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Evaluation of Ventriculoperitoneal Shunt Infections in Children

Çocuklarda Ventrikülоperitoneal Şant Enfeksiyonlarının Değerlendirilmesi

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Abstract

Objective: Ventriculoperitoneal shunt (VPS) infection is an important cause of morbidity and mortality in both adults and children with hydrocephalus. Inappropriately treated shunt infections may cause of mental retardation, neurological deficits and also death in patients. The aim of this study was to determine the demographic characteristics, the causes of hydrocephalus, microorganisms responsible for infection, antibiotic susceptibility of microorganisms and treatment modalities of the pediatric patients treated with VPS infection.

Material and Methods: Medical records of the patients, who were treated with a diagnosis of VPS infection in the Farabi Hospital of Karadeniz Technical University Medical Faculty between 2012-2018, were reviewed retrospectively.

Results: Ventriculoperitoneal shunt was implemented in 362 children. In the follow-up of 26 patients, 29 VPS infection episodes were developed. The most common causes of VPS infection were congenital malformation. *Staphylococcus epidermidis* (34.5%), *Enterococcus faecium* (13.8%), *Escherichia coli* (10.3%), *Serratia liquefaciens* (6.9%), *Bacillus megaterium* (6.9%), *Staphylococcus aureus* (3.4%), *Klebsiella pneumoniae* (3.4%), *Candida albicans* (3.4%) were yielded in the cerebrospinal fluid. Insertion of an extraventricular drain (EVD) was applied five patients, insertion of an extraventricular drain and removal of the infected shunt was applied 13 patients. Of the eight patients whose shunt had not been removed, VPS re-infection was developed in three patients. VPS re-inserted in 12 patients. Three patients died.

Öz

Giriş: Ventrikülоperitoneal şant (VPŞ) enfeksiyonları, hidrosefali nedeniyle şant takılan erişkin ve çocuk hastalarda, morbidite ve mortalitenin önemli nedenlerinden biridir. Hızlı ve uygun tedavi edilmeyen şant enfeksiyonları, hastalarda zeka geriliğine, nörolojik hasarlara, hatta ölüme neden olabilmektedir. Bu çalışmanın amacı VPŞ takılmış ve şant enfeksiyonu nedeniyle tedavi edilmiş çocuk hastaların demografik özelliklerini, hidrosefali nedenlerini, enfeksiyondan sorumlu mikroorganizmaları, mikroorganizmaların antibiyotik duyarlılıklarını ve uygulanan tedavileri ortaya koymaktır.

Gereç ve Yöntemler: Karadeniz Teknik Üniversitesi Tıp Fakültesi Farabi Hastanesi'nde 2012-2018 tarihleri arasında VPŞ enfeksiyonu tanısı ile yatarak tedavi gören 1 ay-18 yaş arası hastaların dosyaları ve bilgisayar kayıtları geriye dönük olarak incelendi.

Bulgular: Üç yüz altmış iki çocuk hastaya VPŞ takılmıştı. Yirmi altı hastanın izleminde, 29 (%8) kez VPŞ enfeksiyonu geliştiği görüldü. Şant takılma nedenleri arasında en sık konjenital nedenler vardı. Beyin omurilik sıvısı (BOS) kültüründe sırasıyla *Staphylococcus epidermidis* (%34.5), *Enterococcus faecium* (%13.8), *Escherichia coli* (%10.3), *Serratia liquefaciens* (%6.9), *Bacillus megaterium* (%6.9), *Staphylococcus aureus* (%3.4), *Klebsiella pneumoniae* (%3.4), *Candida albicans* (%3.4) üredi. Beş hastanın şantı eksternal drenaja alındı. On üç hastanın şantı çekilip, eksternal drenaj uygulandı. Şantı değiştirilmeyen sekiz hastanın üçünde tekrar şant

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Conclusion: The treatment of shunt infections is substantially difficult and consequently have high economic costs. Venticuloperitoneal shunt infections may be presented silent. Suspicion of VPS infection is very important for diagnosis. Simple measures to be applied meticulously during surgery can significantly reduce the infection rate.

Keywords: Hydrocephalus, ventriculoperitoneal shunt infection, children

enfeksiyonu gelişti. Hiçbir hastaya intraventriküler tedavi uygulanmadı. On iki hastaya yeniden şant takıldı. İzlemde toplam üç hasta kaybedildi.

Sonuç: Şant enfeksiyonlarının tedavisi oldukça zordur ve buna bağlı olarak yüksek maliyete sahiptir. VPŞ enfeksiyonlarında klinik sessiz olabilir. Şüphelenmek tanı için çok önemlidir. Cerrahi sırasında titizlikle uygulanacak basit önlemler enfeksiyon oranını önemli ölçüde azaltabilir.

Anahtar Terimler: Hidrosefali, ventrikülöperitoneal şant enfeksiyonu, çocuk

Introduction

The most commonly used method in the treatment of hydrocephalus is the shunt systems that provide the drainage of cerebrospinal fluid (CSF) to the peritoneum, pleural space and atrium. For this purpose, ventriculoperitoneal, ventriculopleval, ventriculoatrial and lumboperitoneal shunt systems have been developed (1). Among these shunt systems, ventriculo peritoneal shunts (VPS) is the most commonly used. One of the major causes of shunt dysfunction is shunt infections and its frequency varies between 0.17% and 33% (2,3). VPS infections are one of the major causes of morbidity and mortality in both adults and children. Shunt infections untreated in a rapid and appropriate way may cause mental deficiency, neurological damage or even death in patients. Risk factors for VPS infection are; small age (< 6 months), especially premature birth, cause of hydrocephalus, development of infection at the shunt entrance, recent shunt revision, previous shunt infection, prolonged operation time, surgeon experience, and systemic infection. Shunt infections are observed more frequently in the first two months after shunt insertion and their frequency decreases after one year (4). A history including ew-developed fever, headache and nausea; and physical examination including lethargy, changes in consciousness, redness and tenderness along the shunt path supports VPS infection. VPS infection should also be considered for the patients with VPS whose fever focus could not be found and whose peritonoid and abdomen tenderness could not be explained in any other way. CSF sampling should be performed for diagnosis. The presence of abnormal CSF cells, glucose and protein does not make a definitive diagnosis of VPS infection, but the fact that it is normal does not exclude VPS infection. Growth in culture ensures the diagnosis. Shunt end culture is recommended to be sent when shunt is removed considering for ventriculoperitoneal shunt infection (5). The most commonly isolated microorganisms in CSF in VPS infections are *Staphylococcus epidermidis* and *Staphylococcus aureus*, respectively, which are found in the skin flora and inoculated during shunt surgery. Other factors include *Escherichia coli, Klebsiella pneumoniae, Proteus, Pseudomonas, Enterococcus* and rarely fungal agents (4,6). The treatment of shunt infections is very difficult and costly. The most effective method in treatment is the administration of appropriate antibiotic therapy along with external ventricular drainage and re-placement of the shunt. Intra-venric antimicrobial therapy should be considered in patients who respond poorly to systemic antimicrobial therapy alone (5,7).

The aim of this study was to determine the demographic characteristics of the pediatric patients who were placed VPS and treated for shunt infection, the causes of hydrocephalus, the microorganisms responsible for infection, the antibiotic susceptibility of microorganisms and the treatments applied.

Materials and Methods

The files and computer records of patients aged between 1 month and 18 years who were diagnosed with VPS infection and hospitalized in the Farabi Hospital of Karadeniz Technical University Medical Faculty between 2012 and 2018 were retrospectively analysed. This is a retrospective descriptive study. Ethics committee approval was received from Karadeniz Technical University Faculty of Medicine.

The demographic data of the patients, etiology of hydrocephalus, date of shunt insertion, CSF biochemical and microbiological laboratory results at the time of shunt infection diagnosis, antibiotics, treatment strategies, length of hospital stay and mortality were recorded.

Diagnosis of ventriculoperitoneal shunt infection was done according to history (headache, nausea, vomiting and seizure) and physical examination findings (fever, change of consciousness, nuchal rigidity, Kernig and Brudzinski symptoms) and pressure, appearance, cell count and gram smear of CSF obtained from ventricle (with fontanelle open ones) or from the shunt reservoir, protein, glucose level and culture results (8).

Data for statistical calculations in the study were expressed as mean ± standard deviation (SD) in continuous variables and as percentage (%) in categorical variables. For the comparison of the quantitative data of the groups, the Student-T test was used for those with normal distribution and the Mann-Whitney U test was used for those with abnormal distribution. The

Chi-square test was used to compare the non-measurable categorical data. Ones of which p value was 0.05 were considered significant.

Results

Between 2012-2018, a total of 362 children undergone shunt. In the course of 26 patients, it was seen that VPS infection was occured 29 times (8%). Of the patients with shunt infection, 15 (57.7%) were female and 11 (42.3%) were male. The mean age of the patients was 4.88 ± 3.16 years (0-11 years). The causes of shunt insertion were respectively; Arnold Chiari malformation type II (38.5%) and meningomyelocele (23.1%)-(61.6%), Dandy Walker malformation (15.4%), astrocytoma (11.5%), colposephaly (7.7%), intracranial hemorrhage (3.8%) and Walker Walburg syndrome (3.8%). The cause of hydrocephalus was not determined in four (13.8%) patients.

An antibiotic free shunt was inserted to 21 (72%) patients and antibiotic impregnated shunt was placed to five patients (24%). 16 of the inserted shunts were without pressure program and 10 of them had medium pressure program. Shunt infection occurred in 12 (41.4%) patients in the first 60 days after the operation, in 8 (27.6%) patients in 60-180 days after the operation and in 9 (31.0%) patients after 180 days. At the time of admission, 14 (48.3%) patients had fever, two (6.9%) had headache, five (17.2%) had nausea and vomiting, two (6,9%) had seizures, seven (24.1%) had consciousness, two (6.9%) had redness and heat increase during the shunt trace. Four (13.8%) patients were diagnosed with VPS infection during routine controls. Demographic and clinical characteristics of the patients are shown in Table 1.

Ventricular dilatation was detected in brain tomography of all patients. Serum and CSF laboratory findings at the time of diagnosis are shown in Table 2. In the CSF cultures, *S. epidermidis* growth was seen in 10 (34.5%) patients, *S. aureus* in one (3.4%) patient *Enterococcus faecium* in four (13.8%) patients, *E. coli* in three (10.3%) patients, *K. pneumoniae* in one (3.4%) patient, *Serratia liquefaciens* in two (6.9%) patients, and *Bacillus megaterium* in two (6.9%) patients. Six of the *S. epidermidis* isolates were methicillin sensitive and four were methicillin resistant. *S. aureus* was sensitive to methicillin. One patient (3.4%) experienced *Candida albicans* growth. Seven (24.1%) patients did not have growth in CSF culture.

For the patients who were diagnosed with ventriculoperitoneal shunt infection, empirical 3rd generation cephalosporin and vancomycin treatment was started after CSF sampling was conducted. According to CSF culture results and clinical response, 14 patients received carbapenem, 8 patients received aminoglycosides, 4 patients received linezolid and 1 patient received quinolones treatment. Liposomal amphotericin B (5 mg/kg/day) was given to the patient who had *Candida albicans* growth until antifungal sensitivity was resulted. The treatment was completed with fluconazole because the *Candida albicans* isolate was sensitive to fluconazole. The shunts of five patients underwent external drainage and te shunts of 13 patients were removed and applied external drainage. Of the eight patients whose shunt had not been replaced, three re-developed shunt infection and two patients died. No intraventricular treatment was applied to any patient. The mean duration of treatment was 54.07 ± 35.73 days. Twelve patients undergone again shunt insertion after averagely 24.92 ± 12.75 days (13-61 days). A total of three patients died during follow-up.

Discussion

Shunt infection continues to be infections with high morbidity and mortality. VPS infections prolong hospital stay and increase health expenses. The clinical findings of shunt infection are not clear and there is no standard definition for them. Therefore, high suspicion is necessary for the diagnosis of shunt infection. The diagnosis is usually based on clinical and laboratory results. Although the frequency of shunt infection varies from centre to centre, it has been reported to be between 2-22% (4, 9). In a retrospective study of 442 pediatric patients with eight hundred twenty consecutive VPSs, 92 shunt (11%) infections were reported (10). Similar to the literature, 8% shunt infection is observed in our hospital. Several studies have shown the etiological causes of patients with VPS infection. The most common cause, as in our study, is congenital malformations (88%) (4).

In the studies, it was determined that most of the VPS infections occurred in the first few months after shunt insertion (10). Approximately 90% of infections were seen in the first 6 months and half of them were seen in the first 2 months after surgery (4). In two different studies conducted in our country, VPS infection was reported in 49.8% of patients in the first month, and in 71.4% in the first 4 months (9,11). In our study, VPS infection occurred in 41.4% of patients in the first 2 months after implantation and in 69% in the first 6 months. These findings can be explained by colonization of the shunt with bacteria during surgery.

The most common clinical findings in ventriculoperitoneal shunt infections are fever, nausea, vomiting and restlessness. Along with these, there may be feeding difficulties, weakness, lethargy irritability, and seizures. In a multicentre study in which children with two hundred and ninety VPS infections were evaluated retrospectively, fever and vomiting were the most common symptoms. In addition; headache, change of consciousness and redness along the VPS path have been reported among other symptoms (5,9). In this study, fever (most frequently), general condition disorder, headache, nausea, vomiting, sei-

Table 1. Demographic and clinical characteristics of patients

Characteristics	Number (n)	Mean ± SD/%
Age	26	4.88 ± 3.16
Gender		
Female	15	57.7%
Male	11	42.3%
Reason for shunt insertion		
Chiari malformation	10	38.5%
Meningomyelocele	6	23.1%
Dandy Walker malformation	4	15.4 %
Astrocytoma	3	11.5%
Colpocephaly	2	7.7%
Walker Walburg malformation	1	3.8%
Intracranial Haemorrhage	1	3.8%
Unknown reason	4	15.4 %
Clinical findings		
Fever	14	48.3%
General condition disorder	7	24.1%
Headache	5	17.2%
Nausea and vomiting	2	6.9%
Seizure	2	6.9%
Redness-swelling in shunt trace	2	6.9%
Control	4	13.8%
Surgical procedure		
Shunt removed + External drainage	13	44.8%
External drainage	5	17.2%
No procedure	16	55.2%
Duration of treatment (day)	26	54.07 ± 35.73
Time of infection after shunt		
< 60 days	12	41.4%
60-180 days	8	27.6.%
> 180 days	9	31%
Shunt re-insertion time (days)	12	24.92 ± 12.75
Patient died	3	11.5%

Table 2. CSF and serum laboratory results

	Mean ± SD
CSF	
Cell count (white cell count/mm^3)	61.19 ± 87.97
Glucose (mg/dL)	47.43 ± 28.51
Protein (mg/dL)	203.63 ± 249.84
Sedimentation (mm/h)	29.11 ± 18.37
CRP (mg/dL)	7.67 ± 11.6
Procalcitonine (ug/L)	6.59 ± 24.91

CSF: Cerebrospinal fluid, CRP: C-reactive protein.

zures and redness-swelling in the shunt trace were observed in the patients, respectively. In our study, when four patients were admitted to the routine control, diagnosis was made upon suspected VPS infection. The findings may be obstructed in ventriculo-peritoneal shunt infection. Therefore, it is important to suspect for diagnosing VPS infection. For diagnosis, the CSF sample should be evaluated. Although the results are variable, there is an increase in polymorphonuclear leukocytes in CSF. CSF glucose and protein levels are variable. Growth in culture ensures the diagnosis. In the absence of growth in culture, the presence of pleocytosis in CSF (> 10/mm^3 white blood cell), low glucose level (< 45 mg/dL) and high protein level (> 100 mg/dL) in patients with suspected VPS infection are considered as VPS infection. In a study evaluating pediatric patients with VPS infection, the median values of CSF glucose, protein and cell count were 31 mg/dL (range: 1-269), 159 mg/dL (range, 5-7240) and 100/mm^3 respectively; (range, 0-80.200) (4,11,12). There was no growth in the CSF culture of 17 patients (9). Similar to other studies, the mean value of CSF glucose, protein and cell count median values were found to be high in our study. In four patients, although there was no growth in CSF culture, VPS infection was considered with clinical and CSF findings.

The most common microorganisms reported to cause ventriculoperitoneal shunt infection are especially *Staphylococcus*

epidermidis, coagulase negative staphylococci (CNS) and *S. aureus*; respectively (4). Considering that staphylococci is the most common agent, most of the VPS infections develop as a result of colonization or contamination of the catheters with skin flora bacteria during surgery (9). Therefore, a number of measures to be taken before and during the surgery will be successful in preventing the shunt infection in the majority of cases. The most common factor in our study was *S. epidermidis* (34.5%). Other factors include gram-negative microorganisms and, more rarely, *Propionibacterium* spp., enterococcus, fungi (eg *Candida, Histoplasma, Cryptococcus*), β-haemolytic streptococci, *Neisseria* spp., *Listeria monocytogenes* (9,10). In a multicenter study conducted in our country, for patients with VPS infection, the most isolated microorganism was (42.5%) CNS in 63, *Pseudomonas aeruginosa in* 22 cases (14.9%), *K. pneumoniae* in 15 cases (10.1%) and *S. aureus* 15 cases (10.1%) (9). In this study, gram negative microorganism was found in eight patients (27.5%) and *Candida albicans* agent was found in one patient.

Treatment of shunt infections is very difficult and overcosting, and the treatment methods are contradictive because there are no controlled clinical studies. It was reported that the highest success rate (70%) and lowest mortality were achieved by the removal of the infected shunt, providing external ventricular drainage and providing re-shunting after appropriate antibiotic treatment (4). Microorganisms which are the most common cause of VPS infection form biofilm layer on shunt which antibiotics cannot be effected on. Therefore, the success rate of treatment of VPS infections with antibiotic treatment alone is low (33%) without shunt removal. In our study, 13 patients underwent external drainage, removing their shunts. Five patients underwent only external drainage. Eight patients were given antibiotic treatment alone. The role of intraventricular antibiotic therapy in VPS infections is controversial. Intraventricular antibiotic treatment may be considered in patients whose infected shunt cannot be completely removed and for whom CSF sterilization cannot be achieved. In a study of thirty-four patients with VPS infection, it was reported that CSF was sterilized faster with simultaneous intraventricular and intravenous antibiotic treatment after shunt removal (13). No intraventricular treatment was performed in this study.

The mortality rate in patients with ventriculoperitoneal shunt infection is 7-13%. While mortality in patients whose shunt was not removed was (34%-36%), it is higher in patients with shunt infections due to Gram negative microorganisms (5). In our study, two patients with Gram-negative microorganism growth in CSF culture died. In the treatment of these patients, shunt was taken to external drainage and systemic antimicrobial treatment was applied. One patient whose CSF culture had *C. albicans* growth was treated with systemic antifungal treatment by removing his/her shunt. A sudden cardiac arrest developed in the patient who was followed up in the service unit for re-insertion. He did not respond to cardiopulmonary resuscitation and died.

Treatment of ventriculoperitoneal shunt infection is an implant-associated infection with the highest cost in the USA and the hospital cost is estimated to be $ 50.000. New developments in surgical technique, perioperative antibiotic applications did not reduce the incidence of shunt infection (14). Antibiotic impregnated shunts have been produced to reduce VPS infections. In a study comparing 1592 patients in control group and five hundred paediatric patients with antibiotic impregnated shunt, a significant reduction in VPS infection was reported in the group using antibiotic-impregnated shunt (15). In a study, it was reported that the cost of infection-related hospital was reduced by $ 442 133 per 100 shunts as a result of decreasing frequency of VPS infection when antibiotic impregnated shunt was used (14). However, contrary to these studies, there are also studies showing that using antibiotic impregnated shunt does not provide additional protection (16). Whether the antibiotic-impregnated shunt is really useful can be demonstrated by multicentre randomized controlled studies. In this study, antibiotic-impregnated shunt catheter was inserted to only five patients. Therefore, no comparison could be made in terms of infection risk.

As a result, the treatment of shunt infections is very difficult and costly. The venticuloperitoneal shunt infections may be asymptomatic. Suspecting is very important for diagnosis. Simple measures to be applied meticulously during surgery can significantly reduce the infection rate.

Ethics Committe Approval: The study was approved by the Ethics Committee of Karadeniz Technical University Ethics Committee with the resolution number 24237859-723.

Informed Consent: Written informed consent was not received due to the retrospective nature of this study.

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