Intrathecal colistin for treatment of highly resistant *Pseudomonas* ventriculitis

Case report and review of the literature

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The emergence of multidrug-resistant Gram-negative organisms causing nosocomial infections represents an increasing therapeutic problem. Patients with CSF diversionary catheters pose a particular challenge given that catheters can serve as both route of inoculation and site of colonization of nosocomial bacteria. Carbapenems are considered to be the treatment of choice for *Acinetobacter* and *Pseudomonas* meningitides, but in recent years there have been numerous reports of carbapenem-resistant isolates of these organisms, particularly in institutions where resistance patterns mandate frequent use of this class of antibiotics. There is no treatment of choice for carbapenem-resistant Gram-negative organisms. In the following report we documented a case in which a woman with a VP shunt demonstrated CSF colonization with *P. aeruginosa* resistant to all available standard antibiotics. Because of this organism’s resistance profile, the polymyxin antibiotic colistin was administered intravenously and intrathecally with successful sterilization of the CSF. Prior case reports on the use of colistin to treat meningitis are also reviewed.

**Case Report**

*First Surgery.* This 51-year-old right-handed woman presented to the hospital with a Hunt and Hess Grade III subarachnoid hemorrhage. Ventriculostomy was performed in the emergency department because of her declining mental status and bradycardia. Results of subsequent cerebral angiography studies revealed a right middle cerebral artery aneurysm at the junction of M1 and M2. She was taken to surgery for aneurysm clip application on posthemorrhage Day 2. Although the aneurysm clip was successfully applied, the bone flap was not replaced and the ventriculostomy catheter was kept in place because of brain swelling. The patient’s bone flap was wrapped in betadine-soaked gauze and stored in the operating room freezer. Postoperatively, she made a good recovery but did not tolerate weaning from the EVD. She received 1 g cefazolin intravenously every 8 hours for prophylaxis per departmental policy for patients with in-dwelling ventricular catheters. Surveillance cultures of her CSF remained negative for infection.

*Second Surgery.* On Day 15 post–clip application, the patient returned to surgery for placement of an occipital right-sided VP shunt. Vancomycin was administered as the perioperative antibiotic. Following completion of the procedure, the left frontal EVD was removed. Cerebrospinal fluid collected intraoperatively from the proximal shunt catheter was sterile. All antibiotic agents were discontinued 48 hours after shunt placement.

*Third Surgery.* Fifteen days after shunt placement, a right cranioplasty was performed without complication by using the patient’s stored bone flap. Cefazolin was used as the perioperative antibiotic. On postcranioplasty Day 1 the pa...
The clinical use of polymyxins has been limited by the nephrotoxicity associated with parenteral use, although various ophthalmic, otic, and topical preparations are available. Colistin sulfate is also available in oral form for use in infants and children with diarrhea caused by susceptible bacteria.

Polymyxin B was first reported to be used intraventricularly, in combination with an intramuscular injection, in the treatment of five infants with meningitis due to \textit{P. pyocyanea}. A survey of 33 cases of \textit{P. pyocyanea} infection at that institution revealed 32 instances of polymyxin B sensitivity, whereas resistances to tetracycline, chloramphenicol, streptomycin, and sulfadimidine were all significantly higher. Of the five reported meningitis cases, all were cleared of infection within 1 month without evidence of direct toxicity or drug resistance. Subsequent use of polymyxins was limited by the emergence of second- and third-generation cephalosporins, which were equally efficacious without the side-effect profile.

Recently, authors have documented outbreaks of organisms, most commonly \textit{Acinetobacter} and \textit{Pseudomonas}, which showed sensitivity to polymyxins only and were treated successfully with intravenous colistin. Notably, these organisms were all resistant to macrolides, carbapenems, and later-generation cephalosporins. One series of 60 infections in 59 patients treated with intravenous colistin included five cases of meningitis, four of which had a good outcome although none had been treated using intrathecal antibiotics. Authors of this series documented iatrogenic renal failure as the most common adverse effect of treatment, which occurred in 27% of treated patients with initially normal renal function. Renal function worsened in 58% of patients with abnormal baseline serum creatinine levels. Two later case reports, featuring the same patient, who had been treated with intravenous colistin for multidrug-resistant \textit{A. baumannii} meningitis, revealed good recovery without evidence of renal compromise.

Modern documentation of intrathecal colistin administration is limited to two reports. Authors of one series documented five cases of catheter-associated carbapenem-resistant \textit{Acinetobacter} ventriculitis; three patients died. The two survivors were treated with intrathecal colistin, although one subsequently died of cardiac arrest approximately 54 days after completing colistin therapy. Postmortem examination in this patient revealed sterile CSF. The first three patients who died in this study all had received intravenous colistin only. Authors of another case report documented a patient who had been treated successfully for highly resistant \textit{Acinetobacter} ventriculitis by using a 21-day regimen of intrathecal colistin. No adverse renal effect was reported among any of these patients.

The patient in the present case was exposed to prolonged cefazolin prophylaxis while the original EVD was in place. A survey of practice patterns among 36 institutions revealed that 72% used prophylactic antibiotics with all EVDs and intracranial pressure monitors, although there are no studies in which investigators report that this practice produces a statistically significant benefit. Prolonged antibiotic use has been linked to broadened resistance profiles in multiple studies, but only with respect to the specific class of agent used. In addition, the routine use of cefazolin as endotoxin in experimental systems. The clinical use of polymyxin for this indication has yet to be established.

Widespread use of polymyxin B and colistin has been associated with parenteral use, although various ophthalmic, otic, and topical preparations are available. Colistin sulfate is also available in oral form for use in infants and children with diarrhea caused by susceptible bacteria.

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an antibiotic prophylaxis is frequently cited as an effective strategy in the context of perioperative use to reduce the incidence of resistance to beta-lactamase-stable penicillins, vancomycin, and carbapenems. The patient in the present study exhibited no evidence of cranioplasty wound infection or osteomyelitis implicating the bone flap as the source of the contaminant.

**Conclusions**

We report the first published case of carbapenem-resistant *Pseudomonas* ventriculitis successfully treated with intrathecal colistin and no appreciable adverse effect. As antibiotic resistance continues to evolve and novel antibiotics emerge at a very slow pace, colistin administered intrathecally and/or intravenously represents what will likely become an increasingly relevant alternative in the treatment of multiresistant organisms. Although the safety and efficacy of its intrathecal administration have been demonstrated in a few isolated cases, further study is warranted to evaluate the full relevance and potential consequences of its more widespread use.

**References**


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