Bacteremic Pneumococcal Pneumonia*
A Community Hospital Experience

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We reviewed our experience with bacteremic pneumococcal pneumonia (BPP) over a 1-year period at a 600-bed community teaching hospital; 26 cases were identified. The mean age was 57.5 years and there were 12 male and 14 female subjects. Cough, sputum production, fever, and mental status changes were the most frequent symptoms. Risk factors included drug abuse in 10, HIV in 4, current smoking in 7, diabetes in 3, and cancer in 3. The mean PaO₂/FIO₂ ratio was 274. Radiographic features included a consolidation pattern in 7, bronchopneumonia in 15, combined in 1, and an initial normal film in 3. Average length of stay (LOS) was 11 days with an overall mortality of 11.5%. Four patients required mechanical ventilation, two meeting the criteria for ARDS (if this group were eliminated, LOS would be 8.4 days). Three of these survived. Four patients had organisms resistant to penicillin and all survived. We conclude that (1) BPP remains a serious but treatable infection particularly when utilizing full supportive care; (2) the bronchopneumonia x-ray film pattern was associated with all the mortality; and (3) the occurrence of penicillin resistance did not contribute to the mortality, since early recognition and the use of appropriate antibiotics saved all of these patients.

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BPP=bacteremic pneumococcal pneumonia; LOS=length of stay; MIC=minimum inhibitory concentration

Key words: bacteremic pneumococcal pneumonia; mortality; Streptococcus pneumoniae

Pneumococcal pneumonia remains the most common form of community-acquired pneumonia associated with bacteremia—up to 60% in one series. Major comorbidities in these patients include neurologic disease, dementia, COPD, smoking, ischemic heart disease, hypertension, malignancy, diabetes mellitus, renal disease, and AIDS. Alcoholics made up the largest group in one series. Mortality from bacteremic pneumococcal pneumonia (BPP) varies between 5 and 67% depending on age, hospital location, and whether the infection is nosocomial or community-acquired. In patients who require mechanical ventilation, particularly if elderly, mortality may approach 60%. As many as 35% of patients with community-acquired disease may not present with typical cough, sputum production, or chest pain. Although lobar consolidation may be more common in bacteremic patients, there are very few studies detailing the radiographic picture in bacteremic patients. In addition, the emergence of penicillin-resistant pneumococci in the last decade may play a role in the outcome of these infections.

In order to assess the incidence, clinical and radiographic presentation, response to therapy, and outcome of BPP in a large tertiary care community hospital, we retrospectively reviewed all adult charts of patients with BPP over a 1-year period.

Materials and Methods

The study took place for the 12-month period between July 1992 and June 1993 at Albert Einstein Medical Center, a 600-bed tertiary care teaching hospital affiliated with Temple University School of Medicine. All adult patients with at least one blood culture positive for Streptococcus pneumoniae were identified. Charts were reviewed with abstraction of demographic data (age and sex) and clinical presentation, with attention to cough and sputum production, fever, hemoptysis, chest pain, and mental confusion. The following risks factors were identified: history of AIDS, alcoholism, diabetes mellitus, smoking, COPD, IV drug abuse, dialysis, or end-stage renal disease, sickle cell anemia or splenectomy, and carcinoma. Laboratory value data abstracted included: maximum WBC and differential cell counts, BUN, creatinine, electrolytes, serum glucose, lactate dehydrogenase, protein, baseline arterial blood gas levels, and antibiotic sensitivities of the organism. The outcome of each patient was assessed with regard to the antibiotics used, dose, susceptibility, and duration of therapy; intensive care utilization; need for mechanical ventilation; length of hospital stay; and the development of complications.
Blood culture isolates of S. pneumoniae were recovered by use of a blood culture system (Bectec 860; Becton Dickinson Diagnostic Instruments Division; Sparks, Md). Patient blood was drawn by venipuncture into blood culture bottles (Bectec 6A and 7A) at the bedside, and the inoculated bottles were transported to the laboratory for incubation and processing. Blood culture bottles giving a positive growth-index indication were subcultured to blood, chocolate, and MacConkey agars, and a smear was examined by the Gram’s stain. The results of the Gram’s stain examination were telephoned to the patient care unit.

Growth on the blood agar plate was tested for catalase production and Gram’s stain morphologic findings. Isolates consisting of Gram-positive cocci that were catalase-negative and that produced α-hemolysis were evaluated with a reagent (Pneumoslide reagent; BBL; Cockeysville, Md). A positive reagent slide result was telephoned to the patient care unit as a presumptive isolation of S. pneumoniae.

All α-hemolytic, catalase-negative Gram-positive cocci were evaluated for optochin susceptibility (Taxo P disk; BBL; Cockeysville, Md) and for oxacillin sodium susceptibility (1-μg disk; BBL; Cockeysville, Md) by standard National Committee for Clinical Laboratory Standards methods. Isolates producing a zone of inhibition of 16 mm or more around the optochin disk were identified as S. pneumoniae. Isolates producing a zone of inhibition of 20 mm or more around the oxacillin disk were reported as “susceptible” to penicillin. Those producing a zone of inhibition of less than 20 mm were reported as “resistant” to penicillin.

Chest x-ray films were reviewed at the time of admission, at 48 h, and at the time of discharge with regard to location of infiltrate, presence or absence of an air bronchogram, atelectasis, pleural effusion, and development of the ARDS. The x-ray films were then categorized according to the classification of Kantor10 (consolidation, bronchopneumonia, interstitial, or combined).

### Results

A total of 29 episodes of pneumococcal bacteremia were identified in 28 patients. A renal patient with two episodes of bacteremia due to sinusitis and an AIDS patient with meningitis both of whom had normal chest x-ray films were excluded. The remaining 26 patients all with radiographic documentation of pneumonia were reviewed. The mean age was 57.5 years with a range of 30 to 92 years; 12 were men and 14 were women. Twenty-two had positive blood cultures at the time of admission; the remainder had a positive blood culture within 48 h. The mean WBC count was 18,300/mm³ with a differential cell count of 63% segmented neutrophils, 23% band cells, and 11% lymphocytes. Means of other pertinent laboratory values were BUN, 25 mg/dL; creatinine, 1.7 mg/dL; Na⁺, 137 mEq/L; Cl⁻, 103 mEq/L; K⁺, 4 mEq/L; CO₂, 24 mEq/L; lactate dehydrogenase (n=5), 655 IU/L; total protein (n=12), 6.6 g/dL; and blood glucose, 154 mg/dL. Arterial blood gas levels were determined in 21 patients; 14 were breathing room air and 7 were receiving supplemental oxygen. The mean PAO₂/FIO₂ ratio was 274, with a range of 136 to 446.

Risk factors are depicted in Figure 1. Current smokers made up the largest group with seven patients or nearly 30% of the group. There were four patients with AIDS and ten patients who abused drugs (five of whom were IV drug abusers and five of whom were crack smokers).

The most common clinical symptom was fever (Fig 2), which was found in 22 of 26 (85%) patients; half the group had cough and sputum production and nearly half had mental status changes. Hemoptysis or rusty colored sputum was rare, occurring in only 3 (12%) patients.

Initial radiographic findings of the 26 patients are outlined in the Table 1. Lower lobe predominance was found in 11 (42%) patients; upper lobe predominance was found in 4 (15%); and multilobe involvement was found in 8 (31%). A normal x-ray film at the time of admission was present in 3 (12%), but all 3 developed pulmonary infiltrates within 72 h of admission. Only 7 (27%) patients demonstrated the consolidation or

### Table 1—Initial Radiographic Findings in 26 Patients

<table>
<thead>
<tr>
<th>X-ray Film Category</th>
<th>Lobe Location, No.*</th>
<th>Effusion</th>
<th>Survival</th>
<th>Other</th>
</tr>
</thead>
<tbody>
<tr>
<td>Consolidation (n=7)</td>
<td>RUL, 2; LLL, 4; LUL, 1</td>
<td>4</td>
<td>All</td>
<td>Atelectasis, 3; Air bronchogram, 5</td>
</tr>
<tr>
<td>Bronchopneumonia</td>
<td>RLL, 4; LUL, 1; LLL, 3; bilobar, 4; trilobar, 3</td>
<td>6</td>
<td>3 deaths</td>
<td>Air bronchogram, 4</td>
</tr>
<tr>
<td>Combined (n=1)</td>
<td>Bilobar</td>
<td>...</td>
<td>Survived</td>
<td>Air bronchogram</td>
</tr>
<tr>
<td>Normal (n=3)</td>
<td>...</td>
<td>...</td>
<td>All</td>
<td>...</td>
</tr>
</tbody>
</table>

*RUL, right lung-upper lobe; LLL, left lung-lower lobe; LUL, left lung-upper lobe; RLL, right lung-lower lobe.
lobar pattern; all of them survived. The vast majority presented with the bronchopneumonic pattern (n=15) with the 3 deaths occurring in this group. Most of the patients with the consolidation pattern had an air bronchogram, while this was a rare finding in those with bronchopneumonia. Volume loss was observed in three patients in the lobar group. There were no patients with an interstitial pattern and only one patient with a combined picture.

Small areas of parapneumonic effusion developed in ten patients; in nine, they were ipsilateral to the side of the infiltrate and in one the effusion was bilateral. In no patient did clinical features suggest an empyema; only two required a thoracentesis to rule out an empyema.

Four patients developed respiratory failure requiring mechanical ventilation and ICU care. The mean age of this group was 53 years, and 3 of 4 had 2 or more risk factors. They spent a mean of 12 days on the ventilator (range, 3 to 22 days) with a length of stay (LOS) of 26 days (range, 22 to 31). Two developed ARDS and both survived. Resistant organisms were present in 1 of 4 and this individual survived after an LOS of 23 days. The overall survival in this subgroup was 75% (3 of 4).

Four patients (15%) had resistant organisms isolated and all survived. Their antibiotic regimens and LOS are depicted in Table 2. Half the patients received a combination of two antibiotics at the time of admission. The most common combination was ceftriaxone disodium and vancomycin. The mean age of this group was 51 years, and 3 of 4 had two or more risk factors. One 84-year-old was a resident of a nursing home. Three of these patients had a LOS of 7 days or fewer, while one remained in the hospital for 23 days as this was also one of the ventilated patients. The remainder of the patients with sensitive organisms were treated with various antibiotics, including ceftriaxone, erythromycin and trimethoprim-sulfa methoxazole. Five patients were treated with penicillin. Five patients received an aminoglycoside at the time of admission, since they were immunocompromised.

The overall LOS was 11 days (range, 1 to 31 days) and was reduced to 8.4 days if the ventilator group was eliminated. Mortality in the group was 11.5% (3 of 26). The mean age of those who died was 72 years (range, 65 to 75 years) and two of 3 had 2 or more risk factors. The initial chest x-ray film demonstrated bilateral infiltrates with an effusion in two patients. The remaining patient had a single bronchopneumonic infiltrate. The interval between admission and death was 1, 4, and 22 days in these individuals. Unique to this group was that two of the three patients who died had a concomitant dissecting or ruptured aortic aneurysm confirmed at the time of surgery. To our knowledge, this association between severe vascular disease and BPP has not been previously reported and must be considered an epiphenomenon. All four patients who were HIV-positive with AIDS survived their infection.

**DISCUSSION**

The overall mortality of pneumococcal bacteremia has recently been reviewed and has been found to range between 15 and 55%. On average, approximately 83% of the patients cited had pneumonia. Mortality continues to correlate with advancing age, particularly in nursing home patients, although Esposito found a less pronounced effect of age on hospital course. In patients with AIDS, the incidence of BPP approaches 50% compared with 20% in non-AIDS patients. Although recurrence is frequent, the mortality in AIDS patients remains low, approximately 6%. Thus, the response to antibiotics in this population appears to be adequate.

The annual incidence of BPP has been estimated by Mufson to be 7.5 per 100,000 people with case fatality rates 2 to 3 times that of nonbacteremic cases. Most deaths will occur within the first 5 days of illness, a feature suggested by our study. Comorbid conditions in addition to age greatly increase the morbidity and mortality of the disease. In an attempt to arrive at a predictive index of death in community-acquired pneumonia, Farr et al found, using multivariate analysis, that a respiratory rate of greater than 30 breaths per minute, diastolic blood...
pressure less than 60 mm Hg, or a BUN level greater than 7 mmol/L were associated with an increase in mortality; however, only 18% of these patients had *S. pneumoniae* pneumonia confirmed by sputum culture. More recently, Ortquist et al. compared two populations in a retrospective analysis of mortality. There was a marked difference in deaths from BPP, 5% in Sweden vs 26% in West Virginia; underlying diseases may have contributed to the increase in the West Virginia group. The most commonly associated comorbid factors in their study included alcoholism, coronary artery disease, COPD, cirrhosis, diabetes mellitus, and neoplastic disease. Thrombocytopenia, leukopenia, renal insufficiency, and the number of lobes involved evidenced on a chest x-ray film are the laboratory parameters most frequently associated with increased mortality.11,12,16,22

With the advent of specialized ICU to care for the critically ill, it would be anticipated that mortality would drop. The data on this issue are conflicting. In 1983, Hook et al. identified a total of 119 cases of BPP over a 6-year period; 45 patients were admitted to the medical ICU. The mortality in this group was 76% compared with a 30% overall mortality. They concluded that critically ill patients died later in their hospitalization, with ICU care delaying the inevitable.24 More recently, Franklin et al. analyzed 150 patients with BPP over a 27-month period and demonstrated an ICU mortality of 41%, considerably less than that found by Hook et al. There is no question that the sickest patients will be selected out for ICU care and as a result will continue to experience the highest mortality from this disease. The impact of ICUs on mortality from BPP would require randomized trials which cannot be justified on ethical grounds. Advanced age and comorbid conditions unfortunately will often determine the outcome.

Several studies have attempted to correlate the initial radiographic appearance of the pneumonia in bacteremic patients with the severity of the disease. Kantor examined 40 patients with confirmed pneumococcal pneumonia from New York Hospital, of which were bacteremic. He described four radiographic presentations: consolidation (lobar), bronchopneumonia (patchy), interstitial, and a mixed type (combined). Underlying diseases were present in 75%. Fifty percent of the bacteremic patients had a lobar pattern; the remainder were distributed equally among the other patterns. There were five deaths, resulting in an overall mortality of 12.5%. There was no statistical association between deaths, radiologic presentation, and the presence of bacteremia. In another study done at a VA hospital, Ort et al. divided 94 patients with pneumococcal pneumonia into lobar (37 patients) and bronchopneumonia (57 patients) radiographic subtypes. The incidence of bacteremia was significantly greater in the lobar (54%) vs the bronchopneumonia (9%) group. Since the interobserver variability with regard to chest x-ray films for the presence of pneumonia was considerable, we utilized a consensus reading of two qualified radiologists in order to establish the presence of pneumonia. Surprisingly, the majority of patients with bacteremia in our study had bronchopneumonia (15 of 26–58%), with all of the deaths occurring in this group. Lower lobe or multilobe involvement were the most common location of the infiltrates. Three patients had normal x-ray films at the time of admission with all developing infiltrates within 72 h.

No attempt was made in this study to assess the degree of resolution of the patient’s infiltrates. Since the average LOS was 8.4 days (nonventilated group), it was not possible to assess all x-ray films to complete resolution. One study has suggested a 6-week interval to complete resolution after discharge in patients with BPP, with further delay especially in patients over age 60 years or with underlying COPD. A more recent review of 81 patients with community-acquired pneumonia correlated clearance of the infiltrates with age, number of lobes involved evidenced on the chest x-ray film and smoking history. Only three patients in this series had BPP.

Only 4 of 26 patients in our study had resistant organisms identified (15%). Of 103 isolates examined by the Centers for Disease Control, 16 (15%) were identified as relatively resistant to penicillin with a minimum inhibitory concentration (MIC) of 0.1 to 0.5 μg/mL. They found no relationship between resistance and prior penicillin administration. The mechanism of resistance does not appear to be mediated by penicillinase. The issue of resistant pneumococci was highlighted by a report from South Africa which described three cases among 85 bacteremic patients, an incidence of 3.5%. All three were black, required mechanical ventilation, developed renal failure, and died. Using a 5-μg disk of methicillin sodium, the MICs of the patients were 0.5, 2, and 4 μg/mL, respectively. Recommended antibiotics for highly resistant strains are chloramphenicol, erythromycin, vancomycin, and rifampin. However, recent reports from Spain reveal an incidence of strains resistant to erythromycin close to 10% and that of those resistant to chloramphenicol close to 30%, 27,28

In assessing the risk factors and response to antibiotic therapy in patients with resistant pneumococci, Pallares et al. examined 25 episodes of bacteremia caused by resistant organisms (MICs from 0.12 to 8 μg/mL). He identified five risk factors: higher use of β-lactam antibiotics, hospitalization 3 months prior to the episode, nosocomial infection, episodes of pneumonia in previous years, and the initial critical condition of the patient. The mortality rate for the resistant
group was 54% in contrast to 25% in the sensitive group. 26,27 Generally, intermediate resistance is defined as an MIC of 0.1 to 1.0 µg/mL and highly resistant as 2 µg/mL or more. Although we were not able to determine the precise MIC in our patients, the zone of inhibition correlates with an MIC of 0.1 or more in all cases. Vancomycin or a third-generation cephalosporin are recommended as drugs of choice in treating resistant pneumococcal infections. 28,29 As a practical initial regimen for BPP, we recommend ceftriaxone and vancomycin or vancomycin alone pending results of sensitivity tests. If the organism is sensitive to penicillin, then usual doses of that drug can be administered. If the organism is resistant, therapy with vancomycin or ceftriaxone can be continued based on the degree of resistance.

In a recent review on the emergence of drug-resistant organisms, Breiman et al. 30 demonstrated an overall incidence of 6.6% in 544 patients from 13 hospitals in 12 states. Only 1.5% had what would be described as highly resistant organisms (MIC greater than 2 µg/mL). All strains were sensitive to vancomycin. 31 The accompanying editorial suggested screening for penicillin resistance utilizing the 1-µg oxacillin disk which was similar to the method used in our study. 32 Finally, it must be kept in mind that the presence of cavitary and necrosis in patients with BPP is more likely due to an accompanying anaerobic infection rather than to an infection with resistant organisms. 33

In summary, we have demonstrated a fairly good outcome (only 11.5% mortality) in patients with BPP admitted to a community hospital. Despite an incidence of pneumococcal resistance and HIV infections of 15% each, all of these patients survived. The radiographic pattern associated with the highest morbidity and all the mortality was the bronchopneumonic one. Respiratory failure requiring mechanical ventilation occurred in four patients which contributed to the high overall LOS. However, aggressive supportive care in the ICU resulted in survival of three of four including both patients who met the criteria for ARDS. If the lung is the only organ system diseased, then ICU care will more likely result in a favorable outcome. This is consistent with data from series of patients with ARDS. The association of either a dissecting thoracic or ruptured abdominal aortic aneurysm with BPP is difficult to explain. It is conceivable that excessive coughing, the febrile state, or the age and debilitated state of these patients contributed to this complication. Which came first is difficult to determine. In our population, BPP remains an eminently treatable disease despite the occurrence of pneumococcal resistance and respiratory failure.

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REFERENCES