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Cerebrospinal fluid shunt infections in infants

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Abstract Infection remains a major cause of morbidity and mortality following CSF shunt procedures. In this study 191 shunt procedures carried out from January 1981 to December 1992 in a series of 81 infants (less than 6 months old) were retrospectively analyzed for possible risk factors. The overall surgical infection rate was 7.8%, with 15 infections occurring in 14 patients (17.2%). No significant difference in the rate of infections was found in relation to sex, birth weight, gestational age, and type of shunt procedure (primary insertion/revision). The occurrence of other infections during the period of shunt surgery did not influence the infection risk either. Intraventricular hemorrhage and central nervous system infections as causes of the hydrocephalus were found to correlate with septic risk. Young age (less than 6 months) seems to represent the main risk factor, and this is related both to the immunologic deficiency and to the particular features of residential bacterial flora in this age group.

Key words Hydrocephalus · Infants · Ventriculoperitoneal shunt · Shunt infection · Risk factors

Introduction

Cerebrospinal fluid (CSF) shunting has developed into the main method of treatment in children with hydrocephalus. Although the improved survival of these children is chiefly due to the success of shunting procedures, the treatment is prone to several complications, among which shunt infections are today the most important cause of morbidity and mortality in hydrocephalic children.

Few studies have analyzed risk factors in detail, making comparisons between reported series difficult and making the relationship between infection rate and the characteristics of patients unclear. In particular, infants and newborns are high-risk patients, both because of the immunologic immaturity in this age group and because of the particular features of neonatal hydrocephalus, often associated with conditions that make it very difficult to obtain real asepsis (spinal dysraphisms for example), and that often require shunt insertion on an emergency basis.

In this study we have retrospectively analyzed our shunt practice to define the infection rate and to identify which factors are associated with an increased infection risk.

Patients and methods

The series consisted of 81 infants (less than 6 months old) affected by hydrocephalus and subjected to ventriculoperitoneal shunt operation over a 12-year period (January 1981 to December 1992). Follow-up was for at least 1 year (range 1–12 years, mean 5.5 years). There were 46 male and 35 female patients, with a mean birth weight of 2790 g (range 750–4100 g) and a mean gestational age of 36 weeks (range 26–41 weeks). At the first shunt procedure, 51 patients (63%) were less than 1 month old, 20 (25%) were less than 3 months old, and 10 patients (12%) were between 4 and 6 months old. The various etiologies of hydrocephalus are shown in Table 1.

The criteria by which CSF shunt infection were diagnosed were those defined by Odio et al. [16]. Infection was considered documented when a pathogenic organism was cultured from ventricular fluid or shunt material, and was associated with one or more of the

Table 1 Etiologies of hydrocephalus in 81 infants who received ventriculoperitoneal shunts

Etiology	No. of cases	%
Myelomeningocele	33	41
CNS congenital anomalies	28	35
Posthemorrhagic	10	12
Postinfective	6	7
CSF cysts	3	4
Neoplasm	1	1
Total	81	100

following: fever, shunt malfunction, neurological or abdominal symptoms, and ultrasonographic images suggestive of infection. When cultures were negative the diagnosis of infection was made if fever, shunt malfunction, abdominal or neurological symptoms, and CSF pleocytosis (>50 leukocytes/mm^3) were present at the same time. Recurrence of infection was defined as reinfection if the isolated germ was different from the previous one and as relapse if the isolated organism was the same as the previous infection and if it occurred within 1 month after the completion of antibiotic therapy.

A "new" implantation was the procedure of the first shunt insertion; this term was also used when a second shunt (in a different site) was required to drain CSF cysts or other collections not communicating with the ventricular system. All procedures of shunt replacement were considered to be revisions. "Complete" revision consisted of the total removal of valve and proximal and distal catheters with implantation of a new shunt on the same or contralateral side; "proximal" and "distal" revisions respectively consisted of the exploration and replacement of the intraventricular or distal catheter.

For shunt procedures the surgeon used a multicomponent system (Heyer-Schulte) made up of a Portnoy ventricular catheter, Pudenz valve (medium pressure), and Raimondi peritoneal catheter (low pressure). In one case a Hakim-Cordis shunt system was used.

Antibiotic prophylaxis was performed during all shunt procedures, both for new implantations and for revisions.

The following parameters were reviewed as possible infective risk factors:

- Gestational age and birth weight
- Age of child at the time of the first shunt insertion
- Underlying cause of hydrocephalus
- Type of shunt procedure (new implantation or revision)
- Number of previous shunt procedures before onset of shunt infection
- Occurrence of other infections during the period of shunt surgery

The results of the study were analyzed using a 2×2 contingency Table (χ^2 test).

Results

A total of 191 shunt procedures were performed in our series of 81 patients during the 12-year period of the study, 95 of which were new insertions and 96 revisions. Fourteen children required the insertion of a second shunt. The mean number of procedures per child was 2.3 (191/81). The revision rate amounted to 1.01 revisions per new implantation (96/95). The reasons for revisions are shown in Table 2.

During the 12-year period of the study, 15 shunt infections resulted from 191 shunt procedures, giving an overall surgical infection rate of 7.8% and involving 14 out of 81 patients (17.2%). The operative infection rate rose to 9.2% (15/168) if we take into account only the shunt procedures performed not as a consequence of a previous CSF shunt infection, but for any other causes of shunt failure.

No relapses or reinfections occurred in this series.

The infections consisted of ventriculitis in 11 patients and of colonization of the distal catheter in 4 cases, in 3 of these with abdominal pseudocyst.

Characteristics of infections

All cases of shunt infections localized in the central nervous system occurred within the 1st year following the primary shunt insertion, with a mean time to onset of 97 days (range 4 days to 1 year); all infections occurred within 2 months except for three that developed respectively 7, 9, and 12 months after surgery. Taking all shunt procedures (new implantations and revisions) into account, the median time to onset was 21 days after surgery (range 4 days to 2 months).

Fever, irritability, meningeal signs, and sometimes seizures were the most common presenting features. In one case a subgaleal purulent collection developed at the site of insertion of the valve.

The microorganisms responsible for infection were isolated in only five cases; in the others the CSF cultures gave a negative result (three patients were receiving antibiotic treatment at the time). All cultured germs were gram-positive cocci (one case of *Staphylococcus aureus*, one of *Streptococcus faecalis*, two cases of *Staphylococcus epidermidis*), except for one case of *Proteus vulgaris*.

The three cases of pseudocysts had a later onset after the first shunt surgery: respectively 9 months, 1 year and 4 months, and 6½ years. Clinically pseudocysts were characterized by an insidious onset with abdominal pain, local swelling, and shunt malfunction.

Risk factors

No significant difference in the rate of infections was found in relation to sex, birth weight, and gestational age. All children were younger than 6 months at the time of the first shunt insertion; when they were divided into two age groups (younger and older than 1 month), no difference in the risk of developing infection could be seen (17.6% or 9/51versus 20% or 6/30).

In our series the etiology of hydrocephalus represented a significant risk factor for infection: posthemorrhagic and postinfectious hydrocephalus had an infection rate of 50% (5/10 in postinfectious hydrocephalus and 3/6 in the post-

Table 2 Types of revision procedures and reasons for revision (n=96) (*VP* ventriculoperitoneal)

Type of procedure	Reason for revision				
	Post shunt-infection	Obstruction	Fracture disconnection	Malposition	Other causes[a]
Total revision	2	6	–	–	5
Proximal revision	–	11	–	3	2
Distal revision	3	9	28	–	–
VP shunt to external drainage	11	–	–	–	1
External drainage to VP shunt	10	–	–	–	1
VP shunt to ventriculoatrial drainage	–	–	–	–	1
Revision of external drainage	3	–	–	–	–
Total	29	26	28	3	10

[a] Skin problems (n=3), loculated ventricles (n=2), abdominal ascites (n=1), underdrainage (n=1), overdrainage (n=1), intracerebral hemorrhages (n=1)

Table 3 Infection rates in hydrocephalus of different etiologies

Etiology of hydrocephalus	No. of cases	No. of clean shunt procedures	No. of infections	No. of infections/child (%)	No. of infections/shunt procedure (%)
Meningomyelocele	33	71	4	12.1	5.6
CNS congenital anomalies	28	51	3	10.7	5.9
Posthemorrhagic	10	17	5	50	29.4
Postinfective	6	19	3	50	15.7
CSF cysts	3	3	0	0	0
Neoplasm	1	1	0	0	0
Total	81	162	15	17.2 (mean)	9.2 (mean)

Table 4 Infection rates associated with first insertions and revisions

Shunt procedure	No.	No. of infections	Infection rate (%)
First insertion	95	6	6.3
Clean revision[a]	67	9	13.4
Total	162	15	9.2

[a] Revision performed for causes other than infection

hemorrhagic one), compared to the mean rate of 17.2% ($P<$ 0.01).

Meningomyelocele, malformative hydrocephalus, and CSF cysts do not seem to be associated with a risk of sepsis (Table 3).

Concurrent infections did not influence the susceptibility to shunt infections, taking as concurrent infections all cases of sepsis that developed at the time of the shunt surgery. Conditions of sepsis associated with postinfectious hydrocephalus with the same pathogen were not considered as concurrent infections. In this study eight cases of sepsis occurred in eight patients, two of whom subsequently developed a shunt infection (P>0.05).

The type of surgical procedure (first implantation/revision) does not seem to represent a predisposing factor for infections, with an infection rate of 6.3% (6/95) after new insertions versus 13.4% (9/67) after revisions (P>0.05; Table 4). Within the revision group however, it is necessary to distinguish some high-risk procedures, such as the insertion of external drainage or revision of the wound on the scalp, performed in four of the nine children who developed an infection after a revision procedure.

The number of early revisions (performed within the first months after primary insertion) represented in our study a highly significant risk factor for shunt infections: the revision rate of children who later developed a shunt infection was much higher (1.8 revision/child) than that of children who had no complications (0.12 revisions/child; $P<$ 0.001). We considered as early revisions all procedures performed within the first 5 months after primary implantation of the shunt, as these 5 months were the mean distance in time of postrevision infections from the initial implantation.

Discussion

Infections remain the major cause of morbidity and mortality following CSF shunt procedures. The reported rate of infection in the literature varies greatly in relation to the characteristics of the series and to the different risk factors considered. Most studies, however, agree in identifying age as an important risk factor. Children in the 1- to 6-month age range have a significantly higher risk of developing shunt infections than older patients [11, 20, 21, 24]. The reason for this increased susceptibility to shunt infections is not clear, but has been postulated to be related to their immunologic immaturity, with particular involvement of the immune response against bacteria [21].

In our study shunt infections occurred after 9.2% (15/191) of surgical procedures, affecting 17.2% (15/81) of children. These results are similar to the rates of infection reported in other series of patients under 6 months of age (15.7% [17], 21% [28], 11.1% [21]. Choux and coworkers [6] have reported a very low infection rate (0.33%) in 600 hydrocephalic children who underwent ventriculoperitoneal shunting. In that series, however, the large majority of patients (68%) were more than 6 months old.

The first 6 months of life are characterized by a progressive decline in the levels of maternal IgG, and the gradual build-up of specific antibodies at this age probably does not yet defend the child from infections. Furthermore, complement activity and cellular immunity are lower and less efficient than in adults. Renier and coworkwers [21] attribute the high incidence of shunt infections occurring in this age to these factors. According to other authors [17], there seems to be no evidence that immunoglobulins (including the specific antibodies against the infecting strain of *Staphylococcus*) are protective against shunt colonization. Moreover, neutrophil function, opsonization, and complement activity seem to exert their defensive function mostly against external infections at the incision sites, but their efficacy is limited once organisms have entered the ventricles or the shunt system [17]. In sum, then, the relationship between increased infection rate and impaired immunity in the first 6 months of life is still controversial.

Some authors suggest an alternative explanation for the increased CSF shunt infection rate in young infants, as coming from the age-related changes in the skin and its residential bacterial flora [7, 17].

There are two main aspects of residential bacterial flora at this age that could be related to the increased shunt infection rate: first, the higher bacterial density of skin in the first months of life [14, 22], and, second, the presence of coagulase-negative *Staphylococcus* and in particular of *Staphylococcus epidermidis*.

Regarding the first point, there seems to be a statistically significant association between skin bacterial density and frequency of bacterial wound contamination during the operation [19]; in addition, the number of organisms necessary to produce an infection is greatly reduced in the presence of foreign material (shunt devices) [9]. Regarding the second point, *Staphylococcus epidermidis*, long regarded as an avirulent residential germ, represents today one of the chief agents responsible for infections in children with CSF shunts as well as in individuals in whom other foreign materials have been implanted [15]. The density of this organism on the skin, very low at birth, rapidly increases during the first weeks of life [7] to become, in favoring environmental conditions (such as the intensive care nursery), the dominant pathogen [7].

These considerations stress the role played by microbic residential flora in determining shunt infections, through direct colonization of shunt devices or wound contamination. In particular, despite measures to isolate skin and wound edges, skin contamination at the site of catheter insertion still occurs and seems to be the main source of shunt infection.

In our study five pathogens were isolated from ventricular fluid specimens during a shunt infection: *Staphylococcus epidermidis* (two cases), *Staphylococcus aureus*, *Streptococcus faecalis*, and *Proteus vulgaris* (one case each). Despite the small number of positive CSF cultures, these results agree with the reports in the literature, where staphylococci are described as the most prevalent pathogens [16–18, 26, 28]. Difficulty in isolating the responsible microorganisms by culturing has been documented in other studies [27], where it has been attributed to adhesion of microorganisms to the foreign material (valve, catheter); consequently they may not be found in circulating CSF but may be detected on the shunt devices by microscopic studies.

Among the risk factors, the etiology of hydrocephalus is a very important one, with a strong influence on the risk of infection. In the literature, posthemorrhagic and postinfectious hydrocephalus are often reported as high-risk conditions [18, 23, 26]. Studies where no association between etiology of hydrocephalus and shunt infection rate are found [13, 28] deal almost exclusively with older children (school age), who are characterized by a lower incidence of these etiologies, so the rarity of these conditions in such studies does not allow comparisons to be made or statistically significant results to be obtained. In our series posthemorrhagic and postinfectious hydrocephalus were significantly associated with an increase in the infection rate (50% of both conditions versus 17.2% mean; $P< 0.005$). On the other hand, our series does not seem to implicate meningomyelocele as a separate risk factor.

The higher infection rate observed in infants with hydrocephalus caused by perinatal intracerebral hemorrhage does not seem to depend only on the frequency of this pathology in premature newborns and therefore on their concomitant immunologic immaturity, but the intraventricular hemorrhage seems to constitute a separate risk factor per se, irrespective of the age of the patient. This special susceptibility may conceivably arise from the predisposing action of remnants of the hemorrhagic material in the

ventricles, which probably opposes local defensive systems [23].

Regarding postinfectious hydrocephalus, the increased septic risk seems to be due to the difficulty of completely sterilizing CSF of the pathogens which caused the ventriculitis and which, despite full clinical remission of the patient and negative CSF cultures after antibiotic therapy, may remain and colonize the inserted shunt system; this, in turn, may keep germs protected from all local defensive systems and consequently favor bacterial multiplication [23]. The sterilization of CSF in the course of ventriculitis is a very difficult goal, because cerebral ventricles respond to infective noxae with the production of proteic material and fibrinic exudate, with the final constitution of adherences and loculated CSF cystic collections, where antibiotics, although locally administered, cannot enter. This pathologic condition (like posthemorrhagic hydrocephalus) would imply that the shunting procedures should be postponed as long as possible, with temporary management of CSF pressure by other therapeutic means such as insertion of a subcutaneous reservoir (which allows serial CSF taps and the simultaneous administration of intraventricular antibiotic therapy), or the insertion of external drainage.

The presence of another source of infection as a risk for shunt sepsis has been infrequently investigated in literature, most studies showing no significant association [12, 24, 25]. A positive correlation between urinary tract infection or pneumonia and shunt infection was documented only by Renier et al. [21]. In our series concurrent infections did not seem to influence susceptibility to developing shunt infections: in two cases only did bacterial sepsis precede a shunt infection, while six unrelated infections occurred in the group of children without shunt complications ($P>0.05$).

Regarding the type of surgical procedure, there is disagreement as to whether primary shunt insertion involves an increased risk of infection. Odio et al. [16] found a higher risk of CSF shunt infection in shunt revisions; a number of papers, by contrast, have reported higher rates in primary shunt insertions than in revisions [12, 21, 25, 28]. Walsh et al. [28] suggest that, where allowances are made for the natural tendency for revisions to be performed in older children than first insertions, this difference is no longer apparent. In our experience no difference was found between infection rates with different types of shunt surgical procedure, even though the incidence of infections after revisions was higher than after initial insertions (13.4% and 6.3% respectively).

Among the revision procedures, scalp wound revision and the management of external ventricular drainage (insertion and subsequent internalization) should be considered separately, carrying a higher risk. In particular, higher infection rates are reported after internalization of external drainages inserted for a previous shunt infection [18, 21]. In our patients all cases of shunt infection were managed by removal of the shunt and insertion of an external catheter, but no reinfection occurred.

In our series the number of early revisions performed in the first months of life significantly correlates with the probability of developing infection ($P< 0.001$). This tendency, also shown by others [16], can easily be explained by the infection risk of each surgical procedure; moreover, the two conditions with which infections are most frequently associated (posthemorrhage and postinfectious hydrocephalus) are the ones that usually require a greater number of revisions, due to the particular characteristics of CSF, easily leading to malfunction of draining catheters.

Sex, gestational age, and birth weight are not associated with significant differences in infection rate.

In our series prophylaxis was performed in all surgical procedures, consisting of preoperative and postoperative intravenous administration of broad-spectrum penicillins, second-generation cephalosporins, and aminoglycosides. At the present time prophylaxis is routinely based on ceftriaxone (80 mg/kg i.v.) for 7–10 days after operation, rarely in combination with netilmycin (6 mg/kg) in high-risk cases. In this study intraventricular antibiotics were not used for prophylaxis.

Unfortunately, antibiotic prophylaxis in shunt surgery does not seem to influence significantly the probability of developing a shunt infection [16–18, 26]. This topic is much debated in the literature, and although some studies have reported a benefit from antibiotics, most authors agree there is no evidence of a correlation between the use of antibiotic prophylaxis and a significant reduction in infection rate. Absence of statistical significance does not, however, mean an absence of effect: on the contrary, the general trend is that the lowest infection rates are found in series where prophylaxis is performed [6, 11]. Moreover, a study by Haines and Taylor [12] showed that preoperative antibiotic prophylaxis, although unable to prevent early infections, significantly reduced the incidence of late shunt obstruction, which they attributed to latent infections. Choux et al. [6] favored the use of preoperative intravenous administration of cloxacillin and oxacillin and intraoperative topical soaking of the shunt material in gentamycin. In sum, despite the absence of absolute evidence of its efficacy, antibiotic prophylaxis is a universally performed practice.

To conclude, the past decade has witnessed a significant reduction in mortality, revision rate, and the frequency of postoperative CSF shunt infections, which nevertheless remain the greatest problem among the various complications of shunt surgery. Despite a large number of publications, very few definitive statements can be drawn up regarding factors influencing shunt infection. The type of surgical procedure (except for the management of external drainage) is probably not relevant, nor is the presence of concurrent infection. The etiology of the hydrocephalus seems to influence significantly the risk of infection, par-

ticularly the postinfectious and posthemorrhagic types, but the dominant determinant of septic risk appears to be young age (less than 6 months). The predisposing role of young age, which may be related to immunologic immaturity, has recently also been attributed to the particular bacterial flora of the skin in the first months of life. At the present time, no study can answer the question as to the efficacy of prophylactic antibiotics, but their use is still required until such data become available.

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