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MAJOR ARTICLE

Characteristics and Treatment Outcome of Cerebrospinal Fluid Shunt–Associated Infections in Adults: A Retrospective Analysis over an 11-Year Period

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Background. Data on infections associated with cerebrospinal fluid (CSF) shunts among adults are limited. Therefore, we performed a retrospective study of shunt-associated infections in adults.

Methods. Patients aged ⩾12 years with infections associated with CSF shunts and admitted to our institution (University Hospital Basel, Basel, Switzerland) from January 1996 through December 2006 were included retrospectively. Hospital charts were reviewed, and follow-up was performed by assessment of later hospitalizations and telephone contact with patients, their families, and general practitioners.

Results. Seventy-eight episodes of infection associated with ventriculoperitoneal shunt (65 episodes), ventriculoatrial shunt (7), lumboperitoneal shunt (5), and central nervous system reservoir (1) were included. Median patient age was 50 years (range, 12–80 years); 49 (63%) of the patients were men. Most infections (48 [62%]) manifested within 1 month after shunt surgery. Fever was present in 61 episodes (78%), neck stiffness was present in 35 (45%), and local signs of infection were present in 38 (49%). In CSF, leukocyte count was $>5 \times 10^6$ cells/L in 80% of episodes, and lactate level was >1.9 mmol/L in 81% of episodes. Leukocyte counts were significantly higher in CSF obtained by use of lumbar puncture (median leukocyte count, 573×10^6 cells/L; $P = .001$) and valve puncture (median leukocyte count, 484×10^6 cells/L; $P = .016$) than in ventricular CSF (median leukocyte count, 8.5×10^6 cells/L). Overall, results of CSF cultures were positive in 66% of episodes (48 of 73 episodes for which CSF was collected), and microorganisms were isolated more often from valve puncture CSF specimens (91% of specimens) and ventricular CSF specimens (70%) than from lumbar CSF specimens (45%). The most prevalent organisms were coagulase-negative staphylococci (found in 37% of specimens), *Staphylococcus aureus* (18%), and *Propionibacterium acnes* (9%). A surgical procedure was performed to treat infection in 63 (81% of the episodes) (shunt removal in 37 episodes and shunt replacement in 26). The shunt was retained without surgery for 15 episodes (19% of episodes). Median duration of patient follow-up was 4.6 years (range, 0.1–11.1 years), with favorable treatment outcome in 75 (96%) of 78 cases. One of the 63 patients who underwent surgical treatment of shunt-associated infection experienced infection relapse; of the 15 patients who received treatment with antibiotics alone, 1 experienced infection relapse and 1 died. The 2 relapses involved rifampin-resistant coagulase-negative staphylococci.

Conclusions. Shunt-associated infections among adults often present with nonspecific clinical signs, and affected patients can have normal CSF leukocyte counts and lactate levels; therefore, a high index of suspicion and improved methods are required for diagnosing shunt-associated infection.

CSF shunts significantly improve the quality of life for patients with hydrocephalus. Infection associated with a CSF shunt is a severe complication with high morbidity and substantial mortality [1]. The incidence of shunt-associated infection has a range of 1%–18% [2–5], and several independent risk factors have been identified, including previous shunt-associated infection,

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shunt revision for dysfunction, postoperative CSF leakage, advanced age, duration of the shunt placement operation, experience of the neurosurgeon, and use of a neuroendoscope [6–8].

Organisms causing shunt-associated infections typically adhere to the device surface and form biofilms, which makes the clinical and laboratory diagnosis difficult and the treatment challenging [9, 10]. Clinical symptoms are often nonspecific, especially when shunt-associated infections are caused by low-virulence organisms, such as coagulase-negative staphylococci or *Propionibacterium acnes* [11]. Often, only signs of intracranial hypertension attributable to shunt malfunction are present, such as headache, nausea, vomiting, and/or change in mental state [12–15]. It is crucial to diagnose shunt-associated infection early and accurately to be able to plan an appropriate medical and/or surgical intervention.

Previous studies have evaluated shunt-associated infections predominantly in the pediatric population, and only limited data are published about infection in adults [12, 15–17]. Moreover, the antimicrobial and surgical treatment approach for shunt-associated infections is not standardized. Current recommendations are supported mainly by case series, are extrapolated from other implant-associated infections (e.g., infections associated with prosthetic joints), or relay on expert opinion.

We performed a retrospective analysis of consecutive episodes of CSF shunt–associated infection among a predominantly adult population, to describe the epidemiological, clinical, laboratory, and microbiological characteristics of shunt-associated infections and treatment outcome.

PATIENTS AND METHODS

Hospital setting. The study was conducted at the University Hospital Basel (Basel, Switzerland), an 800-bed primary and tertiary health care center. It is the major provider of acute medical care for ~300,000 area inhabitants. During the study period, a mean of 240,000 patient-days and 23,300 hospital admissions per year were recorded. Patients with CSF shunts were hospitalized on the neurosurgical ward and, if required, in a specialized intermediate care unit (8 beds), with continuous monitoring of vital functions. During the study period, a mean of 33 CSF shunts were inserted annually (range, 29–41 shunts per year); none of the inserted shunts was coated with antimicrobial agents. As preoperative antibiotic prophylaxis, a single dose of a second-generation cephalosporin was administered intravenously at the time of anesthesia induction. The study was approved by the local Institutional Review and Ethics Board.

Study population. From 1 January 1996 through 31 December 2006, all episodes of infection associated with CSF shunts in patients aged ⩾12 years were included. Episodes of shunt-associated infections were identified using the microbiology database and the infectious diseases consultation list. Each episode was evaluated by 2 independent infectious diseases specialists according to predefined criteria (see below) and was reviewed by a neurosurgeon. Excluded from the study were patients with exclusively external CSF drainage or a subduroperitoneal shunt, patients whose shunt was removed before a diagnosis of infection was determined, and patients whose shunt-associated infection was diagnosed at another hospital.

Definitions. An infection was considered to be associated with a CSF shunt if at least 1 of the following 2 criteria was fulfilled (modified criteria for nosocomial infections of the Cen-

Table 1. Demographic and characteristics of patients with episodes of CSF shunt–associated infection.

Variable	Episodes (n = 78)
Patient age, median years (range)	50 (12–80)
Male sex	49 (63)
Length of hospital stay, median days (range)	26 (1–100)
Underlying neurosurgical condition	
Subarachnoidal bleeding	29 (37)
Intracerebral hemorrhage	19 (24)
CNS tumor[a]	12 (15)
CNS malformation[b]	5 (6)
Cerebral pseudotumor	2 (3)
Subarachnoidal cyst	2 (3)
Unknown	9 (12)
Type of implanted CSF device	
Ventriculoperitoneal shunt	65 (83)
Ventriculoatrial shunt	7 (9)
Lumboperitoneal shunt	5 (6)
CNS reservoir	1 (1)
Reason for shunt placement	
Communicating hydrocephalus	41 (53)
Obstructive hydrocephalus	30 (38)
CSF leakage	4 (5)
Unknown	3 (4)
Route of infection acquisition	
Intraoperative	56 (72)
Contiguous from another anatomical site	
All	21 (27)
Head wound	11 (14)
Perforated gut	7 (9)
Sinus frontalis	2 (3)
External ventricular drainage	1 (1)
Hematogenous[c]	1 (1)

NOTE. Data are no. (%) of episodes, unless otherwise indicated. The percentages were rounded and may not add up to 100%.

[a] Astrocytoma (3 episodes), glioblastoma (2), neurofibroma (2), neuroblastoma (1), meningeoma (1), pituitary adenoma (1), neurocytoma (1), and tumor of the inferior colliculus (1).

[b] Dandy Walker malformation (3 episodes), Arnold Chiari malformation (1), and stenosis of the cerebral aqueduct (1).

[c] Due to *Enterococcus faecalis* in a patient with a ventriculoatrial shunt.

Table 2. Clinical characteristics of patients with episodes of CSF shunt–associated infection.

Variable	Episodes (n = 78)
Temperature >38°C	61 (78)
Neurological signs and symptoms	
Headache	16 (21)
Nausea	11 (14)
Neck stiffness	35 (45)
Decrease in GCS from baseline, points	
Any decrease	24 (31)
1	8
2	4
3	2
4	5
⩾5	5
No neurological signs or symptoms	28 (36)
Local signs and symptoms	
Erythema	23 (29)
Local pain	15 (19)
Swelling	10 (13)
Purulent wound discharge	10 (13)
No local signs or symptoms	40 (51)
No fever or neurological or local signs or symptoms	2 (3)
Duration of symptoms before diagnosis of infection, median days (range)	5 (0–21)
Time between implantation or last surgery and manifestation of infection	
<1 month	48 (62)
1–12 months	22 (28)
>12 months	8 (10)

NOTE. Data are no. (%) of episodes, unless otherwise indicated. The percentages were rounded and may not sum 100%. GCS, Glasgow Coma Scale.

ters for Disease Control and Prevention [CDC]) [18]: (1) growth of a pathogen in the CSF, on the shunt tip, or in wounds overlying the implanted shunt material (if the pathogen was interpreted as relevant), or (2) fever (temperature >38°C), headache, neck stiffness, cranial nerve signs, or irritability without another recognized cause; physician initiation of an appropriate antimicrobial therapy for shunt-associated infection; and a laboratory finding of CSF leukocyte count $>5 \times 10^6$ cells/L, CSF total protein >0.45 g/L, a CSF-to-blood glucose ratio <0.5, organisms seen on CSF Gram stain, or organisms found in blood culture. The onset of infection was defined by the first positive culture of CSF, wound swab, or shunt tip specimen, the initiation of an appropriate antimicrobial treatment for shunt-associated infection, or surgery at the site of the shunt (whichever occurred first).

Data collection. Hospital charts were reviewed with a standardized case-report form to retrieve demographic, clinical, radiographic, and laboratory data. Dual data entry by different operators was performed, with preprogrammed consistency checks. The following data were extracted: age, sex, need for admission to an intensive care unit or a neurosurgical intermediate care unit, length of hospital stay, underlying neurosurgical condition, and reason for shunt implantation (e.g., communicating hydrocephalus, obstructive hydrocephalus, or CSF leakage). Shunt-specific data included date of device insertion and revision (if performed) before infection, type of CSF device (i.e., ventriculoperitoneal, ventriculoatrial, or lumboperitoneal shunt or CNS reservoir), and whether the device surface was coated with antimicrobial agents. Reasons for shunt revision before infection included shunt dysfunction, shunt tip dislocation, or revision because of a postoperative hematoma. Episodes were classified according to the route of infection (i.e., intraoperative, contiguous, or hematogenous acquisition) and whether the manifestation of infection was early (<1 month after shunt surgery), delayed (1–12 months), or late (>12 months). The use of antimicrobial treatment and the type of surgical procedure (i.e., no surgery, complete or partial removal of the shunt, or a 1- or 2-stage exchange procedure) were recorded, as was whether temporary external ventricular drainage was used.

Follow-up and treatment outcome. Treatment outcome was analyzed by review of subsequent hospital admissions (if any) and by contacting patients, their families, and general practitioners by telephone. A relapse (treatment failure) was defined as a shunt-associated infection that occurred within 3 months after remission of symptoms of the previous episode

Table 3. Laboratory analysis of CSF samples from patients with CSF shunt–associated infection.

Variable	Finding
Leukocyte count	
>5 × 10^6 cells/L, no. (%) of episodes	48/60 (80)
Median value, ×10^6 cells/L (range)	61 (0.3–5010)
Granulocyte count	
⩾1 × 10^6 cells/L, no. (%) of episodes	46/60 (77)
Median value, ×10^6 cells/L (range)	32 (0–3006)
Lactate level	
>1.9 mmol/L, no. (%) of episodes	34/42 (81)
Median value, mmol/L (range)	4 (1–14)
Total protein level	
>0.45 g/L, no. (%) of episodes	36/62 (58)
Median value, g/L (range)	0.8 (0.1–36)
CSF-to-blood glucose ratio	
<0.5, no. (%) of episodes	16/31 (52)
Median value (range)	0.4 (0.1–1)

NOTE. Denominators indicate the episodes for which data were available.

and for which the same organism was isolated. A shunt-associated infection was defined as being new if it occurred >3 months after cure of the previous episode or culture revealed an organism other than the organism that caused the original infection. The status of the shunt at last contact was categorized as (1) removed during infection and not replaced within 30 days, (2) initial infection treated and shunt still in place (with or without additional surgery for any reason), or (3) initial infection treated and shunt subsequently removed (including the reason for removal). Death was attributed to shunt-associated infection if the patient died during a clinical course suggestive of persistent infection and no alternative specific cause of death was detected.

Statistical analysis. Continuous variables were compared using the Wilcoxon rank-sum test. A P value <.05 (for a 2-sided test) was considered to be statistically significant. All calculations were performed using the statistical software package JMP, version 7 (SAS Institute). For graphic analysis, Origin software, version 8 (OriginLab), was used.

RESULTS

Demographic and CSF shunt characteristics. During the study period, 78 episodes of CSF shunt-associated infection among 74 patients were identified (table 1); 4 patients developed recurrent infection. At diagnosis of infection, the median patient age was 50 years (range, 12–80 years); 63% of infections (49 episodes) involved male patients. The median duration of hospital stay was 26 days (range, 1–100 days). In 14 episodes (18%), admission to the intensive care unit for a median duration of 3 days (range, 1–19 days) was needed, and in 53 episodes (68%), admission to the neurosurgical intermediate care unit for a median of 9 days (range, 1–45 days) was needed. The most common underlying neurosurgical condition was subarachnoidal or intracerebral bleeding; the main reasons for shunt insertion were communicating hydrocephalus and obstructive hydrocephalus (table 1). Most shunt-associated infections involved ventriculoperitoneal shunts (65 infections [83%]) and were acquired intraoperatively (56 [72%]). Before infection onset in 25 episodes (32%), revision of the shunt site was performed because of shunt dysfunction (20 episodes), shunt-tip dislocation (4), or postoperative hematoma (1).

Clinical characteristics. Table 2 summarizes clinical signs and symptoms at the time of infection diagnosis. Fever >38°C was present in 61 episodes (78%), neck stiffness was present in 35 episodes (45%), and a decrease of Glasgow Coma Scale was present in 24 episodes (31%), whereas headache (21%) and nausea (14%) were less common. Local signs of infection were present in 38 episodes (49%) and included erythema, local pain, swelling, and/or purulent wound discharge. Only 2 episodes (3%) involved neither fever nor neurological or local manifestations of infection; both episodes were caused by coagulase-negative staphylococci. Neurological signs or symptoms were absent in 28 episodes (36%); among those episodes, the most common pathogens were coagulase-negative staphylococci (found in 13 episodes) and *Staphylococcus aureus* (found in 6 episodes).

The median duration of symptoms before hospital admission was 5 days (range, 0–21 days). The median time between shunt insertion or revision (whichever occurred later) and manifestation of infection was 17 days (range, 0 days to 6.9 years). Most infections occurred early (48 episodes [62%]), within a month after shunt placement or revision, 28% (22) involved delayed manifestation (1–12 months after surgery), and 10% (8) involved late manifestation (>12 months after surgery).

Radiological characteristics. The cranial CT scan showed signs of shunt-associated infection in 8 (12%) of 66 episodes, with meningeal enhancement seen in 5 episodes and brain abscess seen in 3 episodes. Shunt-associated meningitis was suspected in 1 (13%) of 8 episodes on the basis of cranial MRI results. For detection of infection associated with the abdominal part of the shunt, CT scan was more reliable than ultrasound; with use of CT, signs of infection were seen in 10 (77%) of 13 episodes and included inflammation of fat or muscle tissue around the shunt (in 4 episodes), thickened gut wall (2), intra-abdominal abscess (2), intraintestinal shunt dislocation (1), or peritoneal cyst (1). Abdominal ultrasound showed signs of infection in 7 (50%) of 14 episodes, including fluid collection around the distal shunt tip (in 4 episodes), thickened gut wall (1), ascites (1), and peritoneal cyst (1).

Laboratory characteristics. Blood leukocyte counts were >12 × 10^9 cells/L in 26 episodes (33%), with a median of 9.8 × 10^9 cells/L (range, 2.2–24 × 10^9 cells/L). C-reactive protein level was >5 mg/L in 57 (76%) of 75 episodes in which it

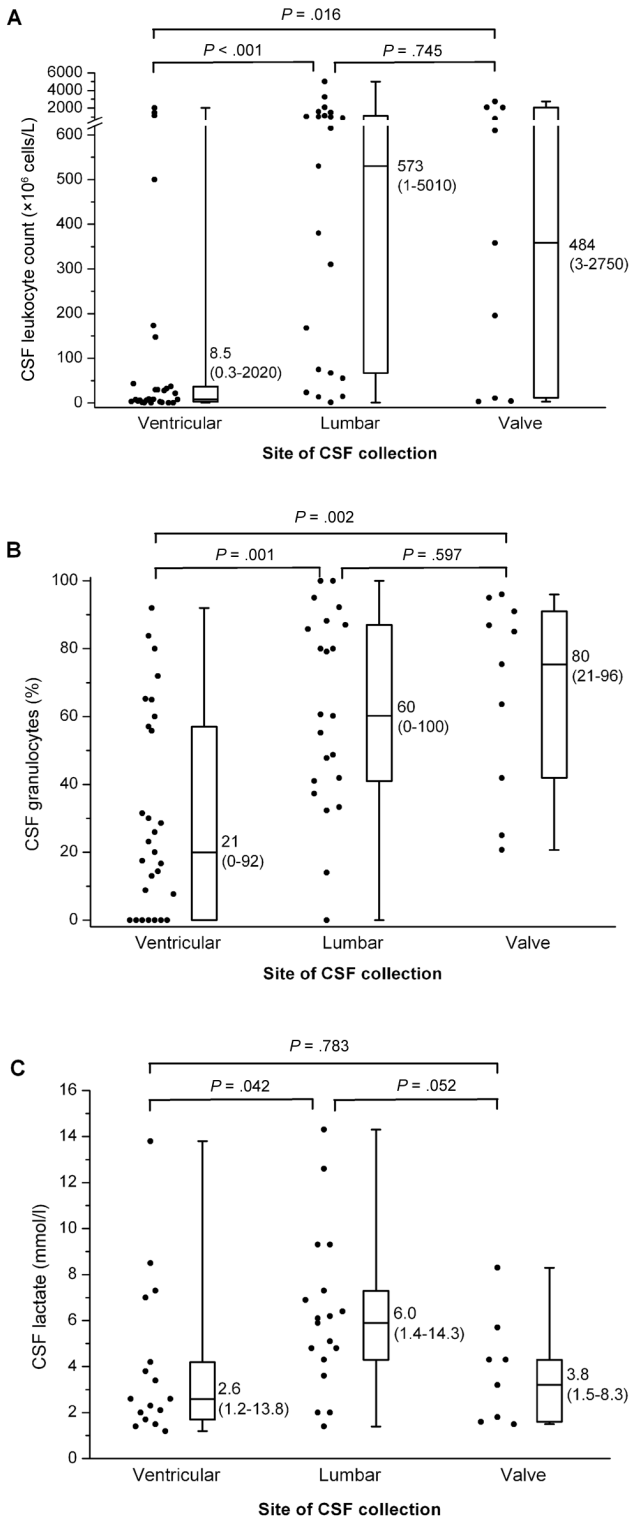

Figure 1. Distribution of leukocytes *(A),* granulocytes *(B),* and lactate *(C)* in CSF, by specimen collection site. Boxes represent the 25th and 50th percentiles, horizontal lines within the boxes indicate median values, and whiskers indicate ranges. Numbers next to boxes denote median values (range) for each group.

was determined, with a median value of 52 mg/L (range, 1–302 mg/L).

Table 3 summarizes laboratory characteristics of CSF. CSF specimens were available for laboratory analysis for 73 episodes (94%). Specimens were collected from the cerebral ventricle during surgery in 40 episodes (55%), by lumbar puncture in 22 episodes (30%), or by valve puncture in 11 episodes (15%). CSF leukocyte counts were abnormal in 80% (48 of 60 episodes in which it was determined), CSF lactate levels were abnormal in 81% (34 of 42), CSF total protein levels were abnormal in 58% (36 of 62), and CSF-to-blood glucose ratios were abnormal in 52% (16 of 31) of episodes.

Figure 1 shows the distribution of leukocytes, granulocytes, and lactate level by site of the CSF collection. Leukocyte counts were significantly higher in CSF obtained from valve puncture (484×10^6 cells/L; range, 3–2750×10^6 cells/L; $P = .016$) and lumbar CSF (573×10^6 cells/L; range, 1–5010×10^6 cells/L; $P = .001$) than in ventricular CSF (8.5×10^6 cells/L; range, 0.3–2020×10^6 cells/L). Similarly, granulocyte percentage was significantly higher in CSF collected from the shunt valve ($P = .002$) and lumbar CSF ($P = .001$) than in ventricular CSF, whereas CSF lactate levels were not statistically significantly different. Only in 2 episodes were the results of CSF analysis completely normal: 1 infection was caused by coagulase-negative staphylococci, and the other episode was a polymicrobial infection.

Microbiology. The infection pathogen was determined in 71 episodes (91%) and was isolated either from swabs of wound overlying the shunt material, culture of the shunt tip, CSF, or blood specimens; in 7 episodes (9%), no organism was determined by culture; 5 of the 7 episodes received prior or concomitant antimicrobial treatment.

Table 4 shows the microbiological findings in terms of time between shunt procedure and infection onset (i.e., early, delayed, or late). Overall, the most prevalent organisms were coagulase-negative staphylococci (in 29 [37%] of 78 episodes), *S. aureus* (14 [18%]), *P. acnes* (7 [9%]), and viridans group streptococci (3 [4%]). Gram-negative rods (enterobacteriaceae and nonfermenters) were identified in culture in only 5 (6%) of the 78 episodes. In 9 additional episodes involving gram-negative rods (*Pseudomonas aeruginosa, Klebsiella* species, *Escherichia coli,* and *Serratia marcescens*), other organisms were also present; 5 of these polymicrobial infections originated from a head wound, and 4 originated from the gut. The pathogen was found by Gram stain of CSF sediment in 26 (38%) of 68 episodes where a Gram stain was performed. In episodes with normal CSF leukocyte counts (12 episodes), coagulase-negative staphylococci (8), *P. acnes* (1), *Enterobacter cloacae* (1), *S. aureus* (1), and >1 organism (1) were isolated.

Figure 2 shows the rate of culture positivity by specimen collection site. Ninety-three percent of wound swab cultures

Table 4. Microbiological findings for episodes of CSF shunt–associated infection.

Pathogen	Overall (n = 78)	Infection onset		
		Early[a] (n = 48)	Delayed[b] (n = 22)	Late[c] (n = 8)
Coagulase-negative staphylococci[d]	29 (37)	19	9	1
Staphylococcus aureus[d]	14 (18)	9	5	…
Propionibacterium acnes	7 (9)	5	2	…
Viridans group streptococci	3 (4)	2	1	…
Enterobacteriaceae[e]	3 (4)	3	…	…
Nonfermenters[f]	2 (3)	…	1	1
Enterococcus species	1 (1)	…	1	…
Polymicrobial[g]	12 (15)	4	2	6
Culture negative	7 (9)	6	1	…

NOTE. Data are no. (%) of episodes. Percentages were rounded.

[a] <1 Month after shunt surgery.

[b] 1–12 Months after shunt surgery.

[c] >12 Months after shunt surgery.

[d] Sixteen (55%) of 29 coagulase-negative staphylococci isolates were methicillin resistant; no *S. aureus* isolate was methicillin resistant. Ten (34%) of 29 coagulase-negative staphylococci isolates were resistant to rifampin; 6 affected patients had shunt removal without immediate replacement, 3 had 2-stage shunt replacement, and 1 had 1-stage shunt replacement. No *S. aureus* isolate was rifampin resistant.

[e] *Escherichia coli, Klebsiella pneumoniae,* and *Enterobacter cloacae* (each isolated once).

[f] *Pseudomonas aeruginosa* and *Comamonas testosteroni* (each isolated once).

[g] Nine (75%) of 12 polymicrobial infections also included gram-negative rods (*P. aeruginosa, Klebsiella* species, *Serratia marcescens, E. cloacae,* and *E. coli*), of which 5 originated from a head wound overlying the shunt material and 4 originated from the gut.

were positive, and 78% of shunt tip cultures were positive. Overall, CSF culture results were positive for 48 (66%) of 73 episodes. The causative pathogen was isolated more often in CSF obtained at the shunt valve (10 [91%] of 11 episodes) and from cerebral ventricles (28 [70%] of 40 episodes) than from CSF obtained by lumbar puncture (10 [45%] of 22 episodes). The rate of negative culture results correlated with prior antimicrobial treatment. Nine (41%) of 22 patients whose lumbar CSF was analyzed had received prior antimicrobial treatment, and 5 of these 9 patients had culture-negative shunt-associated infection. Only 4 (10%) of 40 episodes for which ventricular CSF from valve puncture was analyzed and only 1 (9%) of 11 episodes for which CSF from valve puncture was analyzed received prior antimicrobial treatment. Despite the treatment, culture results in all these episodes were positive.

In 53 (68%) of 78 episodes, blood samples were obtained for culture; results were positive in 5 (83%) of 6 episodes involving ventriculoatrial shunt and in 5 (11%) of 47 episodes involving ventriculoperitoneal shunt. The most prevalent microorganisms isolated from blood cultures were coagulase-negative staphylococci (6 cultures), followed by *S. aureus* (3) and *Enterococcus faecalis* (1).

Antimicrobial and surgical treatment. All patients received systemic antibiotic treatment; none in this case series was treated with intrathecal antibiotics. Median antibiotic treatment duration was 18 days (range, 4–91 days). Initial antibiotic regimen was changed in 33 episodes (42%), for reasons that included adaptation to microbiological culture results (26 episodes), inadequate treatment response (3), allergy (2), and change to an oral regimen (2).

A surgical procedure was performed to treat shunt-associated infection in 63 (81%) of 78 episodes (figure 3). Surgical procedures included shunt removal without replacement within 30 days (37 [47%] of 78 episodes), 1-stage shunt replacement (8 [10%] of 78 episodes), 2-stage shunt replacement with temporary external ventricular drainage (12 [15%] of 78 episodes), and 2-stage shunt replacement without external ventricular drainage (6 [8%] of 78 episodes).

In 15 episodes (19%), no surgical procedure was performed because of good clinical and laboratory response to antibiotic treatment alone (5 episodes), initial uncertainty about the diagnosis of shunt-associated infection (3), the severity of the patient's condition (3), lack of clinical symptoms during shunt implantation but subsequent infection diagnosis by CSF investigation (3), or a concomitant presence of a brain abscess that led to postponement of shunt replacement (1). Infections in which the shunt was retained and that were treated with antibiotics only (without surgery) were either culture-negative (5 infections) or were caused by *P. acnes* (4), coagluase-negative staphylococci (3), *S. aureus* (1), *P. aeruginosa* (1), and viridans group streptococci (1). Among these episodes, 13 infections were acquired intraoperatively. These episodes were clinically

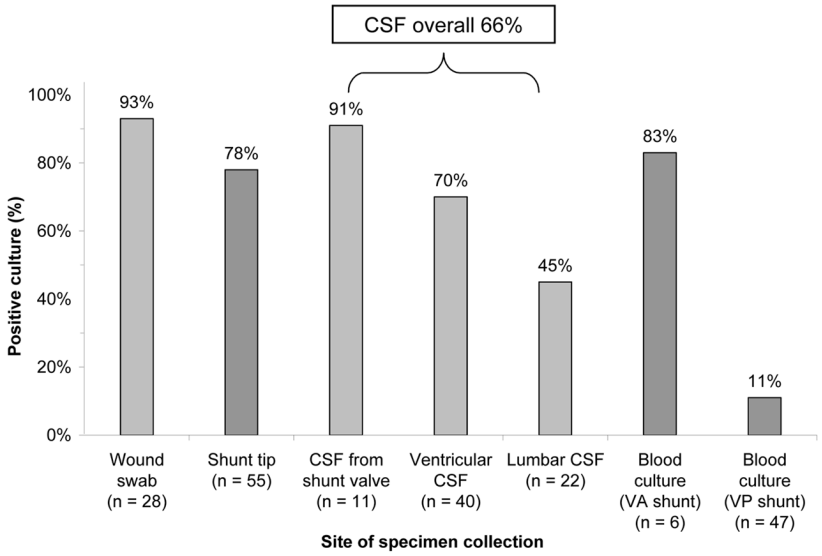

Figure 2. Rate of positive culture results by specimen collection site. VA, ventriculoatrial; VP, ventriculoperitoneal.

more prominent, compared with those in the overall study population, with fever being present in 14 episodes (93%) and neck stiffness present in 13 (87%), whereas local signs of infection were found in only 1. Treatment duration was similar to that for the study group overall (median duration, 22 days; range, 10–91 days), as was length of hospital stay (median duration, 27 days; range, 4–87 days).

Outcome. Figure 3 summarizes the treatment outcome and the status of the shunt at last follow-up. Median duration of patient follow-up was 4.6 years (range, 0.1–11.1 years) after onset of shunt-associated infection. Treatment outcome was favorable in 75 (96%) of 78 episodes; treatment failure occurred in 1 of 63 episodes with surgical treatment and in 2 of 15 episodes treated with antibiotics alone. Among the 3 patients who experienced treatment failure, 1 patient died because of the *P. aeruginosa* shunt-associated infection during the hospital stay (see below). Two patients experienced relapse (treatment failure) during the follow-up period. Both relapses were caused by coagulase-negative staphylococci. In the first relapse episode, no surgical treatment was performed. The infection was caused by a coagulase-negative staphylococcus strain that was initially susceptible to rifampin but that developed rifampin resistance during a 13-week course of combined treatment with vancomycin and rifampin. Relapse occurred 12 days after the discontinuation of antimicrobial treatment. The second relapse episode occurred in a patient who underwent a 1-stage shunt replacement. At that time, 2 morphotypes of coagulase-negative staphylococci were isolated: one strain was susceptible to and the other strain was resistant to rifampin. This patient received treatment with vancomycin and rifampin for 18 days. The relapse occurred 1 day after discontinuation of antimicrobial treatment, and a rifampin-resistant coagulase-negative staphylococcus strain was isolated.

In 4 patients, a new infection occurred in the follow-up period; the shunt was removed during the first infection episode for 2 patients, and a 2-stage shunt replacement with temporary external ventricular drainage was performed for the other 2 patients. New infections occurred 5–29 months after the first episode and were caused by different organisms than those that caused the initial episode.

During follow-up, the shunt was removed in 12 (15%) of the 78 episodes for various reasons. Among the patients who underwent a surgical procedure to treat the initial shunt-associated infection, removal was performed because of shunt dysfunction (for 5 episodes) or new infection (4). Among patients treated only with antibiotics during the initial shunt-associated infection, all shunt removals during the follow-up period were performed because of noninfectious reasons, including no further need for CSF drainage, soft-tissue defect overlying the shunt, or suspected shunt-associated infection, the last of which was subsequently not confirmed. During the follow-up period, 2 patients underwent an additional surgical procedure because of shunt dysfunction.

Overall, 11 (15%) of the 74 patients died, of whom 5 died during their hospital stay and 6 died during the follow-up period. One patient died of a *P. aeruginosa* shunt-associated infection. For this 40-year-old patient with intracerebral hemorrhage, no surgical treatment was performed because of refusal by the patient's relatives. All other in-hospital deaths were unrelated to the shunt-associated infection and included deaths due to cardiac failure (1 patient), glioblastoma multiforme (1), and pneumonia (2).

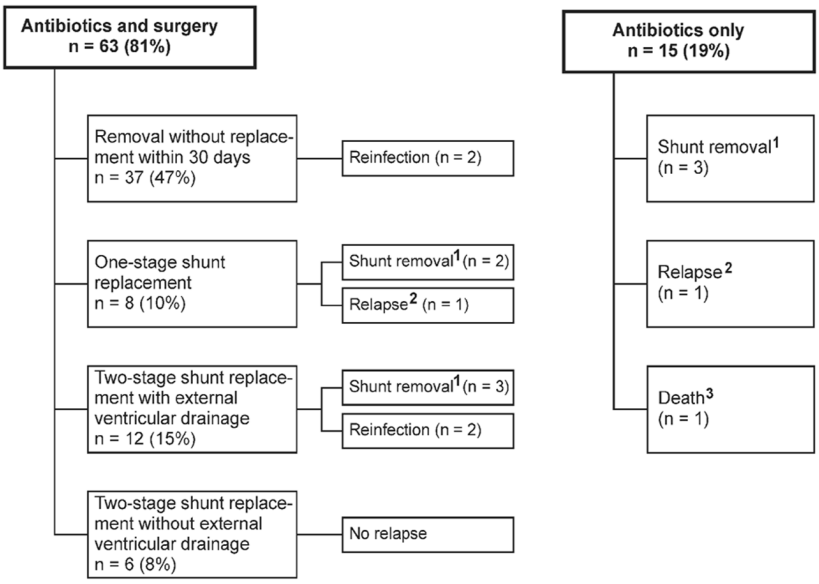

Figure 3. Antimicrobial and surgical treatment strategies and treatment outcomes of CSF shunt–associated infections. During follow-up, 2 relapses and 4 reinfections occurred. [1]Removal, for noninfectious reasons. [2]Relapse, coagulase-negative staphylococci, rifampin resistant. [3]Death, *Pseudomonas aeruginosa* infection associated with ventriculoperitoneal shunt; surgical treatment refused.

DISCUSSION

Most published studies of CSF shunt–associated infections have involved the pediatric population [4, 6, 19]. In the present article, we investigated the characteristics and outcomes of 78 consecutive episodes of shunt-associated infection in the adult patient population. Similar to the findings involving children [16, 20], the majority of shunt-associated infections in our study occurred within the first month after shunt surgery (in 62% of episodes) and were acquired intraoperatively (72%). In approximately one-third of patients, a shunt revision needed for noninfectious reasons, which is a recognized independent risk factor for infection, preceded the infection episode. Most infected patients were admitted to the neurosurgical intermediate care unit (68%), and some were admitted to the intensive care unit (18%), indicating the considerable morbidity related to shunt-associated infections.

In contrast to native meningitis, shunt-associated infections often presented with nonspecific clinical signs and symptoms (e.g., fever), whereas typical neurological manifestations—such as neck stiffness, a decrease in Glasgow Coma Scale, headache, or nausea—were present in less than one-half of the episodes. Remarkably, 22% of patients had no fever, and 36% showed no neurological abnormalities. This fact reflects the nature of implant-associated infections, which are typically caused by low-virulence and slowly replicating organisms growing on the shunt surface in biofilms, such as coagulase-negative staphylococci, the most common cause of shunt-associated infections.

Interestingly, CSF leukocyte count and CSF lactate levels were normal in ~20% of episodes and can, therefore, not be used to exclude a shunt-associated infection. A cutoff for CSF lactate of 4 mmol/L was found to best identify patients with postoperative meningitis [21]. However, in the cited study [21], only 1 patient had a CSF shunt in place. If we had applied this cutoff to our patient group, almost one-half of shunt-associated infections would have been missed. Therefore, we used a lower cutoff of CSF lactate in our study (1.9 mmol/L). The specificity of this value needs to be evaluated in studies that also include patients without CSF shunt-associated infection.

Of note, CSF leukocyte count and granulocyte percentage strongly varied by CSF sampling site and were significantly higher in the CSF obtained through lumbar and valve puncture than in the ventricular CSF. These findings may reflect differences in inflammation in the ventricular system or in the CSF flow in patients with hydrocephalus. An alternative explanation could be that lumbar puncture and valve puncture were performed among patients with advanced shunt-associated infection who presented with fever, whereas ventricular CSF was sampled during shunt surgery at an earlier stage of infection in patients with only local manifestations of infection. Prospective studies with concomitant CSF sampling from different sites are needed to further evaluate differences in CSF values from various collection sites.

In our study, 66% of episodes had positive CSF culture results, and 38% had positive CSF Gram stain results. The CSF culture positivity depended on the collection site and was highest for CSF obtained from valve puncture (91%), potentially

reflecting the high microbial density in biofilms at the site of infection, which is also supported by the high rate of positive shunt tip cultures (78%). Interestingly, lumbar CSF yielded the pathogen in only 45% of episodes, which may be partially explained by preceding antimicrobial treatment; 5 of 12 negative results of lumbar CSF culture were obtained from patients receiving antibiotics before CSF sampling. The high rate of positive wound swab culture results (93%) may represent a selection bias, because wound swab specimens were typically obtained only from patients with clinically evident wound infection.

The most common pathogens in our study were staphylococci and *P. acnes.* This is in accordance with other studies, which have found the most common etiologic agents to be coagulase-negative staphylococci (in 47%–65% of episodes), *S. aureus* (12%–29%), gram-negative rods (6%–20%), and *P. acnes* (1%–14%) [4, 8, 11, 12, 17, 22, 23]. The spectrum of the microorganisms suggests that patient skin flora is an important source of shunt-associated infections [22]. Other means of infection have also been discussed, such as direct inoculation of shunt material from the surgeon or the environment in the operating room, hematogenous spread from a distant focus (especially with ventriculoatrial shunts), or contiguous infection from wounds or perforated gut [2, 24, 25]. Polymicrobial infections were reported mainly when the shunt tip perforated the gut [22, 25]. In our study, most polymicrobial infections presented late and were caused by gut perforation or occurred in patients with head wounds overlying the shunt.

To date, only 1 prospective randomized trial has investigated the outcome of 3 different surgical treatment strategies among 30 children, all receiving antimicrobial treatment [26]. In that study, outcome was favorable in patients with 1-stage or 2-stage shunt replacement with temporary external ventricular drainage (cure rates, 90% and 100%, respectively), whereas without shunt removal, the cure rate was only 30%. Several retrospective analyses underlined these findings [13, 15, 27, 28]. Therefore, a 2- or 1-stage shunt replacement with concomitant administration of intravenous antibiotics is the current recommended treatment strategy. In 1 study, temporary externalization of only the peritoneal shunt catheter with subsequent replacement was effective in 10 (91%) of 11 patients [29].

A conservative management without surgical intervention was investigated in infection associated with ventriculoperitoneal shunt; this study included 43 shunt-associated infections caused by coagulase-negative staphylococci [30]. In this observational study, the success rate was 93%. Similar results were achieved among patients with shunt-associated infections caused by *P. acnes* [11]. In our study, 15 shunt-associated infections (19%) were treated conservatively. In this treatment group, 1 relapse and 1 death attributable to shunt-associated infection occurred. The relapse was caused by a coagulase-negative staphylococcus that was resistant to rifampin, a crucial antibiotic for treating device-associated staphylococcal infections. Another treatment failure was experienced by a patient with a 1-stage shunt exchange and was also caused by a rifampin-resistant coagulase-negative staphylococcus. No treatment failure was observed in the 2-stage shunt exchange group, with or without temporary external ventricular drainage. Overall, treatment outcome in our study was favorable in 75 (96%) of 78 episodes.

This study has limitations inherent to its retrospective design. First, diagnostic and therapeutic procedures did not follow a predefined scheme, which may have biased the interpretation of the results—in particular, the value of different diagnostic tests performed. For example, CSF was collected from different sites, which makes interpretation of sensitivity and specificity difficult. Second, because of the nature of CSF shunt–associated infections with different shunt types and operative procedures, significant associations of one or a group of variables were difficult to find. Third, the sensitivity and specificity of individual laboratory tests could not be determined, because the control group without shunt-associated infection was not evaluated for comparison. Nevertheless, we believe that our mainly descriptive analysis is valuable and has several strengths. This analysis covers an 11-year period and includes a median follow-up of 4.6 years. Although this was done partly in an indirect way—by chart review from rehospitalizations or by contacting patients or their physicians—we were able to estimate the long-term prognosis. A second strength is the in-depth standardized approach that we undertook to investigate all episodes, which demonstrated a detailed picture of shunt-associated infections in predominantly adult neurosurgical patients.

In summary, patients with CSF shunt–associated infections often presented early after shunt placement or revision and with nonspecific clinical signs and symptoms (especially fever) and normal CSF values. Therefore, a high clinical suspicion of CSF shunt–associated infection is needed also in the absence of neurological signs and symptoms. CSF values and culture positivity depended on the CSF collection site; according to our results, it is preferable to collect CSF from the valve, where leukocyte counts and the rate of culture positivity were highest. Shunt-associated infections were caused predominantly by gram-positive skin flora. In selected patients (those with infections due to low-virulence microorganisms that are susceptible to biofilm-active antibiotics, such as rifampin), antibiotic therapy without surgical treatment of shunt-associated infection may be an effective treatment modality. Both treatment failures in our study—one in the 1-stage shunt exchange group and the other in the antibiotic-only treatment group—involved coagulase-negative staphylococci with resistance to rifampin, a

crucial antibiotic for the treatment of device-associated staphylococcal infections.

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