The Clinical Characteristics, Therapeutic Outcome, and Prognostic Factors of Non-Tuberculous Bacterial Spinal Epidural Abscess in Adults: A Hospital-based Study

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Abstract-

Purpose: Nontuberculous bacterial spinal epidural abscess (SEA) is a serious infectious disease of spines. Despite proper management, SEA remains a disease of high morbidity. The epidemiological data in southern Taiwan is still lacking.

Methods: We analyzed the clinical features, laboratory data, magnetic resonance imaging findings, and therapeutic results of 45 bacterial SEA patients, collected during a study period of six years (2003-2008).

Results: The 45 adult SEA patients, 32 were men and 13 women, aged 17-81 years (mean = 62 years). Thoracic and lumbosacral spines were the most commonly affected segments. Staphylococcus aureus was the most commonly implicated pathogen, accounting for infections in 67% (29/43) of the culture-proven cases, and 41% (12/29) of the S. *aureus* strains were oxacillin resistant. Gram-negative pathogens were implicated in 30% (13/43) of the culture-proven cases. Of the 45 patients, 19 underwent antibiotic treatment alone and 26 underwent medical and surgical treatments. The therapeutic results showed that 28 patients had a good prognosis and 17 had a poor prognosis. The significant prognostic factors included higher age, presence of diabetes mellitus and chronic heart disease, and initial presentation of altered consciousness.

Conclusion: S. *aureus* was the most commonly implicated pathogen of adult SEA, and most S. *aureus* strains were oxacillin resistant. A relatively high incidence of Gram-negative infection was observed in this study. The epidemiological characteristics of the implicated pathogens must receive special consideration when selecting the empirical antibiotics. Despite adequate management, many adults with bacterial SEA had a high incidence of poor prognosis.

Key Words: adults, spinal epidural abscess, Staphylococcus aureus, gram-negative pathogen

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INTRODUCTION

Despite the advances in neuroimaging as well as aggressive medical and surgical treatments, spinal epidural abscess (SEA) caused by nontuberculous bacterial infection remains a clinical challenge requiring early medical and surgical intervention to prevent devastating neurologic deficits[1-9]. In the past 2 decades, there has been an increase in the incidence of bacterial SEA because of an aging population, increase in the number of intravenous drug abusers, and the more frequent use of spinal instruments[1]. Other predisposing conditions for its development in adults include the presence of diabetes mellitus (DM), liver cirrhosis, malignancy, chronic renal disease (CRD), autoimmune disease, and use of corticosteroids and immunosuppressants [1,4,10,11].

Early diagnosis and rapid proper treatment are the most important factors in the management of bacterial SEA in adults. Therefore, primary-care physicians are usually the ones who should make the diagnostic and therapeutic decisions based on the clinical presentations, laboratory data, and neuroimaging features of the patients to help them face the challenges of this critical infectious disease [4]. In this study, we analyzed the clini-cal characteristics, therapeutic outcome, and prognostic factors of 45 adult patients with nontuberculous bacterial SEA to delineate the clinical characteristics of this serious infectious disease of the vertebral column.

METHODS

Between 2003 and 2008, 45 adult patients (age ≥ 17 years) were diagnosed with nontuberculous bacterial SEA at Chang Gung Memorial Hospital (CGMH)-Kaohsiung. CGMH-Kaohsiung is the largest medical center in southern Taiwan and a 2,482-bed acute-care teaching hospital, which provides both primary and tertiary referral care. In this study, the diagnostic criteria of bacterial SEA were as follows [2,12]: (1) typical clinical features (fever, back pain, or weakness of the limbs), (2) typical magnetic resonance (MR) imaging features (an example case is shown in Figure 1), (3) positive blood and/or pus culture, and/or (4) evidence of pathological tissue damage (pus, phlegmon, or both). The medical records, imaging findings, and bacteriologic test results of these 45 patients were reviewed for analysis.

In this study, the onset of the clinical symptoms was defined [13] as acute (≤3 days), subacute (>3 days and ≤14
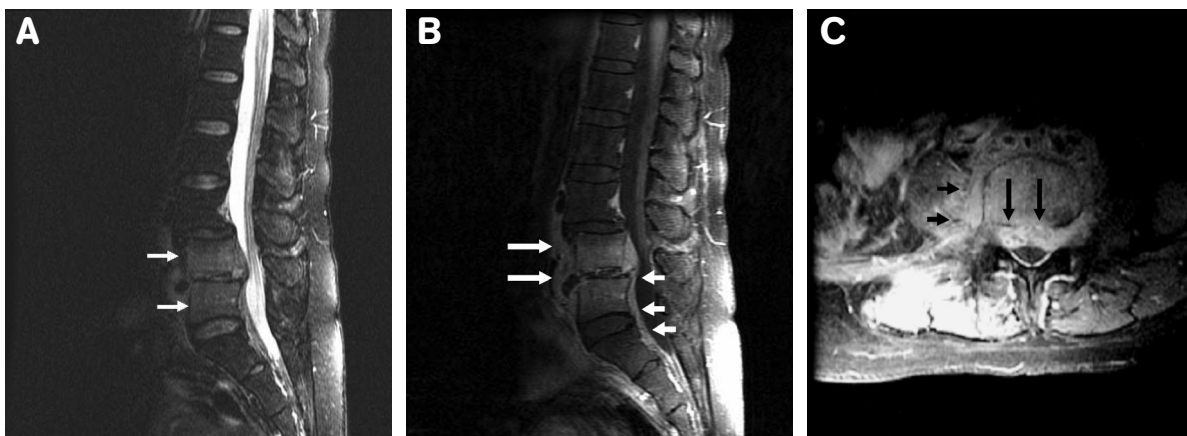

Figure 1. Magnetic resonance imaging findings of the spinal epidural abscess caused by Staphylococcus aureus infection in a 48-year-old woman. Figure 1A (T2-weighted fat-suppression imaging) shows a hyperintense marrow-density change (arrows) at L4 and L5 vertebral bodies. Figure 1B [gadolinium diethylenetriaminepentaacetic acid (DTPA)-enhanced T1-weighted fat-suppression imaging] shows homogenous enhancement at L4 and L5 vertebral bodies, anterior epidural space (short arrows), and prevertebral soft tissue (long arrows). Figure 1C (gadolinium DTPA-enhanced T1-weighted fat-suppression imaging) shows multiple abscesses with ring enhancement at the prevertebral soft tissue (short arrows) and anterior epidural abscess (long arrows).

days), or chronic (>14 days). The severity of clinical manifestations was classified into the following 4 stages [13]: stage 1, back pain at the level of the affected spine; stage 2, radiation of nerve-root pain from the affected spinal area; stage 3, motor weakness, sensory deficit, and bladder and bowel dysfunction; and stage 4, paralysis. In this study, stages 1 and 2 were considered early stages, whereas stages 3 and 4 were considered late stage. "Leukocytosis" was defined as the condition characterized by a white blood cell (WBC) count $> 10\times 10^9$/L. The erythrocyte sedimentation rate (ESR) was considered as abnormal if it was >15 mm/h (both genders; age ≤ 50 years), >20 (men; age >50 years), and >30 (woman; age > 50 years). The levels of C-reactive protein (CRP) were considered as abnormal if they were >5 mg/dL.

For analyzing the prognostic factors, the therapeutic outcomes at 3 months were determined using a modified Barthel Index (BI). A BI score < 12 was defined as a poor outcome, and a score ≤ 12 as a good outcome. Patients who died were also included in the poor outcome group for statistical analysis. Categorical data were compared using the chi-square test. Continuous data were compared using the Mann-Whitney U test. The two-tailed significance level was set at p < 0.05.

RESULTS

The 45 adult SEA patients were 32 men and 13 women, aged 17-81 years (mean = 62 years). Among the 45 patients, 43 had a positive culture result, while the other 2 had a negative result (blood and/or pus cultures). The pathogen was identified using blood cultures in 19 cases, from pus cultures (through surgical drainage) in 12 cases, and from both blood and pus cultures in 12 cases. Of the 43 patients with positive culture results (Table 1), 30 had Gram-positive [G(+)] pathogen infection, while the other 13 had Gram-negative [G(-)] pathogen infection. Of the implicated G(+) pathogens, Staphylococcus aureus was the most common, being found in 29 patients. Of the 29 implicated S. *aureus* strains, 17 were oxacillin-susceptible (OSSA) strains, while the other 12 were oxacillin-resistant (ORSA)

Table 1. Pathogens in the 45 cases of bacterial spinal epidural abscess

Pathogens	Present study
Gram-positive (n = 30)	
Staphylococcus aureus	29
Group B streptococci	1
Gram-negative (n = 13)	
Klebsiella pneumoniae	3
Escherichia coli	2
Salmonella enterica serogroup B	2
Salmonella typhi	1
Enterobacter cloacae	1
Enterobacter sakazakii	1
Pseudomonas aeruginosa	1
Aeromonas hydrophilia	1
Prevotella melaninogenica	1
Culture negative (n = 2)	

strains. Among the implicated G(-) pathogens, Klebsiella pneumoniae, Salmonella spp., and Escherichia coli were the most common.

DM and postneurosurgical state were the most common underlying conditions, being found in 15 and 14 patients, respectively. The other underlying conditions were intravenous substance abuse in 6 patients, CRD in 6, malignancy in 5, chronic lung disease in 4, and liver cirrhosis in 4. With respect to the types of clinical onset, 16 patients had an acute onset; 25, a subacute onset; and 4, a chronic onset. Motor weakness was the most common clinical manifestation, being found in 40 patients. The other clinical manifestations were sensory abnormality in 32 patients, low back pain in 31, bacteremia in 31, fever in 23, bladder dysfunction in 20, psoas muscle abscess in 16, neck pain in 7, altered consciousness in 5, septic arthritis in 5, and concomitant meningitis in 1. The severity of initial clinical manifestations were as follows: stage 1 in 2 patients, stage 2 in 8, stage 3 in 31, and stage 4 in 4. With respect to the involved spinal segments, the lumbar/lumbosacral levels were found to be affected in 23 patients, thoracic/thoracolumbar levels in 15, and cervical/cervicothoracic levels in 7. The range of spinal segment involvement was 1-7 (median = 2).

Table 2. Outcome analysis of the 45 patients with bacterial spinal epidural abscess

	Good outcome (n = 28)	Poor outcome (n = 17)	P value
Age at onset (years), median (range)	58 (17-81)	70 (44-81)	0.014*
Gender			0.382
Male	19	13	
Female	9	4	
Interval before admission (days), median (range)	7 (1-120)	3 (1-30)	0.084
Interval from admission to diagnosis (days), median (range)	2 (1-5)	2 (1-23)	0.489
Underlying disease			
Post-neurosurgical form	9	5	0.537
Diabetes mellitus	6	9	0.030*
Intravenous drug use	5	1	0.252
Chronic renal disease	4	2	1.000
Malignancy	3	2	0.913
Liver cirrhosis	2	2	0.505
Chronic heart failure	0	2	0.040*
Chronic lung disease	2	2	0.457
Clinical presentations			
Fever	16	7	0.299
Low back pain	21	10	0.256
Neck pain	3	4	0.763
Altered consciousness	1	4	0.018*
Onset			0.058
Acute	7	9	
Subacute/chronic	21	8	
Neurologic deficits			0.869
Stages 1-2	6	4	
Stages 3-4	22	13	
Abscess location			0.986
Cervical spines	5	3	
Non-cervical spines	23	14	
Abscess extent			0.900
<3 levels	17	10	
≥3 levels	11	7	
Laboratory findings			
White blood cell count ($\times 10^9$/L), median (range)	12 (6-25)	14 (5-27)	0.773
ESR (mm/h), median (range)	73 (43-89)	96 (59-133)	0.770
C-reactive protein (mg/dL), median (range)	138 (3.4-313)	115 (3.57-400)	0.866
Pathogens			0.134
ORSA	10	7	
Other pathogens	18	10	
Treatment			0.912
Medical alone	12	7	
Combined	16	10	
Length of hospital stay (days), median (range)	45 (17-83)	44 (13-92)	0.584

ESR= erythrocyte sedimentation rate; * p < 0.05

Among the 45 patients, 19 with SEA underwent antibiotic treatment alone and 26 underwent both antibiotic treatment and surgical intervention. Among the latter 26 patients who had undergone surgical intervention, 11 underwent the procedure within 48 h of admission. After medical and/or surgical management, 28 patients had a good prognosis and the other 17 had a poor prognosis. The median duration of hospital stay was 44 days (range, 13-92 days). Among the prognostic factors, age at onset (p = 0.014), presence of DM (p = 0.030) and chronic heart failure (p = 0.040), and presentation with altered consciousness (p = 0.018) were significant (Table 2).

DISCUSSION

Early diagnosis and adequate treatment are known to be important for the management of patients with SEA[6-9]. However, despite early diagnosis and adequate treatment, only 45% of the patients recover fully from this devastating spinal infectious disease [5]. This study revealed that the type of onset of presenting sign and symptoms were 36% (16/45) with acute type and 78% (35/45) searched a medical care in the late stage of SEA. This delay in diagnosis may be one of the important factors that contribute to the therapeutic outcome of bacterial SEA in adults despite the type of onset and the initial severity of neurologic deficit, as shown in Table 2, being statistically insignificant. The clinical presentations, such as motor weakness, sensory abnormality, and low back pain, of these 45 patients were not unique and may be found in other spinal diseases. Moreover, fever was found only in 52% (23/45) of the patients. Therefore, keep the diagnosis in mind is important for early identification of this specific spinal infectious disease.

In this study, the thoracic and lumbosacral levels were the most commonly affected spinal segments, and this finding is consistent with that of other previously reported studies [1-3]. Of the implicated pathogens, S. aureus was the most common; it accounted for 67% (29/43) and 96% (29/30) of the overall culture-proven and G(+) pathogens, respectively. These figures of incidence of S. aureus infection in SEA are consistent with those (56%-87%) of other reports [1,4,6,12-19]. Among the S. aureus strains, 41% (12/29) were oxacillin resistant. This high incidence of ORSA strains as the implicated pathogen in SEA was also noted in other reports from Taiwan [13,14,20], and this has presented a therapeutic challenge in the choice of empirical antibiotics for treating bacterial SEA. Therefore, vancomycin, at least, should be used at the beginning of SEA treatment; this was also suggested in other reports of SEA management [1,2]. The high incidence of ORSA strains usually suggested that the infection control program in the hospital was inadequate, and this observed phenomenon is consistent with other reported findings of rapid dissemination of S. aureus with classic oxacillin resistance, especially in patients with nosocomial infections in Taiwan [21,22].

In this study, G(-) pathogens accounted for the remaining 30% (13/43) of culture-proven bacterial SEA in adults, and this figure of incidence is relatively higher than that reported in other countries [4,14-19], where the incidence ranges from 4% to 18%. Although this relatively high incidence of G(-) pathogen infection has also been noted in other types of central nervous system infection in Taiwan [23,24], this finding deserves further ongoing follow-up study to delineate the epidemiologic trend of implicated pathogens of bacterial SEA in adults. However, the antibiotics, such as 3rd- or 4th-generation cephalosporins and carbapenems that can cover this group of pathogens, should be used empirically in the early stage of treatment. This use of antibiotics has also been suggested in other studies reported recently [1,2].

Many factors, including many underlying conditions, clinical features, and serum biochemical markers, have been found to have prognostic significance in bacterial SEA [12-15]. In this study, the following factors were found to be significantly associated with good and poor outcome: (1) older patients had a poor outcome; (2) patients with DM and chronic heart disease as the underlying conditions had a poor outcome; and (3) patients with a higher incidence of altered consciousness at initial presentation had a poor outcome. Further, we did not observe any prognostic difference between the patients who underwent medical treatment alone and who underwent both medical treatment and surgical intervention.

Optimal management of bacterial SEA is known to involve a combination of medical treatment and surgical intervention, but in recent years, there have been reports of successful cases in antibiotic treatment alone [7,13,25-27]. Further large-scale studies are required for designing a therapeutic strategy for the management of adult patients with bacterial SEA.

In conclusion, most of the adults with bacterial SEA do not undergo early and adequate management. The initial clinical manifestations of this group of patients were not unique; therefore, accurate diagnosis of SEA is important for early identification and treatment. Neuroimaging of spine MRI is very important tool for early identification of patients with SEA. This study revealed a relatively high incidence of infection by ORSA and G(-) strains in the adults with bacterial SEA. In particular, the epidemiological characteristics of the implicated pathogens should be considered while prescribing empirical antibiotics with adequate quality. Despite adequate management, a high percentage of patients had poor outcomes. The important prognostic factors included higher age, presence of DM and chronic heart disease, and initial altered consciousness.

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