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Original Article

Ventriculoperitoneal Shunt Infections in a Tertiary Center: 3 Years Experience

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ABSTRACT

Objective: *Ventriculo-peritoneal shunt infection is the most important complication of shunt applications. In pediatric age, shunt infections are associated with shunt dysfunction, requirement for shunt revision, neurodevelopmental delay, prolonged hospital stay, and high treatment costs. In this study, we aimed to evaluate the characteristics of shunt infections of our patients and to compare the differences between early and late infections, infections caused by staphylococci and other strains and infection that did and did not recur.*

Methods: *In this retrospective study, shunt infections treated in the Pediatric Infection Clinic of Hamidiye Etfal Training and Research Hospital between July 2008 and July 2011 were evaluated.*

Results: *Forty-seven shunt infections in 42 patients were evaluated. Congenital anomalies were the most common etiology of hydrocephalus and fever was the most common symptom of the patients. Higher rates of early shunt infections, shunt infections in early childhood and infections caused by staphylococci species were observed. Patients with infections caused by staphylococci species received shorter duration of antibiotherapy (p=0.024). Infections that recurred in the six months of follow-up had higher rates of positive blood cultures (p=0.022). There was no statistically significant difference between early and late-term shunt infections.*

Conclusion: *Shunt infections were evaluated in different aspects in our study. Direct colonization of the shunt catheter still seems to be most important cause for the shunt infections because early infections and infections caused by skin flora were more common in our patient group.*

INTRODUCTION

Ventriculoperitoneal shunt (VPS) is the most common treatment for hydrocephalus, but despite the improvements in surgical techniques and infection control, complications still remain a problem.[1] Among the complications of VPS application, VPS infections are of serious importance due to shunt dysfunction requiring revision[2] and shunt infections are also associated with an increase in the duration and cost of hospitalization, reduced intellectual performance, neurological dysfunction in children who already have risk of neurodevelopmental problems due to hydrocephalus.[1,2]

Infection rates after VPS applications are reported between 5% and 18%, and the recurrence rate of VPS infection increases up to 26%. Risk of shunt infection has a negative correlation with age. There is also an increased risk in premature babies, in patients who underwent shunt surgery with the indication of post-hemorrhagic hydrocephalus, in patients with history of shunt infection or cerebrospinal fluid (CSF) leakage and intraoperative use of neuro-endoscope. The risk of reinfection is reported to be increased in patients with shunt applied before the sixth months of age, in males, and in patients with intracranial hemorrhage.[3]

Coagulase-negative staphylococci which originate from the skin flora are the most common microorganisms that cause VPS infection. In addition,

gram-negative microorganisms originating from the abdomen can cause shunt infections and fungal infections which can also be seen in patients who receive long-term antibiotherapy.[4,5]

There are differences between centers in terms of the management of shunt infections. Combination of temporary removal of the shunt, application of extra-ventricular drainage (EVD) after removal of the shunt, and intraventricular antibiotherapy are also frequently applied treatment methods in addition to systemic antibiotherapy.[1,3]

In this retrospective study, we aimed to investigate the clinical characteristics of the patients diagnosed as VPS infection and to compare early and late shunt infections, infections caused by staphylococci and other microorganisms and infections that did and did not recur.

MATERIALS and METHODS

Patient Selection and Data Collection

In this study, patients who were hospitalized in the Pediatric Infectious Diseases Clinic of a tertiary center between July 2008 and July 2011 with the diagnosis of VPS infection were evaluated retrospectively. Ethics committee approval was not obtained as it was not obligatory for retrospective studies in 2011. Demographic data and clinical features were recorded from the medical records of the patients.

Diagnosis and treatment protocol for VPS infection

The diagnosis of VPS infection was made by evaluating the patient's history and physical examination findings together with the results of laboratory tests. At least one of the following criteria were accepted as shunt infection; (1) Positive CSF culture, (2) increased leukocyte count (WBC $>10^6/mm^3$), increased CSF protein level (protein> 40 mg/dL) and/or decreased CSF glucose value (CSF glucose <simultaneous blood glucose/2) with the presence of axillary fever higher than 38°C without any other focus), (3) abscess observed at the distal end of the shunt catheter or signs of peritonitis, (4) purulent discharge or signs of local infection at the shunt site.

By examining the patient records; absence of any symptoms of shunt infection and fever (axillary temperature >38°C) observed in the last 48 hours, two consecutive sterile CSF cultures, CSF glucose >20 mg/dL, CSF protein <200 mg/dL, and lack of growth of microorganisms in CSF gram staining were considered successful treatment.[8-10]

Categorization of shunt infections

The patients were grouped as early and late shunt infection, taking into account the time from insertion of shunt to the onset of shunt infection. Shunt infections within and after the first six months following the operation were defined as "early and late shunt infections", respectively. Shunt infections of the patients were evaluated in terms of microorganisms grown in CSF cultures by dividing them into two groups as infections caused by staphylococci and the other microorganisms. The patients were also divided into two groups according to recurrence of the shunt infection in the 6 months of follow-up after the treatment. All these groups were compared in terms of clinical and laboratory characteristics, costs and duration of hospitalization.

Statistical Analysis

SPSS 19.0 (Statistical Package for the Social Sciences) program was used for statistical analysis. Mean, median, standard deviation, ratios and first and third quartiles were used in the descriptive statistics of the data. Mann-Whitney test was used to compare the means between the groups. Wilcoxon test was used for repeated measurements within the group. In the analysis of proportional data, Fischer test was used when chi-square test conditions could not be achieved.

RESULTS

Forty-seven cases of VPS infections diagnosed in 42 patients were included in our study. In 42 cases, the etiologies of the hydrocephalus were spina bifida in 17 (40%), germinal matrix/intraventricular hemorrhage (IVH) due to prematurity in 11 (26%), congenital hydrocephalus in 7 (16%), bacterial meningitis in 3 (7%), encephalocele in 1 (2%) intracranial hemorrhage developed after the neonatal period in 3 (7%) patients. Fever (71%), nausea and vomiting (42%), and change in consciousness (16.6%) were the most common

Table 1. Demographic and clinical features of the patients
*(Values in normal distribution are given as mean±standard deviation. Values not normally distributed are given as median and quartile 1-3 and marked with *. Abbreviations: GM-IVH: germinal matrix -intraventricular hemorrhage)*

Age, months	5* (3-15)
0-6	54.7 (23)
6-12	16.6 (7)
12-24	21.4 (9)
>24	7.1 (3)
Gender n (%)	
Male	15 (35)
Female	27 (55)
Etiologies of Hydrocephalus n, (%)	
Spina Bifida	17 (26)
GM-IVH	11 (26)
Congenital hydrocephalus	7 (16)
Encephalocele	3 (7)
Intracranial hemorrhage	3 (7)
Meningitis	1 (2)
Time between shunt operation and onset of infection, days	172 * (20-220)
Early/Late infection n, (%)	
Early	34/47 (72)
Late	13/47 (28)
Complaints on admission %, (n)	
Fever	71.4 (30)
Nausea/Vomiting	42.8 (18),
Change in conscience	16.6 (7)
Seizure	14.2 (6)
Headache	11.9 (5)
Rubor at the site of shunt	11.9 (5)
Restlessnes	7.1 (3)[d]
Recurrence in follow-up % (n)	40 (19)
Mortality	3 (7)

complaints and 42% (n=18) of the patients had two or more complaints on admission. The demographic data and clinical characteristics of the patients are summarized in Table 1, and their laboratory features in Table 2.

Table 2. Laboratory findings of the patients
(Abbreviations: WBC: white blood cell, Neut: Neutrophils, Hb: hemoglobin, CRP: C-reactive protein, CSF: cerebrospinal fluid)

	On Admission	On Discharge
WBC /uL	16214±9321	10230±2809
Neut /uL	9083±7654	4346±2001
Hb mg/dL	9.9±1.2	10.1±1.1
Platelet /uL	503500±218300	346000±51400
CRP mg/dL	9.7±11.5	0.4±0.15
CSF Glucose mg/dL	24±19.5	36.3±29.4
CSF protein mg/dL	375.9±547.7	84.8±63.4
CSF cell count / mm^3	901±2287	20.1±38.5

The median time from VPS insertion to the onset of infection was 78 days (Q1-Q3; 21-217). Twenty-nine (70%) patients were evaluated as "early shunt infection" due to the development of infection within the first 6 months. In comparison of the groups as early and late VPS infection, there was a significant difference between groups in terms of patients' ages. Patients with early shunt infection was significantly younger (p<0.001) than the patients with late VPS infection (Table 3).

Considering the CSF cultures of the patients, 81% of the patients had positive CSF culture and the CSF culture remained sterile in 8 (19%) patients. The majority of the shunt infections (59%, n=25) were caused by gram-positive bacteria, 26% (n=11) of them by gram-negative microorganisms (Figure 1). The duration of antibiotherapy was significantly shorter in "staphylococcal shunt infections" compared to shunt infections caused by other microorganisms (p=0.024) (Table 4).

Table 3: Comparison of early versus late ventriculoperitoneal shunt infections
*(Values in normal distribution are given as mean±standard deviation. Values not normally distributed are given as median and quartile 1-3 and marked with *. Abbreviations: TL: Turkish Lira, CRP: c-reactive protein, CSF: cerebrospinal fluid)*

	Early infection Mean±SD / n / (%)	Late infection Mean±SD / n / (%)	p
Age (months)	*4 (2-12)	*27 (14-31)	<0.001
Cost (TL)	8965±8906	26402±36175	0.064
Hospitalization duration (days)	33.10±17.79	39.25±27.07	0.856
Average duration of antibiotherapy (days)	27.27±12.90	30.58±19.46	0.944
Neutrophil count (/uL)	9173±8766	8821±5509	0.707
Hemoglobin (gr/dL)	9.70±1.07	10.47±1.42	0.084
CRP (mg/dL)	8.62±9.44	13.69±16.57	0.824
CSF Protein (mg/dL)	385.33±444.35	179.58±119.81	0.427
CSF Glucose (mg/dL)	21.97±17.61	30.33 ±21.98	0.283
Need for intraventricular antibiotherapy, n (%)	13 43.3%	2 16.7%	0.103

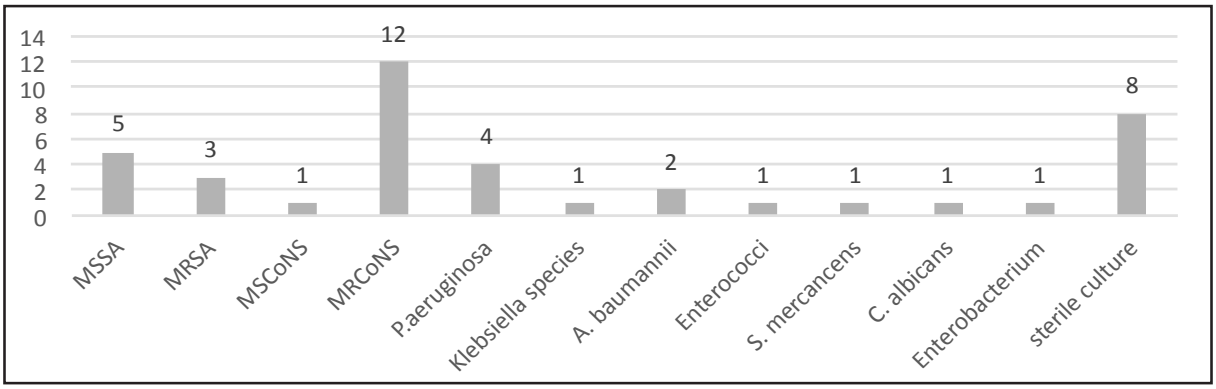

Figure 1. Microorganisms in cerebrospinal cultures
(MSSA: Methicillin- sensitive S. aureus, MRSA: Methicillin-resistant S. aureus, MSCoNS: Methicillin-sensitive coagulase-negative staphylococcus, MRCoNS: Methicillin- resistant coagulas- negative staphylococcus, P. Aeruginosa: Pseudomonas aeruginosa, A. baumannii: Acinetobacter baumanni, S. mercancens: Serratia mercancens, C. albicans: Candida albicans).

Table 4. Comparison of shunt infections caused by staphylocci versus other microorganisms

	Staphylococci Mean±SD / n / (%)	Other microorganisms Mean±SD / n / (%)	p
Cost (TL)	10359±10839	17209±28097	0.497
Hospitalization duration (days)	34.40±22.64	35.27±19.29	0.588
Average duration of antibiotherapy (days)	27.05±18.63	29.27±10.78	0.024
Neutrophil count (/uL)	9029.50±8334.87	9112.73±7695.52	0.910
Hemoglobin (gr/dL)	9.80±1.13	10.04±1.31	0.472
CRP (mg/dL)	7.08±9.55	12.78±13.37	0.166
CSF Protein (mg/dL)	199.70±155.04	441.86±496.45	0.262
CSF Glucose (mg/dL)	26.50±18.57	22.41±19.74	0.378
Need for intraventricular antibiotherapy, n (%)	13 (43.3)	2 (16.7)	0.103

Table 5. Comparison of ventriculoperitoneal shunt infections in terms of recurrence in 6 month follow-up
(EVD: Extra-ventricular drainage).

	Recurrence in 6 months follow-up		
	Yes	No	p
Duration of hospitalization (days)	41.1±39.2	35.9±20.8	0.831
Time between shunt application and onset of infection, days	*135.7±235.5	*274.9±408.4	0.738
Average duration of antibiotherapy (days)	32.3±24.0	27.4±12.6	0.536
Positive blood culture, n (%)	4 33.3%	1 3.6%	0.022
History of shunt infection, n (%)	6 50.0%	8 28.6%	0.193
Need for intratventricular antibiotherapy, n (%)	6 50.0%	9 32.1%	0.285

In the 6-month follow-up after the treatment, 40% (n=19) cases of the VPS infections recurred within 6 months. No statistically significant difference was observed between demographic data, clinical characteristics and laboratory values between the infection attacks that did, and did not recur. But blood culture positivity rates were significantly higher in the VPS infections that recurred (p=0.022) (Table 5).

DISCUSSION

Shunt infections still remain an important cause of morbidity and mortality in pediatric age.[1,11] Shunt infection is an important issue for the health system, considering the length of hospitalization, antibiotics applied and the need for shunt revision.[11] In our study, there was no significant difference between the subgroups of shunt infections in terms of

hospitalization cost.

The most common etiological factor in patients with shunt infection was reported as congenital anomalies.[1] In our study, the most common indication for shunt requirement was spina bifida, in accordance with the literature. When spina bifida, encephalocele and congenital hydrocephalus are evaluated together, it has been observed that congenital anomalies constitute 55% of our patients.

In our study, 71% of the patients were under one year of age, 55% of them were under six months of age and only 7% of them were older than two years of age. In the light of the recent literature, shunt infections are more common under 12 months of age, and it has been shown that the risk of shunt infection is three times higher in patients under 6 months of age.[12] Immaturity of the immune system has been considered as a reason for the increased risk of shunt infections in the early childhood. Morine et al.[13] also reported that the highest complication rate was in children under one year old. In this study, delayed wound healing, longer hospital stay and higher concentration of resistant microorganisms in the skin of infants were accused for higher rates of early shunt infections.

In our study, children under 2 years of age constituted 93% of all patients, consistent with the literature. There are two reasons for this result. Firstly, insertion of VPSs is generally required in a very early period of life. Congenital malformations, hemorrhagic disease of the newborn, germinal matrix-intraventricular hemorrhage due to prematurity, all of which constitute the majority of the indications for VPS applications. Even in the neonatal period shunting may be required.[14] Secondly according to the literature, VPS infections occur within the first 1-2 months after application of VPS[12,13], so that, it is thought that this is the reason why shunt infections were observed more frequently in early childhood.

According to data reported from Turkey[1], Portugal[14] and Korea[12], shunt infection most commonly develops in the first 1-3 months after the shunt procedure. In our study; 70% of shunt infections developed within the first six months in accordance with the literature, but there was no statistically significant difference between early and late shunt infections except the patients' ages. The patients diagnosed as early-onset shunt infection were significantly younger than the patients with late infection.

In previous studies, gram-positive bacteria and especially coagulase-negative staphylococci were reported as the most common cause of VPS infections.[1,12,14-16] Colonization of the shunt during application with direct skin flora is accused for the development of shunt infection. In our study, the most common strain in the CSF cultures of the patients was gram-positive microorganisms with a rate of 60%. In comparison of shunt infections caused by staphylococci and other strains, duration of antibiotic administration was found to be significantly shorter in infections due to *Staphylococci*. This result was thought to be due to microorganism resistance patterns in gram-negative and fungal infections leading to development of shunt infection, suggesting longer antibiotic administration in the treatment guidelines in infections caused by gram-negative strains.[16-18]

When the patients whose infections did, and did not recur in the follow-up after discharge were compared; the rate of microorganism growth in blood culture was significantly higher in patients with recurrence of shunt infection, than the group without. These data suggest that patients with positive blood culture had more severe and generalized infection[17], and the source of recurrent shunt infection in these patients was not only the colonization of the shunt catheter but also it may have had a different focus.

Our study should be interpreted within some limitations. Larger sample size would help to have more statistically significant results. Also a prospective design would provide a better follow up of the patients and chance to determine the risk factors for recurrence of the infection.

Despite advances in medical knowledge and practice, shunt infections continue to be an important complication in the treatment of hydrocephalus. Controversy still continues on the treatment management, risk factors and prevention of shunt infections.[18] Although antibiotic impregnated shunt applications are used to prevent shunt infections and

maximum infection control is applied during shunt application, the rates of shunt infection are not as low as desired.[19] It is thought that antenatal follow-ups and folic acid use to reduce anomalies such as spina bifida, which has an important place in the etiology of hydrocephalus[20], and practices to prevent germinal matrix-intraventricular bleeding in premature babies are considered to be of great importance since they will reduce the need for shunts in the society at the very beginning.[21]

Shunt infections, which were evaluated in many different aspects in our study, are one of the leading causes of central nervous system infections in childhood and, if not managed properly, may result in increased mortality and morbidity. Although shunt technology and intervention techniques have been developed in the last four decades, there is still no consensus on the prevention and management of shunt infections and their recurrence. Comprehensive studies on risk factors and treatment regimens to be carried out in cooperation with neurosurgeons and pediatricians are still required to establish a universal treatment protocol.

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