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Original Article / Özgün Araştırma

Evaluation of Shunt-Related Ventriculitis in Infants

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Abstract

Aims: Shunt-related infections are resistant to antibiotics. This study examined patients aged under two years after ventriculitis. It is the first study on ventriculitis developed in a completely closed system (without skin defect infection, or puncture history), evaluating infants only.

Method: The study included 13 subjects (four females) with ventriculitis who had undergone surgery for hydrocephalus during the neonatal period and were monitored for shunt infection, evaluating certain parameters.

Results: Ventriculitis developed on an average of 2.8 months after surgery. The most common causes of hydrocephalus were spina bifida and intraventricular hemorrhage. Bacteria grown in culture included Staphylococcus epidermidis, Staphylococcus aureus, Klebsiella pneumoniae, Pseudomonas aeruginosa, and Serratia marcescens. Seven (53.8%) patients were treated without complications. Among other patients, three (23.1%) developed multilocular cystic hydrocephalus and three (23.1%) exhibited decreased cerebrospinal fluid production and did not require shunting.

Conclusions: Patients receiving intraventricular therapy showed no complications, warranting further studies on early intraventricular therapy. In the presence of gram-negative bacterial growth, cerebrospinal fluid production may decrease and affected patients do not require shunts.

Key words: Ventriculitis, shunt infections, shunt related ventriculitis

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Bebeklerde Şant İlişkili Ventrikülitlerin Değerlendirilmesi

Öz

Amaç: Şanta bağlı enfeksiyonlar antibiyotiklere dirençlidir. Bu çalışmada ventrikülit sonrası iki yaş altı hastalar incelenmiştir. Tamamen kapalı bir sistemde (cilt defekti-enfeksiyonu, ponksiyon öyküsü olmadan) gelişen ventrikülit üzerine sadece bebekleri değerlendiren ilk çalışmadır.

Yöntemler: Çalışmaya yenidoğan döneminde hidrosefali nedeniyle ameliyat edilen ve şant enfeksiyonu açısından izlenen, ventrikülitli 13 olgu (dördü kadın) dahil edildi ve belirli parametreler değerlendirildi.

Bulgular: Ventrikülit ameliyattan ortalama 2.8 ay sonra gelişti. Hidrosefalinin en sık nedenleri spina bifida ve intraventriküler hemoraji idi. Kültürde üreyen bakteriler Staphylococcus epidermidis, Staphylococcus aureus, Klebsiella pneumoniae, Pseudomonas aeruginosa ve Serratia marcescens idi. Yedi (%53,8) hasta komplikasyonsuz tedavi edilmiştir. Diğer hastalardan üçünde (%23,1) multiloküler kistik hidrosefali gelişti ve üçünde (%23,1) beyin omurilik sıvısı üretiminde azalma görüldü ve şant gerekmedi.

Sonuç: İntraventriküler tedavi alan hastalarda herhangi bir komplikasyon görülmemiştir ve bu durum erken intraventriküler tedavi konusunda daha fazla çalışma yapılmasını gerektirmektedir. Gram-negatif bakteri üremesi varlığında, beyin omurilik sıvısı üretimi azalabilir ve etkilenen hastalar şant gerektirmez.

Anahtar kelimeler: Ventrikülit, Şant enfeksiyonları, Şant ilşkili ventrikülitler.

INTRODUCTION

The ventriculoperitoneal shunt is the most widely used and effective treatment method in the treatment of hydrocephalus. The most common shunt-related complications are infection and obstruction[1].

In shunt-related ventriculitis, leukocytes are present in cerebrospinal fluid (CSF) and CSF cultures exhibit bacterial growth. When the proximal end of the shunt catheter is infected, the infectious agent enters the ventricular system directly and causes clinical findings. These infections are typically resistant to short-term antibiotics, requiring long-term intravenous antibiotics, intraventricular antibiotic therapy, or a combination of these[2,3]. Ventriculitis can result in brain abscesses, adhesions, and septations within the ventricular system[4].

We evaluated patients younger than two years of age who were monitored for ventriculitis. We discussed the etiopathogenesis of ventriculitis, identified potential infectious agents, and evaluated patient outcomes. To our knowledge, this is the first study on ventriculitis developed in a completely closed system (without skin defect infection, or puncture history), evaluating infants only.

METHODS

This study was approved by Health Sciences University Gazi Yaşargil Training and Research Hospital Clinical Research Ethics Committee with the number 361, dated 25/10/2019. The study was conducted by the principles of the Declaration of Helsinki.

We studied 13 patients with ventriculitis in our hospital who had undergone surgery during the neonatal period between June 2017 and September 2019 and were monitored for shunt infection. We evaluated the patients' age and sex, cause of hydrocephalus, infection after shunt placement, the microbial agent used, and patients' final status.

The diagnosis of ventriculitis was based on CSF cell count and CSF culture results, along with contrast enhanced cranial magnetic resonance imaging or computed tomography of the brain (Figure 1). The study excluded patients with incomplete wound healing, open wounds around the shunt system, or a history of post-puncture infection.

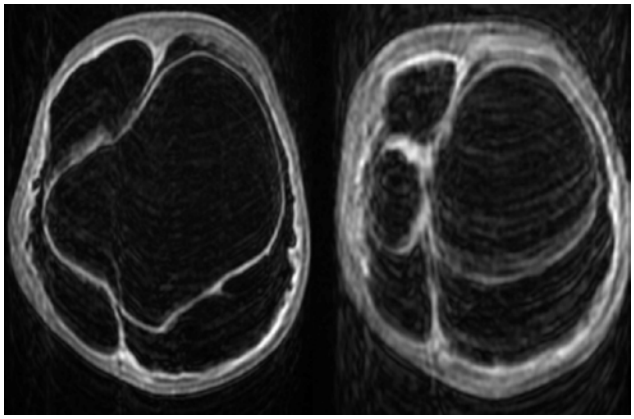

Figure 1. Contrast-enhanced cranial magnetic resonance imaging of a ventriculitis patient, infected with methicillin-resistant Staf. epidermidis

CSF samples for culture were obtained through a shunt pump, lumbar puncture, or transependymal puncture under sterile conditions. The samples were sent to the laboratory in a jel-free tube for direct microscopic examination and culture. First, under direct microscopic examination, the CSF sample was examined on a Thoma slide and the cells were counted. Then a drop of 5% sheep blood was added to the blood agar medium containing the remainder of the CSF sample. Medium plates were kept in an oven at 36°C for 48 to 72 hours. Although biochemical studies (glucose, protein, and chloride) were performed on the CSF sample for diagnosis and treatment follow-up of the patients, the data were not included in the study. This is because the study was conducted to evaluate ventriculitis.

The two authors of the study obtained the data from the hospital database (Hospital Information Management System) and evaluated patient files and separately.

Statistical Analysis

The SPSS for Windows (version 20.0) was used to analyze the study data. The data were expressed as means, numbers, and percentages, along with minimum and maximum values.

The one-way analysis of variance was used to compare the mean of the normally distributed parameters. The nonparametric Kruskal–Wallis H-test was utilized in other cases. The categorical parameters were expressed as percentages and absolute frequencies. A p-value of <0.05 was considered statistically significant.

RESULTS

Shunt-related ventriculitis was detected in 13 (%14.9) of 87 patients who were followed up for shunt infection. Of the 13 patients, four (30.7%) were female and nine (69.3%) were male. The youngest patient was two months old and the oldest was 20 months old, with a mean age of 6.9 months. Nine patients (69.3%) were six months old or younger. Only two patients were older than 12 months (Table 1).

Ventriculitis developed in the first month after surgery for hydrocephalus at the earliest and six months later at the latest, with a mean interval of 2.8 months. Six (46.1%) of the patients had a history of premature birth.

Concerning causes of hydrocephalus, five patients (38.5%) had spina bifida, four (30.7%) had an intraventricular hemorrhage, two (15.4%) had congenital anomalies, one (7.7%) had Dandy-Walker malformation, and one (7.7%) had an encephalocele.

All patients had undergone surgery one to five times and the average number of procedures was 2.85.

The antibiogram of cultures revealed that 53.8% of bacteria were Gram-positive species and 46.2% were Gram-negative species. Staphylococcus epidermidis was found in four patients (30.7%); Staphylococcus aureus, in three (23.1%); Klebsiella pneumoniae, in three (23.1%); Pseudomonas aeruginosa, in two (15.4%); and Serratia marcescens, in one (7.7%). Of these bacteria, 50% of S. epidermidis organisms and 66.6% of S. aureus organisms were methicillin-resistant (Table 1).

In patients with shunt dysfunction, the shunt was removed at the time of admission. In

patients without shunt dysfunction, the shunt was removed when culture findings of CSF obtained from the shunt pump, by lumbar puncture, or by transepidimal puncture were positive. Five patients (38.5%) were subsequently treated with external ventricular drainage.

Table I: Patients Characteristics

	Gender	Age (month)	Time of infection (month)	Etiology	Culture	Number of Surgery
1	Male	4	3	Intraventricular hemorrhage	Staphylococcus aureus	2
2	Male	6	5	Spina bifida	Staphylococcus epidermidis	2
3	Female	4	2	Spina bifida	Staphylococcus aureus	5
4	Female	9	2	Congenital hydrocephalus	Pseudomonas aureginosa	4
5	Male	3	2	Dandy Walker Malformation	Klebsiella pneumoniae	3
6	Male	16	1	Intraventricular hemorrhage	Pseudomonas aureginosa	2
7	Female	3	2	Spina bifida	Staphylococcus epidermidis	2
8	Male	11	5	Intraventricular hemorrhage	Staphylococcus aureus	4
9	Male	3	2	Encephalocele	Staphylococcus epidermidis	2
10	Male	3	2	Spina bifida	Staphylococcus epidermidis	2
11	Female	6	4	Intraventricular hemorrhage	Klebsiella pneumoniae	1
12	Male	2	1	Spina bifida	Serratia marcescens	3
13	Male	20	6	Congenital	Klebsiella pneumoniae	5

Initial antibiotic therapy consisted of a combination of vancomycin and ceftriaxone in seven patients (53.8%), a combination of vancomycin and meropenem in five (38.5%), and a combination of piperacillin/tazobactam and ceftazidime in one (7.7%). Seven patients responded to this treatment. In six patients, the treatment response was insufficient. Subsequently, three (23.1%) received a combination of vancomycin and meropenem as a secondary treatment and three (23.1%) received a combination of vancomycin and linezolid as a secondary treatment. In two of the six patients, the treatment response was still insufficient. One (7.7%) received intraventricular colistin treatment (for five days), and one (7.7%) received intraventricular gentamicin (for five days) as tertiary treatment. Duration of treatment ranged from 14 to 42 days and the average duration was 21.2 days.

While the average treatment duration in patients aged six months and below was 21.00 ± 8.57, the average treatment duration in patients over six months was 20.25 ± 4.92, which was not significant (p=0.875).

Concerning the final status of the patients, seven (53.8%) recovered without complications. Five patients received ventriculoperitoneal shunts, one patient (with the Dandy-Walker malformation) received a ventriculo cystoperitoneal shunt, and one patient received a ventriculo vesical shunt. Multilocular cystic hydrocephalus developed in three other patients (23.1%), who were treated with endoscopic cyst fenestration and multiple shunts. They also had purulent CSF at the time of admission. In the other three patients (23.1%), CSF production decreased and shunts were not needed. One of these three patients died of pneumonia during the 20 months of follow-up. Of the other two, one was monitored for five months and the other for eight months; without requiring shunts.

When categorizing the patients based on the growth results in the culture as gram-negative and gram-positive, there were no statistically significant differences based on sex (p=0.657), etiology of shunt placement (p=0.186), or prematurity (p=0.617).

Considering the final status of patients with gram-negative bacterial growth, 50% of patients did not need it, while 50% needed shunts. Regarding the final status of patients with gram-positive bacterial growth, 42.9% of patients developed multilocular hydrocephalus, while 57.1% required shunts, which was significant (p=0.015).

When patients were categorized based on the growth results in the culture as gram-negative and gram-positive, there were no significant differences based on age (p=0.160), time to the development of infection after surgery (p=0.729), and the number of surgeries (p=0.106).

The average duration of antibiotic therapy in gram-negative bacteria was 25.17 ± 8.519, while in gram-positive bacteria, the average duration of antibiotic therapy was 17.00 ± 3.742, with a significant difference (p=0.042).

DISCUSSION

According to the final status of patients in our study, the probability of developing multilocular cystic hydrocephalus was higher in patients with gram-positive bacterial growth. In half of the patients with gram-negative bacterial growth, shunts were not necessary. This suggests an association with functional impairment secondary to infection in the ventricular ependyma and choroid plexus.

Central nervous system infections are a group of diseases that can be life-threatening, particularly in the childhood period[5]. Bacterial ventriculitis is a complicated disease group of central nervous system infections if early diagnosis and treatment cannot be achieved[4].

Few studies of shunt-related ventriculitis have been conducted. These studies employed adult subjects and used external catheters. They did not focus on the period in which the immune system is underdeveloped, particularly in newborns and older infants.

To assess for ventriculitis, CSF is directly taken from the ventricle and the diagnosis is based on the presence of leukocytes or lymphocytes. Although the literature suggests different definitions of the diagnosis, the most common is the production of the causative microorganism in CSF culture[2]. Despite advances in medicine, the prevalence of neurological sequelae following neonatal central nervous system infections is extremely high. With this, despite the limited information about the definition, pathophysiology, and incidence of ventriculitis, early diagnosis is important to prevent the development of neurological complications[6].

In the literature, there are studies on shunt-related ventriculitis in adults and ventricular puncture, Ommaya pump, etc., related ventriculitis in the neonatal period. However, there is a lack of studies on ventriculoperitoneal shunt-related ventriculitis in infancy. In the present study, we aimed to contribute to the treatment management of ventriculitis by discussing the etiopathogenesis and outcome in ventriculoperitoneal shunt-related ventriculitis in infancy.

In a study of 41 patients with ventriculitis between the ages of five and 69, 22 patients (53.7%) were male. Only two patients had shunt-related ventriculitis. The others developed ventriculitis after various neurosurgical procedures[7]. In a cohort study of patients between the ages of 0 and 18, female sex was reported to be a risk factor for shunt infections[8]. In our study, more than two-thirds of the patients were male infants. However, since our study is not a comparative study of shunt infection and ventriculitis, we cannot conclude that the male gender is a risk factor for the development of ventriculitis.

The risk of shunt infection is known to increase in neonates and very young children due to the insufficient development of the immune system. In the studies of children younger than six months, the frequency of shunt infection is as

high as 19%[9]. However, no study of ventriculitis specifically in this age group was previously conducted. In our study, the youngest patient was two months old, while the oldest was 20 months old, with a mean age of 6.9 months. Furthermore, the majority of the patients were six months old or younger. Therefore, an age of less than six months may also pose a risk factor for ventriculitis[9]. However, our study observed that age did not affect the duration of treatment.

Shunt infections are common in the first three months after shunt placement, but they are rare after one year[10]. According to a study, 69% of shunt infections occur in the first month after shunt insertion and 86% occur in the first six months[11]. In our study, ventriculitis developed one month after surgery at the earliest and 6 months after surgery at the latest. This finding aligns with the literature.

Risk factors for the development of shunt infections can be classified as host-specific and procedure-specific. Host-specific factors include premature birth, young age, history of previous shunt infection, and the cause of hydrocephalus (e.g., intraventricular hemorrhage and spina bifida)[12]. Among our patients, 46% had a history of premature birth and the causes of hydrocephalus included spina bifida and intraventricular hemorrhage.

Procedure-specific factors include a history of three or more shunt revisions, surgical duration, neuroendoscopic procedures, and surgeon's experience[13]. For our patients, all operations were performed by the same neurosurgeon, and for almost all patients, the surgical details (operating room, auxiliary staff, equipment, surgical materials and technique, surgical time) were similar. Neuroendoscopy was not performed for surgery before the onset of ventriculitis. All patients had a history of at least one shunt procedure, with the maximum being five and five patients (38.4%) had undergone at least three shunt procedures. Among the risk factors for ventriculitis examined in our study, we observed premature birth, cause of hydrocephalus, and a history of recurrent surgery.

In a study of 41 patients who were monitored for ventriculitis after neuroendoscopic surgery, the bacteria growing in culture were identified as S. epidermidis, S. aureus, K. pneumoniae, Acinetobacter baumannii, Bacteroides fragilis, Streptococcus species, Enterobacteriaceae, and P. Aeruginosa[7]. In the pediatric population, shunt infections are generally caused by Gram-positive microorganisms with low pathogenicity[11,14]. Pseudomonas, Escherichia, Klebsiella, Propionobacter, and Candida species and Haemophilus influenzae are less common in cultures. Multiple bacteria can be isolated in 20% of cultures[10,14,15]. In our study, we isolated S. epidermidis, S. aureus, K. pneumoniae, P. aeruginosa, and S. marcescens. This suggests that our patients developed infections mostly due to contamination by skin pathogens. However, Gram-negative microorganisms are infectious agents, particularly in the neonatal period due to the underdevelopment of the immune and complement systems[11]. Only one of our patients was still in the neonatal period, and S. marcescens, a Gram-negative bacterium, was identified in that infant's culture.

According to the guidelines of the Infectious Diseases Society of America, the initial treatment for shunt infections should be vancomycin[16]. However, intrathecal or intraventricular administration of antibiotics for resistant and recurrent ventriculitis infections may increase the level of antibiotics in the ventricular system and thereby increase the efficacy of the treatment. Hence, intraventricular therapy may be an effective treatment option[17,18]. In 12 of our patients (92.3%), vancomycin was the initial treatment, while piperacillin/tazobactam and ceftazidime combination therapy was the initial treatment in one (7%). Treatment response varied based on culture findings and treatment response.

When treatment response was insufficient, intraventricular therapy (colistin or gentamicin) was needed. Both patients in need of intraventricular treatment exhibited growth of Gram-negative bacteria (P. aeruginosa and K. pneumoniae).

In a study conducted by Wang et al., although the mean hospital stay was 40.3 days, shunt-related ventriculitis was not the only pathological condition assessed, and hospital stay included the period before onset of ventriculitis[7]. In our study, all patients were evaluated only after the diagnosis of ventriculitis and the mean duration of treatment was 21.2 days. We found that the treatment duration was longer in patients with gram-negative bacterial growth.

The rates of comorbidity and mortality significantly increase among patients who develop ventriculitis[19]. Among our patients, seven (53.8%) were treated without complications. Ventriculitis can result in brain abscess, septations in the ventricles, other sequelae, and death, and long-term hospitalizations are often needed.4 As mentioned, multiloculated cystic hydrocephalus developed in three patients (23.1%). Ten patients (76.9%) underwent shunt reinsertion. According to the findings of experimental studies,20,21 CSF production may decrease due to histopathological changes in the choroid plexus, particularly in infections caused by Gram-negative bacteria[22]. In three patients (23.1%) in whom CSF production decreased and who did not need shunts, Gram-negative species (K. pneumoniae in two and S. marcescens in one) were detected. This finding supports those of previous experimental studies. No complications occurred in two patients who needed intraventricular therapy. None of the children died due to ventriculitis or its complications.

CONCLUSION

Our study is the first to examine shunt-related ventriculitis in patients aged 0 to 24 months with a completely closed system. Male sex predominance was observed among patients with shunt infections. Premature birth, history of recurrent surgery, and cause of hydrocephalus (spina bifida, intraventricular hemorrhage, and other congenital anomalies) were determined to be risk factors for ventriculitis. Ventriculitis, like other shunt infections, is most commonly caused by contamination of the shunt with skin flora, but treatment for ventriculitis can be longer and more complicated. Because the patients receiving intraventricular therapy experienced no complications, studies of the early use of intraventricular therapy are needed. CSF production may decrease with Gram-negative bacterial infections and affected patients do not need shunts. However, because long-term follow-up of such patients has not been reported, physicians should monitor these patients for other complications, particularly multilocular hydrocephalus.

Ethics Committee Approval: This study was approved by the ethics committee of Health Sciences University Gazi Yaşargil Training and Research Hospital with the number 361, dated 25/10/2019. The study was conducted in accordance with the principles of the Declaration of Helsinki.

Conflict of Interest: The authors declared no conflicts of interest.

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