Spontaneous bacterial peritonitis causing *Serratia marcescens* and *Proteus mirabilis* ventriculoperitoneal shunt infection

Case report

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The authors report their experience treating a polymicrobial ventriculoperitoneal (VP) shunt infection in a developmentally delayed 21-year-old woman. Cerebrospinal fluid (CSF) cultures grew *Serratia marcescens* and *Proteus mirabilis*. On admission and throughout her hospitalization, results of physical examination of her abdomen were normal, and radiographic studies showed no evidence of bowel perforation or pseudocyst formation. Contrast-enhanced computed tomography of the abdomen revealed a small fluid collection. After a course of intravenous gentamicin and imipenem with cilastatin in conjunction with intrathecal gentamicin, the infection was resolved and the VP shunt was reimplemented.

Although VP shunt infections are not uncommon, *S. marcescens* as a causative agent is exceedingly rare and potentially devastating. Only two previous cases of *S. marcescens* shunt infection have been reported in the literature. Authors reporting on *S. marcescens* infections in the central nervous system (CNS) have observed significant morbidity and death. Although more common, the presence of *P. mirabilis* in the CSF is still rare and highly suggestive of bowel perforation, which was absent in this patient. Spontaneous bacterial peritonitis was the likely source from which these bacteria gained entrance into the VP shunt system, eventually causing ventriculitis in this patient.

The authors conclude that in light of the high morbidity associated with *S. marcescens* infection of the CNS, intrathecal administration of gentamicin should be strongly considered as part of first-line therapy for *S. marcescens* infections in VP shunts.

**KEY WORDS**  • peritonitis  • shunt infection  • *Proteus mirabilis*  • *Serratia marcescens*  • intrathecal antibiotic therapy  • ventriculoperitoneal shunt

**Abbreviations used in this paper:** CNS = central nervous system; CSF = cerebrospinal fluid; CT = computed tomography; SBP = spontaneous bacterial peritonitis; VP = ventriculoperitoneal.

Both *Serratia marcescens* and *Proteus mirabilis* are classified as members of the Enterobacteriaceae family of bacteria. While *S. marcescens* tends to be an opportunistic pathogen, causing infections of the respiratory and urinary tracts, wounds, and the bloodstream in immunocompromised patients, *P. mirabilis* is commonly present in the gastrointestinal flora, and a *P. mirabilis* infection may be considered community acquired. *Proteus mirabilis* typically causes recurrent urinary tract infections in patients with structural abnormalities of the genitourinary system. It is uncommon for these species, alone or in combination, to cause CNS infections in patients with or without CSF diversion procedures. The presence of *P. mirabilis* in the CSF of a patient with a VP shunt is highly suggestive of an interruption in the alimentary system. In contrast, the presence of *S. marcescens* in the CSF of a patient with a shunt is exceedingly rare and potentially devastating; only two cases have been reported in the literature.

We report our experience in managing a case of infection with a rare combination of pathogens due to SBP. The pharmacological and surgical management is described, and the relevant literature regarding SBP in patients with VP shunts is reviewed along with the two previous reports of *S. marcescens* infection of VP shunts. Despite the presence of the aforementioned pathogens and their postulated route of entry, we concluded that in the absence of clinical symptoms or radiographic abnormalities, the peritoneal cavity remains an acceptable site for CSF diversion.

**Case Report**

**History.** A 21-year-old developmentally delayed woman
Polymicrobial ventriculoperitoneal shunt infection

presented with a 24-hour history of nausea, vomiting, lethargy, and difficulty walking. Her medical history was significant for a Grade III subependymal hemorrhage at birth, requiring VP drainage; epilepsy; and idiopathic thrombocytopenia purpura. The patient had undergone a shunt revision procedure to relieve a proximal obstruction 6 months before this presentation; the peritoneal catheter had not been replaced at that time. The patient experienced vague abdominal symptoms, with no fever or chills, 2 weeks prior to the patient’s presentation. These symptoms resolved spontaneously.

Examination. The patient was afebrile. She had no peri-toneal signs or other evidence of abdominal disease. Blood tests revealed a white blood cell count of 5800/mm³. On neurological examination, the patient was noted to be lethargic and to have right sixth cranial nerve palsy; she had no photophobia or other evidence of meningism. Her previous incisions were well healed with no sign of infection.

An unenhanced head CT scan showed marked interval enlargement of the ventricles and a right parieto-occipital ventricular catheter in a satisfactory position. Anteroposterior and lateral radiographs of the head, neck, chest, and abdomen showed no discontinuity in the shunt apparatus. The tip of the peritoneal catheter was visible beneath the liver. There was no evidence of bowel obstruction, free air beneath the diaphragm, or cardiopulmonary disease.

Attempts to sample CSF from the shunt valve reservoir were unsuccessful.

First Operation. Surgery was undertaken for correction of proximal shunt malfunction. The obstructed ventricular catheter was replaced, but CSF obtained from the new catheter was noted to be grossly cloudy and xanthochromatic, prompting immediate laboratory studies. Gram staining revealed a large number of Gram-negative rods. In light of these findings, the planned proximal shunt revision was aborted, the entire VP shunt system was removed, and the new ventricular catheter was externalized.

Postoperative Course. The results of CSF studies included a glucose level of 27 mg/dl, a protein level of 759 mg/dl, a white blood cell count of 226/mm³, and a red blood cell count of 79/mm³. No gross discoloration or staining of the distal catheter, which was not spring loaded, was seen upon its removal. Gram stains and cultures of specimens from the peritoneal catheter tip were negative for the presence of bacteria. Intravenous treatment with gentamicin and imipenem/cilastatin was initiated. Cultures of CSF revealed the presence of S. marcescens and P. mirabilis. Cultures of blood and urine specimens were nondiagnostic. Sputum was not cultured because the patient had a normal chest radiograph and no respiratory complaint.

Concern over the possibility of an abdominal source of infection prompted a CT scan of the abdomen with oral and intravenous contrast agents. Results of the CT study demonstrated a moderate amount of free fluid in the area of the Douglas cul-de-sac, with surrounding enhancement of the peritoneal surface but no gross abscess cavity (Fig. 1). There was no evidence of fluid collection beneath the liver where the peritoneal catheter had been, or of pelvic or inguinal lymphadenopathy.

Repeated attempts to obtain a specimen of the abdominal fluid transvaginally were unsuccessful, as were CT- and ultrasonography-guided sampling procedures. Throughout these efforts, the patient remained free of abdominal complaints and the physical examination showed no sign of a pathological condition.

Despite bacterial sensitivities for both gentamicin and imipenem, S. marcescens persisted in the CSF surveillance cultures 1 week after commencement of treatment, although the P. mirabilis infection did resolve. The CSF profiles continued to show an elevated level of protein (> 200 mg/dl) and a low level of glucose. Clinically, the findings on sequential neurological examinations indicated continued deterioration in the patient’s condition. She became persistently febrile and had increasing leukocytosis.

Second Operation and Postoperative Course. Seven days after the initial surgery, we replaced the patient’s external ventricular catheter with a catheter impregnated with rifampin and clindamycin. Intrathecal gentamicin (10 mg twice daily) was added to her antibiotic regimen for a total of 10 days.

After these additional measures were undertaken, the findings on CSF surveillance studies improved. Repeated bacterial cultures were negative, and the patient’s neurological condition improved to her baseline. She completed a 21-day course of intravenous imipenem and cilastatin, a 14-day course of intravenous gentamicin, and a 10-day course of intrathecal gentamicin. In light of the abdominal fluid collection and our uncertainty regarding the source of the patient’s polymicrobial ventriculitis, we considered placement of a ventriculoatrial or ventriculopleural shunt. General surgeons were consulted regarding the possibility of an occult perforation. After a comprehensive metabolic evaluation showed no abnormality, the consensus conclusion was that no further intervention was indicated.

At this point, we concluded that SBP had been the source of the patient’s ascending shunt infection.

Third Operation and Postoperative Course. After a repeated abdominal CT scan demonstrated interval resolution of the fluid collection and repeated CSF cultures showed no evidence of infection, a diversion procedure was undertak-
Intraoperative examination of the open peritoneal cavity revealed no fluid collection or other abnormality, and a VP shunt was placed 27 days after the patient’s initial surgery. The patient was discharged home after an uneventful postoperative course. At the most recent follow-up examination, 6 months after surgery, she showed no sign of infection.

Discussion

The concept of Gram-positive bacteria entry into a shunt system is easy to grasp, because the vast majority of these shunt infections are due to otherwise commensal skin flora and are temporally related to recent surgery.\textsuperscript{3,17,18,23,26} Gram-negative infections that occur in the immediate postoperative period are presumed to be caused by bacteria introduced at the time of surgery (assuming colonization or contamination of the skin), whereas later-onset infections are typically related to clinically or radiographically evident bowel perforation.\textsuperscript{21,22} The former and the latter scenarios have plausible mechanisms for entry and subsequent infection. These variants of Gram-negative infection typically manifest with outright clinical signs of perforation or the subtle radiographic finding of a pseudocyst.\textsuperscript{2,6,21,22} The delayed entry of Gram-negative bacteria into the shunt system in the absence of bowel perforation or a pseudocyst is more difficult to understand. It was this ill-defined entry of \textit{S. marcescens} and \textit{P. mirabilis} that prompted us to search exhaustively for an abdominal disease process and consider an alternative site for the distal catheter in the patient in the present case.

In their review of Gram-negative bacterial infections of VP shunts, Stamos and colleagues\textsuperscript{24} acknowledge that the entry of these pathogens into the shunt system remains poorly understood. In the group of patients in their series who presented with a Gram-negative infection at least 3 months after surgery, these authors concluded that a “transient perforation” may have led to those infections for which a mechanism of entry was not identified. Gaskill and Marlin\textsuperscript{8} further developed the concept of transient perforation in patients with shunts and reported a series of patients who met criteria for SBP-associated shunt infections.

Typically seen in patients with cirrhotic ascites, SBP is an infection of the peritoneal fluid in the absence of an abdominal lesion.\textsuperscript{8,27} The organisms most frequently cultured in these cases are commonly found in the intestinal flora. Aerobic Gram-negative organisms, primarily \textit{Escherichia coli} and \textit{Klebsiella pneumoniae}, account for the majority of infections, while aerobic Gram-positive organisms (\textit{Streptococcus, Enterococcus, and Staphylococcus} species) account for less than a third. Of note, despite the polymicrobial nature of the gastrointestinal tract, 92% of cases of infection involve only one organism, while the remaining 8% are polymicrobial.\textsuperscript{8} Gaskill and Marlin\textsuperscript{8} report their experience with seven cases of SBP in patients with VP shunts. These authors identified criteria for diagnosing SBP in such patients, including: a remote history of shunt revision, cultures consistent with normal intestinal flora, and no recent abdominal surgery, gastrostomy, or passage of wire-impregnated catheters. Our patient met all these criteria, but, interestingly, a species normally found in the intestinal flora (\textit{P. mirabilis}) was identified in the CSF culture despite the fact that the Gram stain and culture from the peritoneal catheter were negative for the presence of any bacteria. The two cases of \textit{S. marcescens} infections of a VP shunt that have been previously reported are discussed below. Both of these cases involved abdominal disease processes, which suggests a peritoneal source for this rare pathogen’s entry into the VP shunt system. The fact that 2 weeks before the patient presented to us she experienced vague abdominal symptoms for 2 days suggests that our patient may have suffered from an episode of SBP, which might have allowed \textit{P. mirabilis} and \textit{S. marcescens} to ascend the peritoneal catheter and cause obstructive hydrocephalus and eventually ventriculitis.

It has been postulated that SBP results from the failure of the gut to contain the bacterial flora and the failure of the immune system to kill the virulent bacteria once they are in the peritoneum. Whereas patients with advanced cirrhosis are vulnerable to peritoneal fluid infection by translocation of bacteria from their own gut, patients with VP shunts should generally have intact protective mechanisms.\textsuperscript{27} This may explain the absence of peritoneal signs, the negative culture results, and nondiagnostic abdominal evaluation in our patient, despite the presence of intestinal bacteria and \textit{S. marcescens} in her CSF. Gaskill and Marlin\textsuperscript{8} reported similar findings in three patients in their series of patients with SBP and VP shunts. Two patients presented without peritoneal signs, and in one patient there was no evidence of infection in the ascitic fluid, similar to the findings in our patient.

As there is no other plausible alternative source for the pathogens in this case, we conclude that SBP was the cause of our patient’s shunt infection. To our knowledge, polymicrobial SBP leading to ventriculitis has not been previously reported in a patient with a VP shunt.

After much deliberation, we decided to place the distal end of the catheter into the peritoneal cavity again, instead of placing it into the pleural or vascular space. Various authors\textsuperscript{5,21} have recommended using an alternative site after an abdominal infection. Several factors went into our decision to continue the use of the peritoneal cavity as the CSF diversion site in this patient: the interval resolution of the abdominal infection. Several factors went into our decision to continue the use of the peritoneal cavity as the CSF diversion site in this patient: the interval resolution of the abdominal fluid collection, the results of the general surgical consultation, the normal findings on physical examination of the patient’s abdomen, and the multiple failed attempts to access the fluid collection. We concluded that the absence of clinical and radiographic findings in the abdomen left the peritoneal cavity an acceptable location for CSF diversion.

Our patient’s polymicrobial infection involved a rare combination of pathogens. \textit{Serratia marcescens} is an opportunistic Gram-negative bacillus primarily associated with infections of the respiratory tract, urinary tract, and bloodstream in immunocompromised patients.\textsuperscript{4,11,28} It is an infrequent cause of CNS infection and an even less common cause of VP shunt infection, with only two previous reports in the literature.\textsuperscript{5,18,25} Given that one of the largest series of \textit{S. marcescens} infection in neurosurgical patients demonstrated a substantial mortality rate despite antibiotic therapy, its presence in a VP shunt is cause for alarm.\textsuperscript{12,13,25}

The two previous reports of \textit{S. marcescens} shunt infections are vague in regard to treatment and outcome. Nourissame and colleagues\textsuperscript{16} reported the case of a 10-month-old girl who had presented with symptoms of sepsis 2 months after surgery for shunt revision. The CSF specimen ob-
tained from her shunt reservoir grew *S. marcescens*, and a CT scan of her abdomen demonstrated intraluminal migration of the shunt tubing. These authors reported that the shunt was removed and replaced at a later date, but they did not comment on treatment or outcome.

Bremer and Darouiche* reported the second case of an *S. marcescens* infection of a VP shunt. The patient in their case was a 58-year-old woman who had been treated with methotrexate for severe rheumatoid arthritis and had required shunt placement after an aneurysmal subarachnoid hemorrhage. She was found to have a fluid collection in the right upper quadrant of her abdomen, which, in conjunction with evidence of hydrocephalus on an unenhanced head CT scan, prompted CSF evaluation. The shunt reservoir was accessed and *S. marcescens* was isolated from a specimen. The patient underwent VP shunt removal. Culture of a specimen from the peritoneal catheter also revealed the presence of *S. marcescens*. The patient was treated with intravenous ciprofloxacin and also underwent percutaneous drainage of the abdominal abscess. The authors gave no further information concerning the duration of treatment or outcome.

On the basis of previous reports, *S. marcescens* is known to be an alarming pathogen in a neurosurgical patient, and when it is documented to have infected a VP shunt, surgical intervention and aggressive antibiotic therapy are required.1,4,7,12–15,25 Our experience with the case presented in this report further substantiates this view. Despite documented sensitivity to both imipenem and gentamicin, *S. marcescens* persisted in our patient’s CSF. Even though the results of subsequent sensitivity studies did not show the development of resistance to these antibiotics, the patient’s declining neurological condition, leukocytosis, and persistent fever prompted the addition of intrathecal gentamicin to her antibiotic regimen after replacement of the external ventricular drain. Although intrathecal antibiotic therapy is generally reserved for the treatment of ventriculitis caused by highly resistant organisms, concern about the well-established risk of morbidity and death associated with persistent ventriculitis caused by *S. marcescens* infection supports the intrathecal administration of gentamicin.10,15,19 Our patient experienced improvement in her neurological condition and resolution of the infection only after the second replacement of the ventricular catheter and the intrathecal administration of antibiotic agents.

Conclusions

To our knowledge, this case represents the first report of a polymicrobial VP shunt infection due to SBP and the third reported case of an *S. marcescens*-infected VP shunt. Because the collective series of *S. marcescens* infections of the CNS has entailed significant rates of morbidity and death, the presence of *S. marcescens* in a patient with a VP shunt requires surgical intervention and aggressive antibiotic therapy. Intrathecal administration of gentamicin appears to have been instrumental in the resolution of our patient’s infection. In light of the increased morbidity associated with *S. marcescens* infection of the CNS, intrathecal gentamicin should be considered as part of the first-line therapy in a patient with a shunt infection. Despite the combination of a bowel flora pathogen and a rare opportunistic pathogen isolated from the CSF in this case, the peritoneal cavity remains an acceptable site for CSF diversion in the absence of clinical symptoms and radiographic abnormalities.

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