

Ventriculitis Complicating Use of Intraventricular Catheters in Adult Neurosurgical Patients

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Ventriculitis is a serious complication of intraventricular catheter (IVC) use, with rates of IVC-related infections ranging from 0% to 45% and gram-positive organisms predominating. We prospectively analyzed ventriculostomy-related infections occurring among 157 adult neurosurgical patients (mean age, 54.9 years; 90 [57%] were women) from 1995 through 1998, to determine the incidence of, risk factors for, and organisms that cause ventriculitis. A total of 196 IVC events resulted in 11 infections (5.6%; 9 were caused by gram-negative organisms and 2 by coagulase-negative staphylococci). Independent risk factors for IVC-related infection include length of IVC placement (8.5 days [infected] vs. 5.1 days [uninfected]; $P = .007$) and cerebrospinal fluid leakage about the IVC ($P = .003$). The length of hospital stay (30.8 days vs. 22.6 days; $P = .03$) and mean total hospital charges (\$85,674.27 vs. \$55,339.21; $P = .009$) were greater for infected patients than for uninfected patients. In addition, a microbiologic shift from gram-positive organisms toward gram-negative organisms was noted. This study suggests that IVC-related infections remain serious infections that increase the length of hospitalization.

Intraventricular catheters (IVCs) are vital neurosurgical diagnostic and therapeutic tools that provide for continuous intracranial pressure monitoring and external CSF drainage. Although first introduced in 1875, the technique was not widely used until the 1960s, when Lundberg refined the technique and demonstrated its usefulness for bedside analysis [1, 2]. Lundberg's reports paved the way for widespread use of IVCs for critical neurosurgical patient management. IVCs can be

used to measure intracranial pressure in patients with many conditions, including traumatic brain injury, intracranial hemorrhage, intracranial mass, or any intracranial process that may result in ventricular obstruction or hydrocephalus.

Although IVCs have been useful as monitoring devices and direct portals for removal of CSF or injection of therapeutic agents, their benefits have always been tempered by complications associated with their use. Chief among these complications is infection (either meningitis or ventriculitis), which occurs in 0%–45% of patients, depending on technique of insertion and management of the IVC [1, 3–11]. As might be expected with the use of percutaneous catheters, gram-positive infections traditionally have been predominant; however, gram-negative infections have been reported in association with IVC use and are associated with patient mortality rates of up to 58% [12]. In 1998, we noted an increased rate of IVC-related infections caused by gram-negative organisms at the Johns Hopkins Hospital (Baltimore). Cohort data on neurosurgical patients are prospectively collected and maintained in a detailed database for monitoring purposes by the in-

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fection control department. We systematically analyzed these data to determine the incidence of IVC-related infections, to assess the risk factors for acquiring infection, and to examine the trend of acquisition of pathogenic gram-negative organisms.

PATIENTS AND METHODS

Patients. The Johns Hopkins Hospital is a tertiary-care center with 1002 beds that serves Baltimore, Maryland, and the surrounding areas. All adult neurosurgical patients who were admitted to the 8-bed Neurosciences Critical Care Unit or the 6-bed Neuro-Progressive Care Unit from September 1995 through December 1998 and who underwent placement of an IVC were evaluated. The duration of catheter placement was determined by the Neurosciences Critical Care and Neurosurgery teams, on the basis of the clinical status of the patient and the medical necessity of intraventricular pressure monitoring.

Data collection. At the time of admission to the neurosurgical service, an infection control practitioner (M.O.) evaluated patients on a daily basis and prospectively collected data by use of standardized forms. Data systematically were recorded regarding demographics, diagnosis, date of admission, neurosurgical history and previous illness, type of device, prophylactic antibiotic administration, site and date of IVC insertion, dates of replacement, microbiologic results, and all events that resulted in manipulation of the system (including CSF sampling, irrigation [e.g., therapeutic injection of chemotherapy, antibiotics, urokinase, artificial CSF, or other], inadvertent disconnections of the system, CSF leakage, and dressing changes). In the event of infection, detailed records were collected regarding antimicrobial susceptibility, treatment provided, and patient outcome. *International Classification of Diseases, Ninth Revision*—diagnosis-related group codes for principal diagnosis and primary procedures were obtained from the hospital's case-management system. In addition, data were obtained on length of stay, total and service-specific charges, survival, and neurologic status at discharge.

Insertion of and maintenance technique for IVCs. Decisions regarding the sites of insertion of IVCs were left to the discretion of the neurosurgical staff. Placement of IVCs occurred under sterile conditions at the patient's bedside, in the operating theater, or, rarely, in the emergency department. The patient's skull was shaved and prepared with standard sterile techniques. The skin was incised 2 cm anterior to the coronal suture in a parasagittal plane passing through the pupil of the ipsilateral eye. A twist drill hole was made through the skull, and the dura was nicked for catheter insertion. The catheter was inserted ~5–7 cm until CSF was obtained. The IVC was then tunneled in a retrograde fashion to a distant skin exit site and was connected via a 3-way stopcock to an external pressure transducer and CSF drainage system. The catheter was sutured

in place and a nonocclusive dressing applied. A periprocedure antibiotic, usually oxacillin or cefazolin, was administered to all patients, with administration of prophylactic antibiotic continuing for the duration of catheterization. In the event of β -lactam allergy or known drug intolerance, vancomycin or clindamycin was substituted. After a nonocclusive dressing was applied, the system remained entirely closed. Wounds were redressed only if loose or soiled. Samples of CSF were obtained only if the patient's clinical condition required further assessment—for example, for evaluation of fever or a worsening level of consciousness (obtundation, coma, or delirium).

Microbiologic testing. CSF samples were sent to the microbiologic laboratory for direct examination, Gram stain, and culture. Culture media included 5% sheep blood agar, chocolate agar, MacConkey agar, and Schaedler broth. Inoculated media were incubated at 35°C in 5% CO₂. Bacteria were identified by means of standard biochemical tests. Susceptibility testing was performed by the agar dilution replicate plating method. For organisms that were epidemiologically associated with a cluster of infection, strain similarity was determined by pulsed-field gel electrophoresis [13, 14].

Definitions and exclusion criteria. “Nosocomial ventriculitis” was defined as culture of a recognized pathogen from the CSF either at the time of or 2 days after IVC insertion. The day of insertion was defined as “day 0”. In addition, if common skin flora, such as coagulase-negative *Staphylococcus*, *Corynebacterium*, *Bacillus*, *Micrococcus*, or *Propionibacterium* species were isolated, then ≥ 1 of the following criteria had to be identified: a Gram stain of the original CSF sample that produced a finding consistent with the organism cultured, a decrease in the CSF glucose level (≤ 25 mg/dL), an increase in the CSF protein level (≥ 50 mg/dL), or a finding of neutrophilic pleocytosis (≥ 10 cells/mm³). We excluded the following patients: (1) those whose CSF culture did not yield organisms but who had organisms identified on a smear of the original CSF sample or had only laboratory parameters that were consistent with ventriculitis, (2) those who were given a principal diagnosis of meningitis or ventriculitis *before* the insertion of an IVC, and (3) those whose CSF culture yielded pathogens ≥ 5 days after the IVC was removed.

Analysis of data. Information was recorded onto standard data-entry forms and was entered into EpiInfo, version 6 (Centers for Disease Control and Prevention, Atlanta). If a patient had multiple IVCs placed, each one was recorded separately. Characteristics of infected and uninfected patients were compared, by χ^2 analysis and Fisher's exact test, for all categorical variables and, by ANOVA or 1-sided Student's *t* test, for continuous variables. The level of statistical significance (2-sided) was set at $P < .05$.

To analyze the outcome status of infected patients versus uninfected patients, we categorized neurologic status at dis-

charge by reviewing standardized discharge summaries and then classified patients into 1 of 5 discharge categories for analysis. Patients discharged to home or to outpatient rehabilitation or patients who experienced no additional neurologic impairment as a result of a preexisting condition were defined as having either no impairment or minimal impairment. Patients with neurologic impairment that required inpatient rehabilitation or stable nursing home placement were categorized as having moderate impairment. Patients with severe cognitive or neurologic damage or with ventilatory dependency without future prognosis for self-care were categorized as having severe impairment. All patients who died in the hospital secondary to events that occurred after admission were categorized as patients who died. Patients who were admitted with catastrophic neurologic events without the hope for recovery and who died soon after admission were categorized as expectant patients and were eliminated from outcome analysis, since data on patients in this category would tend to distort outcome data in comparisons of infected and uninfected individuals.

RESULTS

A total of 157 patients underwent placement of 196 IVCs. Individual patients had 1–4 IVCs placed, and 32 patients had ≥ 2 IVCs placed. Among the 196 events, 11 episodes of ventriculitis (5.6%) were identified (table 1). Six additional patients were excluded because they did not meet strictly defined criteria for infection. Three of these excluded patients had evidence of infection on the basis of Gram stain results or CSF laboratory criteria; however, their CSF cultures did not yield organisms. Gram stain results showed gram-negative rods for 2 of the patients, one of whom had concomitant *Serratia marcescens* pneumonia. The third patient was noted to have gram-positive diplococci, according to CSF Gram stain results, in conjunction

with pneumococcal pneumonia. Although these patients did not meet the strict criteria for inclusion in our analysis, they received therapy for presumed ventriculitis at the discretion of the treating doctors. The 3 other patients with CSF culture growth (2 of whom had growth of coagulase-negative *Staphylococcus* species on culture and 1 of whom had growth of *Micrococcus* species) lacked appropriate corresponding laboratory and Gram stain evidence to be considered as having ventricular infection.

The mean age of uninfected patients was 55 years (range, 22–93 years), whereas that of infected patients was 52.2 years (range, 22–69 years; $P = .84$). Seven (7.8%) of 90 women and 4 (6%) of 67 men developed infections. Seven (8.1%) of 86 white patients, 4 (6.1%) of 66 African American patients, and 0 (0%) of 5 patients of other races developed documented IVC infections. No significant differences were noted with regard to the sex or race of the population.

Microbiologic findings. Nine (82%) of 11 cases of ventriculitis were caused by gram-negative organisms. The gram-negative organisms that were yielded by culture included *Klebsiella pneumoniae* (4 cases); *Enterobacter cloacae* (2 cases); and *Klebsiella oxytoca*, *Serratia marcescens*, and *Proteus mirabilis* (1 case each). Both of the gram-positive pathogens were identified as coagulase-negative *Staphylococcus* species. Three of the patients (patients 4, 6, and 7; table 1) had ventriculitis caused by *K. pneumoniae*, and they developed their infections between July 1996 and September 1996. An investigation did not reveal epidemiologic links between the patients. Pulse-field gel electrophoresis analysis determined that the isolates were not related.

Risk factors for ventriculostomy-related infections. The patient's underlying diagnosis was not associated with the risk of developing ventriculitis (table 2). Previous IVC insertion or previous neurosurgical procedures, such as craniotomy, also

Table 1. Microbiologic etiology of nosocomial ventriculitis and associated outcomes among 11 adult neurosurgical patients.

Patient	Age, years	Sex	LOC, days	Organism	Outcome
1	59	F	2	<i>Serratia marcescens</i>	Died
2	22	F	9	Coagulase-negative staphylococci	Home
3	55	M	6	Coagulase-negative staphylococci	Rehabilitation
4	65	M	4	<i>Klebsiella pneumoniae</i>	Hospice
5	49	M	9	<i>Klebsiella oxytoca</i>	Rehabilitation; significant defects
6	53	F	7	<i>K. pneumoniae</i>	Rehabilitation; significant defects
7	52	F	4	<i>K. pneumoniae</i>	Rehabilitation
8	59	F	12	<i>Enterobacter cloacae</i>	Extended care
9	37	M	23	<i>E. cloacae</i>	Died
10	69	F	9	<i>K. pneumoniae</i>	Ventilator dependent
11	54	F	8	<i>Proteus mirabilis</i>	Hospice

NOTE. LOC, length of catheterization before infection.

Table 2. Risk factors for IVC-related infection associated with 196 IVC placements.

Risk factor	No. of IVC placements associated with				<i>P</i>	OR (95% CI) ^a
	Ventriculitis		No ventriculitis			
	Risk factor presence	Risk factor absence	Risk factor presence	Risk factor absence		
Neurosurgical procedure related						
Tumor	4	7	30	155	.086	2.95 (0.59–12.40)
Intracerebral hemorrhage	6	5	126	59	.351	0.56 (0.14–12.43)
Closed head trauma	0	11	6	179	.544	0 (0–15.16)
Open head trauma	0	11	5	180	.581	0 (0–17.79)
Previous neurosurgical procedure	9	2	133	52	.474	1.76 (0.35–17.33)
Additional						
CSF leak	3	8	9	176	.003	7.33 (1.05–37.47)
Previous ventriculostomy	4	7	40	145	.255	2.07 (0.42–8.60)
Involuntary disconnection	2	9	17	168	.327	2.20 (0.21–11.87)
Irrigation of system	1	10	21	164	.818	0.78 (0.02–6.02)

NOTE. IVC, intraventricular catheter.

^a As determined by Fisher's exact test.

did not affect the risk for nosocomial ventriculitis developing in this cohort.

To evaluate whether breaks in the integrity of the closed catheter system increased the rate of infection, we evaluated the risk of CSF leaks at the site of IVC insertion, planned or unplanned disconnections, and irrigation of the system. CSF leaks significantly predisposed patients for the development of ventriculitis (OR, 7.33; 95% CI, 1.05–37.47; *P* = .003). Within the entire cohort, 3 (25%) of 12 CSF leaks were followed by development of ventriculitis. Within the cohort of infected patients, 3 (27%) of 11 patients had a CSF leak occur while the IVC was in place. Other interruptions of the closed system did not appear to increase the risk of infection.

The longer the IVC was in place, the more likely the patient was to develop an infection. For the uninfected patient population, the average duration of catheter placement was 5.07 days (range, 1–23 days). For the infected patient population (before diagnosis of infection), the average duration was significantly longer (8.45 days; range, 2–23 days; *P* = .007). CSF leakage at the insertion site and duration of IVC placement were independent risk factors for the development of ventriculitis.

Patient outcome and information on diagnosis-related group. Two (18%) of 11 infected patients died as a direct result of the ventricular infection. Only 1 patient was discharged directly to home from the hospital; the remaining 8 patients required rehabilitation or admission to extended-care or hospice facilities. The RR of more severe neurologic impairment occurring at discharge or in the hospital after the neurologic event was 5.33 (95% CI, 1.18–32.5) in the infected group as compared with the uninfected group.

To evaluate the direct inpatient costs associated with IVC-related ventriculitis, we compared the length of hospital stay among uninfected and infected groups. For the uninfected group, the mean length of stay was 22.6 days (95% CI, 19.1–26.0), compared with 30.8 days (95% CI, 23.9–37.7) for the infected population (*P* = .03). The total mean charges (in US dollars) associated with hospital stay were \$55,339.21 for uninfected patients and \$85,674.27 for infected patients (*P* = .009).

DISCUSSION

IVC infections remain a serious complication of IVC use. The rate of IVC-related infection at our institution—11 infections occurring during a period of 3 years and 3 months (or 5.6% of all IVCs placed)—matches the rate of infection (range, 0%–45%) reported in the literature [1, 3–11]. A major strength of our study is that we used a strict definition of ventriculitis that was created before data collection. Case definitions traditionally have been difficult to standardize, given the inherent severity of the underlying illness, the potential for skin flora contamination, and the possibility that the IVC, in and of itself, could induce a CSF pleocytosis [3, 5]. The low rate of infection at our institution may reflect improved catheter maintenance techniques and periprocedure antibiotic prophylaxis, which have succeeded in reducing the incidence of nosocomial catheter-related infection [10, 15]. In addition, the lower rate of infection may be related to the patient population, which included a low number of patients with open or closed traumatic brain injury and a higher number of patients with cerebrovascular disease and brain tumor. Nevertheless, the severity of

the infection, coupled with the potential permanent sequelae, makes ongoing review and critical assessment of present procedures vital.

We have evaluated known risk factors for IVC-related ventriculitis [4–11, 16, 17]. They can be broadly categorized into 3 groups: patient characteristics and the underlying mechanism of injury; events that break the integrity of a closed system; and environmental influences. With regard to patient characteristics and underlying mechanism of injury, neither age, sex, nor race increased the risk of developing IVC infections in our study, a finding that is consistent with findings previously reported in the literature [5, 9, 11, 12]. Although some authors report an association between infection and either intraventricular hemorrhage [5, 6], open head trauma [5, 7], or previous neurosurgical procedure (i.e., craniotomy) preceding or coinciding with IVC placement [11, 16], we found no such association in this large prospective cohort. A trend toward the development of ventriculitis in patients who presented with tumors was noted; however, this trend did not achieve statistical significance ($P = .086$).

It seems intuitive that breaks that occur in a closed, sterile CSF drainage system would predispose patients to develop nosocomial IVC-related infection. The mode of acquisition is hypothesized to be retrograde migration of microorganisms that colonize the external catheter [5]. Mayhall et al. [5] noted that irrigation of the ventriculostomy system was a significant risk factor for infection. Aucoin et al. [7] later validated these findings in a series of 255 neurosurgical patients. We found no evidence that irrigation, planned or unplanned disconnections of the IVC drainage system, or IVC drug administration predisposed patients to higher rates of ventriculitis (table 2). Conversely, we found that CSF leakage at the IVC insertion site was a significant risk factor for the development of IVC-related ventriculitis. Such CSF leaks probably provide a more long-standing conduit for retrograde microorganism migration than do the brief interruptions associated with disconnections of the sterile closed IVC system. Our findings thus support those of Bogdahn et al. [8], who reported that CSF leaks, similarly defined by leakage alongside the IVC insertion site, were a significant risk factor for infection.

The duration of IVC placement and the existence of a previous IVC both potentially act as risk factors for the development of IVC-related infection. We found that 73% of the patients who developed ventriculitis did so after 6 days of catheterization and that the IVC had been in place in these patients for, on average, 3 days longer than in the uninfected patients. This finding is generally consistent with the body of literature that reports that infection rates increase after 4–5 days of catheter insertion [4, 5, 7, 9, 16]. Mayhall et al. [5] noted a significant increase in the risk of infection among patients who required ventricular catheterization for >5 days. On the basis

of this finding and the finding that previous IVCs do not predispose patients to nosocomial infection, many experts recommended that IVCs be changed after 5 days if continued intracranial pressure monitoring or CSF drainage is required. Holloway et al. [11] evaluated the effect of routine IVC exchanges, concluded that no benefit was gained, and recommended that IVCs be removed in an expedient fashion, with routine exchange reserved for prolonged monitoring. We likewise found no association between infection and the existence of a previous IVC. Our data support the practices of removing IVCs as early as possible and of routinely exchanging IVCs only when the current device becomes obstructed or when evidence of infection develops.

Microbiologically, one of the findings of most concern in our study is the preponderance of gram-negative infections (82%). Traditionally, gram-positive microorganisms have been the most common pathogens that cause IVC-related ventriculitis [5, 6, 9, 16]. These organisms, represented by *Staphylococcus aureus* and coagulase-negative *Staphylococcus* species, likely originate from skin flora. Furthermore, gram-negative infections are associated with a higher mortality rate, which approaches 58% in some studies [12]. The mortality rate among the patients in our study who developed gram-negative ventriculitis was 22%.

The reasons for this preponderance of gram-negative IVC-related infections is unclear. Although trauma with open head injury may predispose the patient to gram-negative meningitis [18], we had a very low rate of IVC placement due to trauma and no case of trauma-associated ventriculitis in our patient population. We hypothesize that prolonged hospitalization in our study group resulted in gram-negative microbial colonization in patients. The policy at Johns Hopkins Hospital's Neurosciences Critical Care Unit–Neuro-Progressive Care Unit has been to administer prophylactic antibiotics before IVC insertion to protect against skin flora contamination of the wound site. An observational study performed by Wyler and Kelly [15] reduced the rate of infection among neurosurgical patients who underwent ventriculostomy from 27% to 9% with antibiotic prophylaxis. Gram-positive organisms were the predominant pathogens isolated, and gram-positive antibiotic coverage was provided for the entire duration of ventricular catheter placement [15, 19]. At our institution, a single dose of an antibiotic with predominantly gram-positive coverage is given before catheter placement and is continued for the duration of the IVC placement, along with careful monitoring. Thus, it is notable that the infectious pathogens seen at our institution are predominantly gram negative and are not covered by the prophylactic antibiotics. We hypothesize that gram-negative microbial colonization that occurs during a prolonged hospital stay, coupled with selective pressure exerted by administration

of prophylactic antibiotics, may predispose a minority of this ill population to gram-negative ventriculitis.

The clinical outcomes of patients with IVC-related ventriculitis revealed significant morbidity that was attributable to both the underlying neurologic event and the nosocomial ventricular infection. Only 1 (9%) of 11 infected patients was discharged to home, whereas 2 (18%) died, and the remaining 8 patients (73%) required extended rehabilitation, ventilator dependence, or hospice placement (table 1). Admittedly, it is difficult to determine which sequelae can be ascribed to the underlying neurologic event and which can be ascribed to the ventricular infection. Nevertheless, it is useful to keep in mind the significance of this infection with regard to the overall outcome of patients if they experience nosocomial ventricular infections.

In conclusion, IVC-related infections remain a serious complication of IVC use in adults. Our cohort study reveals that CSF leakage at the IVC insertion site and the duration of IVC placement are independent risk factors for IVC-related ventriculitis. These infections increase the crude length of the hospital stay and the overall costs significantly. In addition, our data show a shift in the microbiologic spectrum—from less devastating gram-positive infections toward gram-negative infections—that may relate to organism selection by periprocedure antibiotic administration. Close monitoring and rigorous catheter maintenance remain mainstays of catheter care, and assessment of risk factors is crucial to determine changes in a microbial infection and to identify ways to prevent future complication.

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