Two isolates were recovered, one from the patient's blood and the other from the patient's cerebral spinal fluid. Both isolates were sequenced, and genomes annotated (accession no. SAMN47824484 and SAMN47824485). Both isolates belong to sequence type 199. The only antimicrobial resistance genes carried by the two isolates were the macrolide resistance genes *mef(A)* and *msr(D)*. However, the CSF isolate belonged to serotype 15B while the blood isolate belonged to serotype 15C.

Discussion

This case of *Streptococcus pneumoniae* meningitis in a fully vaccinated 2-year-old underscores the ongoing threat of invasive pneumococcal disease (IPD) in young children despite widespread vaccination. The two *S. pneumoniae* isolates were nearly identically when sequenced from the patient's blood and cerebrospinal fluid, differing by just 4 single nucleotide polymorphisms and an INDEL. Despite their similarity, they belonged to two different serotypes: 15B in the cerebrospinal fluid and 15C in the blood. This divergence was due to a two-nucleotide duplication (c.428_429dup) in the wciZ gene of the blood isolate, causing a frameshift mutation and a truncated WciZ O-acetyltransferase protein. This inactivation prevents acetylation in the capsular pentasaccharide repeating unit, driving a switch from serotype 15B to 15C [7]. This capsular switch is notable because

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it can occur at a high frequency in some isolates, though it may not be reversible in others [8,9]. Since only one isolate was sequenced per site, it remains unclear whether both serotypes coexisted at both locations.

The presence of serotypes 15B and 15C in this case highlights the phenomenon of serotype replacement, a consequence of prolonged use of pneumococcal conjugate vaccines (PCVs) like PCV13. The introduction of PCVs has significantly reduced the incidence of IPD caused by vaccine-targeted serotypes [5]. However, this success has been offset by the emergence of non-vaccine serotypes, such as 15B and 15C, which have increasingly driven IPD cases [10]. In this instance, the patient had received the full schedule of PCV13, which offered no protection against serotypes 15B and 15C, revealing a gap in coverage that allowed this severe infection to develop [11].

Serotype 15B is included in PCV20 (approved for infants in April 2023). While serotype 15C is not directly covered by PCV20, it exhibits limited immune evasion, suggesting that cross-protection from this vaccine is likely [11,12]. In contrast, PCV7, PCV13, and PCV15 do not protect against either serotype 15B or 15C (Table 1) [11]. The patient's progression to meningitis despite the PCV13 vaccination illustrates the urgent need for updated management approaches to address these emerging serotypes.

Table 1. Streptococcus pneumoniae serotypes included in pneumococcal conjugate vaccines (PCV7, PCV10, PCV13, PCV15, and PCV20) and their respective public availability dates for children under 5.

Serotype	PCV7 (2000)	PCV10 (Not U.S., 2009)	PCV13 (2010)	PCV15 (2022)	PCV20 (2023)
4	✓	✓	✓	✓	✓
6B	✓	✓	✓	✓	✓
9V	✓	✓	✓	✓	✓
14	✓	✓	✓	✓	✓
18C	✓	✓	✓	✓	✓
19F	✓	✓	✓	✓	✓
23F	✓	✓	✓	✓	✓
1		✓	✓	✓	✓
5		✓	✓	✓	✓
7F		✓	✓	✓	✓
3			✓	✓	✓
6A			✓	✓	✓
19A			✓	✓	✓
22F				✓	✓
33F				✓	✓
8					✓
10A					✓
11A					✓
12F					✓
15B					✓
15A					
15C					

PCV20 represents a significant advancement in pneumococcal disease prevention. PCV13, introduced in 2010, served as the standard of care until the licensure of PCV20 in 2023, with PCV15 being largely bypassed due to its limited improvement in serotype coverage and established production for PCV13 [13,14]. PCV20 offers enhanced protection by including additional serotypes, such as 15B, that are absent from PCV13 [6]. This broader coverage is critical as non-PCV13 serotypes (22F, 33F, 8, 10A, 11A, 12F, and 15B) have become prominent drivers of IPD following PCV13's widespread use [10]. By addressing serotype replacement, PCV20 provides a more robust defense

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against pneumococcal disease, including meningitis, for the moment until new non vaccine serotypes inevitably increase in incidence.

When given as a single dose to very young children fully vaccinated with PCV13 the PCV20 elicited immune responses expected to provide protection against the 7 additional serotypes included in PCV20, supporting the use of a PCV20 booster shot to children under 5 who were previously vaccinated with PCV13 [15]. Based on this case, we propose a new management strategy: administering a PCV20 booster shot to children under five that only received the PCV13. This suggestion is supported by several key considerations:

1. **Expanded Serotype Coverage:** PCV20 protects against serotype 15B, which are not included in PCV13, potentially mitigating the severity of cases like this one [15].
2. **Cross-Protection Potential:** Although serotype 15C is not in PCV20's formulation, its limited immune evasion suggests cross-protection is achievable [11,12].
3. **Public Health Benefit:** Vaccination with PCV20 can reduce colonization and invasive disease caused by a wider array of serotypes, further decreasing the incidence of pneumococcal diseases like meningitis [14,16].
4. **Vulnerable Population:** Children under five remain especially vulnerable to IPD, with non-PCV13 serotypes increasingly implicated in this age group [17].

Differences in vaccine schedules and catch-up campaigns between the USA and Europe, along with the time needed to observe declines in disease from vaccine-targeted strains, will continue to shape *S. pneumoniae* epidemiology [5,6,18]. This variability underscores the importance of ongoing surveillance and adaptive vaccination strategies to sustain PCV effectiveness. Vaccination, particularly with PCV20, represents a cornerstone of prevention, reducing both colonization and invasive disease [14,16,19]. This is vital for children under 5, where non-PCV13 serotypes increasingly cause IPD [17].

In conclusion, this case reaffirms that *S. pneumoniae* remains a major cause of morbidity and mortality in children worldwide, despite advances in vaccination. While PCVs have markedly reduced IPD, the limitations of PCV13 and the rise of non-vaccine serotypes like 15B and 15C necessitates the adoption of updated vaccines like PCV20 as well as continued awareness of the threat by medical staff. By offering broader serotype coverage and mitigating serotype replacement, PCV20 enhances protection for children under five, a population at heightened risk for invasive disease. We strongly support a PCV20 booster shot in this age group to those who only received the PCV13 to ensure continued comprehensive defense against the changing landscape of pneumococcal serotypes.

Declarations: Material has been reviewed by the Landstuhl Regional Medical Center Public Affairs Office. There is no objection to its presentation and/or publication. The opinions or assertions contained herein are the private views of the author, and are not to be construed as official, or as reflecting true views of the Department of the Army or the Department of Defense.

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