Molecular Characterization of Invasive Streptococcus pneumoniae Serotype 3 Isolates in Pediatric Patients from 2008-2013

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ABSTRACT

Background: Invasive pneumococcal disease (IPD) due to serotype 3 has been a prevalent cause of IPD since the introduction of PCV7. The recent declination in the number of IPD caused by all vaccine serotypes since the introduction of PCV13 suggests a potential need for a modified vaccine to optimally reduce IPD due to serotype 3.

Methods: This study included 62 serotype 3 isolates collected from the US between 2008 and 2013. Isolates were typed by Multilocus Sequence Typing (MLST) and Pulsed Field Gel Electrophoresis (PFGE). Antimicrobial susceptibility testing was performed using CLSI guidelines. Statistical analysis was performed using Fisher’s Exact test and Chi square.

Results: The total number of serotype 3 isolates from 2008 to 2013 was 13,762, of which 104 were serotype 3 isolates. Multilocus typing by MLST and PFGE showed that ST180 represents a common genetic lineage among serotype 3 isolates from the US. More than 90% of all isolates were susceptible to clindamycin. While recent reports suggest a decrease of most vaccine serotypes, post introduction of PCV13, several studies suggested a limited efficacy of the vaccine against serotype 3 compared with other PCV13 serotypes. In a recently published study, serotype 3 was in one recent study identified in 15% of all invasive pediatric infections, which is in agreement with our finding. Since 1993, the US Pediatric Multicenter Pneumococcal Surveillance Network (PMPSN) has monitored the distribution of pneumococci in children <5 years of age. The PMPSN data showed that serotype 3 has been the most common serotype causing invasive pneumococcal disease (IPD) in children throughout the United States over a 6-year period surrounding the introduction of the 13-valent pneumococcal conjugate vaccine, PCV13.

OBJECTIVES

To characterize invasive pediatric infections, caused by S. pneumoniae serotype 3, in children in the United States over a 6-year period surrounding the introduction of the 13-valent pneumococcal conjugate vaccine, PCV13.

INTRODUCTION

Invasive pneumococcal disease (IPD) contributes significantly to the morbidity and mortality of children <5 years of age worldwide. More than 90 different serotypes of S. pneumoniae have been identified and capsular switching has occurred among vaccine serotypes of the past as evident by multilocus sequence typing (MLST). An increase in non-vaccine serotypes was observed after the introduction of the 7-valent pneumococcal conjugate vaccine (PCV7), concurrent with a decrease of IPD in children <5 years of age. In 2000, PCV7 was replaced by the 13-valent pneumococcal conjugate vaccine, PCV13. PFGE, confirming protection against serotype 6B, 4, 6A, 19A, and 23F plus the additional serotypes 1, 3, 5, 6A, 7F, and 19A.

While recent reports suggest a decline of most vaccine serotypes, post introduction of PCV13, several studies suggested a limited efficacy of the vaccine against serotype 3, which has continued to be isolated from pediatric patients. Serotype 3 was in one recent study identified in parapneumonic pleural effusions by PCR from 15 of 20 children immunized with PCV13. (Pediatr Infect Dis 2014;33:81-83).

RESULTS

Demographics and disease presentations

A total of 62 serotype 3 isolates were identified from 2008-2013 (Table 1). The total number of serotype 3 isolates from IPD 2008-2013 made up 6.7% of the total number of IPD isolates identified during this time frame.

Figure 1. Serotype 3 IPD isolates collected from 2008-2013

Table 1. Number of IPD diagnoses per collection site

<table>
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<th>Year</th>
<th>Total Isolate Number</th>
<th>6A</th>
<th>6B</th>
<th>7F</th>
<th>19A</th>
<th>23F</th>
<th>15</th>
<th>2</th>
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CONCLUSIONS

Serotype 3 isolates remain an important cause of IPD since the introduction of PCV13, pneumonia is the most common manifestation, the most commonly isolated serotype was ST180, and genetic change over time was not detected by either MLST or PFGE despite both vaccines and antibiotic pressure.

The MLST database also suggests that ST180 represents a common genetic background among serotype 3 isolates. However, geographic differences in distribution suggest a wider genetic platform from which ST180 could emerge.

Less than 20% of children with a serotype 3 infection had an underlying condition.

The findings in this study, along with previous early studies documenting reduced efficacy of PCV13 against serotype 3 compared with other PCV13 serotypes, indicate that continued surveillance is required to assess the potential for the widespread modified vaccine to optimally reduce IPD due to serotype 3 in children.

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