

Risk factors associated with postcraniotomy meningitis: A retrospective study

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Abstract

Postcraniotomy meningitis (PCM) is a major challenge in neurosurgery, and changing patterns of infectious agents in PCM have been noted. The limited epidemiological data and urgent clinical needs motivated this research. We conducted this study to determine a risk assessment for PCM and the current pattern of infectious agents.

We performed a retrospective case-control study of significant cases of postcraniotomy meningitis in the Changhua Christian Hospital System between January 1, 2008, and December 31, 2012. Postcraniotomy meningitis was diagnosed in 22 out of 4392 surgical patients; this data was reviewed for risk assessment.

This study assessed the risk factors for postcraniotomy meningitis and found that it was more frequently seen in patients who were elderly (OR = 1.57, 95% CI = 1.32–2.98, $P = 0.013$), underwent emergency procedures (OR = 4.82, 95% CI = 1.50–14.53, $P = 0.008$), had leak of cerebrospinal fluid (OR = 4.62, 95% CI = 2.03–10.50, $P = 0.012$), had external ventricular drainage (OR = 4.68, 95% CI = 2.46–8.87, $P = 0.006$), were admitted to the intensive care unit (OR = 2.41, 95% CI = 1.53–8.08, $P = 0.012$), had used drain placement >72 hours (OR = 2.66, 95% CI = 1.04–4.29, $P = 0.007$), had surgery >4.5 hours (OR = 2.38, 95% CI = 1.39–4.05, $P = 0.005$), had repeat operations (OR = 2.74, 95% CI = 1.31–5.73, $P = 0.018$), endured trauma (OR = 5.97, 95% CI = 1.57–17.61, $P = 0.007$), or had 30-days mortality (OR = 5.07, 95% CI = 2.20–11.48, $P = 0.001$). The predominant pathogens isolated from cerebrospinal fluid were *Staphylococcus aureus* in 8 patients (36.7%) and *Acinetobacter baumannii* in 7 patients (31.8%). In our study, the mortality rate was 5.1% among all postcraniotomy patients.

Accurate risk assessment, early diagnosis, and choice of appropriate antibiotics in accordance with epidemiologic information are the cornerstones of reducing mortality and morbidity in PCM. The changing pattern of infectious agents in PCM over time suggests the necessity of further studies to provide the most up-to-date insight to physicians.

Abbreviations: *A baumannii* = *Acinetobacter calcoaceticus*–*Acinetobacter baumannii* complex, ABM = *A baumannii* meningitis, CCH = Changhua Christian Hospital, CCHS = Changhua Christian Hospital System, CI = confidence interval, CSF = cerebrospinal fluid, EVD = external ventricular drainage, HAI = healthcare-associated infection, OR = Odds ratio, PCM = postcraniotomy meningitis, *S aureus* = *Staphylococcus aureus*.

Keywords: *Acinetobacter baumannii*, meningitis, mortality, neurosurgery, *Staphylococcus aureus*, trauma

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1. Introduction

Postcraniotomy meningitis (PCM) is an important challenge in neurosurgery, resulting in severe morbidity and mortality.^[1–3] The rates of PCM that have been reported vary from 0.3% to 10%, and *Staphylococcus aureus* (*S aureus*) is the major pathogen.^[3–5] Some studies reveal that the rate of PCM due to *Acinetobacter calcoaceticus*–*Acinetobacter baumannii* complex (*A baumannii*) has been increasing;^[2,6–8] however, the limited epidemiological data can be perplexing for physicians, in both making accurate diagnoses and choosing effective antibiotics.

PCM results in a high mortality rate and a longer hospital stay;^[1] the most commonly isolated etiologic agents vary between Gram-negative bacilli^[1,9,10] and *S aureus*.^[3,11,12] After Mombelli's report in 1983, Gram-negative bacillary PCM related to traumatic cranial neurosurgery was more widely diagnosed.^[9] *A baumannii* has emerged as a significant nosocomial pathogen in hospitalized patients worldwide, and *A baumannii* meningitis (ABM) causes high mortality and morbidity rates.^[7,13,14] In addition, the rate of PCM due to *A baumannii* has been growing in China, Iran, and Turkey.^[2,6–8]

There have been few studies examining a risk assessment for ABM, especially those investigating the initial clinical features of patients with PMC.^[15] The limited epidemiological data and urgent clinical needs are the motivations for performing this study.

To understand the demographic features of patients with PCM, we conducted this study to determine (i) a risk assessment of PCM and (ii) the current pattern of its infectious agents in our healthcare system.

2. Materials and methods

2.1. Clinical setting and study population

The Changhua Christian Hospital System (CCHS) provides care to most of the Changhua population in Taiwan and has maintained comprehensive clinical records since 1867. Changhua Christian Hospital (CCH) is a member of the CCHS; it is an 1800-bed tertiary referral medical center located in northern Changhua County. More than 1500 craniotomies are performed in our healthcare system every year (Appendix 1, <http://links.lww.com/MD/B148>). Ours is a retrospective case-control study and included 22 patients who developed post-neurosurgical meningitis among the 4392 patients who underwent craniotomy procedures between January 1, 2008, and December 31, 2012. Case group was defined as those patients who developed postneurosurgical meningitis among the 4392 patients who underwent craniotomy procedures between January 1, 2008, and December 31, 2012. Control group was defined as those patients who did not develop meningitis among the 4392 patients who underwent craniotomy procedures between January 1, 2008, and December 31, 2012.

2.2. Case findings and the validity and reliability of methods

Cases of post-craniotomy meningitis were identified from microbiological databases and medical records at CCH in central Taiwan, using the International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM). We used computerized indices to find cases with the following ICD-9-CM codes: 320–324, 326, 038, 038.11, 038.19, 785.59, and procedures involving operation of the nervous system (01.21–01.25, 01.28). We performed a small-scale validity study on our case-finding procedures. We examined the reliability of our case-finding procedure by randomly selecting 20 records of potential cases and having them reviewed independently by 2 infectious disease specialists (CCH and CCY).

2.3. Definitions

The diagnosis of meningitis was based on the following inclusion criteria: a micro-organism must have been isolated either from cerebrospinal fluid (CSF) cultures or from blood cultures taken during the initial diagnostic workup; clinical presentation with acute new onset of fever, headache, stiff neck, meningeal signs, cranial nerve signs, irritability, or turbid CSF in drainage bag; elevated white blood cell count and elevated CSF protein and/or decreased glucose; and organisms seen on Gram stain of CSF. The exclusion criteria were incomplete data; inconsistency between the data from the ICD-9 code and the clinical dataset; and diagnosis of a CNS infection, brain abscess, or meningitis on the first neurosurgical day. The definition of surgical site infection (SSI) was based on Centers for Disease Control and Prevention/National Healthcare Safety Network surveillance definitions.^[16] Polymicrobial meningitis was considered when the etiology was >1 pathogen. We only considered the predominant culturable pathogen of each case when performing statistical analysis. The disease incidence was calculated by considering the entire

admitted patient population of CCH that was at risk for infection. Recurrent meningitis was considered when the patient had >1 episode of meningitis, and only the first episode of PCM in each patient during the study period was included in the statistical analysis. Mortality was defined as the patients with PCM who died within 30 days after diagnosis of PCM. The effective duration of antibiotics was based on clinical presentation and microbiological susceptibility tests. The relationship between a patient's mortality and postoperative meningitis was based on clinical presentation and laboratory data.

2.4. Patient care and protocol for patients with suspected meningitis

All surgical patients received prophylactic antibiotics (cefazolin) before the induction of anesthesia. Lumbar puncture was performed in all patients who did not have external ventricular drainage (EVD) or lumbar drainage and were suspected to have postoperative meningitis. CSF and blood cultures were taken at the same time. Infection of other sites was excluded by taking various cultures. All isolates were routinely examined at the medical laboratory department of CCH and were routinely stored at the bacterial bank of CCH during the study period. The Vitek 2 System (BioMerieux, Marcy l'Etoile, France) was used to identify the phenotype of isolates. Antimicrobial susceptibility was determined using the automated Vitek 2 (BioMerieux) according to the recommendations of the clinical and laboratory standards institute.^[17]

2.5. Statistical analysis

Descriptive statistics were calculated using SPSS version 17.0 for Windows (SPSS Inc., Chicago, IL) in order to analyze the case characteristics and laboratory parameters for each group. The demographic data and clinical characteristics were compared by using the χ^2 test or Student's *t*-test when appropriate. Results were analyzed using the χ^2 test. The multivariate analysis model was used to evaluate the risk factors that affected mortality and were significant according to univariate analysis. Odds ratio (OR) with 95% confidence interval (CI) was calculated. A 2-sided test with a *P* value < 0.05 was considered as statistically significant.

3. Results

3.1. Demographics of postcraniotomy patients

The study flowchart showing the selection of subjects during the study period is shown in Fig. 1. During the study period, PCM was diagnosed in 22 out of 4392 (1.4%) surgical patients (Table 1). The period prevalence of PCM in CCHS was 134.4 ± 76.8 per 100,000 patient-years. The incidence of PCM was 1.4% among 4392 surgical patients in CCHS. A total of 3455 (3455/4392, 78.7%) patients were male and the mean age [\pm SD] was 45 ± 13.8 years. The craniotomies were performed as emergency procedures in 2524 (72.3%) patients. In total, 1256 (28.6%) patients had EVD, and 1160 (26.4%) patients were admitted to the intensive care unit (ICU). The median period from admission to diagnosis of PCM was 10.5 ± 2.1 days (range, 2–30 days). The mean hospitalization duration was 18.6 ± 3.1 days (range, 2–69 days) and the mean postcraniotomy hospitalization duration was 6.32 ± 1.5 days (range, 1–35 days). The overall mortality rate of patients who received craniotomy was 5.5% (242/4392).

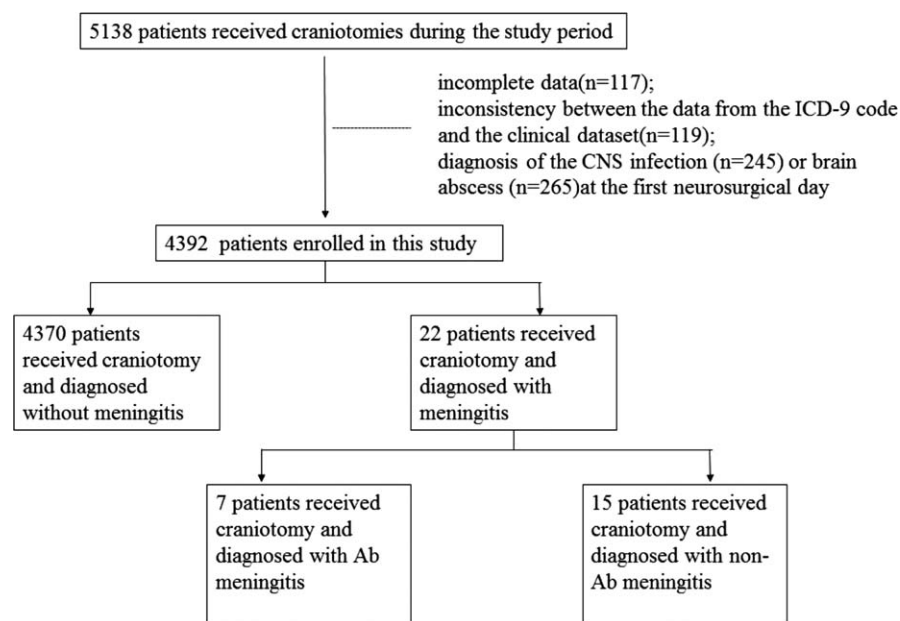


Figure 1. Study flowchart showing the selection of subjects.

3.2. Comparison of postcraniotomy meningitis

The variables used to compare patients with PCM to patients without PCM in the univariate analysis are listed in Table 1. Factors with a *P* value of < 0.05 included age >65 years (OR = 1.57, 95% CI=1.32–2.98, *P*=0.013), emergency procedure (OR=4.82, 95% CI=1.50–14.53, *P*=0.008), CSF leak (OR = 4.62, 95% CI=2.03–10.50, *P*=0.012), EVD (OR=4.68, 95% CI=2.46–8.87, *P*=0.006), ICU admission (OR=2.41, 95% CI=1.53–8.08, *P*=0.012), duration of drain placement longer than 72 hours (OR=2.66, 95% CI=1.04–4.29, *P*=0.007), surgery duration longer than 4.5 hours (OR=2.38, 95% CI=1.39–4.05, *P*=0.005), repeat operations (OR=2.74, 95% CI=1.31–5.73, *P*=0.018), trauma (OR=5.97, 95% CI=1.57–17.61, *P*=0.007), and 30-days mortality (OR=5.07, 95% CI=2.20–11.48, *P*=0.001).

Six patients who had traumatic head injury and received a craniotomy suffered from meningitis; 3 of these had mixed

pathogens and the predominant bacteria of those mixed pathogens were analyzed in this study. The predominant pathogens among those 6 head injury patients with postcraniotomy meningitis were *A baumannii* in 5 and *S aureus* in 1.

3.3. Demographics of patients with postcraniotomy meningitis

Twenty-two (0.5%) patients had PCM. The 5-year longitudinal analysis of HAI, SSI, total number of craniotomies, and total number of PCM during the study period is shown in Fig. 2. Seven of 22 PCM patients did not meet the criteria of SSI because they had open wounds on admission. Fever was observed in 15 (68.2%) patients. There was CSF leak in 15 (68.2%) patients. Four (18.2%) patients had bacteremia. Nineteen (86.4%) patients had leukocytosis with left shift and 19 (86.4%) patients had elevated C-reactive protein at the initial assessment. CSF cell count was >5 elements/mm³ in 22 (100%) examinations. The

Table 1
Demography and clinical characteristics of patients who received postcraniotomy operation between those with meningitis and those without meningitis.

Parameters	Total (n=4392)	Meningitis		<i>P</i> *	OR (95% CI)	<i>P</i> †
		With (n=22) Case	Without (n=4370) Control			
Elderly, age >65 y	1821 (41.7)	15 (68.2)	1806 (41.4)	0.012	1.57 (1.32–2.98)	0.013
EP	2524 (72.3)	16 (72.7)	2508 (72.9)	0.007	4.82 (1.50–14.53)	0.008
CSF leakage	1822 (41.5)	15 (68.2)	1807 (41.4)	0.011	4.62 (2.03–10.50)	0.012
EVD	1256 (28.6)	12 (54.5)	1244 (28.5)	0.007	4.68 (2.46–8.87)	0.006
ICU admission	1160 (26.4)	11 (50)	1149 (26.3)	0.012	2.41 (1.53–8.08)	0.012
DR > 72 h	993 (22.6)	13 (59.0)	980 (28.5)	0.008	2.66 (1.04–4.29)	0.007
SD (h)>4.5	312 (7.1)	6 (27.3)	306 (8.9)	0.006	2.38 (1.39–4.05)	0.005
ROs	565 (12.9)	7 (31.8)	558 (12.8)	0.017	2.74 (1.31–5.73)	0.018
Trauma	351 (8.0)	6 (27.3)	345 (7.9)	0.006	5.97 (1.57–17.61)	0.007
30-d mortality	242 (5.5)	6 (27.3)	236 (5.4)	0.001	5.07 (2.20–11.48)	0.001

Data presents with number with percentage (parenthesis), n (%).

CSF = cerebrospinal fluid, DR = drain placement (external ventricular drainage, lumbar drainage), EP = emergency procedure, EVD = external ventricular drainage, ICU = intensive care unit, OR = odds ratio, ROs = repeat operations, SD = surgery duration, 95% CI = 95% confidence interval.

* *P* value between those with meningitis and those without meningitis.

† *P* value for odds ratio.

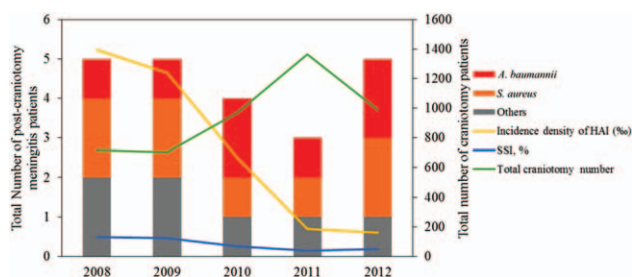


Figure 2. The correlation among healthcare-associated infection, surgical site infection, and total craniotomy number and total postcraniotomy meningitis during the study period.

CSF protein level was $>500\text{mg/dL}$ in 6 (27.2%) cases, and the ratio of CSF glucose level to serum glucose was <0.5 in 19 (86.4%) examinations.

The pathogens isolated from CSF were *S aureus* in 8 patients (36.7%), *A baumannii* in 7 patients (31.8%), *P aeruginosa* in 2 patients (9.1%), *K pneumoniae* in 2 patients (9.1%), *E cloacae* in 1 patient (4.5%), *E coli* in 1 patient (4.5%), and *E faecalis* in 1 patient (4.5%). Six (75%) of 8 *S aureus* isolates were methicillin resistant. The median time from diagnosis to effective treatment (treatment with antibiotics to which the organisms were susceptible) was 3.2 ± 0.6 days (range, 1–5 days) during the empirical therapy. All patients received appropriate antibiotic therapy based on susceptibility tests. Among patients with ABM, carbapenem with colistin was used in 5 patients (71.4%) and ceftriaxone with colistin was used in 2 (28.6%). Two (28.6%) of the patients with ABM died. Four of them were given meropenem treatment. For *K pneumoniae* meningitis, ceftriaxone was used in 2 patients. Vancomycin was given to patients with methicillin-resistant *S aureus* ($n=6$) and *E faecalis* ($n=1$). One (16.7%) of the 6 patients with methicillin-resistant *S aureus* meningitis died.

Of the 22 patients with PCM, 14 (63.6%) of the patients had at least 1 concurrent HAI. The distribution of these infections were as follows: SSI in 15 patients (68.2%), pneumonia in 4 (28.6%), bacteremia in 4 (28.6%), urinary tract infection in 2 (14.3%), and central venous catheter-related infection in 1 (7.1%). Of the 22 patients with PCM, 6 (27.3%) died. Of the 6 patients who died, 5 (83.3%) had ABM. The clinical information for ABM is listed in Appendix 2, <http://links.lww.com/MD/B148>.

4. Discussion

4.1. Risk assessment for PCM

This study assessed the risk factors for PCM. PCM was more frequently seen in patients who had the following risk factors: old age, emergency procedure, CSF leak, EVD, ICU admission, duration of drain placement >4.5 hours, surgery duration >4.5 hours, repeat operations, and trauma. In our study, the 30-day mortality rate of 22 PCM patients was 0.14 % among 4392 postcraniotomy patients.

In our study, the period prevalence of PCM in CCHS was 134.4 ± 76.8 per 100,000 patient-years and the incidence of PCM was 1.4% among 4392 surgical patients in CCHS. The reported incidence of PCM is quite variable in the literature, ranging from 0.5% to 5.5%.^[3,8,12,18] The incidences of PCM in studies by Kourbeti et al (5.5%)^[18] and Srinivas et al (2.2%)^[12] were remarkably higher than in our study (1.4%). The reasons for the lower incidence of PCM in our study included prophylactic

antibiotics given to all patients after the surgery, few SSI events, few traumatic patients, the low use of drainage, and the low number of trans-sphenoidal surgeries. Although the risk factors for PCM are well established, it is nearly impossible to reach the goal of zero HAIs in clinical practice. PCM is still a threat in daily practice. Physicians must pay attention to PCM as it can result in severe morbidity and mortality.^[1–3]

4.2. Changing patterns in pathogens of post-traumatic patients with PCM

This study showed that AMB emerged among post-traumatic patients with PCM. Many studies have described that HAI and postneurosurgical ABM are becoming increasingly more common.^[6,8,9,13,19–23] In the present study, the most commonly isolated agents for PCM were *A baumannii* and *S aureus*, and there was no institutional outbreak of these organisms in CCHS during the study period. The predominance of these PCM pathogens may be related to global emergence. *A baumannii* has emerged as an important healthcare-associated pathogen because it can survive a wide range of environmental conditions and persist for.^[24,25] And, the extensive use of medical equipment in modern institutes has contributed to the emergence of *A baumannii* as a predominant pathogen.^[24,25] An increase of *A baumannii* colonization and infection results from skin or wound colonization, invasive procedures, entry through traumatic wounds, or a type of predominant cluster. In our results, *S aureus* was still the most common pathogen in patients with PCM, but we emphasize that physicians should also consider *A baumannii* when caring for PCM patients.

4.3. Considerations for post-traumatic patients with PCM

In our study, 6 of 22 (27.37%) patients with PCM died. Of the 6 patients who died, 5 (83.3%) had ABM. Five (71.4%) of 7 ABM patients had a history of traumatic injury and died. Regarding the risk factor of traumatic head injury in ABM, there has been a remarkable increase in the incidence of *A baumannii*.^[18,24–26] In this study, we found 8 patients with postcraniotomy *S aureus* meningitis and 7 with postcraniotomy ABM, six of whom suffered from traumatic head injuries. However, the predominant pathogens among patients with PCM in this study were different from those of other studies.^[6,8,9,13,19–23,27] The reasons for this could be due to multiple factors, including geographic difference, local predominant epidemiological features, population, and compliance with infection control guidelines. Thus, we concluded that post-traumatic patients were easily susceptible to *A baumannii* and *S aureus* infection. Because the clinical symptoms of ABM vary and some of causative pathogens include multiple-drug resistant *A baumannii*, it is very important to determine the most effective antibiotic strategy as well as ensure accurate and effective diagnosis and treatment of ABM. Physicians should be alert to the changing patterns of infectious agents in specific individuals with PCM, and promptly prescribe accurate antibiotics at the initial stages.

The present study has several strengths. The most important strength was that we accumulated a complete longitudinal dataset covering 5 years. We had access to excellent data for evaluating the demographic features of PCM and ABM. Secondly, patients with culture positive meningitis were included for analysis, so our results have representational faithfulness. Thirdly, >1500 craniotomies are performed in our healthcare system annually (Appendix 1, <http://links.lww.com/MD/B148>),

and this ensures that we have enough power in our analysis. Overall, the present findings provide invaluable epidemiological information about PCM in central Taiwan.

Nevertheless, this study has several limitations. The individual effect of each intervention was not evaluated, because interventions were performed either individually and simultaneously or sequentially according to the complexity of the clinical conditions. Moreover, compliance with the various measures for infection control during the study period could not be verified because part of study was performed retrospectively, and only the patients with culturable pathogens were enrolled and analyzed. However, these cases are not likely to constitute a large proportion of PCM cases. As this is a retrospective study, history information on antibiotics was possibly inaccurate for the numerous patients who had received antibiotics within 1 month prior to their PCM episode. Due to a lack of adequate workforce, the defined daily doses of the some antibiotics administered during the study period could not be calculated. In addition, we did not perform molecular typing of *A baumannii* isolates owing to no evidence of an outbreak during the study period. Further causal relationship studies and nationwide studies are necessary to elucidate ABM among patients with PCM.

5. Conclusion

In conclusion, PCM should be suspected in patients with new onset fever or unexplained deterioration in neurologic status. Early diagnosis and choice of appropriate antibiotics according to epidemiologic information are the cornerstones of reducing mortality and morbidity. Along with *S aureus*, we found a high rate of PCM due to *A baumannii* among patients with traumatic head injury. The choice of empirical therapy for post-traumatic patients with suspected PCM should cover *S aureus* and *A baumannii*. The changing pattern of infectious agents in PCM over time suggests the necessity of other studies to give the most up-to-date insight to physicians.

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