Recurrent Pneumococcal Bacteremia: 34 Episodes in 15 Patients

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Thirty-four episodes of pneumococcal bacteremia were identified in 15 patients over 5 years in 10 hospitals in Franklin County, Ohio. Twelve patients each had 2 episodes of pneumococcal bacteremia, 2 had 3, and 1 had 4. All patients had predisposing conditions, with lymphoma, multiple myeloma, and chronic obstructive pulmonary disease being the most frequent. The mean interval between the first and second episode was 268 days. Serotyping and genotyping were performed on 29 isolates. The same serotypic and genotypic patterns were found for sequential isolates from four patients; three of these patients had a recurrence between 22 and 90 days after a previous episode. Seven (24%) of the 29 isolates were serotype 23F; four isolates (14%) were not susceptible to penicillin. All of our patients received appropriate antimicrobial therapy and appeared to be clinically cured of their initial infection. For patients with recurrent pneumococcal disease, alternate preventive measures such as immunization with conjugate pneumococcal vaccine and/or prophylactic antibiotic therapy should be considered.

Methods

Between 1991 and 1995, adults (age, 18 years or older) with Streptococcus pneumoniae bacteremia were identified from all 10 hospitals in Franklin County, Ohio, as previously described [1]. Medical records of 15 patients with more than one episode of pneumococcal bacteremia were reviewed.

Blood culture isolates of S. pneumoniae from 29 of the 34 episodes were saved. MICs for isolates obtained before April 1994 were determined by a broth microdilution test [1]. MICs for isolates obtained after April 1994 were performed by the Etest [2]. Isolates were serotyped by using the quellung reaction [3]. DNA sequences were amplified with use of repetitive extragenic palindromic (REP) PCR analysis. DNA was isolated by rapid extraction with use of the QIA amp tissue kit (Qiagen, Chatsworth, CA) following the manufacturer’s recommendations. The PCR mixture consisted of the previously described primers REP2-Dt and REP1R-Dt [4, 5] (each at a concentration of 50 nM), dNTP (at a concentration of 0.2 mM), 5 µL of 10× PCR buffer (500 mM KCl, 100 mM tris-HCl [pH, 8.3], and 15 mM MgCl₂), 5 µL of dimethyl sulfoxide, and 100 ng of template DNA. PCR analysis was performed with use of a 9600 thermal cycler (Perkin-Elmer, Norwalk, CT). The PCR amplification reactions (50 µL) were as follows: initial denaturation (95°C for 7 minutes), 30 cycles of denaturation (90°C for 30 seconds), annealing (40°C for 1 minute), extension (65°C for 8 minutes), and final extension (65°C for 16 minutes). Gels were stained with ethidium bromide. Patterns with less than two band differences were considered the same.

Results

Seven hundred thirty-two adults with pneumococcal bacteremia were identified between 1991 and 1995 in the 10 hospitals in Franklin County. Of these adults, 650 were Franklin County residents. Fifteen patients (12 adult residents of Franklin County) had more than one episode of pneumococcal bacteremia: 12 had 2, 2 had 3, and 1 had 4. Therefore, there were 34 (15 initial and 19 recurrent) episodes of bacteremia in the 15 patients.

The time interval between the first and second episode ranged from 22 to 947 days (mean, 268 days; median, 180 days) (table 1). For the three patients with more than two episodes of bacteremia, the mean time interval between the
second and third episode was 101 days. One patient had a fourth episode 571 days after the third episode. Of the 19 recurrent episodes (i.e., second, third, and fourth episodes), seven occurred between 22 and 90 days after the previous episode. In three of these seven episodes, the isolates matched by both serotyping and PCR pattern. A fourth matching pair of isolates was from a patient with two episodes separated by >1 year. All the other recurrences that occurred >90 days later were associated with different serotypes and genotypes.

Seven patients were male, and eight were female. The mean age of the patients was 57 years (range, 24–75 years), and six patients were 65 years of age or older. Of the 15 patients, one (6.7%; patient 10) died during a recurrent episode of pneumococcal bacteremia. Pneumonia was present in 27 (79%) of the 34 bacteremic episodes. In two of these episodes, meningitis was also present. Meningitis without pneumonia occurred in one episode. In six episodes, no obvious primary site was detected.

Underlying medical conditions were present in all patients (table 1): lymphoma (4 patients), multiple myeloma and diabetes mellitus (2), multiple myeloma (1), chronic obstructive pulmonary disease (3), HIV infection (1), congestive heart failure (1), lung cancer (1), cirrhosis (1), and CSF leak after a craniotomy for treatment of meningioma (1).

Twenty-nine isolates were available for testing. Serotypes identified included 23F (7 isolates), 14 (3), 4 (3), 1 (2), 6A (2), 3 (1), 5 (1), 6B (1), 7F (1), 9N (1), 9V (1), 12F (1), 13 (1), 17F (1), 18C (1), 19F (1), and 37 (1). Serotype 23F was
racial differences were seen in our 15 patients with recurrent pneumococcal bacteremia, although the sample size was small.

Little data on recurrent disease exist [6, 7]. Rodriguez-Creixems et al. [6] reported that of 532 patients with pneumococcal bacteremia, 15 (2.8%) had a second episode within a 10-year period. The presence of multiple myeloma was considered a predictor for recurrent infection. Our patients had similar predisposing conditions, with lymphoma and multiple myeloma being two of the most frequent conditions (table 1).

The mortality rate in this study was relatively low compared with that in the study by Rodriguez-Creixems et al. [6]. One possible explanation is that while only five patients in our study received the pneumococcal vaccine, no patient had received the vaccine in the Spanish study. Only one patient with AIDS was identified in the current study, while AIDS (occurring in four of 15 patients) was one of the most frequent underlying diseases along with multiple myeloma and solid tumors in the Spanish study.

Paired isolates from 10 (71%) of 14 episodes were discordant by both serotyping and DNA banding patterns and clearly represent a new infection (table 1). However, the pathogenesis of recurrent pneumococcal bacteremia is less clear in the four episodes with concordant isolate pairs by serotyping and DNA banding pattern. Our patients received appropriate antimicrobial therapy and appeared to be clinically cured of their initial infection; none of the patients had evidence of endocarditis, osteomyelitis, or abscess. The earliest second infection did not occur until after 22 days; however, it is possible that initial therapy may have been adequate to treat the infection but inadequate to eradicate colonization. Two of our patients with concordant isolate pairs from sequential infections had meningitis due to serotype 23F; one had a recurrent episode separated by >1 year from the first episode. Possibly, long-term colonization overrepresented compared with isolates from patients with a single episode of bacteremia who were from Franklin County (24% vs. 9.7%, respectively; \(P = .03\)) [3]. All serotypes except serotypes 13 and 37 are included in the polysaccharide vaccine.

There were three pairs of sequential isolates with common serotypes, and 10 pairs of isolates with discordant serotypes. An additional pair of isolates with a common serotype was identified in a first and third episode of bacteremia. The isolate from the second episode was not saved (table 1).

There were 25 different banding patterns for the 29 isolates by REP PCR analysis. The banding pattern was the same for each of the four isolate pairs with the same serotypes (figure 1). The other 10 isolate pairs had different banding patterns.

All patients received appropriate antimicrobial therapy. There were no differences in duration of therapy between those patients with concordant isolates from recurrent episodes and those with different isolates from recurrent episodes.

Discussion

The incidence of pneumococcal bacteremia has been reported to be higher among the nonwhite population [1]. No

Figure 1. Results of repetitive extragenic palindromic PCR analysis of pneumococcal isolates from patients with the same serotypes on recurrent episodes of bacteremia in Franklin County, Ohio. Note that the banding patterns were the same for each pair of isolates with the same serotype.
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References