Management of complicated shunt infections: a clinical report

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Object. The authors present their experience with a protocol for the treatment of patients with complicated shunt infections.

Methods. Complicated shunt infections are defined for the purpose of this protocol as multiple compartment hydrocephalus, multiple organism shunt infection, severe peritonitis, or infections in other sites of the body. The initial treatment protocol for these patients was 3 weeks of intravenous antibiotic therapy and 2 weeks of twice daily intraventricular/intrashunt antibiotic therapy. Cerebrospinal fluid (CSF) cultures were monitored during therapy and obtained again 48 hours after completion. The shunt was completely replaced. Additionally, follow-up cultures were obtained in all patients 3–6 months after therapy was completed.

Results. A cure of the infection was achieved in all patients as defined by negative cultures obtained at completion of antibiotic therapy and in follow-up studies. The follow-up period was 2–11 years (mean 4.4 ± 2.5 years). The treatment protocol was modified in the patients treated after 1991, and 18 patients were treated with this modified treatment regime. In these patients, intraventricular antibiotics were administered only once daily for 14 days, and the CSF was cultured 24 hours after antibiotic therapy had been stopped instead of after 48 hours. The results were similar to those obtained with the initial protocol.

Conclusions. Based on their prospective nonrandomized series, the authors believe that patients with complicated shunt infections can be successfully treated with 2 weeks of intraventricular antibiotic therapy administered once daily, concurrent with 3 weeks of intravenous antibiotic therapy. This protocol reduces length of treatment and hospital stay, and avoids recurrence of infection. (DOI: 10.3171/PED/2008/1/3/223)

KEY WORDS • cerebrospinal fluid shunt • infection • therapy

Cerebrospinal fluid shunts are commonly placed to treat hydrocephalus and other conditions, and the most frequent complications are malfunction and infection. The incidence of shunt infection reported in the literature is 1.5–41%,44 and multiple treatment modalities are currently in use.1,9,20,36,43,44 Most authors agree that antibiotic therapy should be administered intravenously to obtain high concentrations of the same in the CSF, but there is very limited consensus as to the duration of therapy, the need for and manner of administration of intraventricular antibiotics, and whether the infected shunt should be removed.1,20,33,36,43,44 Likewise, there is no uniform opinion concerning when the shunt should be replaced if it is removed.1,20,36–38,43,44

There are many factors that mandate an improvement in the timely and effective treatment of shunt infections. The longer a patient stays in the hospital, the more likely that patient is to develop complications. The longer an EVD remains in place, the more likely complications will arise from the drainage system16 and the more likely that microorganisms will contaminate the system.18 A retrospective analysis of patients treated for ventriculostomy and shunt infections16–19 by the lead author has been ongoing. Complicated shunt infections are defined for the purpose of this study as those involving multiple compartment hydrocephalus, multiple organism shunt infection, or severe peritonitis or infections in other sites of the body. The data presented here reflect only the results in this group of patients, and has been subsequently expanded with further patient accrual.

Clinical Materials and Methods

Initial Protocol

Patients were considered to have a shunt infection when shunt aspirate samples obtained by aseptic puncture of the shunt reservoir grew positive cultures. Indications for shunt puncture were recurrent fevers, irritability, peritoneal or meningeal signs, or a combination of all of these.16 On admission, after analysis of their CSF white cell count, chem-
istry, and Gram stain, all patients were promptly given intraventricular fluids and antibiotic therapy, pending the results of the CSF cultures. Following confirmation that the infection was due to >1 organism as documented by bacterial growth in the culture media and/or confirmation that the patient had additional hardware placed because of multiple compartment formation hydrocephalus, the shunt system was either removed and an EVD was placed (ventriculostomy) or the shunt was externalized at the level of the chest wall to a closed external drainage system. In all patients, 1–2 doses of intrashunt antibiotic medication was administered prior to removal while the patient’s clinical course was stabilizing.

Intraventricular antibiotics were administered through the ventriculostomy and/or through the externalized shunt (shunt reservoir). The antibiotic agent was administered into the external ventricular drainage system and/or the externalized shunt twice daily for 2 weeks. In the initial protocol, the antibiotic CSF concentrations were measured or the CSF bactericidal titer was assessed. The dosage was adjusted in an attempt to be 5–10 times greater than the minimal inhibitory concentration of the infecting pathogen; if a CSF bactericidal titer was performed, a titer of 1:8 or more was felt to be adequate.\(^7\)\(^-\)\(^9\)

Throughout treatment, all patients remained in the Neonatal Intensive Care Unit, Pediatric Intensive Care Unit, Intermediate Care Unit, or in other locations where close nursing supervision could be maintained at all times. This was performed to minimize the danger of sudden neurological deterioration from elevated intracranial pressure, disconnections of the external drainage system, superinfections, and also for prompt detection of seizures or other complications.\(^7\)\(^-\)\(^8\)

After 14 days of intrashunt and/or intraventricular antibiotic therapy through the EVD, if the patient had negative daily cultures of the CSF and no further signs of infection, the EVD and/or externalized shunt was completely removed and a new shunt was placed. The patient then received an additional week of intravenous antibiotic therapy. After 3 weeks had been completed, antibiotic therapy was discontinued. Cerebrospinal fluid cultures of samples obtained in the new shunt were obtained at 48 hours after antibiotic therapy was discontinued, and if the cultures were negative after incubation for 24 hours, the patient was discharged from the hospital and received follow-up in an outpatient setting. The CSF was again cultured when the new shunt was placed, and again in an outpatient setting 3–6 months afterwards. The infection was considered cured if all cultures returned negative.

The modified protocol was similar to that used initially, but was adjusted as follows: intraventricular antibiotics were administered once daily instead of twice, and CSF cultures were obtained at 24 rather than 48 hours after antibiotic therapy had been discontinued.

**Results**

**Initial Protocol**

**Patient Population.** Ninety shunt infections were treated from 1975 to 1991 at our institution; infections in 21 patients met the criteria for this protocol. The patient population included 12 boys and 9 girls with an age range of 1 month–14 years (mean 5.1 ± 4.3 years). (Mean values are presented ± standard deviations throughout.) Eleven patients had congenital hydrocephalus, 1 had congenital hydrocephalus with a myelomeningocele, 7 had posthemorrhagic hydrocephalus of prematurity, and 2 patients harbored brain tumors. Of these 21 patients, 4 had multiple organism shunt infections, 14 had multiple compartment hydrocephalus (including 1 patient with infection due to >1 organism), 1 had severe peritonitis, and 2 had infections in other parts of the body (1 at the myelomeningocele repair site and 1 at the halo pin site).

**Cultures.** All patients treated under this protocol had their infection documented on positive culture growth from the CSF aspirate obtained from the reservoir of the shunt system. The infecting organisms in this group of patients are listed in Table 1.

**Intravenous Antibiotic Therapy.** Because the initial protocol was started in 1975, a variety of antibiotic agents were used. In the early years of the protocol, all patients were placed on nafcillin or oxacillin on admission, and these medications were subsequently changed according to the identification of antibiotic sensitivity. The intravenous antibiotics prescribed are listed in Table 2. The initial duration of antibiotic therapy was 21 days.

**Intraventricular Antibiotic Therapy.** All patients treated under this protocol had their infection documented on positive culture growth from the CSF aspirate obtained from the reservoir of the shunt system. The infecting organisms in this group of patients are listed in Table 1.

<table>
<thead>
<tr>
<th>TABLE 1</th>
<th>Summary of infection-causing organisms in patients treated under the initial protocol</th>
</tr>
</thead>
<tbody>
<tr>
<td>Organism</td>
<td>No. of Infected Patients</td>
</tr>
<tr>
<td>------------------</td>
<td>-------------------------</td>
</tr>
<tr>
<td>Single organism shunt infection</td>
<td></td>
</tr>
<tr>
<td>S. epidermidis*</td>
<td>8</td>
</tr>
<tr>
<td>S. aureus</td>
<td>6</td>
</tr>
<tr>
<td>E. coli</td>
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</tr>
<tr>
<td>Enterococcus faecalis</td>
<td>1</td>
</tr>
<tr>
<td>Pseudomonas aeruginosa</td>
<td>1</td>
</tr>
<tr>
<td>Multiple organism shunt infection</td>
<td></td>
</tr>
<tr>
<td>Pseudomonas &amp; Candida albicans</td>
<td>1</td>
</tr>
<tr>
<td>Micrococcus* &amp; S. aureus</td>
<td>1</td>
</tr>
<tr>
<td>S. epidermidis* &amp; S. aureus</td>
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</tr>
</tbody>
</table>

* Coagulase negative.
† Penicillinase positive.

<table>
<thead>
<tr>
<th>TABLE 2</th>
<th>Summary of intravenous antibiotic agents used</th>
</tr>
</thead>
<tbody>
<tr>
<td>Antibiotic</td>
<td>Dose (mg/kg/day)</td>
</tr>
<tr>
<td>amikacin</td>
<td>15</td>
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<tr>
<td>amphotericin B*</td>
<td>1</td>
</tr>
<tr>
<td>ampicillin</td>
<td>200</td>
</tr>
<tr>
<td>carbenicillin</td>
<td>400</td>
</tr>
<tr>
<td>cefepime†</td>
<td>100</td>
</tr>
<tr>
<td>cefotaxime</td>
<td>50</td>
</tr>
<tr>
<td>fluconazole*</td>
<td>6</td>
</tr>
<tr>
<td>methicillin</td>
<td>200</td>
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<tr>
<td>nafcillin</td>
<td>200</td>
</tr>
<tr>
<td>oxacillin</td>
<td>200</td>
</tr>
<tr>
<td>tobramycin†</td>
<td>70</td>
</tr>
<tr>
<td>vancomycin</td>
<td>50</td>
</tr>
</tbody>
</table>

* Agent used in patient with P. aeruginosa and C. albicans shunt infection.
† Agent used in patient with P. aeruginosa shunt infection.
Treatment of complicated shunt infections

der the initial protocol received intraventricular antibiotics via either EVD or direct puncture of the shunt reservoir. The medication was administered by burbotage (diluting it in the patient’s CSF) and injecting slowly. The patients received a morning and late afternoon dose in an attempt to maximize CSF concentration over a 24-hour period, due to the clearance of the antibiotics through the EVD and/or shunt.19,24,25,42 This treatment design was initiated prior to our knowledge of the pharmacodynamics of antimicrobial activity against bacterial pathogens. The type and dosage of intraventricular antibiotics used are listed in Table 3. The duration of intraventricular antibiotic therapy was 14 days and was concurrent with the first 14 days of intravenous antibiotic therapy. In this series, 9 patients underwent EVD placements after shunt removal and 6 had externalized shunts until the shunt was removed and a new one placed. In 1 infant the shunt was completely removed and the child was treated with intermittent ventricular punctures until the shunt was replaced.18,39 In 5 patients, treatment was performed through shunt puncures with the shunts left in place until CSF cultures were negative. The shunts were then removed and replaced with a new shunt13 during the same procedure, and the treatment was continued until completed.

Length of Hospital Stay. The total length of stay in this group was 22–44 days (mean 25.1 ± 8.3 days).

Completion of Therapy. During the treatment course, CSF white cell counts and glucose levels were monitored intermittently, and gram staining of CSF samples was performed and monitored daily. All patients’ fevers resolved within a few days of the initiation of antibiotic therapy. Intraventricular antibiotics were continued for 14 days and intravenous antibiotics were continued for 21 days.

Infection Cure and Follow-Up. All patients in this protocol were considered cured of infection according to the following criteria: a negative CSF culture obtained 48 hours after antibiotic therapy had been stopped, a negative CSF culture obtained intraoperatively at the time of the new shunt placement, and a negative culture of aspirate from the shunt reservoir obtained 3–6 months after hospital discharge. This last aspirate was performed due to the possible late presentation of a recurrent shunt infection.2,20 Finally, these patients were documented not to have another shunt infection during their follow-up. The follow-up period was 2–11 years (mean 4.4 ± 2.5 years).

Complications. There was displacement of the EVD catheter in 1 patient due to lack of patient cooperation. A new catheter was promptly reinserted and closed external ventricular drainage re instituted. There were no additional infections resulting from this displacement. Three patients ex perienced seizures during their hospitalization: 1 had had seizures prior to treatment with intraventricular antibiotics, and the other 2 patients had seizures while receiving intraventricular and intravenous antibiotic therapy. In 1 patient the antibiotic medications used were intraventricular methicillin (1 mg/kg/dose) and intravenous methicillin (200 mg/kg/day). The other patient was receiving intraventricular cefazolin (2 mg/kg/dose) and intravenous nafcillin (200 mg/kg/dose). The seizures were controlled in both patients with the intravenous administration of phenobarbital (5–10 mg/kg/loading dose), and they were maintained on anticonvul sant therapy until completion of their antibiotic regimen and then discontinued without further seizures. In the patient with an underlying seizure disorder, the anticonvulsant therapy was maintained both during the hospital stay and after discharge. Intraventricular antibiotic therapy was withheld for 24 hours in patients who had had seizures after its institution, and then reinstated at a lower dose than previously; neither patient had further seizures.

Subsequent Protocol

Patient Population. In the period 1992–2004, an additional 18 patients who met the same entry criteria as those in the initial protocol were treated. There were 11 boys and 7 girls, with ages ranging from 4 months to 20 years (mean 8.7 ± 6.7 years). Seventeen patients had >1 shunt system and 1 patient had a single shunt system.

Cultures. Seventeen patients had a shunt infection caused by 1 organism, and 1 patient had an infection caused by 2 organisms. The single-agent shunt infections were caused by Staphylococcus epidermidis in 11 children, Enterococcus spp. in 3, Escherichia coli in 1, Propionibacterium spp. in 1, and Staphylococcus lugdunensis in 1 child. The multiple-agent infection was caused by S. auricularis and a non-speciated Staphylococcus coagulase-negative organism.

Intravenous Antibiotic Regimen. The intravenous antibiotic medications used included ampicillin in 3 children, cefuroxime in 1, nafcillin in 6, penicillin in 1, and vancomycin in 7 children. One child was treated with both ampicillin and gentamicin. One patient was started on vancomycin but was switched to nafcillin when renal failure was detected. The duration of intravenous antibiotic therapy in these patients was 21 days.

Intraventricular Antibiotic Regimen. The intraventricular antibiotic agents used included gentamicin in 12 patients, and vancomycin in 6. The patients received intraventricular antibiotic medication for 14 days.

Length of Hospital Stay. The length of hospital stay ranged from 16 to 27 days (mean 19.7 ± 6.6 days). Six patients completed the 21-day intravenous therapy at home.

Infection, Cure, and Follow-Up. All patients were considered cured of infection when they met the following criteria: a negative CSF culture obtained 24 hours after antibiotic treatment had been stopped or after completion of 21 days of therapy, and a negative CSF culture obtained intraoperatively at the time of the new shunt placement. Three patients underwent a repeated CSF culture by shunt aspiration 3–6 months after the new shunt was placed; these cultures were negative. None of the patients had a recurrent shunt infection during the follow-up period. The follow-up period was 1–6 years (mean 3.6 ± 1.7 years).

<table>
<thead>
<tr>
<th>Antibiotic</th>
<th>Dose</th>
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<tbody>
<tr>
<td>amphotericin B*</td>
<td>1–2 mg</td>
</tr>
<tr>
<td>cefazolin</td>
<td>1 mg/kg</td>
</tr>
<tr>
<td>cephalotin</td>
<td>2 mg</td>
</tr>
<tr>
<td>gentamicin</td>
<td>0.5–1 mg/kg</td>
</tr>
<tr>
<td>methicillin</td>
<td>1 mg/kg</td>
</tr>
<tr>
<td>vancomycin</td>
<td>0.5–1 mg/kg</td>
</tr>
</tbody>
</table>

* Agent used in patient with P. aeruginosa and C. albicans shunt infection.
Complications. None of the patients treated under the modified protocol experienced seizures after treatment was initiated. In 1 patient there was a disconnection of the EVD, which was promptly detected and reconnected with an aseptic technique. No other complications were noted.

Discussion

There has been great variability in the treatment of CSF shunt infections, and no uniform consensus exists as to the effectiveness of treatment, especially in complicated shunts and/or shunts infected with > 1 organism. Since CSF shunt placement procedures were first performed, differing therapeutic rationales were already evident in medical reports. The initial report of Schimke et al. of a high-dose intravenous penicillin cure for Staphylococcus shunt infections, together with their reluctance to perform repeated operations in their patients, lead them to recommend intravenous antibiotic therapy as the only initial form of therapy. It must be noted that under the protocol of Schimke and colleagues, 4 of 11 patients had successful outcomes. When the primary shunt was ventriculojugal, there was concern over losing access to the right internal jugular vein if the shunt were removed. Perrin and McLaurin proposed that in a ventriculojugal shunt infection after a brief period of high-dose intravenous antibiotic treatment, the shunt should be removed and a new one installed simultaneously. This would have the advantage of preserving the internal jugular vein. They proposed that intravenous antibiotics then be continued until the infection was resolved. In a subsequent article, Frame and McLaurin recommended that the treatment be modified to include oral and intrashunt antibiotic therapy. Intrashunt antibiotics were to be delivered twice daily to maintain adequate levels of antibiotic agent in the CSF, because the rate of CSF clearance through the shunt would make a single daily dose inadequate. There has been resistance to the use of this form of therapy as recommended, probably due to the reluctance of the treating physician to face the task of puncturing a child’s shunt 2 times a day. However, other authors have recommended intraventricular antibiotic administration to hasten the resolution of ventriculitis.

There were already advocates of shunt removal in the presence of CSF infection at the time of the initial report of Schimke et al., in the publications of Cohen and Callaghan, and others. Authors who advocated shunt removal emphasized that serious consequences would result if the infection were not promptly cured. The authors felt that bacterial colonization of the shunt material made these infections very difficult to eradicate unless the shunts themselves were removed. In support of the removal of infected shunts, Bayston and Penny described the ability of S. epidermidis to produce a mucoid substance that allows it to adhere to the silastic wall of the shunt system. This makes phagocytic eradication of the organism extremely difficult. Subsequent reports have added further information concerning other factors that favor colonization. On scanning electron micrographs of shunts removed from patients with S. aureus and Klebsiella pneumoniae infections, Guevara and colleagues noted that there were numerous bacteria and microcolonies attached to the irregularities, cracks, fissures, and holes that were commonplace in the silastic shunt material. Analysis of new and implanted shunts demonstrated that the silastic surfaces, both inner and outer linings, develop porosities and physical alterations over the period of implantation. These porosities permit microcolonies and bacteria to remain sheltered from leukocytes. Guevara et al. reiterated the concept that infected shunts should be removed to optimize treatment.

There are situations in which the removal of the shunt system to cure an infection may not be necessary; this relates to infections with certain bacteria. In a report on Haemophilus influenzae shunt infection, 1 patient was cured with intravenous antibiotic therapy without shunt removal, and another required shunt removal due to persistent infection.

Most articles document the need for intravenous antibiotics as the mainstay of treatment, but there has been no consensus as to the need for and methodology of intraventricular antibiotic delivery for ventriculitis and CSF shunt infections. Many antibiotic agents enter the brain parenchyma and subarachnoid CSF, and the argument has been made that in itself this provides adequate intraventricular antibiotic therapy. However, when intraventricular antibiotic concentrations have been measured, a wide range of penetration from the serum has been demonstrated. In some patients this variation has been documented to be well below the minimal inhibitory concentration of the infecting organism. Such has been the case for maximum intravenous doses of oxacillin, nafcillin, gentamicin, and cefazolin. Vancomycin intraventricular measurements in 25 CSF specimens were noted to have 6 specimens where the concentrations were below 1.0 µg/ml, with 1 specimen having a concentration as high as 17.3 µg/dl. The mean concentration for all specimens was 5.5 ± 5.2 µg/dl. There was no correlation between ventricular vancomycin concentrations and the dose administered intravenously. There was also no difference in the CSF values defined at various times following intravenous dosing. However, there was a direct correlation between CSF values and protein concentration, and white blood cell count and glucose concentration.

Because of the findings in the other studies, we have used intraventricular antibiotics to maximize therapy as an adjuvant to the intravenous therapy in CSF shunt infections, and to shorten the treatment course and hospital stay. The range of antibiotics used in this protocol reflects the fact that some of the patients included in this study were treated many years ago. We continue to adjust the intravenous and intraventricular antibiotic agents used to organism sensitivity as well as to the patient’s clinical course.

A serious complication of the use of intraventricular antibiotics that should always be considered is neurotoxicity. Neurotoxicity may manifest itself with CSF pleocytosis, irritability, delirium, confusion, and seizures. The seizures may be focal or generalized and may be difficult to control. In an effort to minimize the complications of too high an intraventricular antibiotic dose, it has been recommended that measurements of antibiotic concentration be performed in samples of CSF. This is due to the variability, both high and low, in the amount of antibiotic in the CSF according to the dose prescribed, the adjuvant dosage that may come from the intravenous antibiotic dosing, the degree of underlying inflammation of the ependyma and the choroid plexus, as well as the penetration of the antibiotic. If the patient has an EVD or is being treated through a
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shunt system, the clearance of the medication in the CSF through the shunt will also affect its concentration. If the patient is being treated by ventricular puncture and no drainage system is in place, then the CSF concentrations may be very high for days after a single dose. If > 1 antibiotic agent is administered, or if the in vivo susceptibility to the antibiotic is poor and adequate CSF antibiotic concentrations are a concern, then the patient should undergo a CSF bacterial assay, and the result will permit an adjustment of antibiotic therapy. 19, 41

Our protocol is only relevant to the group of patients who have > 1 organism causing the infection and/or have a complicated shunt system in place due to compartmentalized or multicompartartment hydrocephalus, in which there is additional shunt hardware. This protocol does not address the single organism shunt infection and/or single shunt assembly infection. This is the subject for a separate report.

Conclusions

In patients with multiple organism shunt infections and/or compartmentalized hydrocephalus with complex CSF shunts, the infection may be cleared promptly and effectively if treatment is instituted with intravenous and intraventricular antibiotics. The shunt can be subsequently removed and replaced with a new shunt system if the cultures become negative. Two weeks of intraventricular single daily dose therapy in association with a 3-week course of intravenous antibiotic therapy appears to have been sufficient to cure these infections in our small series. Our results require validation in a larger, prospective, comparative investigational trial. A shorter duration of therapy may also be effective, but would require prospective investigation.

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References


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