MAJOR ARTICLE

Clinical Characteristics and Predictors of Adverse Outcome in Adult and Pediatric Patients With Healthcare-Associated Ventriculitis and Meningitis

Chanunya Srihawan,[1] Rodrigo Lopez Castelblanco,[1] Lucrecia Salazar,[1] Susan H. Wootton,[2] Elizabeth Aguilera,[2] Luis Ostrosky-Zeichner,[1] David I. Sandberg,[3,4] HuiMahn A. Choi,[3,5] Kiwon Lee,[3,5] Ryan Kitigawa,[3,5] Nitin Tandon,[3,4,5] and Rodrigo Hasbun[1]

[1]Department of Internal Medicine, University of Texas Health Science Center at Houston; Departments of [2]Pediatrics, [3]Neurosurgery, [4]Pediatric Surgery, University of Texas Health, and [5]Mischer Neuroscience Institute, Memorial Hermann Hospital, Texas Medical Center, Houston

Background. Healthcare-associated meningitis or ventriculitis is a serious and life-threatening complication of invasive neurosurgical procedures or penetrating head trauma.

Methods. We performed a retrospective study of adults and children with the diagnosis of healthcare-associated meningitis or ventriculitis, as defined by the 2015 Centers of Disease Control and Prevention case definition, at 2 large tertiary care hospitals in Houston, Texas from July 2003 to November 2014. Patients were identified by infection control practitioners and by screening cerebrospinal fluid samples sent to the central laboratory. We collected data on demographics, clinical presentations, laboratory results, imaging studies, treatments, and outcomes.

Results. A total of 215 patients were included (166 adults and 49 children). A positive cerebrospinal fluid culture was seen in 106 (49%) patients, with the majority of the etiologies being *Staphylococcus* and Gram-negative rods. An adverse clinical outcome was seen in 167 patients (77.7%) and was defined as death in 20 patients (9.3%), persistent vegetative state in 31 patients (14.4%), severe disability in 77 patients (35.8%), or moderate disability in 39 patients (18.1%). On logistic regression analysis, age $\geq$45 years (adjusted odds ratio [OR], 6.47; 95% confidence interval [CI], 2.31–18.11; $P \leq$ .001), abnormal neurological exam (adjusted OR, 3.04; 95% CI, 1.27–7.29; $P =$ .013), and mechanical ventilation (adjusted OR, 5.34; 95% CI, 1.51–18.92; $P =$ .01) were associated with an adverse outcome.

Conclusions. Healthcare-associated meningitis or ventriculitis is associated with significant morbidity and mortality.

Keywords. healthcare-associated meningitis; prognosis; risk factors; ventriculitis.

Healthcare-associated meningitis or ventriculitis are serious complications of invasive neurosurgical procedures (eg, craniotomy, placement of internal or external ventricular catheters, intrathecal infusions, spinal anesthesia, or lumbar puncture) or may occur after penetrating head trauma [1].

Early diagnosis of healthcare-associated meningitis remains challenging. Clinical symptoms may be nonspecific and are difficult to distinguish from the underlying neurological disease or postsurgical-related condition, and no standard diagnostic guidelines are available. Although the incidence of meningitis and ventriculitis has been declining, morbidity and mortality rates in patients who do develop these infections patients remain high. Although Gram-positive pathogens, such as coagulase

negative *Staphylococcus*, remain the most common cause [2–4], the increasing incidence of Gram-negative organisms and other multidrug-resistant pathogens have complicated the management of these infections. The goal of our study was to identify risk factors for adverse clinical outcomes among patients with healthcare-associated meningitis or ventriculitis.

PATIENTS AND METHODS

Study Population

The study was conducted at Memorial Hermann Texas Medical Center and Children's Memorial Hermann Hospital, both tertiary care hospitals and primary teaching sites for the University of Texas McGovern Medical School in Houston, Texas. From July 2003 to November 2014, all adult and pediatric patients with possible healthcare-associated meningitis or ventriculitis were screened by infection control practitioners; in addition, from February 2010 until November 2014, all cerebrospinal fluid (CSF) samples sent to the laboratory were screened. Those patients who met the 2015 Centers of Disease Control and Prevention (CDC)'s National Healthcare Safety Network (NHSN) surveillance definition [5] were retrospectively reviewed.

Definition

In accordance with the 2015 CDC/NHSN definition, healthcare-associated meningitis or ventriculitis was defined as either a patient with positive CSF culture or a patient with at least 2 signs and symptoms (fever >38.0 °C, headache, meningeal or cranial nerve signs) along with at least 1 of the following: abnormal CSF analysis (increased white cells, elevated protein, and decreased glucose in CSF per reporting laboratory's reference range); organisms seen on CSF Gram stain; organisms cultured from blood; positive nonculture diagnostic laboratory test of CSF, blood, or urine; or diagnostic single antibody titer (immunoglobulin [Ig]M) or 4-fold increase in paired sera (IgG) for organism. Among patients ≤1 year of age, the definition is similar except that signs include fever >38.0°C, hypothermia <36.0°C, apnea, bradycardia, or irritability [5].

Data Collection

A predesigned, standard case report form was used. Inpatient electronic medical records were retrospectively reviewed to extract the following data: demographic information, comorbidities, immune status, procedures before diagnosis of meningitis or ventriculitis, recent neurosurgical procedure(s), signs and symptoms at presentation, Glasgow Coma Scale (GCS), laboratory tests, imaging studies, treatments received during hospitalization, and clinical outcomes at the time of discharge from hospital or death using the Glasgow outcome scale (GOS). The GOS categories were as follows: 1 = death, 2 = persistent vegetative state, 3 = severe disability (defined as partially or totally dependent on assistance from others in daily living), 4 = moderate disability (defined as independent and can resume almost all activities in daily living, but disabled to the extent that they cannot participate in a variety of social and work activities), and 5 = good recovery. Adverse clinical outcomes were defined as GOS of 1 to 4.

Statistical Analysis

Bivariate analyses to identify variables associated with adverse clinical outcomes were conducted by Pearson χ^2 or Fisher's exact test. All significant variables ($P < .05$) were then evaluated in multivariate logistic regression model to identify risk factors related to adverse clinical outcomes. Bootstrapping was performed to validate the regression model. All statistical analyses were conducted using IBM SPSS program, version 21.

RESULTS

Demographic and Clinical Characteristics

Our study included 215 patients: 166 adults and 49 children. The demographic, clinical, and laboratory characteristics are shown in Table 1. The median age was 45 years old (range, 0.17–87 years), and 115 patients (53.5%) were male. The 2 most common indications for neurosurgical procedures were hemorrhage (49.3%), predominantly subarachnoid hemorrhage, and hydrocephalus (48.4%). The majority of patients had altered mental status with 148 patients (68.8%) having a GCS ≤14 and 33 patients

Table 1. Demographic, Clinical, and Laboratory Characteristics of 215 Adult and Pediatric Patients With Healthcare-Associated Meningitis or Ventriculitis

Characteristics	No. (%)
Median age (years, range)	45 (0.17–87)
Male sex	115 (53.5)
Race	
White	97 (45.1)
Hispanic	56 (26.1)
African American	42 (19.5)
Other	20 (9.3)
Immunocompromised state[a]	15 (7.0)
Indication for neurosurgical procedure	
Hemorrhage[b]	106 (49.3)
Subarachnoid	61 (28.4)
Intraventricular	43 (20.0)
Intracerebral	29 (13.5)
Hydrocephalus	104 (48.4)
Trauma	38 (17.7)
Brain tumor	24 (11.2)
Unknown	2 (0.9)
Fever (temperature >100.4°F)	87 (40.5)
Glasgow Coma Scale	
GCS ≤ 14[c]	148 of 212 (69.8)
GCS < 8[d]	33 of 212 (15.5)
Neurological signs and symptoms[e]	
Headache	63 of 130 (48.5)
Changes in mental status	69 of 170 (40.6)
Nausea/vomiting	62 of 157 (39.5)
Focal neurological deficit	61 of 184 (33.2)
Neck stiffness	23 of 123 (18.7)
Seizures	20 of 192 (10.4)
Photophobia	6 of 93 (6.5)
VP shunt placement	64 (29.8)
CSF leak[f]	46 (21.4)
Had EVD placement	175 (81.4)
Median duration (days, range)	8.5 (1–30)
ICU admission	153 (71.2)
Mechanical ventilation	93 (43.3)
Median duration (days, range)	9 (1–35)
Empirical antibiotics	200 (93.0)
Antibiotics initiated before CSF analysis	109 (50.7)
Steroids	40 (18.6)
CSF analysis (median, range)	
Leukocytes (per mm^3)	272 (0–34750)
Glucose (mg/dL)	49 (1–121)
Protein (mg/dL)	131 (14–1774)
Lactate (mmol/L)	4.65 (1–22.8)
Peripheral leukocytes (per mm^3, median, range)	12.8 (3.6–48.7)
Positive CSF Gram stain	43 of 215 (20.0)
Positive CSF culture	106 of 215 (49.3)
Positive blood cultures	7 of 176 (3.9)

Abbreviations: AIDS, acquired immunodeficiency syndrome; CSF, cerebrospinal fluid; EVD, external ventricular drain; GCS, Glasgow Coma Scale; HIV, human immunodeficiency virus; ICU, intensive care unit, VP, ventriculoperitoneal.

[a] Patients with HIV, AIDS, recent chemotherapy (<1 month), solid organ or bone marrow transplantation, receiving steroids ≥20 mg of prednisone or equivalent for >1 month, congenital immunodeficiency.

[b] Some patients had more than 1 type of hemorrhage.

[c] Indicative of altered mental status.

[d] Indicative of coma.

[e] Results shown as number of positive/total number of documented signs and symptoms (%).

[f] Cerebrospinal fluid leak was defined as patients who had otorrhea, rhinorrhea, or imaging studies of brain/spines revealed traumatic or operative defect associated with focal fluid accumulation. The CSF leak was evaluated and documented in medical records by the neurosurgeons.

(15.4%) presenting in coma (GCS <8) at the time of diagnoses. A total of 40.5% of patients were febrile (temperature >38.0 °C or 100.4 °F), 48.5% of patients reported a headache, and 39.5% of patients had nausea or vomiting. Additional signs included focal neurological deficits (33.2%), neck stiffness (18.7%), seizures (10.4%), and photophobia (6.5%).

An external ventricular drain (EVD) was placed at the time of diagnosis in 175 patients (81.4%) with a mean duration of EVD placement of 8.5 days (range, 1–30 days). A CSF leak was seen in 46 (21.4%) patients. The majority of patients (153, 71.2%) were treated in the intensive care unit (ICU), and 60% of them required mechanical ventilation with mean duration of 9 days (range, 1–35 days). Empiric antibiotics were administered in 93% of patients, and half of them received the treatments before CSF samples were obtained. The median CSF white blood cell count was 272/mm^3 (range, 0–34 750/mm^3), the median CSF glucose was 49 mg/dL (range, 1–121 mg/dL), the median CSF protein was 131 mg/dL (range, 14–1774 mg/dL), and the median CSF lactate was 4.65 mmol/L (range, 1–22.8 mmol/L). A CSF glucose <40 mg/dL and a CSF protein ≥100 mg/dL were found in 78 patients (36.3%) and 135 patients (64%), respectively. A positive CSF culture was seen in 106 patients (49.3%), but Gram stain showed the organisms in only 20%. Only 7 patients (3.3%) had concurrent bacteremia.

Microbiological Findings

Gram-positive organisms were isolated in 67% of patients, and the most common pathogens were coagulase-negative *Staphylococcus* (30.2%) followed by *Staphylococcus aureus* (19.8%), *Streptococcus* species (10.4%), *Enterococcus* species (5.7%), and *Propionibacterium acnes* (0.9%). Gram-negative organisms accounted for 30.2%, as shown in Table 2. *Candida* species was found in 1 patient, and 2 patients had polymicrobial infections.

Clinical Outcomes and Risk Factors

As demonstrated in Table 3, 78% of patients had an adverse clinical outcome at the time of discharge. Twenty patients (9.3%) died, 31 (14.4%) had a persistent vegetative state, 77 (35.8%) had severe disability, and 39 (18%) had moderate disability. A good recovery was seen in 48 patients (22.3%), 30 (62.5%) of whom were pediatric patients. Bivariate analysis identified age ≥45 years (odds ratio [OR], 11.39; 95% confidence interval [CI], 4.58–28.35; P < .001), central nervous system (CNS) hemorrhage (OR, 4.37; 95% CI–2.21, 8.62; P < .001), abnormal neurological exam (OR, 6.51; 95% CI, 3.23–13.13; P < .001), ICU admission (OR, 5.81; 95% CI, 2.90–11.62; P < .001), and mechanical ventilation (OR, 12.59; 95% CI, 4.32–36.68; P < .001) to be associated with a higher risk of having an adverse clinical outcome. Having a ventriculoperitoneal (VP) shunt-associated infection (OR, 0.17; 95% CI, .08–.33; P < .001) was associated with a lower risk of having adverse clinical outcomes. There were no significant differences in sex, race, immune status, or CSF parameters (Table 4). On logistic regression analysis, there

Table 2. Microbiological Data of Patients Who Had Positive CSF Cultures (n = 106)

Pathogen	No. (%)
Gram-positive organisms	71 (67.0)
Coagulase-negative *Staphylococcus*	32 (30.2)
Staphylococcus aureus	21 (19.8)
MSSA	9 (8.5)
MRSA	12 (11.3)
Streptococcus species[a]	11 (10.4)
Enterococcus species	6 (5.7)
Propionibacterium acnes	1 (0.9)
Gram-negative organisms	32 (30.2)
Pseudomonas species[b]	11 (10.4)
Enterobacter cloacae	7 (6.6)
Serratia marcescens	6 (5.7)
Klebsiella species[c]	5 (4.7)
Acinetobacter baumanii	2 (1.9)
Escherichia coli	1 (0.9)
Candida species	1 (0.9)
Mixed infection[d]	2 (1.9)

Abbreviations: CSF, cerebrospinal fluid; MRSA, methicillin-resistant *Staphylococcus aureus*; MSSA, methicillin-sensitive *S aureus*.

[a] Ten patients with α-hemolytic *Streptococcus* (not *Streptococcus pneumoniae* or *Enterococcus*), 1 patient with Group B *Streptococcus*.

[b] Ten patients with *Pseudomonas aeruginosa*, 1 patient with *Pseudomonas fluorescens*.

[c] Four patients with *Klebsiella pneumoniae*, 1 patient with *Klebsiella oxytoca*.

[d] One patient had CSF culture grew *K pneumoniae* and *Enterobacter cloacae*, another patient with *Escherichia coli* and *Serratia marcescens*.

were only 3 variables that remained associated with adverse outcomes: age ≥45 years (OR, 6.47; 95% CI, 2.31–18.11; P < .001), abnormal neurological exam (OR, 3.04; 95% CI, 1.27–7.29; P = .013), and mechanical ventilation (OR, 5.34; 95% CI, 1.51–18.92; P = .010), as shown in Table 5. Bootstrapping analysis internally validated these 3 variables.

DISCUSSION

The incidence of healthcare-associated meningitis or ventriculitis ranges from 1% to 23% [3, 6–11]. A 2011 survey of healthcare-associated infections conducted in 183 US hospitals ranked CNS infections as 11th with an incidence of 0.8% (5800 reported cases annually; 95% CI, 700–20 700) [12]. The wide variation

Table 3. Clinical Outcomes of 215 Adult and Pediatric Patients With Healthcare-Associated Meningitis or Ventriculitis

Glasgow Outcome Scale	No. (%)
Death	20 (9.30)
Persistent vegetative state	31 (14.42)
Severe disability[a]	77 (35.81)
Moderate disability[b]	39 (18.14)
Good recovery	48 (22.33)

[a] Defined as partially or totally dependent on assistance from others in daily living.

[b] Defined as independent and can resume almost all activities in daily living but disabled to the extent that they cannot participate in a variety of social and work activities.

Table 4. Bivariate Analysis of Baseline Variables and Adverse Outcomes[a] in Healthcare-Associated Meningitis or Ventriculitis (n = 215)

Variables	Total No.	Adverse Outcomes,[a] No. (%)	Odds Ratio (95% CI)	P Value
Demographic data				
Age ≥45 y	111	105 (94.6)	11.39 (4.58–28.35)	<.001
Male sex	115	95 (82.6)	0.54 (.28–1.04)	.072
Non-white	118	88 (74.6)	0.67 (.35–1.29)	.253
Immunocompromised state[b]	15	10 (66.7)	0.55 (.18–1.67)	.335
Clinical signs and symptoms				
CNS bleeding	140	122 (87.1)	4.37 (2.21–8.62)	<.001
Hydrocephalus	104	77 (74.0)	0.67 (.35–1.29)	.254
Headache	63	43 (68.3)	0.52 (.23–1.16)	.113
Seizure	20	15 (75.0)	0.79 (.27–2.33)	.773
Abnormal neurological exam[c]	156	137 (87.8)	6.51 (3.23–13.13)	<.001
CSF leakage	46	32 (69.6)	0.58 (.28–1.20)	.162
Had VP shunt placement	64	35 (54.7)	0.17 (.08–0.33)	<.001
Laboratory investigations				
CSF protein ≥100 mg/dL	135	109 (80.7)	1.60 (.83–3.10)	.171
CSF glucose <40 mg/dL	78	55 (70.5)	0.52 (.27–1.01)	.060
Positive CSF Gram stain	43	34 (79.1)	1.07 (.47–2.42)	1.000
Positive CSF culture	106	84 (79.2)	0.79 (.41–1.50)	.514
Positive blood culture	7	6 (85.7)	2.32 (.28–19.37)	.681
Management				
EVD placement	157	129 (82.2)	2.26 (.85–6.00)	.104
ICU admission	153	134 (87.6)	5.81 (2.90–11.62)	<.001
Mechanical ventilation	93	89 (95.7)	12.59 (4.32–36.68)	<.001
Empirical antibiotics	200	156 (78.0)	1.29 (.39–4.25)	.748
Steroids	40	29 (72.5)	0.78 (.35–1.74)	.536

Abbreviations: AIDS, acquired immunodeficiency syndrome; CI, confidence interval; CNS, central nervous system; CSF, cerebrospinal fluid; EVD, external ventricular drain; HIV, human immunodeficiency virus; ICU, intensive care unit; VP, ventriculoperitoneal.

[a] Defined according to Glasgow Outcome Scale of 1 (death), 2 (persistent vegetative state), 3 (severe disability), or 4 (moderate disability).

[b] Patients with HIV, AIDS, recent chemotherapy (<1 month), solid organ or bone marrow transplantation, receiving steroids ≥20 mg of prednisone or equivalent for >1 month, congenital immunodeficiency.

[c] Defined as patients with either focal neurological deficit or Glasgow Coma Scale ≤14, which is indicative of altered mental status.

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of incidence may relate to the variety of diagnostic criteria used in each study [13]. Most studies required only positive CSF cultures, whereas others include cultures and CSF abnormalities (pleocytosis, hypoglycorrhachia, or elevated protein) [14]. Given the heterogeneous diagnostic criteria, we used the 2015

Table 5. Logistic Regression Analysis of Baseline Variables and Adverse Outcomes[a] in Healthcare-Associated Meningitis or Ventriculitis (n = 215)

Variables	Odds Ratio (95% CI)	P Value[b]
Age ≥45 y	6.47 (2.31–18.11)	<.001
CNS bleeding	1.05 (.41–2.65)	.926
Abnormal neurological exam[c]	3.04 (1.27–7.29)	.013
Had VP shunt placement	0.59 (.24–1.47)	.260
ICU admission	1.33 (.50–3.51)	.569
Mechanical ventilation	5.34 (1.51–18.92)	.010

Abbreviations: CI, confidence interval; CNS, central nervous system; ICU, intensive care unit; VP, ventriculoperitoneal.

[a] Defined according to Glasgow Outcome Scale of 1 (death), 2 (persistent vegetative state), 3 (severe disability), or 4 (moderate disability).

[b] All variables validated by Bootstrap (P < .05).

[c] Defined as patients with either focal neurological deficit or Glasgow Coma Scale ≤14, which is indicative of altered mental status.

CDC/NHSN surveillance definition for healthcare-associated meningitis or ventriculitis.

Approximately half (49%) of patients in this cohort had positive CSF cultures for diagnosis. Gram stain was also not helpful because a positive CSF result was found only in 20% of patients. In the absence of positive CSF Gram stain and/or cultures, the diagnosis of this condition is challenging because patients may already have abnormal CSF parameters at baseline due to the underlying neurological condition (hemorrhage, postoperative inflammatory changes, etc). In addition, hospitalized patients may receive broad-spectrum antibiotics empirically for a variety of reasons before CSF cultures are obtained. In our study, 50% of patients received antibiotic therapy before obtaining CSF studies potentially decreasing the yield of the cultures.

Studies evaluating additional CSF testing to improve diagnostic accuracy and earlier detection have been moderately successful. Banks et al [6] reported the beneficial use of polymerase chain reaction (PCR) for specific detection of *P acnes*, *S aureus*, and methicillin-resistant *S aureus*. However, limitations of PCR analysis included no available panel for *Staphylococcus epidermidis*, false-positive results due to colonization, and lower

sensitivity in mixed infection compared with conventional methods [15]. Pfausler et al [16] proposed the use of cell index, which can diagnose meningitis or ventriculitis up to 3 days before conventional diagnosis. Given the requirement of daily CSF analysis, cell index may be difficult to apply. Moreover, use of cell index may increase the potential risk of infection due to frequent manipulation of ventricular devices or multiple lumbar punctures.

Cerebrospinal fluid lactate concentration, a simple and inexpensive assay, has been shown to be a useful marker to distinguish bacterial from aseptic meningitis in previous studies. The cutoff level of ≥4 mmol/L or 35 mg/dL was shown to be optimal in diagnosis [11, 17–19]. However, a meta-analysis performed by Huy et al [20] showed the variable cutoff value for diagnosis ranges from 2.1 to 4.44 mmol/L, depending on the instruments, laboratory, and methods used. Thus, every center must set its own cutoff value for CSF lactate concentration. Moreover, caution is required when interpreting CSF lactate level because a low CSF lactate level cannot entirely rule out bacterial meningitis. In the current study, CSF lactate values had great variability, ranging from 1 to 22.8 mmol/L (median, 4.65 mmol/L). Other biomarkers (such as procalcitonin, C-reactive protein, or serum amyloid A protein in CSF) were studied, but none were useful as an independent tool for the diagnosis of bacterial meningitis [18, 21].

Similar to prior studies, Gram-positive organisms were the most common pathogens (Staphylococcus [30.2%] and S aureus [19.8%]). Propionibacterium acnes was found in only 1 patient, which was much lower than expected. This could possibly be due to CSF cultures being routinely discarded after 5 days at our institution. Because P acnes is a slow-growing organism, the microbiology laboratory should be notified to keep CSF specimens at least 10 days [22] in patients who develop healthcare-associated meningitis or ventriculitis.

Gram-negative pathogens were found in approximately 30% of patients in this study, and only 2 patients had Acinetobacter sp. meningitis. However, the increasing incidence of Gram-negative pathogens continues to be a major concern worldwide. Palabiyikoglu et al [23] reported 67 microorganisms isolated in 49 patients; 61% were Gram-negative bacilli, and 34% were Gram-positive cocci. Gram-negative bacilli gradually increased from 1993 to 2002 when they overtook Gram-positive organisms as more common pathogens.

Patients with healthcare-associated meningitis or ventriculitis tend to have poor clinical outcomes, which could be attributable to both underlying neurological diseases and superimposed nosocomial infections. Gram-negative ventriculitis tends to have high mortality rates [10]. The overall mortality rate in our study was 9.3%, but up to 78% of patients had adverse outcomes.

Risk factors associated with mortality or adverse clinical outcomes have been reported in only a few prior studies. Rodriguez Guardado et al [24] reported 51 patients with EVD-related Acinetobacter meningitis, 17 of whom died from the infection.

In multivariate analysis, mortality was significantly associated with the lack of removal of intraventricular catheters, a high number of CSF leukocytes (4988.35 vs 1341 cells/mm^3), and higher age (50 vs 40 years). However, Kim et al [2] did not find any association between these poor prognostic factors and higher mortality in 27 patients with Acinetobacter meningitis.

In the logistic regression analysis performed in the current study, we identified 3 variables associated with adverse outcomes: age ≥45 years, abnormal neurological exam, and mechanical ventilation. Cerebrospinal fluid parameters and removal of intraventricular catheters were not shown to be associated with adverse outcomes in our cohort. The latter finding could be partly explained by a high success rate in 28 of 30 patients (93%) with coagulase-negative Staphylococcus where the shunt was not removed [25]. However, this treatment approach cannot be extrapolated to other pathogens, especially S aureus and Gram-negative organisms, and we continue to encourage early removal of intraventricular catheters as soon as they are not clinically indicated or if a high clinical suspicion for infection exists.

It is interesting to note that VP shunt placement was found to be the only factor associated with better outcomes in bivariate analysis. The most common pathogens causing VP shunt-related ventriculitis are skin commensal organisms such as coagulase-negative Staphylococcus, which have lower virulence compared with other patients with healthcare-associated meningitis. Alternatively, providers might become more concerned about possible healthcare-associated meningitis or ventriculitis in patients with VP shunts that could result in earlier investigations and aggressive management. However, VP shunt was not statistically significant in the logistic regression analysis.

To our knowledge, this is the largest study of patients with healthcare-associated meningitis or ventriculitis including both adult and pediatric populations. In addition, this study was large enough to perform valid multivariable analysis evaluating risk factors for an adverse outcome. Nonetheless, limitations to this study exist. First, even though the prognostic factors were internally validated by bootstrapping, they need to be externally validated in other centers. Second, even though our study used the standard CDC/NHSN surveillance definition, we found that this definition has limitations. Patients with ventriculo-peritoneal or ventriculo-pleural shunts that presented only with abdominal pain or pleuritis symptoms due to distal shunt infection with negative CSF cultures will be excluded according to this definition. Furthermore, the overlapping signs and symptoms between bacterial meningitis and underlying neurological illnesses (such as subarachnoid hemorrhages or chemical meningitis secondary to postoperative inflammation) are a major hindrance in making a diagnosis, and it is not entirely clear that those with negative CSF cultures had true infections. Whether this surveillance definition provides the best guidance and accuracy in diagnosis is debatable. Finally, the high rates of adverse clinical outcomes in this study could

also be attributed to the underlying diagnosis that prompted the neurosurgical intervention, and further studies should be done to try to delineate the true impact of the infectious complication on the outcomes of the patients.

CONCLUSIONS

Healthcare-associated meningitis or ventriculitis have negative CSF cultures in approximately 50% of patients. The majority of patients have adverse clinical outcomes with independent prognostic factors being an age ≥45 years, an abnormal neurological exam, and requirement for mechanical ventilation.

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