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Vertebral Osteomyelitis and Meningitis due to a Penicillin-Resistant Pneumococcal Strain

Vertebral osteomyelitis is a rare manifestation of *Streptococcus pneumoniae* infection that is difficult to diagnose. Thus, the onset of therapy is often delayed, leading to neurologic sequelae or even death. Since the 1970s, the frequency of penicillin-resistant *Streptococcus pneumoniae* has increased in Europe, particularly in Spain and France, and these infections represent a major therapeutic challenge, especially when they are severe (1). The optimal therapy for penicillin-resistant pneumococcal meningitis has not yet been defined. We report a case of meningitis and cervical osteomyelitis due to a penicillin-resistant pneumococcal strain.

The 52-year-old black man, originating from the French West Indies, was referred to our department in November 1995 for treatment of fever and acute bronchitis. His medical history included chronic alcohol abuse and congestive heart failure. Forty-eight hours before admission, treatment with oral amoxicillin (3 g/day) had been initiated for persistent cough and fever. On physical examination, he was febrile (38.5°C) and lethargic with an altered mental state; neck stiffness was detected without focal neurological defects; the pulmonary examination was unremarkable. The laboratory findings were as follows: white blood cell (WBC) count 14.9×10^9/l (92% neutrophils, 7% lymphocytes), hemoglobin 11.5 g/dl, platelet count 216×10^9/l, erythrocyte sedimentation rate (ESR) 90 mm in the first hour. Serological tests for HIV were negative. The results of cerebral spinal fluid (CSF) analysis are shown in Table 1. Pneumococcal capsular antigen was not sought in CSF. Chest radiograph revealed cardiomegaly and a mild bilateral pleural effusion. Brain and abdominal CT scans were unremarkable. Echocardiography demonstrated dilation and cardiomyopathy; no vegetations were found. Oral amoxicillin was stopped and intravenous cefotaxime (200 mg/kg/day given in 6 doses) was prescribed. Three blood cultures yielded *Streptococcus pneumoniae*, which were subsequently shown to be penicillin-resistant. The MICs of penicillin G, amoxicillin and cefotaxime determined by the broth macrodilution method were 1, 0.45 and 0.38 μg/ml, respectively. This strain was resistant to chloramphenicol, tetracycline, erythromycin and trimethoprim-sulfamethoxazole, and susceptible to rifampicin and pristinamycin. On day 4, the patient's general condition improved and he recovered his normal mental status. A bilateral sensorineural hearing loss was suspected and confirmed by audiometric tests (loss of 30 dB). On day 14, CSF analysis showed persistent infection (Table 1). Because the patient continued to complain of neck stiffness and pain, a radiological examination was performed on day 15, which yielded findings consistent with C5-C6 vertebral osteomyelitis (Figure 1). Oral rifampicin (10 mg/kg b.i.d.) was added to the therapy regimen. By day 20, CSF values had returned to normal. The cefotaxime concentration was measured in CSF and blood 30 min after a 2 g infusion of the drug, the levels being 9.9 and 89 mg/l, respectively (Table 1). After one month of treatment (including two weeks of the combined therapy), the patient was discharged from our unit on intravenous ceftriaxone (4 g/day) in combination with oral rifampicin at the same dosage. On day 50, physical examination of the patient was unremarkable; his hearing had recovered and the vertebral pain resolved. Magnetic resonance imaging (MRI) of the cervical spine showed marked improvement with resolution of the prevertebral inflammatory process, but a persistent enhanced diskitis signal. The patient returned home on prystinamycin (3 g/day) and rifampicin (1200 mg/d)

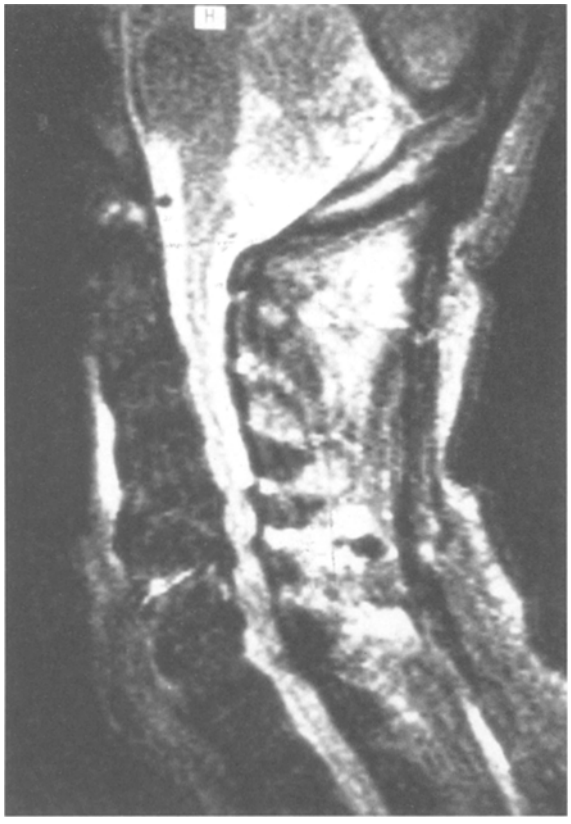

Figure 1: Magnetic resonance image of the cervical spine of a patient with pneumococcal vertebral osteomyelitis, showing enhancement of the C5-C6 disk space, an attenuated C6 signal consistent with anterior spondylitis, and mild enhancement of the C4-C5-C6 prevertebral area consistent with an inflammatory process.

Table 1: Laboratory findings in a patient with vertebral osteomyelitis and meningitis due to a penicillin-resistant pneumococcal strain.

Parameter	Day 1	Day 14	Day 20
CSF			
WBC (/mm^3)	2700	1050	40
Neutrophils (%)	78	90	2
Lymphocytes (%)	13	5	77
Gram stain	negative	negative	negative
Culture	negative	negative	negative
Protein (g/l)	1.59	1.02	0.61
Glucose (mmole/l)	0.2	1.1	2.1
Cefotaxime (mg/l)	ND	ND	9.9
Blood			
WBC (x 10^9/l)	14.9	7.7	5.6
Glucose (mmole/l)	6.7	5.1	7.2
Cefotaxime (mg/l)	ND	ND	89
ESR (mm/h)	84	100	90

prescribed for three months. At the end of therapy he was well, the ESR was 28 mm in the first hour, other laboratory findings were within normal range and MRI showed resolution of the vertebral osteomyelitis. Antimicrobial agents were then stopped.

Vertebral osteomyelitis is a rare complication of pneumococcal bacteremia. Among the 11 cases of pneumococcal vertebral osteomyelitis recently reported by Kutas et al. (2), a prior history of upper or lower respiratory tract infection was found is 45%; none had had meningitis. Alcohol abuse, bone trauma and chronic obstructive pulmonary disease were possible predisposing factors. In our patient no bone biopsy was performed, so our diagnosis of osteomyelitis was indirect, based upon clinical signs and symptoms and MRI findings. Moreover, the CSF culture was negative, raising the question as to whether the meningitis syndrome was a reaction to a parameningeal focus or the result of true bacterial meningitis. Since our patient had received antibiotics just prior to admission, the negative CSF culture was not surprising. Furthermore, the failure of MRI of the cervical spine to demonstrate an epidural abscess, the lower glucose level observed in the CSF and the existence of bilateral sensorineural hearing loss made the diagnosis of bacterial meningitis likely.

Little is known about the optimal therapy of pneumococcal osteomyelitis. According to the literature, parameters such as resolution of vertebral pain, return of the ESR to normal values, and attenuation of bone scan or MRI abnormalities have been shown to reflect a favourable response to therapy. Penicillin G, first-generation cephalosporins and vancomycin followed by oral clindamycin have been used successfully for treatment (2, 3). Intravenous ceftriaxone (2 g/day) given for four weeks was also effective in a case of osteomyelitis caused by pneumococci with intermediate susceptibility to penicillin (MIC 0.25 μg/ml) (4). The rationale for the addition of oral rifampicin to the therapy regimen in our case was its good diffusion into bone, and thus the attainment of higher levels in the area in contact with the osteomyelitis (5).

The choice of regimen for treatment of invasive, penicillin-resistant pneumococcal infections is rendered even more difficult by frequent multiple antibiotic resistance. Furthermore, recent reports have described the failure of extended-spectrum cephalosporins and vancomycin in the therapy of meningitis due to pneumococci with only intermediate susceptibility or resistance to penicillin (6, 7). Thus, the CSF should be analyzed repeatedly in this entity in order to demonstrate persistence or eradication of infection.

Finally, this case is of particular clinical relevance since it demonstrates that persistent neck pain and stiffness after apparently successful therapy of meningitis may be due to associated vertebral osteomyelitis.

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Comparison of Four Methods for Pretreatment of Cystic Fibrosis Sputa

Three methods of sputum sample pretreatment were compared to direct plating of untreated sputa from cystic fibrosis (CF) patients. These methods included chemical liquefaction with the mucolytic agent dithiothreitol (DTT), mechanical homogenisation by use of glass beads and agitation, and combination of these two methods. A quantitative culture technique was used to determine both qualitative differences (number of isolates) and quantitative differences (number of colony-forming units) between the methods.

For the untreated sputum method (Method 1), 20 µl of the specimen were directly spread with a sterile glass rod on the surfaces of each of five agar media (Columbia agar with 5% sheep blood; mannitol salt agar; chocolate agar with 50,000 IU/l bacitracin; MacConkey agar; Sabouraud agar with 100 mg/l gentamicin and 50 mg/l chloramphenicol). Two additional 100-fold dilutions of the sputum were made in saline and cultured in the same manner. The number of colony-forming units (cfu) per milliliter of sputum was calculated after incubation at 36°C for 48 h. For the mechanical homogenisation (Method 2) an aliquot of the same sputum was mixed with sterile glass beads (2 mm in diameter) in a test-tube and agitated on a Vibrax VXR agitator (IKA, Germany) at 800 rpm for 15 min. The specimen was then cultured and diluted as described above. For the chemical liquefaction (Method 3), 0.5 ml of sputum and 0.5 ml of DTT (Sputasol; Unipath, Germany) were mixed, resulting in a final DTT concentration of 50 µg/ml. Subsequently, 0.5 ml of this mixture were left for 15 min at room temperature, then cultured and diluted as described. For the combination method (Method 4) the remaining 0.5 ml of this mixture were immediately transferred into a

Table 1: Performance of four methods of sputum pretreatment (n = 46 sputa) with regard to the most frequently isolated species (≥ 5 isolates).

Species	Total no. of isolates	No. of isolates per pretreatment method			
		None	Chemical	Mechanical	Combined
Pseudomonas aeruginosa	64	63	64	63	64
Candida albicans	41	38	36	37	38
Staphylococcus aureus	21	21	21	21	21
Aspergillus fumigatus	10	10	10	10	10
Candida parapsilosis	6	6	6	6	6
Stenotrophomonas maltophilia	5	5	5	5	5
Total	164	156	157	155	159