

Rifampicin for successful antibiotic eradication and ventriculoperitoneal shunt salvage in staphylococcus epidermidis infection

Abstract

Background: Ventriculoperitoneal Shunt (VPS) infection is a significant and relatively common complication in pediatric patients. Current guidelines recommend empirical treatment with vancomycin and an antipseudomonal beta-lactam antibiotic, followed by surgical removal of the infected VPS. However, adding rifampicin, known for its antibiofilm activity, may allow for successful treatment without the need for shunt removal.

Case presentations

Case 1: An 11-month-old male presented with fever and irritability. Diagnosed with Staphylococcus epidermidis VPS infection, he was successfully treated with vancomycin and rifampicin, without the need for shunt removal.

Case 2: A 2.5-year-old male presented with fever, weakness, and headache. He was also diagnosed with Staphylococcus epidermidis VPS infection and treated successfully with vancomycin and rifampicin, without shunt removal.

Conclusion: For VPS infections caused by Coagulase-Negative Staphylococci (CONS) that are susceptible to rifampicin, and in patients with stable clinical conditions, it may be possible to avoid shunt removal by adding rifampicin to the antibiotic regimen. This approach could potentially reduce the need for additional surgeries.

Introduction

Ventriculoperitoneal Shunt (VPS) placement has become the mainstay of treatment for paediatric hydrocephalus [1]. More than 40,000 Cerebrospinal Fluid (CSF) shunts are placed annually in the United States, with approximately 2,300 becoming infected [2]. VPS infection is a significant complication, occurring in 5%-27% of cases [3]. The most common pathogens responsible for VPS infections are Coagulase-Negative Staphylococci (CONS) and Staphylococcus aureus [1,4].

The Infectious Diseases Society of America (IDSA) guidelines recommend empirical treatment with vancomycin and an antipseudomonal beta-lactam antibiotic, followed by surgical removal

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of the infected VPS and placement of a new shunt once the CSF is sterile [5]. A meta-analysis by Schreffler, covering literature from 1960-1999, concluded that complete removal of the infected shunt is superior to antibiotic treatment alone [6,7].

Another strategy involves initially treating the infection with antibiotics and reserving shunt removal for cases where antibiotic therapy fails [8]. Success rates for this approach range from 15% to 68% [3,8]. For VPS infections caused by CONS or S. aureus that are susceptible to rifampicin, the IDSA recommends incorporating Rifampin into combination therapy [5]. Rifampicin is a potent broad-spectrum antibiotic and a key component of anti-tuberculosis therapy, known for its anti-biofilm activity

ity, which is beneficial in orthopaedic device-related infections [9,10]. Additionally, several clinical trials have investigated the efficacy of rifampicin-coated VPS in preventing shunt infections [11,12].

While shunt removal and replacement are recommended for managing shunt infections, these procedures subject the child to the risks associated with multiple surgeries.

We describe two children with VPS infections caused by CONS who were successfully treated with vancomycin and rifampin alone, without the need for shunt removal.

Patient 1

An 11-month-old baby of Bedouin origin was admitted to the hospital with two days of fever and irritability. His past medical history included a premature birth at 26 weeks. During his admission to the Neonatal Intensive Care Unit (NICU), he suffered from Respiratory Distress Syndrome (RDS), bronchopulmonary dysplasia (BPD), Periventricular Leukomalacia (PVL), and sepsis due to *Staphylococcus aureus* and *Candida*. At eight months, he developed meningitis and ventriculitis due to *Candida albicans*, which was complicated by hydrocephalus. He completed a long course of treatment with amphotericin B and underwent VPS insertion.

At his most recent admission, notable findings upon physical examination included a high temperature of 38.5°C, irritability, and a wound on the scalp above the shunt trajectory. Diagnostic work-up revealed a normal White Blood Cell (WBC) count, moderate elevation of CRP (6 mg/dL), and a head Computed Tomography (CT) scan showing no changes in the size of the ventricles or the position of the VPS. Neurosurgery was consulted for a shunt tap, and 15 mL of clear CSF was aspirated under low pressure and sent for analysis, culture, and pan-bacterial/pan-fungal Polymerase Chain Reaction (PCR). Fluid analysis showed nucleated cells at 148×10^6 cells/L, with 42% neutrophils, 47% lymphocytes, 53 Red Blood Cells (RBCs), glucose of 40 mg/dL, and protein of 261 mg/dL. Empiric antibiotic treatment was initiated with vancomycin, ceftazidime, and fluconazole. The Gram stain revealed Gram-positive cocci. Final culture and pan-bacterial PCR were significant for *Staphylococcus epidermidis*.

Due to his relatively good clinical condition, it was decided to continue antibiotic treatment without removing the VPS, reserving shunt removal only if the antibiotic treatment failed. After the bacteria were isolated, rifampicin was added and ceftazidime was discontinued. After 72 hours of treatment, the patient was afebrile, less irritable, and had an improved appetite, with CRP decreasing to 4 mg/dL. After seven days of treatment, another shunt tap was performed, revealing clear CSF with nucleated cells at 115×10^6 , 25% neutrophils, 65% lymphocytes, protein at 146 mg/dL, and glucose at 33 mg/dL. Gram stain and culture were negative. Ten days later, another shunt tap revealed 40 cells $\times 10^6$, 20% neutrophils, 22% mononuclear cells, 57% lymphocytes, glucose at 40 mg/dL, and protein at 64 mg/dL. Gram stain and culture were again negative.

The patient completed 23 days of intravenous vancomycin and oral fluconazole, along with 21 days of intravenous rifampin. He remained well for the next 33 months without any recurrence of VPS infection.

Patient 2

A 2.5-year-old male of Bedouin origin was admitted to the hospital with fever, weakness, and a headache. His past medical

history was significant for congenital hydrocephalus, seizures, severe hypotonia, severe cognitive delay, and Failure To Thrive (FTT). One month prior to admission, he underwent VPS replacement due to shunt malfunction.

Diagnostic work-up revealed a WBC count of $19 \times 10^3/\text{mm}^3$ with 90% neutrophils and an initial CRP level of 19 mg/dL. Chest X-ray showed no local consolidation, and head CT showed no acute changes compared to an image taken one month prior, right after the VPS replacement. Neurosurgery was consulted for a shunt tap, and 5 mL of clear CSF fluid was aspirated under low pressure and sent for analysis and culture. Fluid analysis revealed 62 cells/ mm^3 , 60% lymphocytes, 22% segments, glucose of 22 mg/dL, and protein of 61 mg/dL. CSF Gram stain revealed Gram-positive cocci, and final culture was significant for *Staphylococcus epidermidis*.

Initially, the patient was started on vancomycin (20 mg/kg every 6 hours) and ceftriaxone (100 mg IV every 24 hours). Due to the patient's overall good condition, it was decided to continue with antibiotics and consider shunt removal only if the antibiotic treatment failed. After 72 hours of treatment, the patient still had a fever but no headache, and his WBC count normalized with a CRP level declining to 7 mg/dL. Another shunt tap was performed, yielding clear CSF with similar parameters. CSF Gram stain again showed Gram-positive cocci, and final culture was significant for *Staphylococcus epidermidis*.

At this point, rifampicin was added and ceftriaxone was discontinued. It was decided to give another trial for shunt salvage. Two days after the initiation of rifampicin, the patient became afebrile, and the CRP declined to 3.3 mg/dL. According to his parents, the patient returned to his baseline condition. Ten days after the second shunt tap, a third tap revealed no cells, normal protein and glucose levels, and sterile CSF culture.

The patient completed a total of 25 days of treatment with vancomycin and 21 days with rifampin. He remained well for the next eight months until he was admitted with fever, although diagnostic work-up showed no signs of VPS infection.

Discussion

We report the clinical features and treatment outcomes of two patients with *Staphylococcus epidermidis* VPS infection who were treated with antibiotics alone, without shunt removal. In the second case, the addition of rifampicin led to an improvement in clinical condition followed by sterilization of the CSF.

The IDSA guidelines for VPS infections recommend the complete removal of the infected VPS and its replacement with an external ventricular drain [5]. While this strategy boasts a success rate of up to 96%, it subjects patients to 1-2 additional surgeries, with both predictable and unpredictable perioperative complications [3].

A less common strategy involves initially treating the infection with antibiotics alone and reserving shunt removal for cases where antibiotic treatment fails. There are no recent prospective studies comparing the outcomes of antibiotic treatment followed by shunt removal versus antibiotic treatment with attempted shunt salvage, with shunt removal only in the case of treatment failure. Reported success rates for this approach vary widely, ranging from 16% to 100% [13,14].

We identified two case reports in the English literature of VPS infections managed without shunt removal by adding rifampin to the antibiotic regimen [15,16]. In both cases, however, the

pathogen was *Streptococcus*. During the work-up for the cases presented here, shunt removal was considered. However, given the patients' clinical appearance and the positive response to the addition of rifampin, shunt removal was postponed. It was clear that any sign of clinical deterioration would necessitate immediate shunt removal.

Our decision to add rifampicin to the regimen was based on its high CSF penetration and its antibiofilm activity. Although shunt removal is generally considered the default treatment for VPS infections, it is possible that with appropriate antibiotic regimens and close monitoring, some patients might benefit from the strategy of treating VPS infection with antibiotics alone, reserving shunt removal for cases of antibiotic failure.

Further carefully designed studies are needed to identify which patients might be effectively managed with antibiotics alone, potentially sparing them from the risks associated with shunt removal.

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