Changing Epidemiology of Adult Bacterial Meningitis in Southern Taiwan: A Hospital-Based Study

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Abstract

Background: Many factors may influence the epidemiologic trend of adult bacterial meningitis (ABM). The objective of this study was to analyze recent epidemiologic trends of ABM in order to provide a better therapeutic strategy.
Materials and Methods: The clinical features, laboratory data, and therapeutic outcomes of 181 ABM cases collected in the last 6.5 years (July 1999–December 2005) were analyzed. The results were compared with those of our previous study (202 cases, January 1986–June 1999).
Results: The 181 cases consisted of 130 men (age range: 18–82 years) and 51 women (age range: 18–78 years). Monomicrobial infection and mixed infection were found in 165 cases and 16 cases, respectively. A preceding post-neurosurgical state was noted in 56.9% (103/181) of cases. Despite a decrease in incidence, *Klebsiella pneumoniae* (25.5%, 42/165) was still the most common pathogen. A marked increase of *Acinetobacter* meningitis (11.5%, 19/165) was noted, which replaced *Pseudomonas* meningitis as the second most common Gram-negative pathogen in ABM. A marked increase in staphylococcal infection, accounting for 23% (38/165) of all cases, was also noted, of which 76% (29/38) were methicillin-resistant strains. The therapeutic result showed a mortality rate of 30.3% (55/181). Significant prognostic factors included septic shock and age at infection.
Conclusions: This study revealed a change in the epidemiologic trend of ABM, with an increase in the number of patients with a postneurosurgical state and a rising incidence of *Acinetobacter* and staphylococcal infections. Clinicians should pay greater attention to these changes, which may affect their management of ABM.

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Introduction

The prevalence rate of pathogens causing bacterial meningitis is influenced by several clinical factors, including age, preceding medical, and/or surgical conditions, mode of contraction, geographic distribution, status of vaccination, and the time period of the study [1–16]. Changing epidemiology of bacterial meningitis has been noted in several studies [5, 8, 10, 12]. Because early appropriate antibiotic therapy is one of the important and explicit steps in the management of potentially fatal central nervous system (CNS) infection, these recent epidemiologic trends have influenced the choice of initial empiric antibiotic treatment [17, 18]. Even as the final identification of the involved pathogen by culture needs time, epidemiologic factors, including the prevalence and relative frequency of the causative pathogen(s) of adult bacterial meningitis (ABM), should be reviewed constantly [4, 17–19]. Our previous study [4] had disclosed the epidemiologic trend of ABM in southern Taiwan, in which 202 ABM patients collected in a 13.5-year time period (January 1986–June 1999) were included. In present study, we analyzed the epidemiologic trend of culture-proven ABM in southern Taiwan in the past 6.5 years (July 1999–December 2005) and made clinical and laboratory comparisons with the earlier study results [4]. We also compared the pathogens of ABM which occurred after neurosurgery to those of spontaneous ABM. The change of epidemiologic trend of ABM in southern Taiwan was explored to help bring about a better therapeutic strategy.

Materials and Methods

We retrospectively reviewed the microbiological records of cerebrospinal fluid (CSF) and blood cultures, laboratory data,

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and medical records of adult patients (> 17 years) with culture-proven bacterial meningitis admitted to Chang Gung Memorial Hospital (CGMH)-Kaohsiung over a period of 6.5 years (July 1999–December 2005). The aim of this study was to compare the causing pathogens of the time period (13.5 years, January 1986–June 1999) of our previous study [4]. CGMH-Kaohsiung is the largest medical center in southern Taiwan. This facility is a 2,482-bed acute-care teaching hospital, which provides both primary and tertiary referral care. Southern Taiwan consists of two cities and three counties with a population of approximately 5,441,000 as of October 1998. The annual population increase for Taiwan is reported to be 0.75% [20]. During this study period, 181 adult patients were determined to have culture-proven bacterial meningitis.

In this study, the criteria for a definite diagnosis of bacterial meningitis included the following: (1) positive CSF culture of bacterial pathogen(s); (2) clinical features of meningitis, including fever, consciousness disturbance, seizure, and signs of meningeal irritation; and (3) purulent CSF features, including at least one of the following parameters: leukocytosis with leukocyte count $> 0.25 \times 10^9$/l and predominant polymorphonuclear cells, lactate concentration > 3.5 mmol/l, glucose ratio (CSF glucose/serum glucose) < 0.4 or glucose level < 2.5 mmol/l if no simultaneous blood glucose level was determined. Because viridans streptococci and coagulase-negative staphylococci (CoNS) are common contaminants of cultures, the diagnosis of meningitis caused by these two groups of pathogens was defined by a stricter criteria [1, 21, 22]: only if repeated CSF cultures demonstrated positive results or if they were cultured from the tip of an indwelling neurosurgical device. Patients with evidence of concomitant chronic meningitis or encephalitis not due to bacterial pathogens were excluded. Patients were considered to have ''mixed bacterial meningitis'' if at least two bacterial organisms were isolated from the initial CSF culture [23].

For study, ABM was classified as either being nosocomial or community-acquired. Nosocomial meningitis was defined as a positive bacterial infection not present when the patient was admitted to the hospital, clinical evidence of an infection no sooner than 48 hours after admission, or clinical evidence of meningitis within a short period of time (i.e. usually within one month after discharge from the hospital where the patient had received an invasive procedure, especially a neurosurgical procedure). Otherwise, the patient was considered to have ''community-acquired'' infection. Patients who developed meningitis related to head trauma with skull fractures or neurosurgical procedures were classified as ''postneurosurgical'' meningitis. Otherwise, patients who demonstrated no clear distinctive disease characteristics and who had not undergone any invasive procedures were classified as ''spontaneous'' meningitis.

The initial consciousness level of adult patients was classified into two groups. Group I had normal consciousness (Glasgow coma scale (GCS) score = 15), while group II had disturbed consciousness (GCS < 15). ''Leukocytosis'' was defined as a peripheral white blood cell (WBC) count $> 10 \times 10^9$/l, ''leukopenia'' as a WBC count $< 5 \times 10^9$/l, and ''thrombocytopenia'' as a platelet count $< 140 \times 10^9$/l. Bacteremia was considered to be ''positive'' only when multiple blood cultures grew the same bacterial pathogen. Over the study period, intravenous administration of penicillin G or vancomycin with one of the third generation cephalosporins (ceftriaxone, ceftazidime) or cefepime were the initial empiric antibiotics used in the treatment of adult patients with clinical evidence of bacterial meningitis. Further antibiotic adjustment was guided according to the results of pathogen identification and antibiotic susceptibility tests. Antibiotic susceptibility of the isolated pathogen was tested using the Kirby-Bauer diffusion method (BBL, Muller-Hinton II agars; Becton Dickinson Microbiology Systems, Cockeysville, MD, USA). Other antibiotics used after the final bacterial culture and antibiotic susceptibility test results came out included oxacillin, imipenem, and meropenem.

For statistical analysis, the 181 adult patients were divided into two groups (fatal and non-fatal groups). Data, such as sex, type of acquisition of infection, type of infection, underlying conditions, clinical manifestations, and therapeutic outcomes between these two patient groups, were analyzed by χ^2-test or Fisher's exact test. Age between the two patient groups was analyzed by Student's t-test. Consciousness levels at the time of admission between the two patient groups were analyzed by Mann-Whitney test. CSF data for WBC count, glucose, total proteins and lactate concentrations for the two groups were logarithmically transformed to improve normality. The two patient groups were compared using Student's t-test.

Relationships among variables and the two patient groups were analyzed using multiple logistic regression analysis and adjusted for other potential confounding factors. Variables with zero cell counts were eliminated for logistic analysis, and only variables with statistical significance ($p < 0.05$) were included in the final model. All analyses were conducted using SAS (SAS Statistical Institute) [24].

Results

The 181 patients consisted of 130 men, with the age range of 18–82 years, and 51 women, with the age range of 18–78 years. Their underlying medical and postneurosurgical conditions are listed in tables 1 and 2. Of the 181 patients, 103 had a postneurosurgical state as the preceding event of ABM, while the other 78 had spontaneous ABM. Of the patients with spontaneous infections, diabetes mellitus (DM) was the most common underlying condition, followed by liver disease, especially liver cirrhosis, and alcoholism. Ninety-six patients had community-acquired infection while the other 85 had nosocomial infections. As to the clinical manifestations (Table 3), fever was the most common clinical manifestation, followed by altered consciousness, bacteremia, hydrocephalus, and seizure.

Table 1
Underlying medical conditions of the 181 adult bacterial meningitis cases.

	Spontaneous form (n = 78)	Postneurosurgical form (n = 103)
Diabetes mellitus	34	17
Liver disease	13	2
Alcoholism	12	4
End-stage renal disease	6	0
Malignancy	6	9
Chronic otitis media	5	1
Intravenous drug abuser	4	0
Systemic lupus erythematosis	1	1

Table 2
Neurosurgical conditions of the 103 cases with postneurosurgical adult bacterial meningitis.

Postneurosurgical conditions	Case number
s/p V–P shunt	31
s/p EVD	21
s/p Craniectomy	16
Spontaneous ICH s/p craniotomy s/p EVD	6
Head trauma s/p craniotomy	5
Head trauma	4
Traumatic ICH s/p EVD, craniectomy, V–P shunt	4
Others[a]	16

[a]One patient may have ≥ 1 neurosurgical condition; others = ICH (4), SDH (4), SAH (2), braintumor (2), EDH (1), craniotomy (5), craniectomy (3), EVD (4) and VP shunt (1); s/p: post-state; ICH: intracerebral hemorrhage; EVD: extraventricular drainage; VP shunt: ventriculoperitoneal shunt; SDH: subdural hemorrhage; EDH: epidural hemorrhage; SAH: subarachnoid hemorrhage

Table 3
Clinical manifestations of the 181 adult bacterial meningitis cases.

	Spontaneous form, n = 78 (%)	Postneurosurgical form, n = 103 (%)
Fever	70 (89.7)	90 (87.3)
Altered consciousness	51 (65.3)	57 (55)
Bacteremia	28 (35.9)	18 (17.3)
Seizure	26 (32.9)	29 (27.8)
Brain abscess	13 (16.4)	6 (5.7)
Hydrocephalus	11 (13.9)	62 (60.2)
Septic shock	6 (7.5)	9 (8.6)
Liver abscess	6 (7.5)	0 (0)
Multiple septic abscess	6 (7.5)	2 (1.9)
HHNK or DKA	5 (6.3)	3 (2.8)
Cerebral infarction	5 (6.3)	7 (6.79)
Infections endocarditis	2 (2.5)	0 (0)

HHNK: hyperosmolar hyperglycemic non-ketoacidosis; DKA: diabetic ketoacidosis

The causative pathogens of the enrolled 181 ABM cases are listed in table 4. Of these, 165 had monomicrobial infection while 16 had mixed infection. Of the 165 monomicrobial infections, Gram-negative pathogens accounted for 101 episodes and Gram-positive accounted for the other 64. Among the implicated Gram-negative pathogens, *Klebsiella* (*K.*) *pneumoniae* was the most common (42), followed by *Acinetobacter* (*A.*) *spp.* (19), *Escherichia* (*E.*) *coli (12)*, and *Pseudomonas* (*P.*) *spp.* (10). Of the implicated *Acinetobacter* spp., *A. baumannii* was the most common (18), followed by *A. lwoffii.* Of the *Pseudomonas* spp., *P. aeruginosa* was the most common (7), followed by *P. mendocina* (2), and *P. stutzeri* (1). The leading causative pathogens of spontaneous and postneurosurgical ABM were *K. pneumoniae* and staphylococcal spp., respectively. In this study, *Acinetobacter* spp. was also an important pathogen of postneurosurgical ABM. If the types of infection were considered, the case number in the age groups of 40–60 years and ≥ 60 years was about the same, while those in the age group of ≤ 40 years, most of the cases were in the postneurosurgical form.

Of the 42 cases with *K. pneumoniae* infection, 35 belonged to the spontaneous group and 7 to the postneurosurgical group. Of the former 35 cases, 24 had DM and 10 had liver disease. Of the 19 cases with *Acinetobacter* infection, 17 cases belonged to the postneurosurgical group. Of the 12 cases with *E. coli* infection, 6 were spontaneous and 6 were postneurosurgical ABM. Of the 10 cases with *Pseudomonas* infection, 6 were postneurosurgical and 4 were spontaneous ABM.

Among the Gram-positive pathogens, staphylococcal spp., including CoNS (19), and *Staphylococcus* (*S.*) *aureus* (19) were the most common, followed by viridans streptococci (8) and *Streptococcus pneumoniae* (6). All of the 19 cases with CoNS infection had a postneurosurgical condition as the preceding event and 18 of the implicated CoNS strains were methicillin-resistant. Of the 19 *S. aureus* infections, 12 were postneurosurgical and 7 were spontaneous. Nine postneurosurgical and 2 spontaneous *S. aureus* infections were methicillin-resistant strains. Despite this, all 38 staphylococcal strains still retained their susceptibility to linezolid. Of the eight viridian streptococcal infections, six were spontaneous and two were postneurosurgical. Of the six *Streptococcus pneumoniae* infections, four were spontaneous infections, while the other two were postneurosurgical.

Of the 16 cases with mixed infections, 13 were postneurosurgical and 3 were spontaneous. The implicated pathogens for mixed infections included *Pseudomonas* spp. (6), *Acinetobacter* spp. (5), CoNS (3), *K. pneumoniae* (3), *E. coli* (3), viridans streptococci (3), *Prevotella* spp. (2), *Brevundimonas dimiunda* (2), *Fusobacterium* spp. (2), *Bacteroides fragilis* (1), *Aeromonas caviae* (1), *Alcaligenes faecalis* (1), *Citrobacter diversus* (1), *Comamonas acidovorans* (1), *Enterococcus fecalis* (1), *Proteus mirabilis* (1), *Shewanella putrefaciens* (1), Gr D streptococcus (1), *Streptococcus pneumoniae* (1), and *Veillonella* spp. (1).

A comparison of the causing pathogens of this study period and those of our previous study (13.5 years, January 1986–June 1999) was done. The results showed that the leading Gram-positive pathogens of this study were CoNS (20, 10.9%), *S. aureus* (20, 10.9%), viridans streptococci (8, 4.4%), *Streptococcus pneumoniae* (6, 3.3%) and *Enterococcus* spp. (5, 2.7%), and in the previous study period, *Streptococcus pneumoniae* (19, 10.6%), *S. aureus* (15, 8.3%), viridans streptococci (13, 7.2%), CoNS (12, 6.7%), *Enterococcus* spp. (4, 2.2%). The leading Gram-negative pathogens of this study period were *K. pneumoniae* (42, 23.0%), *Acinetobacter* spp. (19, 10.4%), *E. coli* (12, 6.6%), *Pseudomonas* spp. (10, 5.5%), and

Table 4
Causative organisms of the 181 adult bacterial meningitis cases.

Pathogen	Spontaneous meningitis			Postneurosurgical meningitis		
	Age (y/o)			Age (y/o)		
	≤ 40 (n = 10)	40–60 (n = 35)	≥ 60 (n = 33)	≤ 40 (n = 28)	40–60 (n = 38)	≥ 60 (n = 37)
Gram-negative pathogens						
Klebsiella pneumoniae	3	18	14	4	2	1
Escherichia coli	1	2	3	0	5	1
Pseudomonas species	1	2	1	4	0	2
Acinetobacter species	0	1	1	4	5	8
Proteus mirabilis	0	0	2	0	0	1
Neisseria meningitides	2	0	0	0	0	0
Salmonella species	0	1	1	0	0	0
Fusobacterium nucleatum	1	0	0	0	0	0
Sphingomonas paucimobilis	0	1	0	0	0	0
Enterobacter species	0	0	0	0	1	6
Serratia marcences	0	0	0	1	0	0
Citrobacter diversus	0	0	0	0	0	1
Gram-positive pathogens						
Staphylococcus aureus	1	3	3	1	6	5
Coagulase-negative staphylococci	0	0	0	7	8	4
Viridan streptococci	0	4	2	1	1	0
Streptococcus pneumoniae	1	1	2	1	1	0
Others streptococci	0	0	0	0	1	1
Listeria monocytogenes	0	1	1	0	0	0
Enterococcus species	0	0	1	0	2	2
Corynebacterium species	0	0	0	1	0	1
Micrococcus	0	0	0	0	1	0
Mixed infections	0	1	2	4	5	4

Enterobacter spp. (7, 3.9%), and in the previous study period, *K. pneumoniae* (57, 31.6%), *Pseudomonas* spp. (20, 11.1%), *E. coli* (9, 5.0%), *Acinetobacter* spp. (6, 3.3%), and *Enterobacter spp.* (5, 2.8%).

The CSF findings of the 181 patients are listed in table 5. CSF glucose levels ranged from 1 to 235 mg/dl, total protein 4 to 2,188 mg/dl, lactate 4 to 401 mg/dl, and white blood cell (WBC) count 10 to 72,000 cells/mm^3. Blood cultures were conducted for all of the 181 cases, with positive blood culture in 46 cases. In the peripheral blood study, leukocytosis was found in 119 cases, leukopenia in 4, and thrombocytopenia in 8. The overall therapeutic results showed a mortality rate of 30.3% (55/181).

The potential prognostic factors are listed in table 5. Statistical analysis of the clinical manifestations, laboratory data, and underlying diseases between the two patient groups (fatal and non-fatal group) revealed the following significant factors: mean age (p = 0.007), presence of septic shock (p = 0.0001), type of infection (spontaneous and postneurosurgical meningitis) (p = 0.017), and CSF total protein (p = 0.014) and lactate (p = 0.007) concentration, and WBC count (p = 0.04). Variables used in logistic regression included mean age, presence of septic shock, type of infection, CSF total protein, lactate concentration, and WBC count. After analysis of the aforementioned variables, only the presence of septic shock (p = 0.004) and mean age at infection (p = 0.019) were independently associated with the therapeutic outcome. Furthermore, stepwise logistic regression analysis demonstrated a 4% increase of fatality rate per age increase and the adjusted risk of fatality for patients who had septic shock had an OR equal to 10 compared with those who did not (reference group).

Discussion

There are different epidemiologic trends of ABM between Western and Eastern countries [1, 4, 8, 9]. These differences are also observed among the different countries in the Asia [4, 6, 7, 9]. The epidemiologic trend of ABM is influenced by several factors and changes may alter the behavior of clinicians in terms of managing this potentially fatal CNS infection, especially in the choice of initial empiric antibiotics [18, 19]. When compared with the findings of our previous study [4], there has been an annual increase of ABM in recent years, from 15 (202/13.5) cases/year to 27.8 (181/6.5) cases/year. This increase may be explained by the increase of neurosurgeons and

Table 5
Prognostic factors of the 181 adult bacterial meningitis cases.

	Fatal group (N = 55)	Non-fatal group (N = 126)	OR	95% CI	p-value
Age at meningitis (year)	58.3 ± 13.0	51.9 ± 17.6			0.007
Sex					
Female	14	37	0.821	0.401–1.684	0.591
Male	41	89			
Clinical feature					
Fever	47	113	1.48	0.476–3.803	0.414
Disturbed consciousness	38	70	0.559	0.286–1.094	0.088
Seizure	19	36	0.758	0.385–1.491	0.422
Septic shock	12	3	0.087	0.024–0.325	0.0001
Hydrocephalus	21	52	1.138	0.594–2.178	0.697
DKA/HHNK	3	5	0.716	0.165–3.108	0.701
CSF leakage	2	7	1.559	0.313–7.755	0.725
Infectious endocarditis	1	1	0.432	0.027–7.034	0.517
Acquisition of infection					
Community acquired	34	62	0.598	0.313–1.142	0.118
Nosocomial acquired	21	64			
Types of infection					
Spontaneous meningitis	31	47	0.461	0.242–0.877	0.017
Postneurosurgical meningitis	24	79			
Antimicrobial therapy					
Appropriate	53	122	0.434	0.06–3.166	0.588
Inappropriate	2	2			
GCS at the time of admission	8.0 ± 4.4	10.0 ± 4.3			0.003
Underlying diseases					
Diabetes mellitus	16	35	0.938	0.465–1.89	0.857
Liver cirrhosis	7	8	0.465	0.160–1.35	0.239
Alcoholism	5	11	0.957	0.316–2.897	1
Chronic otitis media	3	3	0.423	0.083–2.164	0.37
Intravenous drug abuser	1	3	1.317	0.134–12.59	1
End-stage renal disease	5	1	0.08	0.009–0.702	0.01
Systemic lupus erythematosus	1	1	0.432	0.027–7.034	0.517
Malignancy	8	7	0.346	0.119–1.007	0.074
Peripheral blood study					
Thrombocytopenia	3	5	0.716	0.165–3.108	0.701
Bacteremia	20	26	0.455	0.226–0.915	0.025
Leukocytosis	38	81	0.805	0.409–1.587	0.531
Laboratory data at the time of admission					
Glucose (mmol/l)	2.5 ± 2.8	2.9 ± 2.5			0.161
Total Protein (g/l)	5.0 ± 4.9	2.9 ± 3.1			0.014
Lactate (mmol/l)	14.0 ± 8.2	10.3 ± 8.0			0.007
White cell count ($\times 10^6$/l)	27,106 ± 10,804	2,531 ± 6,001			0.04

GCS: Glasgow coma score; HHNK: hyperosmolar hyperglycemic nonketotic coma; DKA: diabetic ketoacidosis; OR: odds ratio; CI: confidence interval

neurologists and the subsequent expansion of their services in our hospital [25].

In this study, fever, altered consciousness, hydrocephalus, bacteremia, and seizure were the leading clinical features of ABM patients. However, these clinical manifestations were not distinct from those of our previous reports [4] or from those of other large-scale studies of ABM [1–3]. As to underlying conditions with regards to our 181 ABM cases, 56.9% had a neurosurgical condition as the preceding event. An increasing incidence (from 25% to 49% in the two study periods) of postneurosurgical conditions as the preceding event of ABM had been noted in our previous study [4]. In this study, the total case number of ABM patients with postneurosurgical conditions had outnumbered those with spontaneous infection, which may also reflect the expansion of neurological and neurosurgical services in our hospital. However, an inadequate infectious control program in the hospital may also have contributed to the development of bacterial meningitis in postneurosurgical patients [26].

Compared with our previously documented causative pathogens of ABM (1986–1999) reported in 2000 [4], changes of prevalence of causative pathogens of ABM had been noted. This study had shown that *K. pneumoniae* was still the most common pathogen of ABM, although its incidence has declined from 31.7% (57/180) to 25.5% (42/165). In Taiwan, *K. pneumoniae* has been a very common pathogen of ABM [4, 27–29] and most cases belonged to spontaneous, community-acquired infection. Therefore, its decrease in incidence could be explained by the increased number of postneurosurgical patients. Moreover, despite the decrease in incidence, 57.1% (24/42) and 23.8% (10/42) of the *K. pneumoniae* ABM patients had DM and liver disease, respectively. This high incidence of DM and liver disease among the *K. pneumoniae* ABM patients was consistent with the findings of previous reports [29–31].

In the previous study [4], *Acinetobacter* meningntis accounted for 3.3% (6/180) of monomicrobial ABM. But in this study, its incidence has increased markedly to 11.5% (19/165) and replaced *Pseudomonas* ABM as the second most common Gram-negative ABM. If only the patients with a postneurosurgical state were considered, *Acinetobacter spp.* was the most commonly implicated Gram-negative pathogen. This change has resulted in a serious challenge in the choice of empiric antibiotic in the treatment for ABM because there is a very high incidence of 3rd- or 4th-generation cephalosporin-resistant *Acinetobacter* strains [32–34]. Furthermore, 89.5% of the implicated *Acinetobacter* strains belonged to postneurosurgical infection. Therefore, the use of carbapenem as one of the initial empiric antibiotics should be highly considered in those patients with suspected postneurosurgcial ABM [33, 34]. *E. coli and Pseudomonas spp.* were the other common Gram-negative pathogens, in which 50% (6/12) and 60% (6/10) of patients, respectively, were postneurosurgical. In this study, mixed infection accounted for 8.8% (16/181) of the cases. Although polymicrobial ABM is usually seen in patients with postneurosurgical infection [23], its incidence did not increase when compared with the incidence (10.9%, 22/202) of mixed infections in our previous study [4].

As to the Gram-positive pathogens, this study showed a marked increase in the incidence of staphylococcal infection and a decrease in the incidence of *Streptococcus pneumoniae* infection. Staphylococcal *spp.* accounted for 23% (38/165) of the implicated pathogens of the monomicrobial ABM, in which 81.6% (31/38) belonged to the postneurosurgical infections, and they were also the most commonly implicated pathogen of postneurosurgical ABM. This increase can be explained by the increased number of patients with postneurosurgical state as their preceding event [26, 35, 36]. Moreover, among the implicated staphylococcal strains, 76% (29/38) were methicillin-resistant. The high incidence of methicillin-resistant staphylococcal strains noted especially in the postneurosurgical infection is a serious problem of CNS infection in Taiwan [26, 35, 36]. This has also resulted in a therapeutic challenge in the choice of initial empiric antibiotics. In facing this specific group of ABM patients, the use of linezolid should be seriously considered [37, 38].

Streptococcus pneumonia is an important leading pathogen of ABM, especially in those with spontaneous, community-acquired infection [1, 39]. In our previous study [4], *Streptococcus pneumoniae* was the most common Gram-positive pathogen of community-acquired, spontaneous ABM, accounting for 10.6% (19/180) of all monomicrobial infections. In this study, its incidence decreased, accounting only for 3.6% (6/165) of monomicrobial infections. The exact cause of this decrease is not clear, but it can be explained partially by the increase in nosocomial, postneurosurgical ABM in this study group of patients.

In this study, of ABM cases that were younger (≤ 40 years), 73.7% (28/38) had a postneurosurgical state as the preceding event of their meningitis. Therefore, most of the implicated pathogens of this age group of patients belonged to those that usually appeared in postneurosurgical ABM [22, 23, 34, 40], including CoNS, *Pseudomonas* and *Acinetobacter* spp, and mixed infections. Most of the implicated pathogens of this specific group of ABM patients have been reported to have a higher incidence of antimicrobial resistance [22, 23, 34, 41] and have also caused a therapeutic challenge.

Although the overall mortality rate (30.3%, 55/181) shown in this study was lower than that of our previous report (35.6%, 72/202) [4], ABM is still a disease of high morbidity and mortality. The causes of mortality, especially in postneurosurgical cases, are complicated. In this study, many potential prognostic factors were revealed, but only the presence of septic shock and the age at infection were able to influence the prognosis independently. Many studies have been conducted to analyze the prognostic factors of ABM patients with different preceding events, different environment of contraction, and different therapeutic regimens [17, 42–44]. The concluded prognostic factors among these studies were similar, including septic shock and age at infection.

In conclusion, more ABM cases have been identified due to the expansion of neurology and neurosurgical services, and the epidemiologic trend of ABM has changed. Patients with postneurosurgical ABM outnumbered those with spontaneous meningitis. Although the incidence of *Klebsiella* ABM decreased, *K. pneumoniae* remained the most commonly implicated pathogen. *Acinetobacter* meningntis had replaced *Pseudomonas* meningitis as the second most common Gram-negative infection. The incidence of staphylococcal infections had also increased markedly, and most of the implicated strains were methicillin-resistant. Most cases with *Acinetobacter* and staphylococcal meningitis had a postneurosurgical state as the preceding event. Lastly, these resistant strains result in a therapeutic challenge in the choice of empiric antibiotics in the initial management of ABM. Yet despite advances in antibiotic therapy, the mortality rate of this CNS infectious disease remains high. Therefore, constant epidemiologic trend analysis is needed to further improve therapeutic outcome.

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