Primary *Pseudomonas aeruginosa* meningitis in a 2-year-old boy

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Pseudomonas aeruginosa is a common cause of infections in hospitalized patients, but meningitis due to this organism is rare. Since the first proven case was described by Kossel[1] in 1894, many cases have been reported.[2-20] In children primary *P. aeruginosa* meningitis has been described after lumbar puncture, in those with spinal malformation such as spina bifida or meningocele, and after cranial or spinal surgery.[3] Secondary involvement of the meninges from a distant focus of infection is less frequent; such cases are secondary to septicemia, otitis media, umbilical infection or enteritis.[2]

We report a case of primary *P. aeruginosa* meningitis in a 2-year-old boy following diagnostic lumbar puncture, which was treated successfully with combined systemic and intrathecal administration of gentamicin.

Case report

Clinical course

A 2-year-old boy was admitted to Hôpital Sainte-Justine, Montreal, because of persistent fever, anorexia and apathy.

One month previously, while on vacation in Haiti, he had been treated for 10 days with ampicillin, 160 mg/kg•d, for *Hemophilus influenzae* meningitis. Three days after his discharge from hospital in Haiti, fever had reappeared and he was described as being listless and anorexic. He was readmitted to the same hospital. Gentamicin, 2 mg/kg•d administered intramuscularly, produced no improvement. The high fever persisted and the patient was therefore transferred to our hospital.

He was febrile but showed no signs of toxicity and was conscious. Nuchal rigidity was pronounced. A lumbar puncture revealed turbid cerebrospinal fluid (CSF). Intravenous administration of ampicillin, 400 mg/kg•d, was started immediately but no improvement occurred. Three days later, bacteriologic study of the CSF collected at the time of admission yielded *P. aeruginosa*.

A second lumbar puncture, done on day 4, also yielded turbid CSF. Ampicillin therapy was stopped the same day and replaced by intravenous administration of carbenicillin, 400 mg/kg•d, and gentamicin, 6 mg/kg•d. When culture of the second CSF sample confirmed the presence of *P. aeruginosa*, intrathecal therapy with gentamicin was begun. Six injections of 4 mg each were given. After the second injection the CSF became sterile.

With this regimen the patient's condition rapidly improved and no side effects were encountered. Intravenous administration of antibiotics was stopped after 16 days, and 3 days later the patient was discharged from hospital. He was seen 1 and 6 months after discharge and found to be perfectly healthy. Audiography, performed 1 month after discharge, did not reveal a hearing deficit. Further investigation eliminated a craniospinal malformation or immunodeficiency as the cause of the meningitis.

The patient's clinical course in hospital is summarized in Fig. 1.

Bacteriologic study

Methods: P. aeruginosa isolated from the CSF was identified by standard bacteriologic methods.[21] Drug sensitivity was studied by the disc method of Kirby and Bauer[22] and by the tube dilution method in Mueller–Hinton broth. Antibiotic concentrations in the CSF (Table I) were estimated with a microbiologic assay based

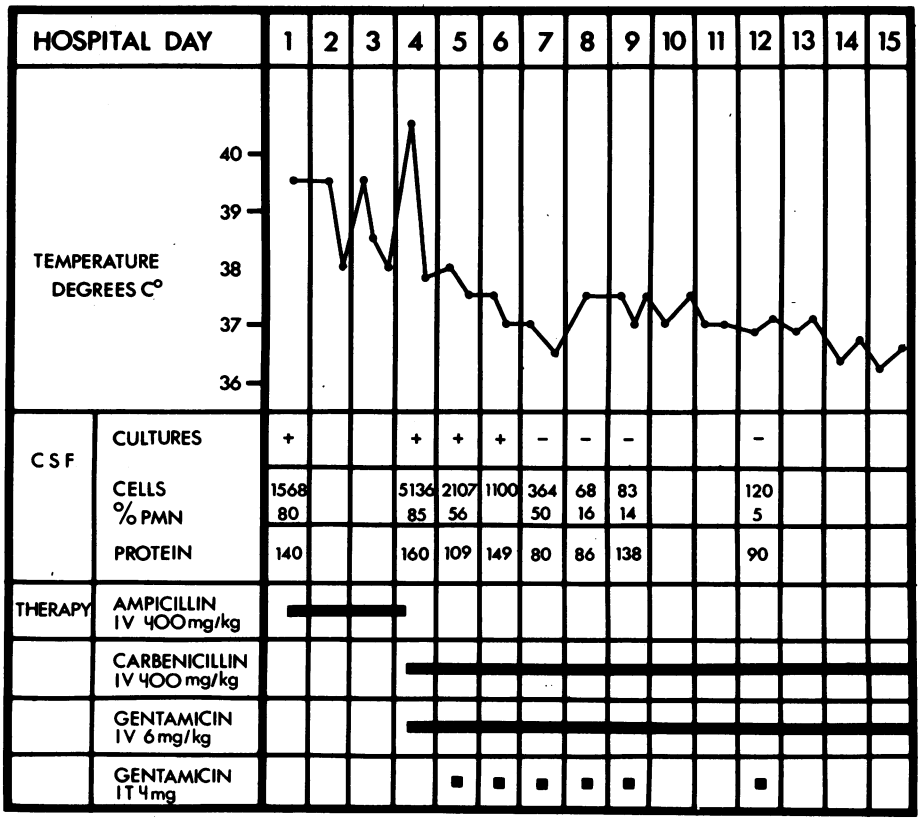

FIG. 1—Clinical course in hospital of 2-year-old boy with primary *Pseudomonas aeruginosa* meningitis.

Table I—Results of cerebrospinal fluid (CSF) studies in 2-year-old boy with primary *Pseudomonas aeruginosa* meningitis

CSF sample no.	Hospital day	CSF concentration (μg/mL); time (h) after last dose of drug*		Growth of *P. aeruginosa* in CSF culture
		Gentamicin	Carbenicillin	
1	5	< 0.25; IV, 8	< 12.5; IV, 1	Yes
2	6	< 0.25; IV, 6; IT, 22	< 12.5; IV, 3	Yes
3	7	0.5; IV, 6; IT, 24	< 12.5; IV, 3	No
4	8	< 0.25; IV, 6; IT, 24	< 12.5; IV, 3	No
5	9	0.4; IV, 6; IT, 24	< 12.5; IV, 3	No
6	12	< 0.25; IV, 6; IT, 72	< 12.5; IV, 3	No

*IV = intravenous; IT = intrathecal.

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on the agar diffusion method.[23] Concentrations of carbenicillin were determined with a strain of *Bacteroïdes fragilis*, and those of gentamicin were determined after inactivation of carbenicillin by β-lactamase. Preliminary tests with known concentrations of the antibiotics in various combinations established the value of these methods for determining concentrations of each antibiotic.

Results: The strain isolated in this case was very sensitive to gentamicin and tobramycin, with a minimum inhibitory concentration (MIC) less than or equal to 0.12 μg/mL for both antibiotics. The MIC for carbenicillin was 32 μg/mL. With intrathecal injections of 4 mg of gentamicin the highest CSF concentrations of drug were 0.4 to 0.5 μg/mL, as shown by samples 3 and 5 (Table I). Before intrathecal injections were begun and 72 hours after the last such injection the gentamicin concentrations in the CSF were less than 0.25 μg/mL, as shown by samples 1 and 6. The particularly low values in samples 2 and 4, collected while the patient was receiving intrathecal injections, were probably due to technical difficulties encountered in performing the injections. Carbenicillin concentrations in the CSF were always less than 12.5 μg/mL.

Discussion

Until 1960 most of the primary cases of *P. aeruginosa* meningitis described in the literature were due to contamination during lumbar puncture performed as a diagnostic, therapeutic or, more frequently, anesthetic procedure. Since then fewer cases have been described after lumbar puncture.[10]

In our case it is impossible to be certain of the source of infection but the organism may have been acquired while the child was being treated for his *H. influenzae* meningitis, possibly by lumbar puncture. The relatively mild symptoms of the second episode of meningitis before the diagnosis was established were surprising. We would have expected a fulminant onset and a rapidly fatal course. Such a relatively benign presentation is also mentioned by Forkner.[3]

Several antibiotics have been used in the past without satisfactory results. Increased survival was obtained with both intrathecal and intramuscular administration of polymyxin B.[16,19] In vitro synergy between gentamicin and carbenicillin against *P. aeruginosa* is well known,[24] but even in the presence of meningeal inflammation both drugs diffuse poorly in the CSF.[25,26] Therefore, intrathecal administration of gentamicin has been proposed as the preferred treatment in combination with systemic administration of gentamicin and carbenicillin.[27]

In a pharmacologic study of intrathecal therapy with gentamicin in 21 adults Rahal and colleagues[28,29] found that the drug had a geometric mean half-life of 5.5 hours in the CSF, and they suggested an initial regimen of 8 mg intrathecally every 24 hours. With this regimen Turgeon, Laverdière and Perron[20] successfully treated *P. aeruginosa* meningitis in an adult with leukemia and neutropenia. Gentamicin concentrations in the CSF 24 hours after intrathecal injection varied widely, from 1 to 27 μg/mL, in the studies of Rahal and Turgeon and their colleagues.

In children, except for neonates, no data have been reported concerning the intrathecal use of gentamicin in cases of *Pseudomonas* meningitis. We gave 4 mg of gentamicin intrathecally at 24-hour intervals. This dose is low in comparison with that given by Turgeon and colleagues[20] but exceeds the MIC of the strain of *Pseudomonas* isolated in our case.

Carbenicillin concentrations in the CSF of our patient were below 12 μg/mL, which confirms the poor diffusion of this antibiotic in the CSF. No side effects were observed in our patient.

From our data we cannot conclude that intrathecal gentamicin therapy was critical in the cure of our patient's meningitis, although the fact that the CSF cultures became sterile only after institution of intrathecal therapy suggests that systemic antibiotic therapy alone might not have been sufficient.

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