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REVIEW

Spinal and paraspinal pneumococcal infections—a review

D. M. Siddiq · D. M. Musher · R. O. Darouiche

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Abstract Spinal and paraspinal infections caused by *Streptococcus pneumoniae* remain a rare event. We present two cases from our institution, discuss the pathophysiology, and present a literature review of an additional 50 cases of spinal pneumococcal infections. Spinal epidural abscess and vertebral osteomyelitis as well as paraspinal abscesses caused by pneumococcus were included in the analysis. As has been reported for spinal infections due to other bacteria, persistent localized back pain with an elevation in inflammatory markers was almost universal. The lumbar spine was the most commonly involved. Pneumococcus was most frequently isolated from material obtained at the site of the infection; blood cultures were a less common source. The majority of patients with neurologic deficits had spinal epidural abscess or phlegmon, and had a higher mortality. Most patients were treated with 6 weeks of parenteral antimicrobials, and surgical intervention was not associated with a mortality benefit.

Introduction

Spinal and paraspinal infections due to *Streptococcus pneumoniae* are uncommonly reported. Several large case series on bacteremic pneumococcal disease do not mention spinal infections [1–4]. A recent case series of 136 patients with invasive pneumococcal disease revealed a single patient with vertebral osteomyelitis [5]. In a large case series of patients with vertebral osteomyelitis, pneumococci were identified as the causative organism in 1.3 % [6]. A search of the medical records at two large teaching hospitals in Houston, Texas revealed only two cases of spinal infection due to *S. pneumoniae* in the last decade. We now report these two cases, along with a review of the literature.

D. M. Siddiq (✉) · D. M. Musher · R. O. Darouiche
Baylor College of Medicine and the Michael E. DeBakey Veteran Affairs Medical Center, 2002 Holcombe Blvd., Room 4B-370, Houston, TX 77025, USA
e-mail: danish.m.siddiq@gmail.com

Case 1

A 71-year-old man presented to the emergency department (ED) with pain in the left knee and lower back that had progressed over a period of one week. His temperature was 99.2 °F, lungs were clear, and no heart murmur was noted. His gait was normal, and he had good anal sphincter tone. Plain X-rays of the lumbosacral spine and left knee showed degenerative changes. He was sent home with a prescription for ibuprofen.

Three days later, he was unable to walk, and he returned to the ED. His temperature was 103.3 °F. He had tenderness over the T12-L1 spinous processes and right-sided pulmonary rales. A grade III/VI blowing diastolic murmur was heard at the left upper sternal border. He was awake, alert, and fully oriented. Cranial nerves were normal. His left side was weak, and he had dysmetria of his right hand. Deep tendon reflexes and sensory examination were normal. No peripheral stigmata of endocarditis were noted. His white blood cell (WBC) count was 17,100 cells/mm^3 (14 % band forms). Chest X-ray showed a questionable right middle lobe infiltrate. Blood cultures were drawn, and he was treated empirically with intravenous vancomycin and cefepime.

A contrast-enhanced magnetic resonance imaging (MRI) of the lumbosacral spine (Fig. 1) showed L3–4 vertebral body osteomyelitis and a paraspinal abscess at the level of L4 possibly causing nerve root compression. No epidural abscess was seen. MRI of the brain with contrast showed multiple brain abscesses, consistent with emboli. A transthoracic echocardiogram showed partial destruction of one aortic valve cusp with moderate aortic regurgitation and no definite vegetation or perivalvular abscess.

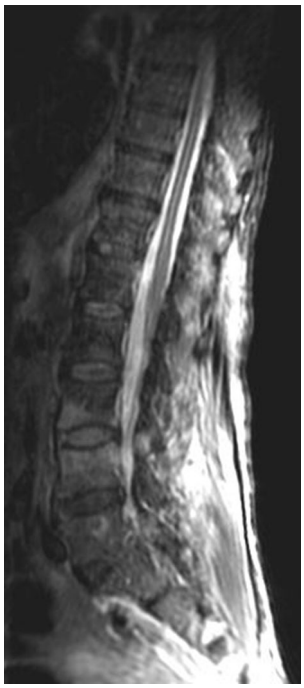

Fig. 1 Case 1, magnetic resonance imaging (MRI) enhanced with gadolinium contrast showing the lumbosacral spine. Enhancement of the L3–4 vertebral bodies with marrow edema signifying osteomyelitis also with L3–4 disk enhancement consistent with diskitis. Small area of enhancement seen in the L5 vertebral body. No cord impingement seen

Admission blood cultures grew *S. pneumoniae* sensitive to ceftriaxone. No neurosurgical intervention was pursued, and intravenous treatment was continued with 2 g ceftriaxone every 12 h. All subsequent blood cultures were negative. A preoperative evaluation for aortic valve surgery was initiated, but he developed worsening congestive heart failure, refractory shock, and died three weeks after admission.

Case 2

A 64-year-old, non-diabetic man presented with right-sided otalgia and otorrhea for 3 days. He was afebrile. His tympanic membranes were noted as normal and he was diagnosed with right-sided otitis externa, for which ciprofloxacin otic drops were prescribed. He returned twice over the next 3 days for persistent pain in his right ear. Five days later, he was admitted for progressive weakness of the left arm and foot. The remainder of the physical and neurological examination, including higher mental function, cerebellar function, and proprioception, were within normal limits. His WBC count was 19,300 cells/mm^3 (13 % band forms), and the erythrocyte sedimentation rate (ESR) was 97 mm/h. Two sets of blood cultures were drawn and he received empiric intravenous vancomycin and piperacillin–tazobactam. A non-contrast-enhanced computed tomography (CT) of the head showed opacification of the right mastoid air cells. A transthoracic echocardiogram did not show valvular vegetations.

The morning after admission, the patient developed rapidly progressive quadriplegia. A contrast-enhanced MRI (Fig. 2) showed edema and enhancement of the C6 and C7 vertebral bodies and intervertebral disk, without impingement on the spinal column. The patient underwent emergent decompressive laminectomy from C2–C7 and hemilaminectomy of T1. Upon entry in to the C6–7 disk space, purulent material was immediately expressed; no epidural abscess was noted. One of two blood cultures and cultures of the infected disk space grew *S. pneumoniae* susceptible to penicillin. He was treated with intravenous ceftriaxone, 2 g twice daily, for 6 weeks, after which he could ambulate with a single-point cane and climb up and descend down at least three steps. His ESR was 17 mm/h at the end of treatment.

Methods

We searched PubMed from 2000 to the present, using combinations of the following search terms: "vertebral osteomyelitis", "spondylodiskitis", "diskitis", "spinal epidural abscess", "paravertebral abscess", "paraspinal abscess", "*Streptococcus pneumoniae*", "pneumococcus", "otitis media", and "mastoiditis". Historical references were reviewed from the articles selected. Most reports were in the English language.

We included cases in which *S. pneumoniae* (or in historic cases, Gram stain showing predominant Gram-positive diplococci) was isolated from an aspirate or biopsy specimen of the vertebral bone, intervertebral disk space, epidural

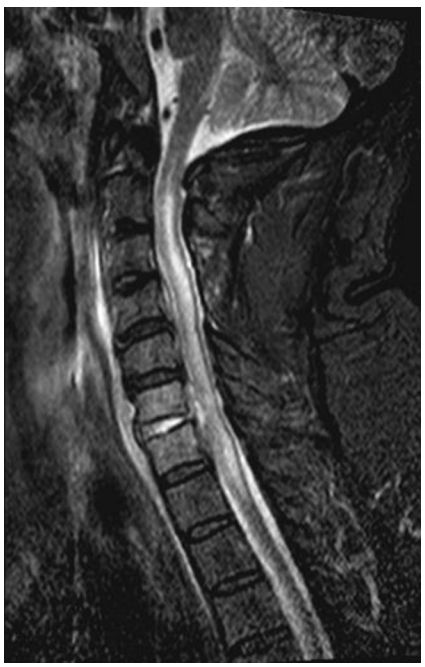

Fig. 2 Case 2, MRI of the cervical spine with gadolinium contrast showing spinal cord edema extending from C2–7, C6–7 disk hyperintensity consistent with diskitis, and some mild enhancement of the C6–7 vertebral bodies and marrow edema concerning for early osteomyelitis

purulence, cerebrospinal fluid, paraspinal abscess, or positive blood cultures, and there was radiographic evidence of spinal epidural or paraspinal abscess, diskitis, and/or vertebral osteomyelitis. We included all cases of spinal (other than isolated pneumococcal meningitis) and paraspinal infections caused by pneumococcus.

Osteocartilagenous forms of spinal infection include vertebral osteomyelitis (VO) and diskitis. Bacterial infections generally begin in the disk space, causing diskitis, and spread upward and downward to involve the adjacent vertebral bodies. Theoretically, VO and diskitis can occur in isolation, but diskitis is most likely present in the disk between consecutive infected bones. Within the spinal canal, the space between the spinal cord and the dura mater is the epidural space, wherein an epidural abscess or phlegmon may form. We differentiate between spinal epidural abscess (SEA) and spinal epidural phlegmon (SEP) depending upon whether purulent material or inflamed tissue, respectively, was detected radiographically or at the time of surgery.

All identified cases were reviewed and the variables of interest were tabulated (Table 1). The strengths of associations among variables of interest were calculated using odds ratios (OR) with 95 % confidence intervals (CI), and the statistical significance for categorical variables was studied using Fisher's exact test.

Results

We identified 50 additional cases of spinal and paraspinal infections due to pneumococcus (Table 1). There were 34 males and 16 females. The distribution as with other invasive pneumococcal disease appears to be bimodal, with eight cases reported from the age of 3 months to 15 years and a much more pronounced second peak with 31 cases between 50 to 79 years of age. There were nine cases of isolated pneumococcal SEA and 11 cases of isolated VO. All 17 cases of paraspinal abscess (PA) co-existed with either SEA (on case) or VO alone (nine cases), or both (six cases). Forty-two of the cases had VO, 25 cases had SEA, four cases had SEP, and there was one case of spinal subdural abscess. All four cases of SEP were in conjunction with VO.

Localized vertebral pain was a prominent symptom; if we exclude children <2 years of age and one case in which information was unavailable, 44 of 47 (93.6 %) patients included here had localized back pain. The time to diagnosis after the development of symptoms was highly variable, ranging from 1 to 150 days (median 14 days). Fever was present at admission in only 62 % of cases in which the temperature was recorded. Neurologic deficits were present in 23 (50 %) cases. Twenty-one of 23 (91.3 %) patients with neurologic deficits had SEA or SEP. Leukocytosis (WBC count>10,000/mm^3) was present in 82 % of cases, but inflammatory markers (ESR and/or C-reactive protein) were elevated in all 31 cases in which they were reported. The lumbar vertebrae were involved in 46.0 % of cases (Table 2).

The radiographic modalities used to make the diagnosis of spinal infection changed with time. In the 1970s, the diagnosis of epidural abscess was made by myelography, i.e., X-ray after the injection of radio-opaque contrast into the subarachnoid space. This technique was replaced in the 1980s by computerized axial tomography, again following intrathecal injection of contrast material. The fact that these invasive procedures were done only in patients who had demonstrated neurological deficits led to a high proportion of patients with spinal infection undergoing surgical intervention; 8 of 11 (72.7 %) patients with pneumococcal SEA/SEP who were reported from 1970–1990 and for whom information is available underwent a surgical procedure, generally laminectomy. Once MRI with contrast became available, this more sensitive non-invasive radiologic technique replaced plain X-ray or computerized axial tomography following epidural injection for the diagnosis of SEA. Since 1990, 18 patients were found to have pneumococcal SEA/SEP, but only 11 (61.1 %) underwent laminectomy; others had aspiration or just received antibiotics without surgical intervention. The sources for isolation of pneumococcus were spinal samples in 67.3 % of cases and blood cultures in 46.2 % (Table 3). Seventeen of the isolates were serotyped and included ten unique serotypes, with three cases each of serotypes 3, 6, and 23. Reduced susceptibility to penicillin was reported in eight pneumococcal isolates and four also exhibited reduced susceptibility to cephalosporins.

All 45 patients in the post antibiotic era received antibiotics. Information on the duration of therapy was available in 38 cases; treatment ranged from 2 to >30 weeks. Eleven patients were treated for 6 weeks. Six patients died while on antibiotics. Before 2000, most cases were treated with penicillin or ampicillin, unless resistance to penicillin was documented, in which case third-generation cephalosporins were used. During the past decade, ceftriaxone has been the preferred antibiotic for treating spinal pneumococcal infections. Vancomycin was used with good outcomes in three cases where resistance to cephalosporins was documented.

Patients with SEA/SEP (OR=10.67, 95 % CI; 2.12 to 68.04, $p<0.001$) or neurologic deficit (OR=6.75, 95 % CI; 1.11 to 70.43, $p=0.035$) had a higher mortality than those with isolated VO or without neurologic deficit, respectively. Mortality was not decreased by operative intervention (OR= 1.01, 95 % CI; 0.21 to 5.05, $p=1$). In the 19 patients without SEA/SEP, only two had neurologic deficits (Case 35, Table 1 and case 2). All three deaths (15.8 % mortality) in this group were related to disseminated disease. In contrast, 21 of the 27 patients with SEA/SEP had neurologic deficits; 18 of the 21 patients underwent surgical intervention, of whom three had persistent deficits, four showed improvement, and five had

Table 1 Summary of cases of spinal and paraspinal pneumococcal infections

Case [reference]	Country/year	Age/ sex	Concomitant conditions, localized pain (LP)	Temp (°F)	WBC ($\times 10^3/mm^3$)	ESR (mm/ h)/CRP (mg/L)	Level of infection	Type of infection (level)	Source of isolate/ resistance pattern (serotype)	Antibiotic (duration)	Surgical intervention	Neurologic deficit	Mortality
1 [31]	Netherlands/ 1906	8/F	Leptomeningitis, LP	Fever	NS	NS	Thoraco-lumbar	SEA	CSF, "Frankel's diplococcus" (NS)	None	NS	UMNS	Died
2 [32]	Germany/ 1909	40/M	Bronchitis for 11 d, meningitis, LP	NS	NS	NS	Lower cervical, upper thoracic on autopsy	SEA	CSF, "Frankel's pneumococcus" (NS)	None	NS	BLE paralysis, BUE paresis	Died
3 [33]	USA/1928	19/M	Acute OM → mastoiditis, pleural empyema, LP	NS	NS	NS	T7	VO, PA	Middle ear, blood, and mediastinal purulence (1)	None	Drainage and debridement	None	Survived
4 [33]	USA/1928	59/F	Pneumonia 4 w prior, buttock abscess tracking to sacrum, purulent peritonitis, LP	NS	13.6	NS	L3–4	VO, PA	Abdominal purulence, autopsy: L3–4 bone (4)	None	Drainage of buttock abscess	None	Died
5 [34]	USA/1929	49/M	Pneumonia 10 d prior, LP	NS	21.0	NS	C4–7	VO (C5), SEA, myelitis	Sputum, autopsy: C5 purulence gs+ve (NS)	None	C5-T1 laminectomy	LUE → RUE weakness → BLE UMNS	Died
6 [33]	USA/1932	51/M	Chronic OM for 7 m, mastoiditis, bacteremia 3 m prior, LP	NS	21.0	NS	L2–3	VO, PA	Paraspinal abscess, urine (3)	None	Drainage and debridement	None	Survived
7 [35]	USA/1934	3/M	Purulent tonsillitis 1 w, meningitis, LP	105.8	13.2	NS	NS	SEA	Autopsy: SEA and tonsillar abscess gs+ve (NS)	None	L3–5 laminectomy	BLE absent reflexes, NS	Died
8 [36]	UK/1971	36/F	Tubal ligation, 1 m postpartum, LP	NS	NS	NS	C3–4	VO, PA	Blood (NS)	Given but NS	None, fusion 1 y later	None	Survived
9 [37]	USA/1972	3 m/F	Recent URI	102.6	19.5	NS	T5–10	VO (T7), SEA, PA (T7–8)	Epidural and paraspinal purulence (3)	Met iv → PCN iv/ po (6w)	T5–10 laminectomy	BLE weakness resolved	Survived
10 [38]	USA/1972	NS	NS	NS	NS	NS	NS	VO	Needle aspiration of disk (NS)	NS	NS	NS	NS
11 [39]	USA/1980	58/NS	Endocarditis and meningitis, LP	102	13.7	NS	T5–6	SEA	Blood, epidural purulence, and CSF (NS)	NS	NS	NS	Died
12 [15]	USA/1984	55/M	MVA with rib fractures 6 m prior, LP	Afeb	11.3	48/NS	T4–5	VO, SEP	Bone and phlegmon (NS)	PCN iv (6 w)	T4–5 laminectomy, debridement	BLE paresis resolved	Survived
13 [40]	USA/1987	77/M	Fall 3 w prior, meningitis, LP	104	20.4	NS	T11-L2	SEA, PA	Blood and CSF (NS)	Naf+Gen iv → PCN/Chl iv	Laminectomy, drainage	BLE UMNS and paralysis	Died
14 [41]	USA/1984	52/M	Chronic alcoholism, CAD, possible sinusitis, LP	Afeb	7.5	115/NS	L4–5	VO, SEP	L5 bone(NS)	CFZ iv (2 w) → Cephradine po (4 w) - PCN all	Debridement	None	Survived
15 [42]	Canada/1988	11/F	Recent URI, LP	100.4	17.6	45	L4–5	VO	Blood (NS)	PCN iv (6 w)	None	NS	Survived
16 [43]	USA/1986	55 m/M	Recent URI	Afeb	20.1	NS	C3–7	VO (C5) SEA	Epidural purulence (NS)	Ery iv/it (2 w) → po (4 w)	C4–7 laminectomy, debridement and drainage	BUE paralysis, BLE paresis, and UMNS all improved	Survived

Table 1 (continued)

Case [reference]	Country/year	Age/ sex	Concomitant conditions, localized pain (LP)	Temp (°F)	WBC ($\times 10^3/mm^3$)	ESR (mm/ h)/CRP (mg/L)	Level of infection	Type of infection (level)	Source of isolate/ resistance pattern (serotype)	Antibiotic (duration)	Surgical intervention	Neurologic deficit	Mortality
17 [44]	USA/1988	69/F	Recent URI, NIm, endocarditis, DM, LP	98.6	32.0	142/NS	L4–5	VO, SEA	Blood, epidural/disk purulence (NS)	Naf/Gen (8 d) → PCN iv (6 w+)	L4–5 laminectomy and drainage	BLE quadriceps paresis resolved	Survived
18 [45]	USA/1992	71/F	Febrile illness 4 w prior, NIm, LP	Afeb	15.3	122/NS	L3–4	VO	Disk purulence, PCN-R (NS)	CTX iv (4 w)	Percutaneous aspiration	None	Survived
19 [46]	UK/1992	61/F	Endocarditis and meningitis, LP	104	23.0	116/NS	L5-S2	VO	Blood, CSF LPA+(3)	PCN iv (4 w) → Clinda po (3 m)	None	Back pain resolved	Survived
20 [47]	USA/1993	66/M	Bacteremic pneumonia 3 m prior, DM, chronic alcoholism, LP	97	6.8	113/NS	L4–5	VO, SEA, PA	Disk purulence (NS)	Vanc iv (6 w) → Clinda po (6 m) - PCN all	None	BLE paresis, dysesthesiae resolved	Survived
21 [48]	Spain/1995	11/M	None, LP	Afeb	NS	92/1.5	L5-S1	VO, PA	Disk specimen (NS)	Clox iv (2w) → CTX iv (3w)	Diskectomy and debridement	None	Survived
22 [49]	France/1996	52/M	Bronchitis, meningitis, chronic alcoholism, CHF, LP	101.3	14.9	90/NS	C5–6	VO, SEP	Blood, PCN-R (NS)	Cefotax iv (4 w) → CTX iv (3 w) → Prist po (12 w)+ Rif po (last 17 w)	None	None	Survived
23 [50]	France/1996	43/M	New diagnosis of HIV with "normal" CD4, URI, LP	Feb	NS	NS	NS	VO, SEA	Blood (NS)	NS	NS	NS	NS
24 [51]	Spain/1996	15/M	Lumbar sprain 6 w prior, gingival hypertrophy, LP	101	8.9	65/NS	L4–5	VO	Lumbar FNA, PCN-I (NS)	CTX iv (4 w)	None	None	Survived
25 [52]	UK/1997	31/F	Epidural anesthesia 8 d prior, URI	NS	NS	NS	T4-L1	SEA	NS (NS)	NS	Hemilaminectomy	BLE paresis, dysesthesiae	Survived
26 [53]	USA/1997	56/F	Back sprain 4 w prior, LP	98.2	6.9	73/NS	L1–2	VO	L1 and L2 bone, PCN-R, CTX-R (NS)	Vanc iv+Rif po (6 w)	None	None	Survived
27 [7]	UK/1985–1997	71/M	Chronic alcoholism, recent URI, LP	NS	8.3	25/NS	L2–3	VO, PA	L2–3 disk space aspirate (NS)	Amp iv (17 d) → Amox po (6 w)	None	NS	Survived
28 [7]	UK/1985–1997	74/F	DM, recent back injury, LP	100.4	17.1	50/NS	L5	VO	Blood (34)	PCN iv (2 w) → Amox po (4 w)	None	NS	Survived
29 [7]	UK/1985–1997	51/M	Crohn's disease, arthropathy, LP	101.3	24.6	NS	C3-T1	SEA	Epidural purulence (22)	PCN iv (3 w) → Amox po (3 w)	Drainage and debridement	Present but NS	Survived
30 [7]	UK/1985–1997	65/M	Cervical spondylosis, LP	99	24.7	>90/NS	C3–4	VO, SEA	Blood, epidural purulence (6)	PCN iv (3 w) → Amox po (4 w)	Drainage and debridement	Present but NS	Died
31 [7]	UK/1995	75/M	Cervical spondylosis, bullous pemphigoid, prednisolone therapy, recent URI, LP	96.8	13.4	69/NS	C6-T1	VO, SEA	Blood, epidural purulence (6)	PCN iv (6 w) → Amox po (NS)	Decompression and debridement	BUE paresis, BLE paralysis	Died
32 [7]	UK/1985–1997	59/M	DM, Recent URI, LP	98.4	12.6	>90/NS	L4–5	VO, SEA, PA	Epidural purulence (18)	PCN iv (5 w) → PCN po (5 w)	Drainage and debridement	NS	Survived
33 [7]	UK/1997	72/M	Spondylosis, chronic alcoholism, LP	98.2	11.2	>90/NS	C6–7, T9–10, L4–5	VO, SEA	Blood, epidural purulence (23)	PCN iv (23 d)	L4–5 laminectomy, T9–10 R costotransversectomy BLE paresis	Died	

Table 1 (continued)

Case [reference]	Country/year	Age/ sex	Concomitant conditions, localized pain (LP)	Temp (°F)	WBC ($\times 10^3/mm^3$)	ESR (mm/ h)/CRP (mg/L)	Level of infection	Type of infection (level)	Source of isolate/ resistance pattern (serotype)	Antibiotic (duration)	Surgical intervention	Neurologic deficit	Mortality
34 [7]	UK/1997	79/F	Meningitis and endocarditis, LP	104	10.7	>90/NS	L1–2	VO, PA	Blood, CSF (6)	PCN iv (47 d)+ Gen iv (14 d)	Drainage and debridement	None	Survived
35 [54]	US/1999	52/F	Fall 2 m prior, mycotic AAA, LP	98.5	8.6	130/NS	L3–4	VO, PA	Blood, PCN-R, CTX-R	Naf iv+Gen iv	None	BLE paresis	Died
36 [55]	US/2000	26 m/M	URI 8 d prior, day care	100.4	5.7	100/NS	T4–7	SEA	Epidural purulence, PCN-R, CTX-I (NS)	Vanc iv+Cefotax iv (2 w)	T5–7 laminectomy, debridement	BLE paresis, UMNS, resolved	Survived
37 [56]	US/2000	60/M	HIV (CD4=320) off ARV for 6 m, pneumococcal sepsis 10 y prior, Im ×2 in the past 6 y, LP	102.2	13.7	118/NS	L4-S1	VO (L5-S1) SEA (L4-S1)	Blood(NS)	CTX iv (6 w) → Amox po (8 w)	None	None	Survived
38 [57]	Turkey/2001	51/F	Meningitis, LP	101.3	20.2	125/NS	L3–4	VO, SEA, PA	CSF, L3 bone (NS)	CTX iv (6 w) → NS po (4 w)	Psoas abscess aspiration	BLE paresis resolved	Survived
39 [58]	US/2003	46/M	Pneumonia and bacteremia 2 w prior, concomitant tricuspid endocarditis, LP	103.6	NS	NS	L4-S1, C3–6	VO, SEP	Blood PCN-I, Cefur-R, lumbar SEP (23)	Vanc iv+Rif po (3 d)+PCN iv (3 m) → Amox po (3 m)	Lumbar decompression	BLE dysthesiae	Survived
40 [59]	Spain/2004	43/M	HIV (CD4=521) on ARV, Im ×1, LP	100.8	22.3	107/8.3	C1–2	VO, SEA, PA	Blood, retropharyngeal/ epidural purulence (9)	Vanc iv (NS)+ Cefotax iv (3 w)	Transoral drainage	None	Survived
41 [60]	Germany/ 2004	54/M	Chronic alcoholism, pneumonia 6 m prior, mycotic TAA with lung fistula, LP	Afeb	13.1	120/NS	T8	VO	T8 body bone (NS)	Cefotax+Fluclox+ Metro (6 w) → Clinda po (1 y)	Resection of aneurysm and Dacron graft, T8 resection	Postop BLE paresis persisted	Survived
42 [61]	Denmark/ 2004	70/M	Concomitant bilateral endophthalmitis, LP	NS	NS	NS	T10–11, L2–4	VO, SSA (L2–4)	Blood (NS)	PCN iv+Gen iv (NS)	None	None	Survived
43 [62]	France/2006	58/M	Sinusitis 1 m prior, LP	Afeb	16.4	NS/271	L2-S1	VO (L5-S1) SEA, PA	PA aspirate purulence (NS)	Cefotax iv (2 w)+ Fosfo iv (2 w)+ Gent iv (5 d) → Moxi po (10 w)+ Rif po (10 w)	None	None	Survived
44 [18]	Netherlands/ 2008	51/M	Chronic low back pain, meningitis 4 w prior, LP	96.4	NS	NS	L1–2	VO	CSF 4 w prior (10)	Fluclox iv (6 w)	None	None	Survived
45 [18]	Netherlands/ 2008	39/F	Meningitis 2 w prior, lumbar spondylodesis, LP	101	NS	NS	L4–5	VO	CSF and blood 2 w prior (10)	Fluclox iv (6 w)	None	None	Survived
46 [63]	Japan/2008	73/M	LP	Feb	High	NS/high	C4–7, L4–5	VO, SEA	Blood (NS)	Given (NS)	NS	"little paralysis remained"	Survived
47 [64]	France/2010	49/M	Bacteremia, knee septic arthritis, gingival hypertrophy, and gingivitis	101.3	NS	NS	C5–6	VO	Blood and purulence from knee joint (NS)	Amox iv (12 w)+ Gen iv (8 d)	None	None	Survived

Table 1 (continued)

Case [reference]	Country/year	Age/ sex	Concomitant conditions, localized pain (LP)	Temp (°F)	WBC ($\times 10^3/mm^3$)	ESR (mm/ h)/CRP (mg/L)	Level of infection	Type of infection (level)	Source of isolate/ resistance pattern (serotype)	Antibiotic (duration)	Surgical intervention	Neurologic deficit	Mortality
48 [65]	Japan/2011	53/F	Bronchitis, SLE on steroids, DM, h/o lumbar surgery, CAD, NIm, LP	100.4	23.1	NS/5.5	L5/S1	VO, PA	Blood, psoas purulence (NS)	Vanc iv (6 d) → CTX iv (9 w) → Cefpod iv (NS)	PA percutaneous drainage	None	Survived
49 [66]	India/2011	2.5/M	Meningitis, NIm	Feb	High	High	Lower thoracic, L4-S1	SEA, myelitis	Epidural purulence (NS)	Vanc iv (NS)+ CTX iv (6 w)	Lumbar laminectomy and drainage	BUE paresis (resolved), BLE paralysis (improved)	Survived
50 [67]	Morocco/ 2011	35/M	Meningitis, cavernous sinus thrombosis, otitis media/externa, petrositis	101.7	25.2	NS/9	T4–9, L2–3	SEA	CSF (NS)	CTX iv (8 w)+ Metro iv (NS)+ Vanc iv (NS)	Laminectomy	RLE paralysis, LLE paresis (improved)	Survived
Cases reported in this series													
51, case 1	USA/2005	73/M	Endocarditis, brain abscesses, DM, CVA, Im-PPV 8 y ago, LP	103.3	17.1	48/NS	L3–4	VO, PA (L4)	Blood, PCN-I, CTX-S (23)	Vanc iv+CTX iv	None	LUE paresis	Died
52, case 2	US/2012	64/M	Otitis extema, mastoiditis, prior cervical laminectomy, NIm, LP	100.4	19.3	97/NS	C6–7	VO	Blood, disk purulence (NS)	Vanc iv (4 d)+Pip-Tazo iv (4 d) → CTX iv (6 w)	C2–C7 laminectomy T1 hemilaminectomy	L hemiparesis, dysthesiae → quadriparesis, improved	Survived

LP – localized pain, URI – upper respiratory infection, OM – otitis media, MVA – motor vehicle accident, CAD – coronary artery disease, DM – diabetes mellitus, Im – immunized, NIm – not immunized, CHF – congestive heart failure, LPA – latex particle agglutination, ARV – anti-retrovirals, CVA – cerebrovascular accident, SLE – systemic lupus erythematosus, TAA – thoracic aortic aneurysm, AAA – abdominal aortic aneurysm

Feb – febrile, Afeb – afebrile, NS – not specified, UMNS – upper motor neuron signs, SEA – spinal epidural abscess, VO – vertebral osteomyelitis, SEP – spinal epidural phlegmon, PA – paraspinal abscess, SSA – spinal subdural abscess, d – day(s), w – week(s), m – month(s), y – year(s), BLE – bilateral lower extremities, BUE – bilateral upper extremities, LUE – left upper extremity, RLE – right lower extremity, LLE – left lower extremity, gs+ve – seen on Gram stain, C – cervical vertebra, T – thoracic vertebra, L – lumbar vertebra, S – sacral vertebra, → – followed by, all – allergy

PCN – penicillin, Met – methicillin, Naf – nafcillin, Gen – gentamicin, Chl – chloramphenicol, CFZ – cefazolin, Ery – erythromycin, CTX – ceftriaxone, Clinda – clindamycin, Vanc – Vancomycin, Clox – cloxacillin, Cefotax – cefotaxime, Prist – pristinamycin, Rif – rifampin, Amp – ampicillin, Amox – amoxicillin, Fluclox – flucloxacillin, Metro – metronidazole, Fosfo – fosfomycin, Moxi – moxifloxacin, Cefpod – cefpodoxime, Cefur – cefuroxime, Pip-Tazo – piperacillin–tazobactam. -R – resistant, -I – intermediate, -S – sensitive, iv – intravenous, po – per oral, it – intrathecal

Table 2 Spinal levels of pneumococcal infection

Spinal level	Cases (%)
Cervical (C1–7)	14 (20.9)
Thoracic (T1–12)	16 (23.9)
Lumbar (L1–5)	31 (46.3)
Sacral (S1–5)	6 (8.9)

resolution of their deficits, but six patients died (29.6 % overall mortality). All the deaths in this group were in patients with neurologic deficits (adjusted OR=8.185, p=0.06), but this result was not statistically significantly likely due to the small numbers in the subgroup. Endovascular involvement was present in 15.4 % of cases, including six cases of endocarditis and two cases with mycotic aortic aneurysms. Meningitis was present or recently diagnosed in 21.2 % of cases.

Discussion

Spinal pneumococcal infections are an uncommon occurrence. In two large tertiary care centers, we found only two cases in the first decade of this millennium. The largest case series described eight cases over a span of 13 years from Nottingham, UK [7]. Even case reports have been relatively infrequent. Pneumococcus is a virulent organism, so the lack of more reports of spinal infections is somewhat unexpected. Our review has insufficient data to make any inference regarding incidence or causative serotypes. Studies of SEA have found that up to 44 % of patients have radiographic features suggesting co-existent VO [8, 9]. Conversely, 17 % of patients with VO have confirmed epidural abscess [10].

The epidural space contains adipose tissue and vasculature; it extends from the foramen magnum to the sacrum, posterior to the spinal cord. Anterior to the spinal cord, it is more a potential epidural space, as the dura mater is attached to the vertebral bodies from the foramen magnum to around L-1. SEA may either spread deeper spontaneously or, if a lumbar puncture is performed through the SEA, into the subdural or subarachnoid space, resulting in subdural empyema or purulent meningitis, respectively. This pattern of spread was confirmed by a study in which patients with SEA had negative CSF Gram stains and positive cultures in 25 % of those who underwent lumbar punctures [11]. Meningitis can also exist with other spinal pneumococcal infections. *Locus minoris resistentiae* presents as a risk factor in a major series of spinal infection [11]. Trauma or degenerative changes predispose the bony vertebral column to infection [12]. Neurological damage can be caused by compression of the spinal cord or vascular supply, vascular thrombosis, bacterial toxin mediated, and exuberant inflammatory response due to the pathogen [13]. The time to develop irreversible neurological deficits after spinal cord compromise is variable. Based on the pathogenesis, local compression has greater theoretical odds of being reversible compared to ischemic damage [11, 14].

Infection can reach the spinal column by local extension or hematogenous spread; the latter may be characterized as venous or arterial. The arterial vasculature of the vertebral column is well defined, and was likely involved in case 1 [15]. The venous arm is underappreciated and is imperative to explain the pathophysiology in case 2. The intracranial and vertebral venous systems lack valves, and, as a result, there may be bidirectional venous flow of blood to a vertebral body [16]. Venous Doppler studies in healthy volunteers have shown that much of the cranial blood return in the upright position is via the cerebrospinal venous system [17]. This might explain the spread from an infected mastoid to the cervical spine. This may offer an alternate path, namely, via the azygous system that communicates with the vertebral

Table 3 Sources of pneumococcal isolates

Culture source	Cases (%)
Blood	24 (46.2)
Spine	35 (67.3)
Epidural purulence	15 (28.8)
Disk purulence	7 (13.5)
Vertebral bone	7 (13.5)
CSF	9 (17.3)
Epidural phlegmon	2 (3.8)
Paraspinal abscess	4 (7.7)
Sputum	1 (1.9)

Table 4 Concomitant conditions with spinal and paraspinal pneumococcal infections

Concomitant conditions	Cases (%)
Respiratory/ENT	27 (51.9)
Pneumonia, bronchitis, empyema	9 (17.3)
URI	9 (17.3)
Pharyngotonsillitis	1 (1.9)
Otitis media, mastoiditis	4 (7.7)
Sinusitis	2 (3.8)
Gingival hypertrophy	2 (3.8)
Endovascular involvement	8 (15.4)
Endocarditis	6 (13.5)
Mycotic aneurysm	2 (3.8)
Meningitis	11 (21.2)
Back trauma or degenerative spine disease	13 (25)
Alcoholism	6 (11.5)
Heart disease	3 (5.8)
Diabetes	4 (7.7)
HIV	3 (5.8)
Rheumatic disease	3 (5.8)

venous system in patients with pneumococcal pneumonia. Back pain after the diagnosis of bacterial meningitis should prompt further workup for spinal or paraspinal infection [18].

The widespread use of antibiotics to treat acute otitis media has resulted in a drastic decrease in intracranial complications. Mastoiditis develops during untreated otitis media if inflammation blocks the opening of the mastoid air cells. Infection from the bony air cells can spread via the emissary veins or, in children, the unossified petrosquamous suture can serve as a direct path from the middle ear to the middle cranial fossa [19–21].

Concomitant conditions seen with spinal and paraspinal pneumococcal infections are listed in Table 4. Although many cases of pneumococcal osteomyelitis have been reported in patients with sickle cell disease including many long bones, no case of pneumococcal VO or SEA has been reported in a patient with known sickle cell disease or asplenia, possibly because vertebral bodies have a much better blood supply and are not as susceptible to infarction as long bones in the context of sickle cell disease [22, 23]. Roughly one-half the patients have associated infection of the respiratory tract, ear, nose, or throat infections. Supporting the concept of *locus minoris resistentiae*, one-quarter of the cases had some spinal trauma or degenerative spine disease. Endovascular involvement was present in 15.4 %; this included six cases of endocarditis and two cases with mycotic aortic aneurysms. Meningitis was present or recently diagnosed in 21.2 % of cases.

Localized back pain in adults was present in almost all cases reviewed, and persistent back pain after a bacteremic pneumococcal infection should prompt further evaluation. Contrast-enhanced MRI is now the study of choice in patients with neurologic deficits [24]. The absence of fever or leukocytosis cannot be used to exclude spinal or paraspinal pneumococcal infections, as they were only present in 62 and 82 % of cases, respectively. In contrast, inflammatory markers were universally elevated in cases in which they were measured, and their normalization in cases of spinal infection with diverse etiology correlates with the response to treatment [25, 26]. In the 1960s and 1970s, when a preoperative diagnosis of SEA was confirmed only by myelography, patients did not undergo this invasive diagnostic study unless they had neurologic abnormalities, and the teaching was that, once spinal infection was detected, surgical intervention was mandated. Contrast-enhanced MRI is now the study of choice in patients with neurologic deficits, but this sensitive procedure regularly demonstrates phlegmon or early abscess in patients who have no neurologic abnormalities [24]. Thus, in patients who have no neurologic abnormalities, medical therapy should be considered. The appearance of such abnormalities should raise strong consideration of immediate surgical intervention [14].

Initial empiric therapy for pyogenic spinal infections should cover methicillin-resistant *Staphylococcus aureus* until proven otherwise, because this organism is, by far, the most common cause of VO and SEA; this regimen would also be effective against drug-resistant pneumococci. Once a diagnosis of pneumococcal spinal infection is made and sensitivities are available, treatment should be given with an intravenous beta-lactam antibiotic for at least the first 2 weeks. Some experts have suggested that the use of fluoroquinolones is reasonable due to their excellent bioavailability, once-daily dosing, uptake by bone, and ability to cross the blood–brain barrier to complete 6 weeks of therapy for VO in general [27, 28]. In our opinion, fluoroquinolone therapy for pneumococcal spinal infections should only be used in patients with severe beta-lactam allergies. The duration of parenteral antibiotics after adequate drainage for SEA was usually 3 to 4 weeks, but it is sometimes impossible to rule out VO and, therefore, treatment is extended to 6 weeks [29]. In our review, patients most frequently received a 6-week course of parenteral antibiotics for spinal pneumococcal infections. Repeating an imaging study is usually not warranted for the evaluation of treatment unless the inflammatory markers do not respond or clinical symptoms persist [30].

In our study, outcomes were worse for patients who had pneumococcal SEA/SEP when compared to those patients who had VO. The subgroup of pneumococcal SEA/SEP had a significantly higher proportion of neurologic deficits and mortality. Early detection may have prevented the outcome in case 1, and using inflammatory markers to guide further workup when the patient presented for the first time with back pain may have prompted the physician to establish a spinal infection at an earlier stage. Case 2 highlights otitis media and mastoiditis, resulting in hematogenous translocation of pneumococcus to the cervical spine. The rapid progression and resolution of neurologic symptoms with surgery posits cord edema as the cause rather than ischemic damage, especially when no purulence was detected in the epidural space. In conclusion, it is important to consider spinal infection in an individual who has had a recent pneumococcal infection, especially if bacteremia was present.

Conflict of interest The authors declare that they have no conflict of interest.

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