Chapter 44
Shunt Infection

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44.1 Introduction

Ventriculoperitoneal shunt (VPS) remains the gold standard treatment for multiple forms of hydrocephalus. Although its success has been amply demonstrated, the rate of event-free survival is around 70% in the first year and 40% at 10 years [1]. Among the different causes of shunt failure, in this chapter we will focus on shunt infection requiring long-term hospital admission, removal of the shunt system in the majority of cases, and intravenous antibiotic therapy for a variable period of days or weeks. Hence, the importance of its early detection and the protocolization of its management.

44.2 Definition

Multiple definitions of shunt infection exist. They mostly include a combination of symptoms and signs of shunt dysfunction and infectious semiology, supported by complementary tests that indicate an infectious process, confirmed by the isolation of the causative microorganism. One of the most widely used and broadest definitions is that recommended by the HCRN [2]:

1. Microbiological determination of organisms on culture or Gram stain from cerebrospinal fluid (CSF), wound swab, and/or pseudocyst fluid.

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2. Shunt erosion (wound breakdown with visible shunt hardware).
3. Abdominal pseudocyst (even in the absence of positive cultures)
4. Positive blood cultures in a child with ventriculoatrial shunts.

The Centers for Disease Control and Prevention's National Healthcare Safety Network (CDC/NHSN) definition of health-care-associated ventriculitis or meningitis [3] is more complex. It includes at least 1 of the following criteria:

- Organism cultured from CSF
- At least 2 of the following symptoms with no other recognized cause in patients aged >1 year: fever >38 °C or headache, meningeal signs, or cranial nerve signs, or at least 2 of the following symptoms with no other recognized cause in patients aged ≤1 year: fever >38 °C or hypothermia <36 °C, apnea, bradycardia, or irritability and at least 1 of the following:

  – Increased white cells, elevated protein and decreased glucose in CSF
  – Organisms seen on Gram stain of CSF
  – Organisms cultured from blood
  – Positive nonculture diagnostic laboratory test from CSF, blood, or urine
  – Diagnostic single antibody titer-(immunoglobulin M) or four-fold increase in paired sera (immunoglobulin G) for organism.

The IDSA guidelines [4] present a practical approach for the management of shunt infections and give the evidence of their recommendations. Regarding diagnosis, they suggest several issues to consider:

- Symptoms of infection, CSF pleocytosis and positive culture are indicative of ventriculitis or meningitis.
- An altered CSF biochemistry does not diagnose an infection, just as a normal biochemistry does not rule it out. Likewise, a negative CSF Gram stain does not exclude infection. Although CSF culture is the most important test to establish the diagnosis of meningitis and ventriculitis, it is recommended that cultures be held for at least 10 days to identify slow-growing organisms.
- An elevated CSF lactate or an elevated CSF procalcitonin, or the combination of both, may be useful in the diagnosis of bacterial ventriculitis and meningitis and an elevated serum procalcitonin may be useful in differentiating CSF abnormalities due to surgery or intracranial hemorrhage from those due to bacterial infection.

The fact that there exist different definitions of shunt infection in the literature may due to the variety of clinical situations we can find in practice: from a small erosion on the patient's skin or small abdominal discomfort to bacterial meningitis with a wide spectrum of symptoms, whether or not linked to shunt disfunction. Thus, a high degree of clinical suspicion is necessary and this diagnosis should be considered whenever shunt dysfunction occurs without an obvious explanation.

44.3 Epidemiology

The incidence of shunt infection is variable. Rates between 5% and 41% can be found in different series in the literature, although in recent years the rate has been limited to 4–17%. The incidence of infection by procedure or operative incidence is between 2.8% and 14%. Most authors consider a rate below 10% acceptable, although most series have described a rate lower than 4% [4].

Our center published data on surgical outcome after shunt surgery in 2016, reviewing 166 patients in whom 425 procedures were performed between 2000 and 2015 [5]. This retrospective noncontrolled study showed the following infection rates: shunt infections occurred in 7% of the procedures (30/425) and 15.7% of the patients (26/166) and the percentage of shunt revisions secondary to infection was 11.6%.

A retrospective review of infections for the period between 2000 and 2020, with data yet to be published, showed the following: shunt infection rates per patient and per procedure were 14.64% (41/280) and 6.67% (49/734), respectively.

44.4 Risk Factors

Over the last few years, several case-control studies have reported the main risk factors related to shunt infection. Some factors depend on the patient: prematurity, a history of infectious disease such as sepsis or ventriculitis, complex cardiopulmonary disease, previous CSF fistula … The relationship between the patient's age and the risk of infection is disputed, although most of the literature agrees that the younger the age, the greater the risk of infection. Other factors of a surgical nature include: previous external ventricular drainage, surgery time for shunt implantation, whether the surgery was performed urgently, or the experience of the surgeon. On the other hand, surgical factors such as the use of standardized protocols [6] or the use of antibiotic-impregnated catheters have been found to be protective [7].

Regarding the type of catheters, several publications have confirmed the decrease in rates of shunt infection in those centers that have introduced the use of antibiotic-impregnated catheters. The IDSA guidelines recommend their use with "a strong rating for the quality of the evidence and a moderate grade for the recommendation". However, the most commonly used antibiotics for impregnation of these catheters are rifampicin and clindamycin and several studies have published a relative increase in the frequency of gram-negative infection [8].

One of the most important risk factors is a history of previous shunt revision. The risk of infection is three times higher in those patients with a history of shunt revision compared to those without (HR 3.9, 95% CI, 2.2, 6.5) and up to 13 times higher in those with 2 or more shunt revisions compared to those with no review (HR 13.0, 95% CI, 6.5, 24.9) [9].

In our series, infection was the reason for shunt failure mainly in younger patients soon after the first ventriculoperitoneal implantation or later on in the context of distal dysfunction secondary to a peritoneal pseudocyst [5].

44.5 Pathogenesis

There are four mechanisms by which shunt infection can occur.

- First, the contamination of the VPS during implantation surgery. Here, the infection occurs early in time and is caused by microorganisms that typically colonize the skin of patients, such as gram-positive cocci. However, if the infection is caused by slow-growing bacteria (P. Acnes, S. Epidermidis) that are expressed in a paucisymptomatic manner, the diagnosis may be reached late.
- Second, infection can migrate retrogradely from the distal part of the shunt because of abdominal complications from the shunt, such as pseudocysts or peritonitis, or may be secondary to infectious/inflammatory diseases originated in the abdominal cavity.
- Third, the shunt can be infected through the skin, either by invasive maneuvers such as puncturing the reservoir or by small erosions or ulcerations on the patient's skin that cause exposure of the "hardware".
- The fourth mechanism is hematogenous, characteristically in patients with a ventriculoatrial shunt, which is a foreign body in the bloodstream that exposes them to colonization if bacteremia occurs.

Some authors differentiate between early infection when it occurs before 6 months after implantation surgery and late infection when it occurs beyond that period. The mean time from shunt implantation to infection is 19 days, which is consistent with the general idea that the most common infection mechanism is intraoperative contamination [10]. These early infections are mostly caused by bacteria such as coagulase-negative Staphylococcus species and S. aureus. Late infections are less frequent and a higher proportion of these are caused by gram-negative bacilli, suggesting that this type of infection is caused by a mechanism of retrograde contamination from the distal part of the shunt.

In our series, 35 of 49 (71.42%) infections occurred early (within 6 months of shunt implantation) and 14 of 49 (28.57%) occurred late (more than 6 months after shunt implantation). Regarding the bacterial etiology in our series, coagulase-negative cocci was the most frequent group, causing 20 of the 49 infections (40.81%). Infections caused by S. aureus (6 of 49, 12.24%) and gram-negative bacilli (6 of 49, 12.24%) followed in frequency.

In the pathogenesis of shunt infection, the role of the bacterial biofilm should be mentioned. Bacteria have the ability to adhere to inert material, such as the shunt catheter or valve hardware, thanks to the polysaccharides on the bacterial wall. Bacteria accumulate in a matrix made up of macromolecules such as proteins, DNA,

and other products from bacterial lysis. The result is the formation of a biofilm adhered to the shunt, which is formed by a plactonic layer that is susceptible to the action of antibiotics, and another deep layer, which is inert to their action. For this reason, as we will see below, the complete removal of the shunt is recommended, since antibiotic treatment may be insufficient to eliminate all the bacteria in the biofilm. In addition, the biofilm together with the products of the patient's CSF can cause obstruction and shunt failure [11].

44.6 Clinical Characteristics

The clinical characteristics of shunt infection can be highly variable and depend on its pathogenesis, the virulence of the microorganism, and the type of shunt. For example, some of the bacteria that most frequently produce shunt infection, such as coagulase-negative staphylococci or P. acnes, are indolent and therefore cause minimal inflammation, resulting in minimal ventriculitis without meningeal involvement or shunt dysfunction without inflammation due to the formation of a biofilm on the catheter or shunt hardware [12]. Figure 44.1 shows the symptoms registered in our series of cases. Note that up to a third of patients did not present fever at diagnosis.

The most frequent form of presentation is a patient with new-onset headache, nausea and/or lethargy. This clinical profile generally occurs when the infection settles in the proximal part of the shunt, causing a condition that resembles shunt dysfunction. On the other hand, signs such as erythema or tightness in the

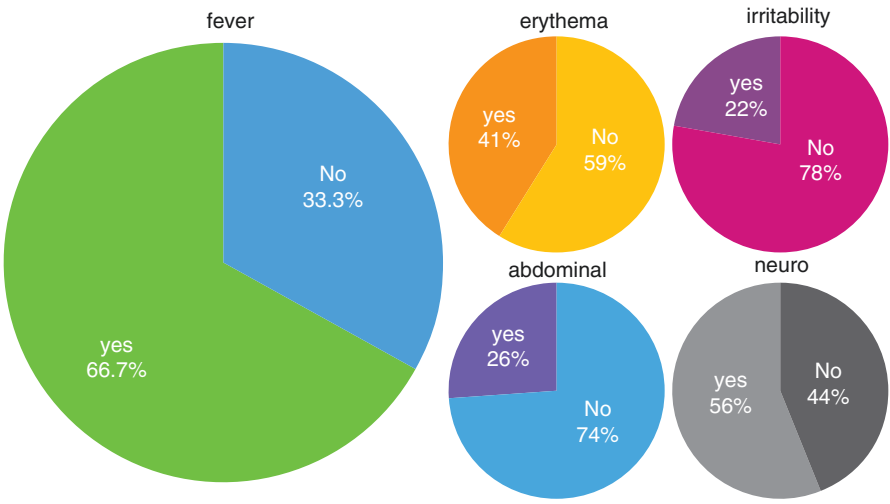

Fig. 44.1 Frequency of symptoms in our series of shunt infections

subcutaneous path of the VPS should suggest its infection. Finally, the symptoms related to distal shunt infection are caused by inflammation of the peritoneum in VPS and of the pleura in a ventriculopleural shunt.

It should be noted that, with low-virulence microorganisms, the symptoms of infection may be nonspecific, such as abdominal pain or tightness. Sometimes the scarring process in the abdomen leads to the formation of an abdominal pseudocyst around the distal catheter in an attempt to contain the infection.

44.7 Diagnosis

The diagnosis of shunt infection can be challenging and requires a high index of suspicion. Faced with a patient with compatible symptoms, a directed anamnesis should be carried out in which information is obtained about the reason for shunting, date of implantation and type of shunt valve. After a physical examination that should include a complete neurological study and inspection of the VPS tract, it is recommended to request blood tests with acute phase reactants such as CRP and more specifically for bacterial infection such as serum procalcitonin. A CT scan should be done as an urgent neuroimaging test to perform the accurate diagnosis of shunt dysfunction. After that, CSF should be obtained by one of the following methods: by puncturing the shunt reservoir, a CSF collection, abdominal collections or an externalized catheter, in order to study the biochemical parameters of the CSF, as well as microbiological studies such as gram staining and CSF culture.

Alterations in CSF biochemical parameters can be subtle, making it difficult to distinguish whether these alterations are due to an infection or some other disease causing the hydrocephalus (tumor, hemorrhage…) or even some other neurosurgical process performed. Although the increase in leukocytes, decrease in glucose and increase in proteins in CSF correlate with the infection, it can nevertheless occur in patients with normal biochemical parameters [13]. Gram stain is commonly used when infection is suspected, although its negative result does not rule out the presence of bacterial infection, especially if the patient has previously received antibiotic treatment.

Given this clinical scenario, we must use more specific infection parameters to guide the diagnosis of the condition, such as CSF lactate. Two meta-analyses have shown that elevated CSF lactate is better than the use of a leukocyte count, glucose or protein in differentiating between bacterial meningitis and aseptic meningitis [14, 15]. Regarding the recommended cut-off number, a CSF lactate greater than 4 mmol/L has a high sensitivity (88%) and very high specificity (98%) in the diagnosis of bacterial meningitis after neurosurgical intervention [16].

CSF culture is the most important diagnostic test in detecting VPS infection, since the result will generally be positive even in those patients without CSF biochemical alterations. Its culture requires several days or weeks of incubation before

determining a negative result, because the presence of slow-growing microorganisms such as P. acnes is not uncommon. If the result is negative and the suspicion of infection remains high, the test should be repeated, especially if the patient is already receiving antibiotic treatment as the sensitivity of the CSF culture decreases from 88% to 70% with the use of any antibiotic therapy. Sensitivity decreases to 59% if antibiotics have been administered more than 24 h before CSF extraction [17].

When a shunt revision surgery is performed and the suspicion of infection is plausible, culture of the catheters and the valve hardware is recommended. However, if a valve system or catheter is removed for some other reason during revision surgery, "routine" culture of these components is not recommended [4].

44.8 Treatment

44.8.1 Surgical Management

When the suspicion of infection is high and the data from the complementary tests support the diagnosis, the patient should be admitted to hospital in order to plan medical and surgery treatment. Different approaches have been published. Several studies have described series in which removal of the infected shunt system is not carried out, in an attempt to avoid the morbidity of repeated surgical interventions and to maintain a CSF shunt. The efficacy described was low (34–36%) and a relatively high mortality rate was found, together with prolonged hospitalization periods and adverse events associated with the instillation of intrathecal antibiotics, sometimes used in this conservative approach [18]. However, an observational study described better results, with up to 92% success in infections caused by microorganisms other than S. aureus, suggesting that the conservative approach may be appropriate for more indolent bacteria like coagulase negative staphylococci or P. acnes [13]. In the only randomized study carried out in children, non-removal of the shunt system was associated with a 70% recurrence rate [19]. In our center, the absence of complete removal of the infected shunt is considered only exceptionally, in patients with a very poor prognosis regardless of the infection or with a very high surgical risk.

The surgical management used in most centers is the complete removal of the shunt system plus the implantation of an external CSF drainage. The presence of external ventricular drainage (EVD) allows the monitoring of CSF biochemical parameters, as well as serial cultures every 24–48 h. In addition, it can be used to administer intrathecal therapy when necessary [20]. After the end of the antibiotic treatment (see below), a new shunt can be implanted, preferably in the contralateral ventricle. The persistence of pleocytosis, hypoglycorrhachia or hyperproteinorrhachia should not delay the placement of the new VPS beyond the recommended periods, as CSF biochemistry can remain altered for a long time.

An intermediate option for surgical management is externalization of the shunt. This may be an option to consider for patients whose infection is limited to the distal portion of the shunt (for example, in those with an abdominal pseudocyst and negative CSF cultures) or in those patients in whom the infection is combined with a situation of shunt overdrainage or slit ventricles, in which insertion of an EVD can be difficult.

On the other hand, patients with old catheters or those attached to the choroid plexus present a technical difficulty for shunt removal and a relatively high risk of bleeding, which may justify the inability to remove the shunt completely. These patients should be closely followed, since the recurrence of infection by the same microorganism supports the indication to carry out a surgical intervention in a programmed way to remove the abandoned part of the previous shunt.

44.8.2 Antibiotic Treatment

After obtaining CSF cultures, antibiotic treatment should be started empirically and intravenously. Current guidelines recommend the use of vancomycin plus a beta-lactam with anti-psudomonal effect such as cefepime, ceftazidime or meropenem. The choice of the beta-lactam antibiotic should be made based on local susceptibility patterns. In case of allergy to beta-lactams, or if meropenem is contraindicated, aztreonam or cirpofloxacin may be an alternative. Table 44.1 shows the recommended doses.

If gram-positive microorganisms are observed during admission, the recommended treatment is vancomycin with or without rifampicin. In the case of gram negative microorganisms, the treatment would be the chosen beta-lactam. Once the germ has been identified in the culture, targeted treatment should be performed. Figure 44.2 shows some examples of targeted antibiotic therapy.

Intraventricular antibiotic therapy is reserved for restricted cases, such as failure of intravenous therapy, difficult-to-eradicate infections caused by multi-resistant bacteria (for example, carbapenem-resistant), or when the indicated antibiotic does not adequately penetrate the CSF. It could also be indicated in patients who cannot immediately undergo removal of the shunt system [21]. Antibiotic dosage depends

Table 44.1 Pediatric doses of the most used antibiotics

Antibiotic	Pediatric dose
Vancomycin	60 mg/kg/day every 6 h
Meropenem	120 mg/kg/day every 8 h
Ceftazidime	200 mg/kg/day every 8 h
Cefepime	150 mg/kg/day every 8 h
Rifampicin	20 mg/kg/day every 24 h
Linezolid	<12 years: 30 mg/kg/day every 8 h >12 years: 20 mg/kg/day every 12 h (maximum 600 mg/dose)

Staphylococcia Methicillin sensitive	Nafcillin or oxacillin = cloxacillin
Staphylococcia Methicillin resistant	Vancomycin
Propionibacterium acnes	Penicillin G / Amoxicillin
Streptococcus pneumoniae	Third-generation cephalosporin
Pseudomonas aeruginosa	Cefepime, ceftazidime, or meropenem
Haemophilus influenzae	Ampicillin / Third-generation cephalosporin
Extended spectrum β-lactamase-producing gram-negative bacilli	Meropenem
Acinetobacter baumannii	Meropenem
Other Enterobacteriaceae	Third-generation cephalosporin
Candida species	Lipid formulation of amphotericin B ± flucytosine

Fig. 44.2 Targeted antibiotic therapy recommendations

on the ventricular size and the drainage debits. In children, the dose should be reduced by 60%. It is recommended to use intrathecal vancomycin for gram positive and intrathecal gentamicin or amikacin for gram negative bacilli. Penicillins and cephalosporins should not be administered by this route, since they have been significantly associated with neurotoxicity, especially seizures [22].

44.8.3 Duration of Antibiotic Therapy

The duration of antibiotic treatment is not completely defined and depends on the cultured microorganism, the clinical impact of the infection and the biochemical parameters of the CSF. According to the recommendations of the IDSA guidelines (Table 44.2), in infections caused by coagulase negative staphylococcus or P acnes without an increase in leukocytes in CSF or minimal increase, normal glucose in CSF and few symptoms, treatment should last 10 days. In the event that the infection caused by these bacteria does cause an increase in leukocytes in CSF, decrease glucose in CSF, or produce considerable neurological or systemic symptoms, treatment should be prolonged between 10 and 14 days. For infections caused by more aggressive germs such as S. aureus or gram negative bacilli, regardless of the CSF

Table 44.2 Recommendations for the duration of antibiotic treatment based on the microorganism causing the infection

Microorganism	Days of antibiotics after VPS removal
Coagulase-negative staphylococcus or P acnes **without** pathological CSF biochemistry and **without** neurological or systemic symptoms	10 days
Coagulase-negative staphylococcus or P acnes **with** pathological CSF biochemistry or **with** neurological or systemic symptoms	10–14 days
S. aureus or gram-negative bacilli	10–14 days (some authors recommend 21 days if gram-negative bacilli)
Repetitive positive cultures	10–14 days from last positive culture

biochemistry, treatment should last between 10 and 14 days, although some experts recommend extending up to 21 days for infections caused by gram negative bacilli.

During antibiotic treatment, a CSF sample should be extracted every 24 or 48 h to examine the evolution of the biochemical parameters and ensure that the cultures are negative. For patients who return to a positive CSF culture, antibiotic treatment should be continued for up to 10–14 days from the last positive culture. Replacing the EVD is highly recommended to improve the evolution of the infection.

44.8.4 New Shunt Reimplantation

The time of reimplantation must be individualized according to the cultured microorganism, the evolution of the CSF biochemical parameters and the clinical severity of the infection. Reimplantation too early can increase the risk of reinfection, while delaying it excessively exposes the patient to the risk of superinfection of the external CSF drainage.

Negative CSF cultures are a fundamental requirement to consider reimplantation of the new shunt. The IDSA guide [4] recommends different waiting periods depending on the isolated microorganism, similar to the duration of antibiotic treatment.

- For an infection caused by coagulase-negative staphylococci or P. acnes, if no associated CSF abnormalities are detected and CSF cultures are negative for 48 h after externalization, a new shunt should be reimplanted as soon as the third day after removal. If there are abnormalities in CSF but negative repeat CSF cultures, a new shunt should be reimplanted after 7 days of antimicrobial therapy. However, if repeat cultures are positive, antimicrobial treatment is prolonged until CSF cultures remain negative for 7–10 consecutive days [23].
- When the infection is caused by *S. aureus* or gram-negative bacillus, the new shunt can be repositioned 10 days after the cultures are negative [24].

The pleocytosis, hypoglycorrhachia, and hyperprotein in the CSF samples obtained for monitoring the biochemical parameters should not delay the placement of the new shunt, since these parameters can remain altered for a long time.

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