Infections of the Central Nervous System Due to Pseudomonas Aeruginosa

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PSEUDOMONAS AERUGINOSA, formerly called B. pyocyanea, is one of the group of gram-negative organisms that have caused an increased percentage of hospital-acquired infections in recent years.\(^1,^5\) Because pseudomonas rarely produces primary infections in man,\(^6\) it has been referred to as an "opportunist" organism, a term suggesting a micro-organism that is part of the normal flora of man but that occasionally produces progressive infections in a host with impaired defenses. Pseudomonas infections may be relatively indolent, producing only slow host reactions, and therefore may persist for long periods before being diagnosed and properly treated.

The characteristics noted above are particularly pertinent to pseudomonas infections of the central nervous system. Pseudomonas is the cause of about 5% of neonatal meningitis.\(^13,^14\) In most instances pseudomonas meningitis has been superimposed on underlying disease, wound infection or cerebrospinal-fluid fistula; has extended from adjacent foci; or has been introduced by lumbar puncture, spinal anesthesia, or indwelling catheters draining cerebrospinal fluid.\(^1,^2,^5,^9,^12\) In one large series, covering 10 years, pseudomonas was the causative organism in four out of 294 cases of bacterial meningitis (1.4%).\(^5\) An extensive review of reports of pseudomonas meningitis through 1955 is found in Forkner's monograph.\(^4\)

We are reporting 16 cases of pseudomonas infections of the central nervous system seen at the University of California Hospitals, and Fort Miley Veterans Administration Hospital, San Francisco, in the past 18 years. Two of the cases included in this series were described in detail previously.\(^7,^8\)

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Description of Cases

Terminal Sepsis. Pseudomonas meningitis occurred as a terminal infection in five patients. Three of these had extensive neoplastic disease, one had pancytopenia complicated by pseudomonas septicemia, and one had acute tubular necrosis complicated by pseudomonas septicemia. None had adequate antibiotic therapy and all five patients died.

Brain Abscess. Two men, each about 65 years old, had brain abscesses due to pseudomonas. One died without treatment after a convulsive seizure, and an unruptured temporal-lobar abscess was encountered at autopsy. Pulmonary emphysema was also present, and pseudomonas was cultured from the bronchi. The other patient had a multilocular temporal-lobar abscess in direct continuity with a cholesteatoma of the middle ear. Twelve days after craniotomy, signs of meningitis appeared and pseudomonas was cultured from the cerebrospinal fluid. Subsequent therapy with Polymyxin B (30 mg every 8 hours for 8 days) resulted in a cure.

Meningitis. There were nine cases of meningitis due to pseudomonas diagnosed during life (Table 1). Four of these patients died, but one of these deaths was due to pulmonary embolism (Case 8) and CSF and blood cultures were negative at autopsy. One child (Case 3) died without having received adequate therapy now known to be necessary; the other child who died (Case 2) had had meningitis for about 3 weeks before specific intrathecal therapy was begun. The fourth patient who died (Case 6) had had a long debilitating course of illness before the meningitis occurred.

Another child with pseudomonas ventriculitis (Case 9) was cured of his infection by intraventricular Polymyxin B; however, extensive adhesions and webs within the ventricular system, noted prior to the start of
therapy with Polymyxin B, remained and resulted in recurrent blockage of ventriculostomy shunts. This child finally died of uncontrolled hydrocephalus approximately 7 months after cure of the infection.

In the other cases, the infection was cured by intrathecal or intraventricular Polymyxin B. In Case 4,7 two courses of intramuscular Polymyxin B were ineffective in eradicating the meningitis, whereas intrathecal Polymyxin B (50 mg in 17 days) without any systemic antibiotics effected a cure. Similar treatment was effective in Case 18 and Case 5. In one patient (Case 7), infection was suppressed by brief intrathecal administration of Polymyxin B but flared up when a ventriculostomy shunt was inserted. The infected shunt could not be sterilized by prolonged treatment with Polymyxin B, and the Holter valve had to be removed. The infection was then promptly eradicated and 10 days later another shunt was inserted without recurrence of infection. This patient is alive and free from infection 7 years later.

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**TABLE 1**

_Survey of nine cases of meningitis due to Pseudomonas aeruginosa_

<table>
<thead>
<tr>
<th>Case No.</th>
<th>Age (yrs)</th>
<th>Sex</th>
<th>Underlying Disease</th>
<th>Source of Meningitis</th>
<th>Treatment</th>
<th>Outcome</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>24</td>
<td>F</td>
<td>Compound skull fracture, burr holes</td>
<td>Scalp wound infection</td>
<td>Intrathecal Polymyxin B; 1 week—relapse 3 weeks—cure</td>
<td>Cure</td>
<td>Reported in ref. 8</td>
</tr>
<tr>
<td>2</td>
<td>3</td>
<td>F</td>
<td>Cerebellar astrocytoma incomplete resection</td>
<td>Wound dehiscence with CSF leak</td>
<td>Intramuscular penicillin &amp; terramycin Intrathecal Polymyxin B, 3 doses</td>
<td>Death</td>
<td>Meningitis present about 3 weeks before therapy begun</td>
</tr>
<tr>
<td>3</td>
<td>10</td>
<td>F</td>
<td>Cerebellar astrocytoma, incomplete resection</td>
<td>Indwelling lumbar intrathecal catheter</td>
<td>Intramuscular penicillin &amp; terramycin</td>
<td>Death</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>70</td>
<td>M</td>
<td>Neurilemmoma, C-7 nerve root</td>
<td>Wound dehiscence &amp; infection (pseudomonas urinary infection)</td>
<td>Intramuscular Polymyxin B, 2 courses, for 12 &amp; 8 days, ineffective. Intrathecal Polymyxin B, 5 mg—doses, 50 mg in 17 days</td>
<td>Cure</td>
<td>Reported in ref. 7</td>
</tr>
<tr>
<td>5</td>
<td>35</td>
<td>M</td>
<td>Subdural hematoma</td>
<td>Postcraniotomy 7 days after drainage through burr holes</td>
<td>Intrathecal Polymyxin B, 5 mg—doses to total of 40 mg, in 14 days</td>
<td>Cure</td>
<td>Received intraventricular Polymyxin B for 2 days prior to intrathecal dose</td>
</tr>
<tr>
<td>6</td>
<td>46</td>
<td>M</td>
<td>Glioma, spinal cord</td>
<td>Wound dehiscence with CSF leak</td>
<td>Erythromycin, tetracycline chloramphenicol, penicillin, Intrathecal Polymyxin B, 10 mg./day for 7 days</td>
<td>Death</td>
<td>Long debilitating course before meningitis</td>
</tr>
<tr>
<td>7</td>
<td>5</td>
<td>F</td>
<td>Cerebellar astrocytoma</td>
<td>Wound dehiscence &amp; CSF leak, constant ventricular drainage, 6 days Previous meningitis recurred after ventriculostomy shunt with pseudomonas septicaemia</td>
<td>Intraventricular Polymyxin B, 75 mg, in 31 days plus intramuscular penicillin</td>
<td>Apparent cure but recurrence after ventriculostomy shunt</td>
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<td></td>
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<td>Penicillin &amp; chloramphenicol intrathecal Polymyxin B, 15 mg, in 6 days</td>
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<td></td>
<td>Intraventricular Polymyxin B, 13 mg, in 16 days &amp; intramuscular neomycin</td>
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<td></td>
<td></td>
<td>Intra-ventricular Polymyxin B, 70 mg, in 14 days, intramuscular Polymyxin B, 100 mg./day for 14 days</td>
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<td></td>
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<tr>
<td>8</td>
<td>27</td>
<td>M</td>
<td>Colloid cyst of third ventricle</td>
<td>Wound infection</td>
<td>Intraventricular Polymyxin B, 70 mg, in 14 days, intramuscular Polymyxin B, 100 mg./day for 14 days</td>
<td>Cure of infection; died of pulmonary embolus</td>
<td></td>
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<tr>
<td>9</td>
<td>6 wks</td>
<td>M</td>
<td>Lumbar meningocoele</td>
<td>CSF leak through repair</td>
<td>Intraventricular Polymyxin B, 13 mg, in 16 days &amp; intramuscular neomycin</td>
<td>Cure-subsequent V-A shunt without infection</td>
<td>Died at 9 mos, shunts blocked by adhesions</td>
</tr>
</tbody>
</table>
Discussion

Infections of the central nervous system and cerebrospinal fluid due to pseudomonas are extremely serious and carry a high mortality. This is partly due to the fact that these infections often appear during the terminal phase of an incurable illness. Pseudomonas meningitis may appear late in the course of a long debilitating illness, and a fatal outcome may result from this combination of conditions. Finally, the infection is often indolent and may not be recognized for a long period of time.

However, our experiences described above, as well as those of others, suggest that meningitis or ventriculitis due to pseudomonas may be cured readily and without serious sequelae if proper therapy is begun soon after onset of the infection and reinfec-

Cure of pseudomonas meningitis with intrathecal Polymyxin B was first reported by Schoenbach, and this has proved to be the best therapy available. Intrathecal dosage is 1 to 2 mg in infants, 3 to 5 mg in children over 2 years, and 5 to 10 mg in adults. These amounts administered daily for 3 days, then on alternate days for 2 to 3 weeks, have been successful in eradicating the infection. At this level, untoward drug effects have been minor, consisting only of occasional transient increase of signs of meningeal irritation. If pseudomonas infection is limited to the CNS, systemic Polymyxin B is unnecessary. If the CNS infection is suppressed but not eradicated, it may be reactivated by a ventriculoatrial shunt (Case 7), but after adequate treatment ventriculoatrial shunting may be done without reactiv-

Summary

Our experience with 14 cases of pseudomonas meningitis and two cases of pseudomonas brain abscess has been described. Five of the cases of meningitis were terminal infections in the presence of other serious illnesses and adequate antimicrobial therapy was not used. Of the nine patients whose meningitis was diagnosed and treated, four died, but of these, one did not receive adequate intrathecal therapy and one died of pulmonary embolism after cure of the infec-

References