Original Article

A Fifteen-year Epidemiological Study of Ventriculoperitoneal Shunt Infections in Pediatric Patients: A Single Center Experience

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Purpose : Ventriculoperitoneal (VP) shunt insertion is an important treatment modality in children with hydrocephalus. VP shunt infection is a major complication and an important factor that determines the surgery outcome. This 15-year study was performed to evaluate the epidemiology of VP shunt infections in pediatric patients treated at our center.

Methods : A retrospective review of medical records was performed in patients 18 years old or younger who underwent VP shunt insertion surgery from April 1995 to June 2010.

Results : Three hundred twenty-seven VP shunt surgeries were performed in a total of 190 pediatric patients (83 females, 107 males). The median age of the patients was 2.4 years (range, 0.02-17.9 years). Having a malignant brain tumor was the most frequent cause for VP shunt insertion. The shunt infection rate was 6.7% (22/327) per 100 operations and 9.5% (18/190) per 100 patients, and the incidence rate was 0.45 infection cases per 100 shunt operations-year. The most common pathogen was coagulase-negative staphylococcus (n=7) followed by methicillin resistant *Staphylococcus aureus* (n=1). Ten cases were treated with vancomycin and beta-lactam antibiotic (cephalosporin or carbapenem) combination therapy and 7 cases were treated with vancomycin monotherapy. The median duration of antibiotic treatment was 26 days (range, 7 to 58 days). Surgical intervention was performed in 18 cases (18/22, 81.8%).

Conclusion : Epidemiologic information regarding VP shunt infections in pediatric patients is valuable that will help guide proper antibiotic management. Additional studies on the risk factors for developing VP shunt infections are also warranted.

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Key Words : Ventriculoperitoneal shunt, Infectious complications, Children

Introduction

Ventriculoperitoenal (VP) shunts have an important role in managing hydrocephalus in pediatric patients [1]. Shunt infections are one of the most important causes of postoperative complications[2] and can lead to an increased risk of seizures and mortality in pediatric patients[3, 4]. Shunt infections are generally known to occur within the first two months after surgery[5] with an infection rate of 5-20%[6-9]. Patients with shunt infections can present with typical symptoms such as fever and seizures, but can also present without any symptoms[10]. To treat these infections, administering parenteral antibiotics is generally recommended, along with removing the device until the cerebrospinal fluid (CSF) becomes sterile again[11-15]. The aim of this study was to determine the epidemiological, clinical, laboratory and microbiological characteristics and treatment outcomes of VP shunt infections in the pediatric patients at a single center.

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Materials and Methods

The medical records of patients younger than 18 years of age who underwent VP shunt insertion surgeries at Samsung Medical Center from April 1995 to June 2010 were reviewed retrospectively and data were collected including age, sex, hydrocephalus etiology, date of shunt placement, and the number of shunt revisions. Among these VP shunt operation recipients, patients with VP shunt infections were identified and infection-related data were analyzed, including the onset of infection from the first surgery, symptoms, WBC count, differential and protein in CSF, pathogens in CSF culture, method of medical treatment and duration, surgical treatment, and treatment outcome.

The definition of VP shunt infection varies[10, 16-18]. In our study, we used the Centers for disease control (CDC) definitions for nosocomial infection[19, 20]. Shunt infections were defined when at least one of the three following criteria were satisfied: 1) patient had organisms cultured from CSF, 2) patient had at least one of the following signs or symptoms with no other recognized cause: fever (>38℃), headache, stiff neck, meningeal signs, cranial nerve signs, or irritability and at least one of the following: increased white cells (> 5 cells/μL), organisms seen on gram stain of CSF, organisms cultured from blood, a positive antigen test of CSF, blood or urine, or 3) patients ≤1 year of age had at least one of following signs or symptoms with no other recognized cause: fever (>38℃), hypothermia (<37℃), apnea, bradycardia, stiff neck, meningeal signs, cranial nerve signs, or irritability and at least one of the following: increased white cells (>5 cells/μL), organisms seen on gram stain of CSF, organisms cultured from blood, or positive antigen test of CSF, blood or urine.

Results

Three hundred twenty-seven VP shunt operations were performed in 190 patients (107 male and 83 female). Among them, 75 patients (39.5%) were younger than 1 year. The median age of the included patients was 2.4 years (range, 0.02 to 17.9 year). The most common cause of hydrocephalus that needed a VP shunt was a brain tumor (41.3%), followed by a congenital anomaly (25.5%) (Table 1).

Twenty-two episodes of VP shunt infection occurred in 18 patients. Four patients developed shunt infections twice during the follow-up period. The shunt infection rate was 6.7% (22/327) per 100 operations and 9.5% (18/190) per 100 patients and the incidence rate was 0.45 infection cases per 100

Table 1. Characteristics of Children Who Underwent Ventriculoperitoenal Shunt Operations

Characteristic	N=190 (%)
Median age at initial shunt replacement (Median age/year)	
0.35 (range 0.02-0.98)	75 (39.5)
1.73 (range 1.02-2.92)	29 (15.3)
9.78 (range 3.00-17.88)	86 (45.2)
Gender	
Male	107 (56.4)
Female	83 (43.6)
Etiology of hydrocephalus	
Malignancy-brain tumor	79 (41.3)
Congenital anomaly	49 (25.5)
Post-meningitis hydrocephalus	24 (11.3)
Post-hemorrhagic hydrocephalus in neonate	22 (12.0)
Posttraumatic hydrocephalus	11 (5.7)
Tuberous sclerosis	3 (1.5)
Others*	2 (1.0)

*Posthemorrhagic hydrocephalus due to arteriovenous malformation and hydrocephalus due to mucopolysaccharides

shunt operations-year. The median duration from the shunt insertion day to the first infection onset was 26 days (range, 2 to 884 days). Thirteen patients (13/18, 72.2%) developed the first VP shunt infection within three months of surgery.

VP shunt infections were most commonly observed in patients with post-meningitic hydrocephalus (4/24, 16.7%), followed by congenital anomalies (5/49, 10.2%), post-hemorrhagic hydrocephalus in neonates (2/22, 9.1%), post-traumatic hydrocephalus (1/11, 9.1%), and brain tumors (5/79, 6.3%)

In twenty-one episodes of shunt infection (21/22, 95.5%), a fever of above 38℃ was observed. One patient did not have a significant fever but did have pleocytosis in the CSF on post-operative day 12, and had coagulase-negative staphylococcus (CoNS) grow from CSF samples. Additional symptoms included vomiting, wound redness, seizure, abdominal pain, irritability, apnea and headache (Table 2).

From CSF analyses of the 22 infection episodes, the median WBC count was 115 cells/μL (range, 1 to 1470 cells/μL), the median polymorphonuclear cell percentage was 13% (range, 0 to 95%), and the median protein level was 157.5 mg/dL (range, 4.6 to 2,100 mg/dL).

Responsible pathogens were identified from the CSF in 14 cases (14/22, 63.6%). Bacteria grew in 12 cases and a virus was isolated in 2 cases. Gram positive bacteria were identified in 9 cases. CoNS was the most common cause (n=7), followed by methicillin resistant *Stapylococcus aureus* (MRSA), *Bacillus cereus, Enterobacter cloacae* and *Pseudomonas fluorescens* coinfection, *E. coli* and *Candida tropicalis*. In one patient, echovirus was detected twice in the CSF by RT-PCR. In one patient, CoNS grew both in cultures from CSF and blood simultaneously.

In all cases, patients received parenteral antibiotic treatments; the median treatment duration was 26.5 days (range, 7 to 58 days). Ten cases were treated with vancomycin and beta-lactam antibiotics (cephalosporin or carbapenem) combination therapy and 7 cases were treated with vancomycin monotherapy. Among them, the 2 patients on vancomycin monotherapy continued to have positive CSF cultures

Table 2. Ventriculoperitoneal Shunt Infection Details

	N=22 (%)
Symptom	
Fever*	21 (95.5)
Vomiting	3 (13.6)
Wound redness	3 (13.6)
Seizure	2 (9.1)
Abdominal pain	1 (4.5)
Irritability	1 (4.5)
Headache	1 (4.5)
Apnea	1 (4.5)
Pathogens in CSF	
Coagulase-negative staphylococci	7 (31.8)
Methicillin resistant *Stapylococcus aureus*	1 (4.5)
Bacillus cereus	1 (4.5)
Enterobacter cloacae and Pseudomonas luorescens/putida	1 (4.5)
Gram (-) *E. coli*	1 (4.5)
Fungus *Candida tropicalis*	1 (4.5)
Virus Echovirus	2 (9.0)
No growth	4 (18.2)
Antibiotics treatment at infection	
Vancomycin + beta-lactam	10 (45.5)
Vancomycin monotherapy	7 (31.8)
Vancomycin + bactrim	1 (4.5)
Amphotericin B	1 (4.5)
Others†	3 (13.6)
Surgical approach to treatment	
EVD and shunt reinsertion	11 (50.0)
Shunt removal and shunt reinsertion	6 (27.3)
Shunt removal only	1 (4.5)
No surgical intervention	4 (18.2)

*Fever is defined as having a temperature of over 38℃. Other symptoms overlapped with fever.
†Ceftriaxone, ceftazidime and tobramycin, piperacillin/tazobactam and amikacin

Table 3. Characteristics of Patients with Shunt Infections

Pt	Disease	Onset*	Symptom	Pathogen	Antibiotics (days)	Surgery
1	tumor	38	fever, redness	MRSA	vanco (55), rifampin (31)	EVD, reinsertion
2	meng	7	fever, seizure	no growth	ceftriaxone (7)	not done
3	cHCP	224	fever	no growth	vanco (10)	shunt revision
	recur		fever, redness	no growth	ceftazidime + vanco (15)	EVD, reinsertion
4	cmHCP	16	fever	CoNS	vanco (46)	EVD, reinsertion
5	cHCP	25	fever	CoNS	vanco (38)	EVD, reinsertion
6	cHCP	9	fever	CoNS	vanco (24)	EVD, reinsertion
					teico (20)	EVD, reinsertion
7	tSDH	12	none	CoNS	vanco (16)	
8	tumor	2	fever	CoNS	vanco (30)	shunt revision
9	tumor	26	fever abd pain	*Bacillus cereus*	meropenem + vanco (30)	shunt removal
10	tumor	12	fever, headache	*Enterobacter cloacae* *Pseudomonas fluorescens*	ceftizoxime + tobramycin (12)	shunt revision
11	HCP (MPS)	4	fever	CoNS	vanco (48) bactrim (22) rifampin (14)	EVD, reinsertion
12	meng	50	fever vomiting	no growth	vanco (58),	shunt revision
13	tumor	68	fever. vomiting	no growth	cefepime + vanco (14)	not done
	recur		fever	CoNS	ceftazidime + vanco (15)	not done
14	hHCP	95	fever irritability	no growth	ceftazidime + vanco (21)	shunt revision
	recur		fever	*Candida tropicalis*	amphotericin-B (33)	EVD, reinsertion
15	meng	884	fever	Echovirus	cefotaxime + vanco (41) amikacin + pi/tazo (15)	shunt revision
	recur		fever, seizure	Echovirus		not done
16	IVH	132	fever, apnea	ESBL (+) *E.coli*	meropenem + vanco (23)	EVD, reinsertion
17	cHCP	158	fever vomiting	no growth	cefotaxime + vanco (38)	EVD, reinsertion
18	tumor	6	fever, redness	no growth	meropenem + vanco (15)	EVD, reinsertion

Abbreviations : Pt, patient; meng, meningitis; cHCP, congenital hydrocephalus; recur, recurrent infection; cmHCP, communicating hydrocephalus; tSDH, traumatic subdural hemorrhage; HCP, hydrocephalus; MPS, mucopolysaccharide; hHCP, posthemorrhagic hydrocephalus; IVH, intraventricular hemorrhage in preterm infant; abd pain, abdominal pain; vanco, vancomycin; teico, teicoplanin; pi/tazo, piperacillin/tazobactam; EVD, external ventricular drain.
*The number of days after surgery that the symptoms began occurring.

for CoNS. The culture eventually became negative after the regimen was changed to a rifampin and vancomycin combination therapy. In one case, amphotericin B was administered to treat a Candida infection. Surgery was performed in 18 cases (18/22, 81.8%). External ventricular drainage (EVD) and insertions of new shunts after antibiotic treatment was performed in 11 cases, initial shunt removal and reinsertion after antibiotic treatment was performed in 6 cases, and shunt removal without reinsertion was performed in one case.

Four patients had two shunt infection episodes. The median length of time between the two episodes was 120 days (range, 65 to 420 days). In two patients, no pathogen was identified during the first infection episode but during the second episode,

Candida tropicalis was identified in one patient and CoNS in the other. Echovirus was isolated twice from another patient who had X-linked agammaglobulinemia and developed a chronic echovirus infection. In the fourth patient, the CSF culture grew no organism in both occasions. There was no VP shunt infection-associated mortality.

Discussion

Shunt infections are a serious complication after VP shunt insertions. Therefore, updating the epidemiology of shunt infection at each institution is important. This study summarized the epidemiology of VP shunt infections of pediatric patients in a single center. We found that a rate of 0.45 shunt infection cases per 100 shunt operations-year (6.7% per 100 operations and 9.5% per 100 patients) occurred over a consecutive 15-year period.

Shunt infections have been reported to be more common in pediatric patients than in adults[10, 18]. There are few studies in pediatric patients covering an extended period of more than 10 years[21]. Our study is a retrospective study that analyzed pediatric data from 15 consecutive years in a single center.

VP shunt infection rates in pediatric patients have been reported to range from 8-20%[22, 23], depending on factors such as age, immune status, and comorbidities[5]. In pediatric patients, hemorrhage is less common than in adults, and brain tumors are the main cause for hydrocephalus. Since our center is one of the major referral centers for pediatric cancer in our nation, brain tumors were the leading cause of hydrocephalus in this study. Having a brain tumor may play a role in increasing VP shunt infection rates in children when compared with adults. Since these patients typically receive chemotherapy in addition to operations, they may be predisposed to infection due to their immunosuppressive condition. However, in our study, the lowest infection rate was observed in patients with brain tumor-associated hydrocephalus (6.3%).

Diagnosis of VP shunt infections in children is challenging because the symptoms of VP shunt infection are nonspecific and young children typically cannot communicate properly. It can be very confusing to differentiate VP shunt infections from other common childhood infections. VP shunt infections commonly occurred within 3 months of surgery[10, 17] and we also observed that 72.2% of our first VP shunt infection cases occurred within 3 months of surgery. Therefore, it is important to rule out VP shunt infections in patients with a history of recent VP shunt insertion and pertinent infection symptoms such as fever. Fever and shunt malfunctions are known to be the leading signs of a VP shunt infection [5]. In our study, 95.5% of VP shunt infection episodes were associated with fever. However, no VP shunt malfunctions were observed. Shunt revision operations were performed in 137 cases due to shunt malfunction, all of which did not satisfy the shunt infection definition and therefore were not considered infection cases.

CoNS was reported as the most commonly identified pathogen in cases of VP shunt infection[17, 24-27]. In our study, CoNS was also the most common cause of infection (7/22, 31%). Of note, two patients had persistent VP shunt infections due to CoNS. Despite the parenteral vancomycin treatment for more than 2 weeks with appropriate serum drug levels (15-20 μg/mL), the CSF was not sterilized and CoNS continued to grow from EVD samples. Rifampin (15-25

mg/kg/day) was added to the therapy and the CSF culture finally became negative after this combination therapy without complications (9 days and 15 days of combination therapy, respectively). The EVDs were removed and new VP shunts were inserted. Failure at bacterial eradication could have been due to the sub-therapeutic levels of vancomycin in the CSF because of its low blood-brain barrier penetration, and also due to the formation of a biofilm on the VP shunt itself. Therefore, the drug might have not reached adequate concentrations at the appropriate sites[28]. It has been reported that increased bactericidal effects are observed when rifampin or trimethoprim/sulfamethoxazole are co-administered with vancomycin for a biomaterial infection caused by CoNS or *S. aureus*[29, 30]. Since our patients had appropriate serum levels of vancomycin and the infection was treated by combination therapy with rifampin, it is assumed that biofilm formation played a more important role in these cases. Although removing the offending material is the most important treatment, for critical patients who cannot undergo immediate surgical procedures, combination therapies may be beneficial.

Four patients had two episodes of VP shunt infections. One patient had congenital agammaglobulinemia and developed prolonged enterovirus meningoencephalitis. The other three patients did not have congenial immunodeficiencies and the interval between the two infection episodes in these three patients was 105 days. In another study from 100 patients who developed VP shunt reinfections, reinfection occurred an average of 21 days after the initial infection[31]. Risk factors for reinfection were reported to include treatment without surgical intervention in the previous infection episode and having two prior shunt infections[31, 32]. They reported that the surgical removal of infected materials played an important role in the treatment of VP shunt infections[31]. In our study, we could not identify the risk factors for reinfection due the low number of patients. One of our patients who had a reinfection did not have a surgical intervention for the first infection (culture negative) episode, and developed a second infection due to CoNS. This patient did not receive a shunt revision. Of note, this patient was one of the four patients who did not have their shunt removed during the first infection episode.

Limitation to our study includes the fact that it is a retrospective single center study with only a small number of VP shunt infection cases. For this reason, we could not further investigate risk factors or the efficacy of different treatment modalities. However, the duration of this study period was 15 consecutive years and we have tried to summarize the important aspects of VP shunt infection epidemiology in children.

In conclusion, epidemiologic information regarding VP shunt infections in pediatric patients is valuable that will help guide proper antibiotic management. Additional studies on the risk factors for developing VP shunt infections are also warranted.

한 글 요 약

소아 환자에서의 뇌실-복강 단락 감염의 역학적 고찰: 15년 간의 단일 기관 연구

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목 적 : 뇌실-복강 단락 수술은 수두증이 있는 소아 환자에서 중요한 치료 방법 중 하나이다. 뇌실-복강 단락에

서 단락 감염은 중요한 합병증이며 수술의 예후를 결정하는 중요한 요인이다. 이 연구는 소아 환자에서의 뇌실-복강 단락 감염의 역학적 특성과 임상 증상, 치료와 예후를 파악하고 진단 및 치료에 도움이 되고자 하였다.

방 법: 1995년 4월부터 2010년 6월까지 뇌실-복강 단락 수술을 시행 받은 18세 이하의 환자를 대상으로 하였으며 후향적으로 의무 기록을 분석하였다.

결 과: 총 190명(여자 82명, 남자 107명)의 환자에서 327건의 뇌실-복강 단락 수술을 시행하였다. 중위 연령은 2.4세이며(0.02-17.9세) 뇌실-복강 단락 수술의 가장 흔한 원인은 악성 뇌종양이었다. 수술 1건 당 감염률은 6.7% (22/327건), 환자 1명 당 감염률은 9.5% (18/190명)이며 100건의 수술-년 당 감염은 0.45건 이었다. 가장 흔한 원인 균은 coagulase-negative staphylococcus (7건) 이며 methicillin resistant *Staphylococcus aureus*에 의한 감염은 1건 이었다. 10건의 감염에서 vancomycin과 beta-lactam antibiotics (cephalosporin or carbapenem)의 복합 정주 치료를 시행하였으며 7건의 감염에서 vancomycin 단독 정주 치료를 시행하였다. 치료 기간의 중앙값은 26일(7-58일)이었으며 수술적 치료는 18건에서 시행하였다(18/22건, 81.8%).

결 론: 본 연구는 단일 기관에서 15년 동안의 뇌실-복강 단락 감염의 역학을 요약한 연구로 소아 환자에서의 뇌실-복강 단락 감염의 역학적 정보는 적절한 치료를 시행하는데 큰 도움이 될 것이다. 향후 단락 감염의 발생과 관련한 위험 인자에 대한 추가적인 연구가 필요할 것으로 사료된다.

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