Posttraumatic meningitis due to ampicillin-resistant *Hemophilus influenzae*

Case report

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Two men who sustained skull fractures secondary to blunt head trauma developed meningitis due to *Hemophilus influenzae* type b. The isolates in both cases were resistant to ampicillin but susceptible to chloramphenicol. Based on this experience and recent epidemiological trends, it is suggested that chloramphenicol, rather than penicillin G, might be the initial therapy of choice for posttraumatic meningitis when no micro-organisms are recognized on Gram-stained smears of the cerebrospinal fluid.

**KEY WORDS**  skull fracture  meningitis  *Hemophilus influenzae*  antibiotic therapy

Appropriate initial antibiotic therapy of life-threatening infections, when no pathogen is demonstrated by Gram-stained smears or other studies, depends upon knowledge of the pathogens most likely to be encountered. There have been few tabulations of the pathogens encountered in posttraumatic meningitis. Hand and Sanford reviewed the findings in 16 patients encountered between 1958 and 1970, and concluded that pneumococcus was the usual infecting agent. They suggested that, unless Gram-stained smears demonstrate a different etiology, therapy should be initiated with high-dose penicillin G. Our recent experience suggests the need to consider also *Hemophilus influenzae* infection.

**Case Reports**

**Case 1**

This 40-year-old alcoholic man suffered blunt head trauma during an altercation and was admitted to the hospital with multiple scalp lacerations, rupture of the left tympanic membrane, and a left central seventh nerve palsy. Radiographic studies revealed a comminuted fracture of the left frontal and temporal bones and also a fracture of the lateral wall of the left orbit and zygomatic bone. Neither cerebrospinal fluid (CSF) rhinorrhea nor otorrhea was demonstrated. Penicillin G, one million units intravenously every 6 hours, was begun soon after admission.

The patient was disoriented and had a fever of 103°F on the second hospital day. Lumbar puncture revealed cloudy CSF containing 368 red blood cells, 3000 polymorphonuclear leukocytes, and 413 lymphocytes per cu mm, a protein content of 975 mg/dl, and a glucose content of 4 mg/dl. Gram-stained smears disclosed no micro-organisms. There was no response to high-dose penicillin G therapy. Cultures of CSF and of blood revealed *Hemophilus influenzae* type b, which was susceptible to chloramphenicol (minimum inhibitory concentration 0.5 μg/ml) but resistant to ampicillin (minimum inhibitory concentration greater than 16 μg/ml). Chloramphenicol, 1 gm intravenously every 6 hours, was begun. The patient made an uneventful recovery.

**Case 2**

This 25-year-old alcoholic man suffered blunt head trauma during an altercation and was admitted to the hospital with an extensive fracture involving the left frontal and parietal bones and extending to the frontal sinus and roof of the left orbit. A major motor seizure...
occurred on the second hospital day and was followed by fever of 101.2°F. Blood cultures were obtained, and phenoxyethyl penicillin V potassium, 500 mg orally every 6 hours, was begun.

On the fourth hospital day, the patient had a stiff neck and a fever of 102.4°F. Lumbar puncture disclosed cloudy CSF with 2076 red blood cells, 1088 lymphocytes per cu mm, a protein content of 390 mg/dl, and a glucose content of 5 mg/dl. No micro-organisms were apparent on Gram-stained smears. There was no response to high-dose intravenous penicillin G therapy. Cerebrospinal fluid and blood cultures revealed *Hemophilus influenzae* type b, resistant to ampicillin (minimum inhibitory concentration greater than 16 μg/ml) but susceptible to chloramphenicol (minimum inhibitory concentration 1.0 μg/ml). He was placed on chloramphenicol, 1.5 gm every 6 hours (75 mg/kg/day), and made an uneventful recovery.

**Discussion**

Both of our patients suffered skull fractures from blunt head trauma and probably sustained dural tears even though neither CSF otorrhea nor rhinorrhea was demonstrated. Both received low-dose penicillin prophylaxis, which may be ineffective in this setting, and both developed meningitis due to ampicillin-resistant *Hemophilus influenzae* type b. Three of the last four instances of posttraumatic bacterial meningitis encountered on our service (the present cases, and one due to *Salmonella enteritidis*) have been due to agents for which chloramphenicol was the antibiotic of choice.

Hand and Sanford reported in 1970 that pneumococcal infection was the definite or probable cause of 20 of 24 episodes of posttraumatic meningitis. In only one other instance (due to a *Hemophilus* species) did they isolate a different pathogen from the CSF. Therefore, they concluded that "intravenous penicillin in large doses should be administered unless organisms likely to be penicillin resistant are seen in the spinal fluid smear." Since Hand and Sanford's study, three trends pertinent to the epidemiology of *Hemophilus influenzae* infection have emerged. First, the prevalence of bactericidal antibodies against this pathogen in the adult population may have decreased. Whereas Fothergill and Wright found in 1933 that all persons over 10 years of age possessed such antibodies, Norden found that only 22% of 1021 persons over 10 years old studied between 1962 and 1972 possessed bactericidal antibodies against *Hemophilus influenzae* type b. While the relationship of bactericidal antibodies to susceptibility to invasive disease remains unproven, it is of interest that acute ethanol ingestion, present in our patients, may abolish such antibodies.

Second, recent studies suggest an apparent increased incidence of serious *Hemophilus influenzae* infection in adults. Finally, ampicillin resistance among clinical isolates of this pathogen is becoming widespread.

An ongoing multi-center surveillance of the microbial etiologies of posttraumatic meningitis would be useful. At present, we suggest that chloramphenicol may be the initial therapy of choice when Gram-stained smears and other preliminary studies fail to suggest an etiology. Chloramphenicol and penicillin G are equally effective agents for pneumococcal meningitis. Although chloramphenicol is usually considered to be a "bacteriostatic" agent, concentrations achieved in the CSF are bactericidal against the pneumococcus and other commonly encountered pathogens. Chloramphenicol is a first-line drug for therapy of Gram-negative bacillary meningitis, which is being encountered with increasing frequency in neurosurgical patients. Although fatal bone marrow aplasia from chloramphenicol remains rare and unpredictable, the more common dose-related marrow toxicity can be minimized by careful attention to dosage and to hematological parameters.

**References**


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