Successful Treatment of Ventriculitis Due to Carbapenem-Resistant Acinetobacter baumannii with Intraventricular Colistin Sulfomethate Sodium

Over the past 2 decades, Acinetobacter baumannii has developed one of the most alarming patterns of antibiotic resistance ever observed [1]. Nowadays, since an increasing proportion of isolates are resistant to all antibiotics tested routinely, therapy is a serious challenge [2]. Beginning in 1992, a large outbreak due to multiresistant A. baumannii was noted in our 1,000-bed tertiary teaching hospital, causing considerable imipenem overuse [3]. In January 1997, two clones resistant to carbapenems emerged: clone D, moderately resistant to imipenem (MICs, 4–16 mg/L) and tobramycin (MIC, 8 mg/L) and susceptible only to sulbactam and polymyxins (MICs, <4 mg/L), and clone E, highly resistant to imipenem and sulbactam (MICs, >256 mg/L), moderately resistant to tobramycin (MIC, 8 mg/L), and susceptible only to polymyxins. Since then, five patients have developed catheter-associated ventriculitis due to carbapenem-resistant A. baumannii strains (table 1). Of these five patients, three died of their infection after receiving inadequate therapy (patients 1–3). The other two were, to our knowledge, the first reported to date who survived after treatment with intraventricular colistin sulfomethate sodium (patients 4 and 5).

Patient 4 was a 16-year-old boy who underwent surgery and the insertion of an external ventriculostomy tube for continuous drainage because of hemangioblastoma of the fourth ventricle. On day 7 after surgery, meropenem at 2 g/8 h was started empirically to treat his fever, although CSF cultures had been sterile. On day 16, his fever increased, and CSF analysis revealed 27,900 cells/mm³ (95% polymorphonuclear cells), and cultures of CSF yielded A. baumannii. Meropenem was discontinued, and intraventricular tobramycin (10 mg/12 h), intravenous tobramycin (5 mg/kg once a day), and intravenous sulbactam (2 g/6 h) were then initiated. On day 19, because CSF cultures remained positive, the ventriculostomy tube was replaced and intraventricular tobramycin was switched to intraventricular colistimethate sodium (5 mg/12 h), intravenous tobramycin was maintained, and intravenous sulbactam was discontinued. Intraventricular colistin was administered in a 5-mL solution of saline serum through the ventriculostomy tube after previous extraction of 5 mL of CSF, and thereafter, the drainage was interrupted for 3 hours. On day 21, cultures of CSF were negative and remained so until colistin sulfomethate sodium therapy was ended on day 39, when a ventriculoperitoneal shunt was inserted. During therapy, CSF bacterial titers at 3 hours after colistin sulfomethate sodium administration (peak) were 1/2, and before doses were administered (trough), titers ranged from <1/2 to 1/4. Similarly, CSF bacteriostatic titers at peak were 1/8 and at trough ranged from 1/4 to 1/16. Levels of tobramycin in CSF varied from 7.9 mg/L (peak) to 0.7 mg/L (trough). No adverse reactions were documented during therapy. On day 82, the patient was alert with spontaneous mobilization of the extremities, but he died suddenly of cardiac arrest. Postmortem examination ruled out ventriculitis, and cultures of CSF were negative for A. baumannii.

Patient 5 was a 34-year-old woman who required an external ventriculostomy tube because of subarachnoid hemorrhage with hydrocephalus. The catheter was removed 6 days after insertion; however, 24 hours later, the patient developed high fever and neurological symptoms worsened, with purulent secretion from the catheter insertion site. CSF obtained through a new ventricular drainage site was cloudy, showing 2,000 cells/mm³ (95% polymorphonuclear cells) and short gram-negative rods on gram stain. Cultures from the purulent secretion and CSF yielded A. baumannii. Intraventricular colistimethate sodium (5 mg/12 h), given following the above-mentioned procedures, and intravenous tobramycin (4 mg/kg once a day) were administered without complications. Although a rapid decrease in the bacterial count in CSF

References


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was observed, cultures of CSF remained positive through the fifth day of therapy. Dosages of colistin sulfomethate sodium were then increased to 10 mg/12 h, and 24 hours later, cultures of CSF yielded negative results (CSF peak bactericidal and bacteriostatic titers were 1/2 and 1/16, respectively). Cultures of CSF continued to be negative until day 30 of the patient’s stay in the intensive care unit (6 days after the end of colistin sulfomethate sodium therapy), when a ventriculoperitoneal shunt was inserted. Two months later, the patient was discharged from the unit, remaining on therapy), when a ventriculoperitoneal shunt was inserted. Two months later, the patient was discharged from the unit, remaining on

In view of these results, search for new therapeutic strategies is urgently needed for the treatment of CNS infections due to A. baumannii that is resistant to carbapenems. In the meantime, intraventricular colistimethate sodium may be life-saving in circumstances in which there are no other options.

**Table 1.** Clinical characteristics of the five patients with carbapenem-resistant *Acinetobacter baumannii* ventriculitis.

<table>
<thead>
<tr>
<th>Patient no.</th>
<th>Age/sex</th>
<th>Underlying condition</th>
<th>Surgery/ventricular tube*</th>
<th>Clone</th>
<th>Intrathecal colistin¹</th>
<th>Intravenous antibiotics¹</th>
<th>Infection outcome²</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>47/F</td>
<td>Subarachnoid hemorrhage</td>
<td>No/yes (7)</td>
<td>E</td>
<td>No</td>
<td>Mer (2) + Tm (2)</td>
<td>Died (2)</td>
</tr>
<tr>
<td>2</td>
<td>61/F</td>
<td>Ependymoma</td>
<td>Yes/yes (11)</td>
<td>E</td>
<td>No</td>
<td>Sulb (7) + Tm (7)</td>
<td>Died (7)</td>
</tr>
<tr>
<td>3</td>
<td>64/M</td>
<td>Epidermoid tumor</td>
<td>Yes/yes (21)</td>
<td>E</td>
<td>No</td>
<td>No</td>
<td>Died (1)</td>
</tr>
<tr>
<td>4</td>
<td>16/M</td>
<td>Hemangioblastoma</td>
<td>Yes/yes (16)</td>
<td>D</td>
<td>Yes (19)</td>
<td>Sulb (3) + Tm (19)</td>
<td>Cured¹</td>
</tr>
<tr>
<td>5</td>
<td>34/F</td>
<td>Subarachnoid hemorrhage</td>
<td>No/yes (7)</td>
<td>E</td>
<td>Yes (17)</td>
<td>Tm (17)</td>
<td>Cured</td>
</tr>
</tbody>
</table>

NOTE. Mer = meropenem; Sulb = sulbactam; Tm = tobramycin.

* Parentheses indicate the days from catheter insertion to diagnosis of infection.

¹ Parentheses indicate the days of treatment.

¹ Parentheses indicate the days from diagnosis of infection to death.

¹ The patient died of a noninfectious cause, 66 days after treatment ended.

References


