Streptococcus pneumoniae Spinal Infection in Nottingham, United Kingdom: Not a Rare Event

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Pneumonia and meningitis are the most frequent manifestations of Streptococcus pneumoniae infection. Spinal infection is considered to be a rarity. Between 1985 and 1997, 8 patients with spinal infection (vertebral osteomyelitis, 3; spinal epidural abscess, 1; both, 4) due to S. pneumoniae were seen at University Hospital (Nottingham, U.K.). Predisposing factors for pneumococcal infection were documented for five patients and included diabetes mellitus, alcoholism, and corticosteroid therapy. One patient presented with concomitant meningitis and endocarditis. Clinical features of note were prolonged symptoms and a lack of febrile response. S. pneumoniae was isolated from the blood of five patients. Magnetic resonance imaging was used to localize the spinal infection in five patients. Two cases were managed medically. Three patients died after a protracted illness. A literature search revealed 20 other cases of spinal infections due to S. pneumoniae. The salient features of the cases are summarized.

Vertebral osteomyelitis (VO) and/or spinal epidural abscess (SEA) due to Streptococcus pneumoniae is extremely uncommon. Except for isolated case reports [1–18], the pathogen is rarely mentioned in major reviews on VO [19–27] or SEA [5, 28–34]. Furthermore, spinal infection is not even mentioned as a focus of infection in nine large series of pneumococcal bacteremia published between 1974 and 1996, documenting a total of 2,451 episodes of pneumococcal bacteremia [35–43]. We have elected to report the patients with VO and/or SEA in this series as a single group and have used the all-embracing term of spinal infection to include both of these clinical entities, but we refer to each separately whenever relevant.

We report eight patients with spinal infection due to S. pneumoniae encountered between 1985 and 1997 and review 20 other cases reported in the literature.

Patients and Methods

Clinical, laboratory, and epidemiological findings for each case of spinal infection due to S. pneumoniae were documented. All isolates of S. pneumoniae were identified by standard methods and were tested for susceptibility to penicillin as described previously [44]. S. pneumoniae isolates were sent to the Respiratory and Systemic Infection Laboratory of the Central Public Health Laboratory (Colindale, London) for typing.

A search of the English-language literature from 1970 to 1997 was conducted via MEDLINE for other reported cases of spinal infection caused by S. pneumoniae. Additional cases were identified by a review of cited articles.

Results

The salient features of the eight patients encountered in Nottingham (U.K.) at University Hospital and the 20 previously reported cases of spinal infection due to S. pneumoniae are summarized in table 1 in chronological order, according to the year of their report.

Illustrative Cases Occurring in Nottingham (Table 1)

Patient 5. A 75-year-old man with a 12-day history of pain in the neck and shoulders was admitted to University Hospital in September 1995. Rigors and a nonproductive cough preceded these symptoms. In 1991 bullous pemphigoid had been diagnosed, and he had been taking prednisolone regularly (5–40 mg/d) for 18 months. On examination his neck was held in flexion by muscle spasm and was tender posteriorly. On day 2 he developed a sudden flaccid quadraparesis; power was of grade 2/3 in both arms and grade 0 in both legs, anal tone was absent, and a sensory level was present at T2.

MRI showed an anterior SEA extending from C6 to T1 with cord compression and osteomyelitis of C6–C7. Blood cultures were performed and he underwent anterior decompression, debridement, and spinal stabilization from C5 to C7. Gram staining of the pus obtained from the C6–C7 disk and epidural space showed gram-positive diplococci. Intravenous therapy with ampicillin, fluoxacillin, and metronidazole was commenced. A reducing course of hydrocortisone was given. Cultures of both blood and pus yielded S. pneumoniae (type 6) that was susceptible to penicillin. After 2 days, therapy with benzylpenicillin (1.2 g every 4 hours) was commenced.
Table 1. Characteristics of patients, sites of infection, treatment, and outcome in 28 cases of *Streptococcus pneumoniae* spinal infection (1933–1997), from the current series and the literature.

<table>
<thead>
<tr>
<th>Case or patient no., reference</th>
<th>Country</th>
<th>Patient’s age (y)/sex</th>
<th>Underlying disease/risk factor(s)</th>
<th>Duration of back/neck pain</th>
<th>Temperature (°C)</th>
<th>WBCs (×10^9/L)</th>
<th>ESR (mm/h)</th>
<th>Site of infection (diagnosis)</th>
<th>Source of isolate (serotype)</th>
<th>Antimicrobial agent (duration, in d)</th>
<th>Drainage/ debridement</th>
<th>Outcome</th>
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<tr>
<td>Cases in literature (1933–1997)</td>
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<tr>
<td>1 [1] USA 51/M</td>
<td>Chronic otitis media; recent episode of pneumococcal septicemia</td>
<td>11 w</td>
<td>NS</td>
<td>21.0</td>
<td>NS</td>
<td>L2–L3 (VO + PA)</td>
<td>Spinal pus + urine (3)</td>
<td>None</td>
<td>Yes</td>
<td>Survived</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2 [1] USA 59/F</td>
<td>Recent RTI</td>
<td>3 w (buttock)</td>
<td>NS</td>
<td>13.6</td>
<td>NS</td>
<td>L3–L4 (VO + PA)</td>
<td>Abdominal pus + (post-mortem) lumbar vertebrae (4)</td>
<td>None</td>
<td>Yes</td>
<td>Died</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3 [1] USA 19/M</td>
<td>Acute mastoiditis; recent mastoidectomy</td>
<td>4 w</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>T7–T8 (VO + PA)</td>
<td>Ear pus + blood + mediastinal pus (1)</td>
<td>None</td>
<td>Yes</td>
<td>Survived</td>
<td></td>
<td></td>
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<tr>
<td>4 [2] USA 49/M</td>
<td>Concomitant pneumonia</td>
<td>5 d</td>
<td>39.0</td>
<td>16.4</td>
<td>NS</td>
<td>C4–C6 (SEA + VO)</td>
<td>Sputum (culture-positive); autopsy spinal pus (gram film-positive only) (NS)</td>
<td>None</td>
<td>Yes</td>
<td>Died</td>
<td></td>
<td></td>
</tr>
<tr>
<td>5 [3] UK 36/F</td>
<td>Tubal ligation 1 mo post-partum; severe neck pain since surgery</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>C3–C4 (VO + PA)</td>
<td>Blood (NS)</td>
<td>NS</td>
<td>No</td>
<td>Survived</td>
<td></td>
<td></td>
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<tr>
<td>6 [4] USA 12 w/F</td>
<td>Recent RTI</td>
<td>1 w</td>
<td>39.2</td>
<td>19.5</td>
<td>NS</td>
<td>T5–T10 (SEA + VO + PA)</td>
<td>Epidural pus (3)</td>
<td>Penicillin iv → po (42)</td>
<td>Yes</td>
<td>Survived</td>
<td></td>
<td></td>
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<tr>
<td>7 [5] USA 58/NS</td>
<td>Concomitant endocarditis and meningitis</td>
<td>2 d</td>
<td>39.0</td>
<td>13.7</td>
<td>NS</td>
<td>T5–T6 (SEA)</td>
<td>CSF + blood + epidural pus (NS)</td>
<td>NS</td>
<td>Yes</td>
<td>Died</td>
<td></td>
<td></td>
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<tr>
<td>8 [6] USA 55/M</td>
<td>Multiple rib fractures following traffic accident 6 mo previously</td>
<td>5 mo</td>
<td>Apyrexial</td>
<td>11.3</td>
<td>48</td>
<td>T4–T5 (VO + SEA)</td>
<td>Vertebra (NS)</td>
<td>Benzylpenicillin iv (42)</td>
<td>Yes</td>
<td>Survived</td>
<td></td>
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</tr>
<tr>
<td>9 [7] USA 77/M</td>
<td>Fall from a ladder 3 w prior to admission; concomitant meningitis</td>
<td>1 w</td>
<td>40.0</td>
<td>20.4</td>
<td>NS</td>
<td>T11–L2 (SEA + PA)</td>
<td>CSF + blood (NS)</td>
<td>Nafcillin iv + gentamicin iv (NS) → penicillin + chloramphenicol (NS) Cefazolin iv (14) → cephradine po (28); patient was allergic to penicillin</td>
<td>Yes</td>
<td>Died</td>
<td></td>
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<tr>
<td>10 [8] USA 52/M</td>
<td>Chronic alcoholic pancreatitis; ischemic heart disease</td>
<td>4 mo</td>
<td>Apyrexial</td>
<td>7.5</td>
<td>115</td>
<td>L4–L5 (VO)</td>
<td>Spinal granulation tissue (Not typed)</td>
<td>Cefazolin iv (14) → erythromycin iv (14) → erythromycin extradurally → erythromycin po (28); patient was allergic to penicillin</td>
<td>Yes</td>
<td>Survived</td>
<td></td>
<td></td>
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<tr>
<td>11 [9] Canada 11/F</td>
<td>Recent RTI</td>
<td>1 w</td>
<td>38.0</td>
<td>17.6</td>
<td>45</td>
<td>L4–L5 (VO)</td>
<td>Blood (NS)</td>
<td>Penicillin iv (42)</td>
<td>No</td>
<td>Survived</td>
<td></td>
<td></td>
</tr>
<tr>
<td>12 [10] USA 5.5 mo/M</td>
<td>Recent RTI</td>
<td>2 d</td>
<td>Apyrexial</td>
<td>20.1</td>
<td>NS</td>
<td>C3–C7 (SEA + VO)</td>
<td>Epidural pus (NS)</td>
<td>Yes</td>
<td>Survived</td>
<td></td>
<td></td>
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<tr>
<td>Case or patient no., reference</td>
<td>Country</td>
<td>Patient’s age (y)/sex</td>
<td>Underlying disease/risk factor(s)</td>
<td>Duration of back/neck pain</td>
<td>Temperature (°C)</td>
<td>WBCs ($\times 10^9$/L)</td>
<td>ESR (mm/h)</td>
<td>Site of infection (diagnosis)</td>
<td>Source of isolate (serotype)</td>
<td>Antimicrobial agent (duration, in d)</td>
<td>Drainage/debridement</td>
<td>Outcome</td>
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<tr>
<td>13 [11]</td>
<td>USA</td>
<td>69/F</td>
<td>DM; recent RTI; concomitant endocarditis</td>
<td>5 d</td>
<td>37.0</td>
<td>142</td>
<td>L4–L5 (SEA) + blood (NS)</td>
<td>Spinal pus</td>
<td>Nafcill 4 (8) + gentamicin 4 (8) + penicillin iv (28)</td>
<td>Yes</td>
<td>Survived</td>
<td></td>
</tr>
<tr>
<td>16 [14]</td>
<td>USA</td>
<td>66/M</td>
<td>DM; alcoholism; lumbar stenosis; recent episode of bacteremic pneumococcal pneumonia</td>
<td>3 mo</td>
<td>36.1</td>
<td>113</td>
<td>L4–L5 (VO + SEA + PA)</td>
<td>L4–5 disk space aspirate (NS)</td>
<td>Vancomycin iv (42) + clindamycin po (180); patient was allergic to penicillin</td>
<td>No</td>
<td>Survived</td>
<td></td>
</tr>
<tr>
<td>18 [16]</td>
<td>France</td>
<td>52/M</td>
<td>Recent RTI; alcoholism; congestive cardiac failure; concomitant meningitis</td>
<td>2 d</td>
<td>38.5</td>
<td>14.9</td>
<td>C5–C6 (VO)</td>
<td>Blood; PRS (NS)</td>
<td>Cefoxanted (28) + rifampin po (14) + ceftriaxone iv (NS) + rifampin (NS) + pristinamycin + rifampin (90) + ceftriaxone iv (30)</td>
<td>No</td>
<td>Survived</td>
<td></td>
</tr>
<tr>
<td>19 [17]</td>
<td>Spain</td>
<td>15/M</td>
<td>Recent injury to back whilst playing basketball; chronic gum hypertrophy</td>
<td>2 w</td>
<td>38.3</td>
<td>8.9</td>
<td>L4–L5 (VO)</td>
<td>Needle biopsy specimen of lumbar vertebra (NS)</td>
<td>Vancomycin iv (42) + rifampin iv (42)</td>
<td>No</td>
<td>Survived</td>
<td></td>
</tr>
<tr>
<td>20 [18]</td>
<td>USA</td>
<td>56/F</td>
<td>None</td>
<td>7 w</td>
<td>36.8</td>
<td>6.9</td>
<td>L1–L2 (VO + PA)</td>
<td>Needle biopsy specimen of L1–L2 vertebrae; PRS (NS)</td>
<td>Vancomycin iv (42) + rifampin iv (42)</td>
<td>No</td>
<td>Survived</td>
<td></td>
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</tbody>
</table>

Patients in series reported herein (1985–1997)

<table>
<thead>
<tr>
<th>Case or patient no., reference</th>
<th>Country</th>
<th>Patient’s age (y)/sex</th>
<th>Underlying disease/risk factor(s)</th>
<th>Duration of back/neck pain</th>
<th>Temperature (°C)</th>
<th>WBCs ($\times 10^9$/L)</th>
<th>ESR (mm/h)</th>
<th>Site of infection (diagnosis)</th>
<th>Source of isolate (serotype)</th>
<th>Antimicrobial agent (duration, in d)</th>
<th>Drainage/debridement</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 UK</td>
<td>71/M</td>
<td>Alcoholism; recent RTI</td>
<td>14 w</td>
<td>L2–L3 (VO + PA)</td>
<td>8.3</td>
<td>25</td>
<td>Blood (34)</td>
<td>Spinal pus</td>
<td>Ampicillin iv (17) + amoxicillin po (42)</td>
<td>No</td>
<td>Survived</td>
<td></td>
</tr>
<tr>
<td>2 UK</td>
<td>74/F</td>
<td>DM; recent back injury</td>
<td>2 d</td>
<td>L2–3 disk space aspirate (not typed)</td>
<td>38.0</td>
<td>17.1</td>
<td>L5 (VO)</td>
<td>Spinal pus</td>
<td>Benzylpenicillin iv (14) + amoxicillin po (28)</td>
<td>No</td>
<td>Survived</td>
<td></td>
</tr>
<tr>
<td>3 UK</td>
<td>51/M</td>
<td>Crohn’s disease; seronegative arthopathy</td>
<td>2 w</td>
<td>C3–T1 (SEA)</td>
<td>38.5</td>
<td>24.6</td>
<td>Blood (22)</td>
<td>Spinal pus</td>
<td>Benzylpenicillin iv (21) + amoxicillin po (21)</td>
<td>Yes</td>
<td>Survived</td>
<td></td>
</tr>
<tr>
<td>4 UK</td>
<td>65/M</td>
<td>Cervical spondylosis</td>
<td>10 w</td>
<td>C3–C4 (SEA + VO)</td>
<td>37.2</td>
<td>24.7</td>
<td>C5–C6 (VO)</td>
<td>Spinal pus</td>
<td>Benzylpenicillin iv (21) + amoxicillin po (28)</td>
<td>Yes</td>
<td>Died</td>
<td></td>
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</tbody>
</table>
Three days after surgery he developed pulmonary edema and a chest infection and was transferred to the intensive care unit for ventilation. His respiratory function deteriorated and the tetraparesis did not improve. He died 78 days after admission. An autopsy was not performed.

**Patient 7.** A 72-year-old Afro-Caribbean man with a 9-week history of severe back pain that had worsened over the past 2 weeks and radiated to his legs was admitted to University Hospital in March 1997. Apart from a 20-year history of back pain, his medical history was unremarkable. He drank 1.5 L of whisky per week. On examination, flexion of the spine precipitated lightening pains in both legs. A working clinical diagnosis of spondylosis was made, and he was given analgesia and observed. On day 6 he suddenly became doubly incontinent and had weakness in both legs. MRI of the spine showed osteomyelitis at C6–C7, T9–T10, and L4–L5 with an SEA at L4–L5 (figure 1). Blood cultures were subsequently performed.

In the meantime, the patient had developed pain in the right eye and swelling over the right sternoclavicular joint. Blood cultures yielded *S. pneumoniae* (type 23) that was susceptible to penicillin. Therapy with intravenous benzylpenicillin (2.4 g every 4 hours) was commenced. By this stage he was consid- ered to be too ill for open surgery. An ultrasound-guided needle aspiration of the spine at the L4–L5 vertebral level yielded ~1 mL of pus. This specimen yielded *S. pneumoniae* (type 23) that was susceptible to penicillin.

Gram staining and culture of pus from the corneal abscess were negative, but a gram stain of pus from the area of swelling over the sternoclavicular joint showed gram-positive diplococci, although culture was negative. His condition deteriorated, and on day 20 surgical exploration of the spine was undertaken that included a total laminectomy at the L4–L5 level and a right costotransversectomy at the T9–T10 level. Except for some granulation tissue, no free pus was detected.

Postoperatively his condition deteriorated further, and he subsequently died. An autopsy revealed gross bony involvement of the T7–T10 vertebrae and a left psoas abscess, which appeared to extend from the lumbar vertebrae. An abscess in the region of the right sternoclavicular joint was also confirmed. The cardiac valves were normal.

**Patient 8.** A previously fit 79-year-old woman was brought to University Hospital in July 1997, having been found unresponsive by her daughter. She had been confused and anorexic for 2 days and had a 6-week history of back pain that radiated to the left leg. On examination, the Glasgow coma scale score was 7/15 and she was photophobic and had a stiff neck. On fundoscopy, the right optic disk margins were blurred. After two sets of blood cultures were performed, she received a single dose of cefotaxime (2 g). A CT scan of the head was normal, and a lumbar puncture was subsequently performed. Analysis of the CSF revealed the following values: neutrophils, 85/µL; RBCs, 25/µL; protein, 2.4 g/L; and glucose, 0.1 mg/L (blood glucose concentration was 5.4 mg/L). A gram-stained film of the CSF deposit revealed scanty gram-positive diplococci. Therapy with intravenous benzylpenicillin (2.4 g every 4 hours) and gentamicin (120 mg once daily) was commenced.

*S. pneumoniae* (type 6) that was susceptible to penicillin was isolated in cultures of blood and CSF. On day 3, a systolic murmur and splinter hemorrhages were noted. A transthoracic echocardiogram demonstrated vegetations on the mitral valve.
Figure 1. Magnetic resonance images from a 72-year-old patient with spinal infection due to S. pneumoniae showing osteomyelitis at T9–T10 (left) and L4–L5 (center left). There is an associated epidural abscess at L4–L5, with compression of the thecal sac (center right and right).

and mitral regurgitation. Benzylpenicillin and gentamicin were withdrawn after 17 and 14 days, respectively, and therapy with oral amoxicillin was started. On day 18, however, she developed worsening low-back pain. A bone scan showed increased isotope uptake in the L1–L2 vertebrae. MRI of the spine showed osteomyelitis at L1–L2, with an associated paravertebral mass. Therapy with intravenous benzylpenicillin (2.4 g every 6 hours) was restarted. She underwent debridement and stabilization of the spine between the T11 and L3 vertebrae. She recovered slowly and was discharged 5 months after presentation. At follow-up 2 months later, she had no neurological deficit but residual thoracic kyphosis was present.

Summary of the Salient Features of Patients with Pneumococcal Spinal Infection

Nottingham Series (Eight Patients)

The mean age of the eight adult patients was 68.3 years. There was a distinct male predominance (3:1). Recent or concurrent respiratory tract infection in three patients was documented. Alcohol abuse (2 patients), corticosteroid therapy (1) possible hyposplenism (secondary to Crohn’s disease; 1), diabetes mellitus (2), recent nonpenetrating trauma to the back (1), and spondylosis (2) also were noted. One patient had concomitant meningitis and endocarditis. The mean duration of back or neck pain prior to hospital admission was 6 weeks. Highest temperature in the first 24 hours of hospitalization was ≥38°C in three (43%) of seven patients. The WBC count was >11 × 10⁹/L in 6 of 8 patients (75%), the erythrocyte sedimentation rate (ESR) was ≥90 mm/h for 4 of 7 (57%), and the C-reactive protein (CRP) level was ≥100 mg/L in 6 of 6 (100%).

Neurological deficit on admission was documented in patient 3; in another three (patients 4, 5, and 7), neurological deficits appeared later. S. pneumoniae was isolated in the blood cultures of 5 of 7 patients (71%), and for 3 of these 5 patients the organism was also isolated from epidural pus. For three other patients (numbers 1, 3, and 6), the organism was isolated from spinal pus only. Blood was the source of the causative agent in the remaining two patients. S. pneumoniae from all eight patients was susceptible to penicillin. Of the 8 patients, MRI of the spine was performed on 5 (patients 4–8), CT scanning on 1 (patient 1), myelography plus CT on 1 (patient 3), and bone scan on 1 (patient 2). The lumbar and cervicothoracic regions were involved in four and three patients, respectively, and in the remaining patient (number 7) the spine was involved at multiple levels. Of the 8 patients with spinal infection, 4 presented with complicated VO (SEA in 2), 1 with uncomplicated VO, and 3 with SEA (with associated VO in 2). Three patients in whom the spinal infection was not initially suspected died after protracted illness.

Literature Survey (20 Cases)

The mean age of the 15 adult patients was 55.4 years. The remaining five patients were children. There were 11 males and 8 females, and the gender information was missing in 1 report. Recent or concurrent respiratory tract infection (10 patients), alcohol abuse (3), spinal trauma (3), and diabetes mellitus (2) were documented. Three patients had concomitant endocarditis, and two of them also had meningitis. Another two patients had concomitant meningitis. The mean duration of symptoms before presentation was 4.9 weeks. On admission, a temperature of ≥38°C in 8 of 16 patients (50%), a WBC count of ≥11 × 10⁹/L in 13 of 17 (76%), and an ESR of ≥90 mm/h in 7 of 11 (64%) were noted. CRP values were rarely recorded.

Neurological status was not specified for two patients (cases 5 and 7). Six patients (cases 6, 8, 9, 12, 13, and 16) had signs of neurological deficit on admission, and in another (case 4) it developed later. Blood cultures were positive for 8 of 14 patients (57%); S. pneumoniae was also isolated from pus, bone, tissue or aspirates from 15 patients and from the CSF from 2 patients. Blood was the only source of the causative agent for
four patients. Penicillin-resistant strains of *S. pneumoniae* were isolated from three patients (cases 14, 18, and 20), and the isolate in case 20 was found to be resistant to the extended-spectrum cephalosporins as well.

Diagnosis of spinal infection was made at surgery for two patients (cases 3 and 10) and at autopsy for another two (cases 2 and 4). MRI of the spine was performed on the last five patients (cases 16–20). For the remaining 11 patients, various other radiographic imaging techniques were used, including myelography (cases 6–9 and 11–13), CT scanning (cases 8, 9, 12, and 14), and bone scanning (cases 11 and 15). Of the 20 patients with spinal infection, 8 presented with complicated VO (SEA in 2), 6 with uncomplicated VO, and 6 with SEA (with associated VO in 3). There were 4 deaths; 2 were in the preantibiotic era and the other 2 were of patients with SEAs.

**Discussion**

**Etiology and Epidemiology**

Hematogenous VO and SEA are classically monomicrobial infections. *Staphylococcus aureus* is by far the commonest etiologic agent, but coliforms, *Pseudomonas aeruginosa*, and various streptococci have also been implicated [5, 19, 20, 23, 26, 28, 29, 34]. *Mycobacterium tuberculosis* remains an important and not infrequent cause of spinal infection, even in developed countries [5, 26]. Of course, any organism can on occasion produce spinal infection, including *Salmonella* species [45], *Yersinia enterocolitica* [46], *Brucella* species [47], and fungi [48]. The astonishing fact is that although *S. pneumoniae* is considered to be a virulent and invasive organism [49] and indeed is the third most common pathogen isolated in blood cultures [50], pneumococcal osteomyelitis in adults in any location appears to be a rare event [6]. Apart from isolated case reports (table 1), pneumococcal spinal infection has rarely been reported.

In a literature review that documented 587 cases of VO [19–27] and 260 cases of SEA [5, 28–34], *S. pneumoniae* was mentioned as a causative agent in 1 [20] and 7 cases [5, 28, 29, 31, 34], respectively. In University Hospital between 1985 and 1997, we encountered 84 cases of hematogenous pyogenic spinal infection (authors’ unpublished observations), out of which eight (9.5%) were due to *S. pneumoniae*. Over the same period there were 639 episodes of pneumococcal bacteremia (unpublished observations), and spinal infection was documented in five (0.8%) of these episodes. Therefore, the lack of information in published reports of pneumococcal bacteremia about the spine as the focus of infection remains an enigma.

**Predisposing Factors and Clinical Presentation**

Recent or concurrent respiratory tract infection was noted in 13 (46%) of 28 patients. It is conceivable that hematogenous spread of *S. pneumoniae* to the spine occurred at some stage of the illness. Alcohol abuse and corticosteroid or other immunosuppressive therapy are accepted risk factors for pneumococcal infection [49]. In large reports of spinal infection, ~20% of the patients had diabetes mellitus [19, 26, 27, 29–31]. Overall, 14% of the patients in this report were diabetic. Earlier literature on VO commented on blunt trauma to the back as an important predisposing factor, but in recent years its significance has declined [51]. Nevertheless, in this report, trauma to and/or abnormality of the spine was documented in six of 28 patients (21%), similar to the findings of other investigators [33, 34].

Concomitant endocarditis was documented in four patients. Pneumococcal endocarditis in the antibiotic era has become a rare event [37, 49, 52]. Therefore, this overrepresentation and/or overassociation of pneumococcal endocarditis and spinal infection is interesting but not altogether surprising. Presumably, seeding of an unusual site is more likely to occur with unchecked and continuous bacteremia than when the episode is transient. An insidious, chronic pain in the affected region of the spine is standard in patients with VO and is present in 92% of all patients [19]. Except the elderly [53, 54], most patients with invasive pneumococcal infection present dramatically, with overt signs of sepsis. It does come as a surprise, therefore, to see *S. pneumoniae* produce an indolent type of infection, with a lack of febrile response in almost half of the patients, and behave in a manner not unlike the other common etiologic agents of spinal infection [19, 21].

Back or neck pain associated with neurological findings is suggestive of spinal cord involvement. Heusner [55], in 1948, summarized the progression of acute SEA in the following four clinical stages: stage 1, focal vertebral pain; stage 2, root pain; stage 3, deficits of motor, sensory, or sphincter function; stage 4, complete paralysis. On admission the neurological findings in four patients (cases 6, 8, 13, and 16) corresponded to stage 3, and those of three patients (cases 9 and 12 and our patient 3) corresponded to stage 4. Another four patients, in whom spinal infection was not suspected initially, suddenly developed neurological deficits after admission over a period of time ranging from 1 to 11 days. The neurological status on examination corresponded to stage 3 for all four patients.

It is not unusual for patients whose SEA is eventually diagnosed to have the illness initially misdiagnosed. This is partly due to a variety of patient presentations and the rarity of the disease process [29, 34]. All 11 patients in this report who developed neurological signs had evidence of SEA with or without VO, whereas the patients whose diagnosis was VO only, without any local complications (cases 10, 11, 14, 15, 18, and 19 and our patient 2), remained neurologically intact.

**Laboratory Investigations**

Overall, the WBC count was elevated (>11.0 × 10⁹/L) on admission in 19 of 25 cases (76%). This is in sharp contrast to findings regarding pyogenic VO of alternative etiology, in
which the WBC count was raised in only 42% of cases [19]. An elevated ESR, although nonspecific, is seen in up to 95% of patients with VO [19, 21, 24]. The ESR was grossly elevated (≥90 mm/h) in 11 (61%) of 18 cases of pneumococcal spinal infection in this report (table 1). Serial estimation of the ESR during therapy in patients with VO has been found to be useful for following the response to therapy [19, 21].

Positive blood cultures in the context of an appropriate clinical setting provide strong evidence of the causative agent of spinal infection and, indeed, may be the only evidence for patients who received antibiotics before diagnostic and/or surgical specimens were obtained or in circumstances where nonsurgical management is pursued. In earlier reports of VO [19] and SEA [28], blood cultures were found to be positive for 25% of patients. More recently, however, blood cultures have been found to be positive in 30%–56% of cases of VO [21–23, 26] and in 25%–82% of cases of SEA [29, 31, 33, 34]. This difference may be partly due to heightened awareness of the importance of obtaining blood culture specimens before any antibiotic therapy is commenced and partly due to improvements in blood culture methods. Overall, blood cultures were positive for 13 of 21 patients (62%) with pneumococcal spinal infection. The importance of obtaining diagnostic material from the spine cannot be overemphasized.

Diagnostic Imaging, Site(s) of Infection, and Complications

In recent years, MRI has replaced myelography and CT scanning in patients with suspected SEA [30, 31, 56]. Indeed, it is also considered to be a sensitive means of investigation in patients with VO [24]. MRI was used to evaluate not only the last five patients in the Nottingham series but also the last five patients in the literature survey.

In hematogenous VO the lumbar vertebrae are involved in at least 50% of cases [19]. The thoracic spine is the next most common site, whereas the cervical spine is least commonly involved, except in intravenous drug abusers [19]. SEAs often involve several vertebral segments, and in recent reports the majority of the abscesses have involved the lumbar region [29, 31, 34]. However, the cervical level is again commonly affected in intravenous drug abusers [33]. Overall, of the 19 patients who presented with pneumococcal VO, in 14 (74%) the lumbar or lumbosacral region was the site of infection. In the nine patients who presented with SEA, the thoracic and cervical regions were more commonly involved (table 1).

Patients with VO should be observed closely for the onset of root pain, weakness, or reflex changes that may herald the onset of SEA. VO may be complicated by SEA and/or paravertebral abscess in 15%–50% of cases [21, 22, 24]. Overall, in this report VO was the primary diagnosis for 19 patients and was complicated by SEA in four patients (table 1). Of the nine patients with SEA, an associated VO was present in five (56%), not unlike the findings of others [30, 31, 56].

Management

Medical treatment alone is suitable for most cases of VO, provided there is no danger of significant spinal instability, there is no obvious neurological deficit, and a bacterial etiology has already been established by blood cultures and/or cultures of percutaneous samples obtained from the spine. Indeed, in the antibiotic era, 10 (63%) of 16 cases of VO were managed successfully with medical therapy alone. Surgical intervention becomes mandatory not only for patients with neurological deficit and/or frank paravertebral collection but also for those whose disease is progressive despite appropriate antimicrobial therapy. It is imperative that the causative agent is isolated and its precise susceptibility determined. This is underpinned by the fact that there are now worldwide reports of the increasing prevalence of penicillin-resistant strains of S. pneumoniae [57–59] and, even more disturbing, reports of resistance to the extended-spectrum cephalosporins [18, 59, 60].

There appears to be a lack of consensus in the literature regarding the duration of intravenous therapy and the role of oral antimicrobial therapy in the management of pyogenic VO. The duration of intravenous therapy varies from as short as 3–4 weeks [22, 23, 26] to as long as 6–8 weeks [19, 21, 27]. Shorter intravenous courses have usually been followed by an appropriate course of oral antibiotics [22, 23, 26]. Those recommending prolonged courses of parenteral antibiotics [21, 27] point out that intravenous therapy of <4 weeks’ duration has been associated with a significant incidence of therapeutic failures and that the role of subsequent oral antimicrobial therapy is yet to be determined [19].

The management of SEA is surrounded by controversy. There is general agreement that urgent surgical intervention is required once there is evidence of neurological impairment, for there is the potential risk of rapid progression to complete and permanent paralysis. Furthermore, if the paralysis has been present for >48 hours prior to surgery, the chance of complete recovery is greatly diminished [28, 29]. However, there are reports in the literature of adequate results with antimicrobial therapy alone, and the long-established practice that all patients with suspected or proven SEA should undergo urgent surgical intervention in the context of an appropriate clinical setting provide strong evidence of the causative agent of spinal infection and, indeed, may be the only evidence for patients who received antibiotics before diagnostic and/or surgical specimens were obtained or in circumstances where nonsurgical management is pursued. Indeed, in the antibiotic era, 10 (63%) of 16 cases of VO were managed successfully with medical therapy alone. Surgical intervention becomes mandatory not only for patients with neurological deficit and/or frank paravertebral collection but also for those whose disease is progressive despite appropriate antimicrobial therapy. It is imperative that the causative agent is isolated and its precise susceptibility determined. This is underpinned by the fact that there are now worldwide reports of the increasing prevalence of penicillin-resistant strains of S. pneumoniae [57–59] and, even more disturbing, reports of resistance to the extended-spectrum cephalosporins [18, 59, 60].
era were treated with an appropriate course of intravenous antibiotics, which was in some cases followed by a course of oral antimicrobial therapy (table 1).

Outcome

The mortality rate associated with uncomplicated VO has fallen from 25% in the preantibiotic era to <5% in recent years [19, 21–27]. The mortality rate associated with SEA, which has always been considerably higher than that of VO, has shown a similar decline, from ~55% in the preantibiotic era [63] to a range of zero to 23% in recent years [31, 32]. Of the 16 patients with pneumococcal VO in the antibiotic era, one patient (6%; patient 7) in whom VO was complicated by SEA died. Of the eight patients who presented with SEA in the antibiotic era, four died. The fact that despite the availability of highly active antimicrobial agents, improved radiological diagnostic techniques, and advances in surgical technique and postoperative intensive care the incidence of death [29, 31] or irreversible paralysis [34] was persistently high among patients with SEA probably reflects a delay in the diagnosis of this condition, which is not uncommon [29, 34] and was seen in this series. In an endeavor to reduce mortality, we should perhaps aim at heightening awareness of this relatively uncommon, potentially fatal, but eminently treatable condition.

Conclusions

This unusual cluster of eight patients with *S. pneumoniae* spinal infection seen in Nottingham between 1985 and 1997 may be due partly to the presence of regional centers for neurosurgery since 1985 and for spinal surgery since 1993. Additional factors may include the excellent relationships between clinicians and microbiologists, the maintenance by one of us (P.I.) of prospective records of all patients with serious infections, and a long-established practice within our facility’s Department of Microbiology to prompt our clinical colleagues to exclude the spine as a focus of infection if the blood culture result for an adult patient is not explained by an obvious focus of infection.

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