MAJOR ARTICLE

Vertebral Osteomyelitis: Long-Term Outcome for 253 Patients from 7 Cleveland-Area Hospitals

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We report a retrospective study of 253 patients with vertebral osteomyelitis (VO) who had long-term follow-up. Eleven percent of the patients died, residual disability occurred in more than one-third of the survivors, and relapse occurred in 14%. Median duration of follow-up was 6.5 years (range, 2 days to 38 years). Independent risk factors for adverse outcome (death or qualified recovery) were neurologic compromise, time to diagnosis, and hospital acquisition of infection ($P \leqslant .004$). Surgical treatment resulted in recovery or improvement in 86 (79%) of 109 patients. Magnetic resonance images (110 patients) were often obtained late in the course of infection and did not significantly affect outcome. Often, relapse developed in individuals with severe vertebral destruction and abscesses, appearing some time after surgical drainage or debridement. Recurrent bacteremia, paravertebral abscesses, and chronically draining sinuses were independently associated with relapse ($P \leqslant .001$). An optimal outcome of VO requires heightened awareness, early diagnosis, prompt identification of pathogens, reversal of complications, and prolonged antimicrobial therapy.

Long known as a formidable clinical challenge [1–5], vertebral osteomyelitis (VO) may have serious consequences. Pitfalls in diagnosis have received considerable emphasis, but little attention has been paid to long-term outcome [6, 7]. In studies reported elsewhere, follow-up has often been of limited duration and the outcomes have been reported only as "death" or "survival." Few authors have evaluated prognostic factors, and relapse has received scant attention. Our study was undertaken to review the clinical features of VO in a large number of patients and to determine the outcome after long-term follow-up. We sought to identify the factors associated with poor outcome and relapse. We assessed the effect of time to diagnosis, findings of MRI, and surgical treatment on outcome.

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MATERIALS AND METHODS

Case ascertainment. Records were reviewed for all patients with VO who attended The Cleveland Clinic Hospital (CCH) from 1950 through 31 December 1994 and for those with the condition during an 11-year period from 1972 through 31 December 1982 who attended 6 additional teaching hospitals in the greater Cleveland area. Records were obtained from the files of the departments of infectious diseases and from files coded in the medical records departments with a discharge diagnosis of VO or disk-space infection. Cases from before 1978 from 3 hospitals were included in the study of Eismont et al. [8]. The MRI findings for some patients at CCH have been described elsewhere by Modic et al. [9] and Dagirmanjian et al. [10].

Case definitions and classifications. Patients were included only if there was illness compatible with vertebral infection and evidence of spinal involvement on conventional radiographs or MRIs. We included 1 patient for whom there were no radiographs or MRIs and for whom open biopsy and cultures of an infected spinous process were diagnostic of VO.

Diagnosis was defined as "definite" when a microorganism was isolated from the involved vertebra, in-

tervertebral disk space, or paravertebral or epidural abscesses; as "probable," when the results of ⩾2 blood cultures were positive during a compatible illness; or as "presumptive," when an organism was isolated from a sinus tract specimen in contiguity with the vertebral lesions. Seven patients with only 1 positive blood culture result were also included in the presumptive category; none of these isolates were coagulase-negative staphylococci. Patients with no positive results of cultures of samples from clinically significant sites were excluded. Sixteen patients with tuberculous VO were seen during the study period but were not included. The severity of underlying noninfectious disease(s) was classified according to the following categories of McCabe and Jackson [11]: rapidly fatal disease, ultimately fatal disease, nonfatal disease, or no underlying disease.

Follow-up and outcome. Patients and/or their physicians or closest relatives were contacted by M.C.M. on ⩾1 occasion when the duration of the patient's follow-up was <5 years. In patients with ⩾5 years of follow-up, we contacted patients whenever the outcome was inconclusive or the patient's health status was otherwise uncertain. Outcomes were classified as follows: "recovery," survival and disappearance of all signs and symptoms of active infection with no residual disability; "qualified recovery," survival and disappearance of all signs and symptoms of infection, but persistence of clinically significant residual disability, such as motor weakness or paralysis, neurogenic bladder, or pain that limited activity or required analgesic therapy; or "death," either caused by or associated with persistent infection. Patients with adverse outcomes (i.e., death or qualified recovery) were compared with patients who recovered.

Because 1 patient who had 2 separate episodes of VO experienced relapse with the first episode and died during the second, the first episode was used for the analysis of relapse and the second for outcome. Another patient who had 2 episodes of VO recovered from both; the first episode was used for the analysis of outcome.

Statistical methods. Categorical factors, according to outcome (i.e., adverse outcome or recovery), were compared by use of the χ^2 test or Fisher's exact test. Time to diagnosis, according to outcome, was compared by use of the Wilcoxon rank-sum test. The 1-year cumulative mortality rate and 1-year rate of relapse with SEs were estimated by means of the Kaplan-Meier method. The equality of relapse and mortality curves between groups were tested with the log-rank test. The 95% CIs were provided for the 1-year mortality and relapse rates. Multivariate logistic regression and the Cox proportional-hazards regression model with forward and backward stepwise variable selection were used to examine the joint effects of prognostic factors on the risk of adverse outcome and the risk of relapse, respectively. Only factors that were significant ($P \leqslant .05$) in the univariate analysis were included in the multivariate analyses. All statistical tests were 2-sided.

RESULTS

Demographic characteristics. There were 253 patients with a total of 255 episodes of VO, including 160 male patients and 93 female patients, ranging in age from 10 weeks to 85 years (median, 60 years). A total of 193 patients (76%) were from CCH, and 60 were from the other hospitals. Of these patients, 142 (56%) had been hospitalized at other institutions for a median of 20 days before referral to the teaching hospital.

Sites of involvement. The location of lesions is shown in table 1. Infection usually involved ⩾2 contiguous vertebral bodies and intervening disk spaces. Involvement of noncontiguous vertebrae with normal intervening vertebrae occurred in 7 patients. In 27 patients (11%), VO presented as disease of a single vertebra, usually with a collapsed vertebral body that resembled a benign or malignant spinal compression fracture. In 17 patients, subsequent radiographs revealed lesions in contiguous vertebrae; this was usually a late finding. In the remaining 10 patients, disease was confined to 1 vertebral body. This deceptive radiologic presentation often led to delayed diagnosis. Six of these patients have been described elsewhere [12].

Paravertebral, epidural, and disk-space abscesses were frequent (table 1). Meningitis developed in 7 patients. Four patients had mycotic aneurysms of the contiguous abdominal or thoracic aorta; 1 of these patients has been described elsewhere [13]. Two patients had infected aortic grafts adjacent to the involved vertebrae. One or more comorbid diseases were present in 201 (79%) of 253 patients. Diabetes mellitus was the most common disease; it occurred in 79 patients (31%). Twenty-nine (11%) of the patients had chronic alcoholism. Approximately 4% each had concomitant malignant neoplasms, collagen vascular disease, hepatic cirrhosis, or end-stage renal disease or were injection drug abusers. Comorbid disease was rapidly fatal in 2 patients (1%), ultimately fatal in 42 patients (17%), and nonfatal or not present in 209 patients (82%).

Microbiologic findings. Causative organisms and diagnostic categories are listed in table 2. Cultures of specimens obtained by percutaneous CT or fluoroscopically guided aspiration or biopsy of the spine, intervertebral disk space, or paravertebral abscesses were positive for pathogens for 86 (69%) of 124 patients. Cultures of samples obtained during surgery were positive for 88 (78%) of 113 patients. For 13 patients with negative cultures of samples of ⩾1 percutaneous aspiration or biopsy specimen, subsequent cultures of samples obtained during surgery were positive in 8.

Pathogenesis and associated conditions. Eighty-three patients (33%) acquired VO in the hospital. VO developed after spinal surgery or penetrating spinal trauma in 39 patients

Table 1. Location of lesions in 255 episodes of vertebral osteomyelitis in 253 patients.

Location	No. of episodes	Epidural abscess	Paravertebral abscess	Disk-space abscess
Cervical	27[a]	7[a]	7[a]	0
Cervical-thoracic	1	1	0	0
Thoracic	61	16	23	4
Thoracolumbar	16	1	10	0
Lumbar	110	9	22	5
Lumbosacral	39	9	4	4
Sacral	1	0	0	0
Total episodes (%)	255[b]	43 (17)[c]	66 (26)[d]	13 (5)[e]

[a] In 2 episodes with cervical myelopathy due to epidural abscess, lumbar infection was present as well; paravertebral abscesses were in the lumbar region rather than in the cervical region in those episodes.

[b] Lesions involved vertebral bodies in 252 episodes and spinous processes in 3 episodes.

[c] Epidural abscess confirmed at operation (40 episodes) or at autopsy (1 episode); in 2 episodes with myelopathy, epidural abscess was diagnosed on MRI.

[d] Paravertebral abscess confirmed during surgery (52 episodes) or by percutaneous aspiration (8 episodes); in 6 episodes, diagnosis was based solely on findings of CT (4 episodes) or MRI (2 episodes).

[e] Abscess found in intervertebral disk space at operation (12 episodes) or by percutaneous aspiration of 50 mL of pus from disk space (1 episode).

(15%). Nosocomial trauma included diskography, epidural catheterization or block, translumbar aortography, or lumbar puncture; community-acquired disease was due to bullet or stab wounds. VO was secondary to a contiguous abscess or an adjacent infected aortic graft in 7 patients (3%; "contiguous VO"). Predisposing extravertebral infections were identified in 130 patients (51%); in 122, this focus was the apparent source of hematogenous VO. The most common portals of entry for hematogenous VO were the urinary tract, skin and subcutaneous tissues, infected vascular access sites, endocarditis, and bursitis or septic arthritis. Bacteremia was documented in 156 patients (62%); ⩾2 blood cultures were positive for 141 (56%). Recurrent episodes of bacteremia due to the same genus and species of organism occurred in 36 patients (14%); intervals between episodes ranged from 12 days to 12 years (median, 1.2 months).

Among 56 patients who did not have fever, bacteremia was detected in 12 patients (21%). Fifty-eight patients with ⩾2 positive blood culture results ultimately had a definite diagnosis established by positive cultures of surgical or percutaneous biopsy specimens. This occurred in individuals who had bacteremia that antedated the drainage of abscesses or surgical debridement (34 patients); in those in whom bacteremia resolved with therapy, but illness persisted or recurred (10 patients); and in those with atypical radiologic presentations or in whom the relationship of bacteremia to vertebral lesions was otherwise uncertain (6 patients). In the remaining 8 patients, bacteremia developed shortly after percutaneous (in 6 patients) or open surgical (in 2) biopsies.

Neurologic complications. Motor weakness or paralysis developed in 62 patients (25%); it was caused by compression of the spinal cord in 33 patients, of the cauda equina in 15, and of isolated nerve roots in 13. Femoral neuropathy occurred in 1 patient who had a psoas abscess. Spinal instability was diagnosed in 21 patients, 12 of whom had motor dysfunction. Weakness [14] was severe in 36 patients, moderate in 12, and mild in 14. The frequency of motor dysfunction was highest among patients with infections of the cervical spine (44% of patients), followed, in descending order, by infections of the thoracic (32%), thoracolumbar (25%), and lumbar and lumbosacral spine (17%; $P = .001$, determined by the Jonckheere-Terpstra test). Other factors that were significantly associated with neurologic compromise were diabetes mellitus ($P = .016$) and advanced age (i.e., ⩾50 years; $P = .001$). These findings are similar to those reported by Eismont et al. [8].

Time to diagnosis. Only 71 (28%) of the episodes of VO were diagnosed within the first month of onset of symptoms. The median time to diagnosis was 1.8 months, which reflects the subacute nature of the illness and/or diagnostic delay. VO was infrequently mentioned in the early differential diagnosis. Of 229 patients in whom the early impressions of attending physicians were available, VO was noted in only 54 (24%).

MRI. MRIs were obtained for 110 patients (43%), 45 of whom had a single scan; ⩾2 scans were performed for 65 patients. The primary radiologic diagnosis on the initial MRI, classified according to the method of Carragee [15], was diskitis or VO for 81 patients (74%). For 29 patients (26%), the initial MRI findings were interpreted as a noninfectious disease, but

Table 2. Causative organisms in 255 episodes of vertebral osteomyelitis (VO) in 253 patients.

Causative organism(s)	No. of episodes[a]	No. (%) of episodes of VO, by diagnostic category		
		Definite (n = 162)	Probable (n = 83)	Presumptive (n = 10)
Staphylococcus aureus	123	76 (62)	42 (34)	5 (4)
Coagulase-negative staphylococci	17	10 (59)	6 (35)	1 (6)
Gram-negative bacilli[b]	59	39 (66)	18 (31)	2 (3)
Streptococci	24	12 (50)	11 (46)	1 (4)
Polymicrobial infection	20	15 (75)	4 (20)	1 (5)
Miscellaneous[c]	12	10 (83)	2 (17)	0 (0)

[a] Two patients each had separate episodes of VO. In 1, the first episode (T9–T11 vertebrae) was caused by *S. aureus* and the second (T8–T11) by coagulase-negative staphylococci. In the other patient, the first episode (T12–L1) was caused by *Listeria monocytogenes* and the second (L3–L4) by *Streptococcus viridans*.

[b] *Escherichia coli* (in 30 episodes), *Pseudomonas aeruginosa* (in 13), *Proteus mirabilis* (in 5), *Klebsiella pneumoniae* (in 5), *Salmonella* species (in 4), *Enterobacter cloacae* (in 1), and *Serratia marcescens* (in 1).

[c] *Nocardia asteroides* (in 2 episodes), *Propionibacterium acnes* (in 2), *Brucella melitensis* (in 1), *Mycobacterium avium intracellulare* (in 1), *Neisseria meningitidis* (in 1), *Bacillus* species (in 1), *Corynebacterium* group JK (in 1), *Candida albicans* (in 1), *Candida tropicalis* (in 1), and *L. monocytogenes* (in 1).

VO was listed as an alternative for 8 patients. The most frequent noninfectious diagnoses were degenerative arthritis, degenerative disk disease, and metastatic neoplasm. Follow-up MRIs, which were obtained for 21 of the 29 patients, were diagnostic of VO for 20. The patient with a nondiagnostic follow-up MRI had undergone surgical removal of an osteomyelitic vertebral body; only postoperative changes were evident on the scan.

Follow-up and outcome. Of 187 patients with an initial duration of follow-up of <5 years, additional information was obtained for 173 (93%). The duration of follow-up for patients with nonfatal cases ranged from 2 days to 38 years (median, 6.5 years). The outcome of 255 episodes was recovery in 146 (57%), qualified recovery in 80 (31%), and death in 29 (11%). The 1-year cumulative mortality rate was 11.3% ± 2.0% (95% CI, 7.4–15.2). For the 80 patients who had qualified recovery, disability was caused by pain in 53, motor weakness or paralysis in 27, impaired mobility in 21, and neurogenic bladder in 4; >1 problem was present in some patients.

Antimicrobial drug therapy. More than 90% of the patients received ⩾4 weeks of specific antibiotic therapy. We defined "definitive antimicrobial therapy" as the treatment regimen administered by physicians at the teaching hospital. This therapy was classified into 1 of 5 categories on the basis of the definitive therapeutic regimen after the diagnosis of VO or after the final relapse of VO (table 3). The largest category involved patients who received specific parenteral antibiotic therapy, on the basis of the results of in vitro susceptibility tests, for ⩾4 weeks. Oral antimicrobial drug therapy was administered most frequently as a follow-up to parenteral therapy, but it constituted definitive therapy in some patients. The most common oral medications were β-lactam antibiotics. Patients who received <4 weeks of specific antibiotic therapy (group 4) did poorly compared with those who received ⩾4 weeks of treatment. However, 13 patients in group 4 died while receiving the appropriate parenteral antibiotic therapy (duration, 6–26 days); this poor outcome appeared to be related to the severity of illness rather than to the short-course of therapy.

Operative management. Surgical treatment was performed for 109 (43%) of 253 patients. The most frequent indications were drainage of abscesses (for 85 patients); relief of compression of the spinal cord, cauda equina, or nerve roots (for 48); and spinal stabilization (for 32). Other indications included debridement, excision of sinuses, removal of infected hardware, and resection of contiguous infected aortic aneurysms or grafts with extra-anatomic bypass. The outcome was favorable (i.e., recovery or improvement) for 86 patients (79%) and unfavorable (i.e., no change or worsening) for 21%.

Forty-eight patients with neurologic impairment underwent surgical treatment; the outcome was favorable for 33 (69%). Of 41 patients with paresis or paralysis caused by compression of the spinal cord or cauda equina, decompression was performed by an anterior approach in 18 patients and by a posterior or posterolateral approach in 23. Of the 18 patients who underwent decompression by an anterior route, the outcome was favorable for 15 (83%), whereas the outcome was favorable for only 13 (57%) of the 23 patients who underwent decompression by a posterior or posterolateral approach. However, the difference was not statistically significant ($P = .067$).

Seven patients with neurologic dysfunction due to spinal cord compression were treated nonoperatively. Muscle func-

Table 3. Outcome, according to specific antimicrobial drug therapy (SAMDT) received, for 255 episodes of vertebral osteomyelitis (VO) in 253 patients.

Group	Therapy	Death (n = 29)	Qualified recovery (n = 80)	Recovery (n = 146)	Relapse preceding SAMDT[a] (n = 36)
1	⩾4 Weeks of parenteral SAMDT plus concomitant or subsequent oral SAMDT[b,c]	16	62	118	27
2	<4 Weeks of parenteral SAMDT plus oral SAMDT for a combined total of ⩾4 weeks	0	10	15	4
3	⩾4 Weeks of oral SAMDT	0	5	6	2
4	<4 Weeks of SAMDT	13[d]	2	4	3
5	Duration of therapy unknown or uncertain	0	1	3	0

[a] None of these courses of SAMDT were followed by relapse; relapse antedated the institution of SAMDT in 36 episodes of VO. Courses of antibiotic therapy that preceded relapse in those 36 patients are not included in this table.
[b] In 3 episodes of VO, patients received ⩾4 weeks of simultaneous parenteral and oral SAMDT.
[c] Of the 196 episodes in this group, 78 episodes (78 patients) were treated with supplemental oral antibiotic therapy for 1 week to 6 years (median, 5 months).
[d] These patients died while receiving appropriate parenteral antibiotic therapy (duration, 6–26 days).

tion improved with antibiotic therapy in 2 patients, but each was left with significant residual disability. Five patients died of uncontrolled infection despite having received appropriate antibiotic therapy—1 died of rupture of a mycotic aneurysm of the contiguous aorta and 4 died of undrained epidural abscesses complicated by paraplegia or quadriplegia. Each of the patients with epidural abscesses was considered unacceptable for surgery because of severe comorbid disease. The outlook for patients with radiculopathy was good. Of 13 patients with isolated nerve root compression, 7 were treated without operation and the outcome was favorable for 6; 6 patients underwent surgery, and 3 had favorable results.

Relapse. Recurrence of the symptoms of infection after apparent resolution developed after hospital discharge in 36 patients (14%); >1 relapse (range, 2–6) occurred in 11. Intervals between the initial illness and relapse ranged from <1 month to 12 years, but they were <1 year for 27 patients (75%). The 1-year cumulative relapse rate was 11.8% ± 2.1% (95% CI, 7.6–16.0). For 30 patients, relapse was confirmed by positive results of cultures of samples of bone, intervertebral disk space, abscesses, or blood. For 6 patients, the diagnosis of relapse was based on clinical findings alone.

For 29 of the 30 patients with culture-confirmed relapse, the same genus and species of the microorganism isolated during the first episode was recovered during relapse. In 1 patient with relapse caused by *Staphylococcus aureus, Escherichia coli* was isolated concomitantly with *S. aureus* from the infected intervertebral disk space, whereas only *S. aureus* was recovered from the same disk space during the first episode. Acute urinary tract infection due to *E. coli* during the first episode probably seeded the infected spinal column. In 1 patient, an initial culture of a sample from the infected disk space yielded *Bacteroides fragilis* and α-hemolytic streptococci, whereas culture of a psoas abscess specimen obtained during relapse yielded *Proteus mirabilis;* further investigation found a colonic fistula in communication with the abscess.

Nineteen patients with relapse had severe destructive changes and deformities of vertebrae that may have retarded healing and allowed organisms to persist despite the administration of antibiotic therapy, including vertebral collapse or severe compression fracture (in 9 patients), gibbous deformities (in 9), and a large cavity that replaced most of a vertebral body (in 1). In patients who had involvement of ⩾3 contiguous vertebral bodies, relapse occurred significantly more often than it did in patients who had infection of <3 adjacent vertebrae ($P < .001$; table 4).

Twenty patients with relapse had undergone evacuation of abscesses or debridement of infected bone before recurrence, which suggests that incomplete debridement or drainage was involved in pathogenesis; 14 of these patients required additional surgery. Relapse developed after suboptimal antibiotic therapy in 13 patients (36%). Therapy was considered suboptimal when the duration of treatment was <4 weeks (for 10 patients) [2], the dosage was lower than that ordinarily recommended for serious osseous infections (for 2), or the pathogen was resistant to the administered drug (for 1). Relapse developed after completion of apparent optimal antibiotic therapy in 23 (64%) of 36 patients.

The results of univariate analysis of factors related to relapse are shown in table 4. In the multivariate analysis (table 5), only recurrent bacteremia, chronic draining sinuses, and paravertebral abscesses remained independent factors associated with relapse.

Risk factors for adverse outcome. Adverse outcome was not significantly associated with the age or sex of patients, the causative organism(s), bacteremia, the location of spinal lesions,

Table 4. Univariate analysis of factors associated with relapse in patients with vertebral osteomyelitis (VO).

Factor	No. of patients with relapse/ no. with factor (%)	1-Year relapse rate ± SE	P^a
Sex			
Male	21/160 (13)	10.4 ± 2.5	.53
Female	15/93 (16)	14.3 ± 3.8	
Place of acquisition of VO			
Hospital	18/83 (22)	17.5 ± 4.4	.009
Community	18/170 (11)	9.1 ± 2.3	
Epidural abscess			
Present	8/43 (19)	17.9 ± 6.2	.36
Absent	28/210 (13)	10.6 ± 2.2	
Paravertebral abscess			
Present	18/66 (27)	19.1 ± 5.2	<.001
Absent	18/187 (10)	9.4 ± 2.2	
Motor weakness or paralysis			
Present	12/62 (19)	21.4 ± 5.8	.09
Absent	24/191 (13)	9.1 ± 2.2	
Gibbous deformity			
Present	9/27 (33)	23.9 ± 8.5	.002
Absent	27/226 (12)	10.4 ± 2.2	
Chronically draining sinus			
Present	7/13 (54)	25.0 ± 12.5	<.001
Absent	29/240 (12)	11.1 ± 2.1	
Recurrent bacteremia			
Present	20/36 (56)	53.0 ± 8.6	<.001
Absent	16/217 (7)	4.7 ± 1.5	
Diabetes			
Present	16/79 (20)	20.3 ± 4.9	.036
Absent	20/174 (11)	8.1 ± 2.2	
Contiguous involvement of ⩾3 vertebrae			
Present	13/37 (35)	26.7 ± 7.7	<.001
Absent	23/216 (11)	9.3 ± 2.1	

[a] Determined by means of the log-rank test.

or relapse. The median interval between the onset of symptoms and diagnosis was significantly longer for patients with adverse outcomes (2.1 months) than it was for those who recovered (1.4 months; $P = .025$). The outcome of patients evaluated by MRI did not significantly differ from the outcome for those who were not ($P = .6$). MRI was frequently not performed early during the illness. The median time between the onset of symptoms and performance of MRI was 1.4 months; this did not differ significantly between patients with MRIs who recovered and those who had an unfavorable outcome ($P = .5$).

The results of the univariate analysis of factors related to outcome are shown in table 6. In the multivariate analysis (table 7), only motor weakness or paralysis, longer time to diagnosis, and hospital acquisition remained as independent risk factors for adverse outcome.

Hospital acquisition as an unfavorable prognostic factor was unexpected. Age or sex of patients, location of spinal lesions, severity of comorbid diseases, and the rate of complications of spinal infection were not significantly associated with the place of acquisition of VO. Patients with hospital-acquired VO had a significantly higher incidence of antecedent spinal surgery or penetrating spinal trauma ($P = .001$) and predisposing contiguous foci of infection ($P = .04$) than did patients with community-acquired disease.

DISCUSSION

A longer time to diagnosis, neurologic compromise, and hospital acquisition were major independent risk factors for adverse outcome of VO. To our knowledge, the present study contains, to date, the largest number of patients with microbiologically diagnosed pyogenic VO. Malawski and Lukawski [16] described 442 patients, but diagnosis was established bacteriologically for only 80. Six additional studies [4, 17–21] each included slightly more than 100 patients. Although the difficulties of an early diagnosis of VO have long been known and well documented, the present study may be the first to demonstrate that diagnostic delay is an independent risk factor for an unfavorable outcome. Because VO is an uncommon disease, physicians are often unaccustomed to thinking about the diagnosis; erroneous initial clinical impressions are common [18, 22–24]. The average reported duration from the onset of symptoms to diagnosis has ranged from 6 weeks to nearly 7 months [23–31].

A striking finding was that MRI results did not exert a significant effect on outcome, probably because MRI was often performed late during the illness. Recently, Carragee [15, 19] reported that MRI scans, which were obtained for 103 of 111 patients with pyogenic VO, were obtained a median of <3 weeks after onset of spinal symptoms; diagnosis was confirmed within the first month of illness for 69% of patients, and the mortality rate was 11.7%. Patients with impaired immune systems appeared to be at increased risk of death. These results indicate that prompt referral to experienced physicians and the timely use of MRI shortens time to diagnosis. Unfortunately, patients are often not referred to tertiary care hospitals until they are in the advanced stages of disease. More than 50% of our patients had been hospitalized at other institutions for a median of 20 days before referral. Clearly, there is a pressing need for increased awareness of VO and for early diagnosis. When VO is first suspected, MRI with gadolinium is the imaging procedure of choice.

Severity of comorbid illness was not an independent risk factor for adverse outcome, possibly because of the relatively small number of patients with rapidly or ultimately fatal underlying diseases. The unfavorable effect of hospital acquisition appeared to be due, in part, to the high incidence of antecedent

Table 5. Multivariate analysis of factors associated with relapse for patients with vertebral osteomyelitis (VO).

Risk factor	RR (95% CI)	*P*
Recurrent bacteremia, yes/no	18.9 (8.8–40.8)	<.001
Chronically draining sinus, yes/no	7.6 (2.8–20.5)	<.001
Paravertebral abscess, yes/no	3.2 (1.6–6.5)	.001

spinal surgery, penetrating spinal trauma, and contiguous VO in patients with nosocomial disease and to the high rate of unfavorable outcome associated with these conditions. Because many studies of spinal osteomyelitis exclude patients with postoperative, posttraumatic, and contiguous VO, we believe that the poor outcome associated with these conditions warrants emphasis.

Postoperative spondylodiskitis has been reported by some as having a uniformly good prognosis [32], which is attributed to the rarity of deaths and uncommon relapses [33]. Some patients with postoperative diskitis have recovered without antimicrobial therapy [34], but, even when drug therapy is administered, relapses and deaths that occur years after the initial episode have been reported [35, 36]. Reports of favorable prognosis have been based on small numbers of cases with limited follow-up. Larger studies with longer follow-up periods [20, 37] have conveyed a vastly different message: up to 75% of patients with postoperative diskitis had severe chronic back pain and an inability to work or perform the normal activities of daily living. Moreover, the incidence of chronic pain and vocational handicap was significantly greater in patients with diskitis than it was in matched control patients who had undergone spinal surgery without infection [20].

Relapse has been noted in 1%–22% of patients treated for pyogenic VO during the antibiotic era [2, 6, 7, 18, 28, 32, 37–52]. It should be considered in any patient with previously treated VO—even years later—when there is recurrence or intensification of pain, unexplained fever, night sweats or weight loss, renewed elevation of the erythrocyte sedimentation rate (ESR), or recurrent bacteremia. Patients with severe destructive vertebral lesions and patients who have undergone surgical drainage or debridement should be monitored closely for persistent or recurrent infection. A longer duration of antibiotic therapy may be indicated when there is any suspicion of residual disease.

Persistent pain should be viewed with concern. Five of our patients who had relapse had persistent severe back pain at the conclusion of therapy; in the absence of fever, this was erroneously attributed to causes other than infection. Diagnostic studies were delayed, and relapse was diagnosed only later, when systemic symptoms reappeared. When relapse is diagnosed, microbiologic diagnosis should be pursued, because different microorganisms may occasionally be involved. Moreover, a thorough investigation for surgically correctable lesions is critical.

In a classic review of pyogenic VO, Sapico and Montgomerie [2] found that parenteral antibiotic therapy of <4 weeks' duration resulted in therapeutic failure significantly more often than did therapy for ⩾4 weeks. Although 4–6 weeks is a minimum acceptable duration, a much longer duration of treatment may be required for cure in individual patients. Treatment must continue until a favorable outcome is secured, with improvement or disappearance of pain, improved mobility, absence of fever, and progression of the ESR and C-reactive protein, hemoglobin, and hematocrit values toward normalization. When patients are improving but have not attained baseline levels, we believe that oral therapy for 3–6 months or longer is beneficial after completion of parenteral therapy.

Table 6. Univariate analysis of factors associated with adverse outcome in patients with vertebral osteomyelitis (VO).

Factor	No. of patients with adverse outcome/ no. with factor (%)	*P*[a]
Sex		
Male	66/160 (41)	.54
Female	42/93 (45)	
Age, years		
<50	25/68 (37)	.25
⩾50	83/185 (45)	
Comorbid disease		
Rapidly or ultimately fatal	26/44 (59)	.016
Nonfatal or none	82/209 (39)	
Place of acquisition of VO		
Hospital	48/83 (58)	.001
Community	60/170 (35)	
Epidural abscess		
Present	29/43 (67)	.001
Absent	79/210 (38)	
Motor weakness or paralysis		
Present	47/62 (76)	.001
Absent	61/191 (32)	
Paravertebral abscess		
Present	34/66 (52)	.09
Absent	74/187 (40)	
Relapse		
Present	17/36 (47)	.55
Absent	91/217 (42)	
Bacteremia		
Present	62/156 (40)	.23
Absent	46/97 (47)	
Time to diagnosis, months		
<2	48/138 (35)	.005
⩾2	60/115 (52)	

[a] Determined by means of the χ^2 test. There was no significant difference in outcome for patients in the last decade of the present study, compared with that in patients treated before January 1985 ($P = .6$).

Table 7. Multivariate analysis of factors associated with adverse outcome for patients with vertebral osteomyelitis.

Risk factor	OR (95% CI)	*P*
Motor weakness or paralysis, yes/no	7.1 (5.0–10.1)	<.001
Hospital acquisition, yes/no	2.5 (1.9–3.4)	.002
Time to diagnosis of >2 months, yes/no	2.3 (1.7–3.1)	.004

Because neurologic impairment is a major risk factor for adverse outcome, there can be no substitute for repeated, careful neurologic examinations for early detection. In our patients with neurologic compromise, the outcome of surgery was favorable in nearly 70%; even better results might have been achieved in the absence of diagnostic delay.

In conclusion, pyogenic VO has evolved from an acute stormy illness of young patients that had a high mortality rate [53–55] to a more indolent illness of elderly individuals that has a lower mortality rate but that relapses and has frequent disabling sequelae. Early diagnosis is a major challenge. Heightened awareness and the prompt use of MRI are necessary to avoid diagnostic delay. Prolonged antimicrobial therapy and the judicious application of timely surgical intervention are essential for an optimal outcome.

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