Recurrent Ventriculoperitoneal Shunt Infection Due to
Nontypeable Haemophilus influenzae

Nontypeable *Haemophilus influenzae* strains are commonly thought to cause only noninvasive infections such as otitis media and sinusitis, whereas invasive diseases, including meningitis and sepsis, are usually due to known typeable encapsulated strains. *H. influenzae* type b is the most virulent of these strains, due to the antiphagocytic effects of the type b capsular polysaccharide and its resistance to complement-mediated bacterial killing. Nontypeable *H. influenzae* strains, on the other hand, generally lack such virulence factors. These organisms commonly reside in the upper respiratory tract of healthy individuals and are considered part of the normal respiratory flora [1].

Population-based studies evaluating the rate of invasive nontypeable *H. influenzae* infection have reported an incidence rate of 0.5 per 100,000 per year in children <10 years old [2] and 3.6 per 100,000 per year in children <5 years old [3]. These numbers correspond to ~5% of invasive *H. influenzae* disease due to all strains. In a study from Sweden of *H. influenzae* meningitis in children <5 years old, of 274 cases in which serotype was determined, none were due to nontypeable strains [4]. To our knowledge, we report the first case of recurrent ventriculoperitoneal shunt infection due to nontypeable *H. influenzae*.

In March 1998, a 3½-year-old girl—twin A of a 27-week gestation, with a history of intraventricular hemorrhage, hydrocephalus, and ventriculoperitoneal shunt placed at 1 month of age—was admitted to an outside hospital because of fever, vomiting, and abdominal pain. She was transferred to Childrens Hospital Los Angeles (CHLA) on the following day. Her ventriculoperitoneal shunt had been revised once in March 1995 and was fully functional until this presentation. Laboratory studies revealed a complete blood cell count (CBC) with a WBC count of 13.6 × 10^9/L (78% neutrophils, 12% lymphocytes, 5% monocytes, 3% eosinophils, 1% myelocytes, and 1% metamyelocytes). Gram staining of a ventricular fluid aspirate from the patient’s ventriculoperitoneal shunt done at the outside hospital revealed 2+ polymorphonuclear (PMN) cells and no organisms. Analysis of a CSF specimen obtained by lumbar puncture at that time revealed the following: glucose, 68 mg/dL; protein, 292 mg/dL; RBCs, 91/μL; and WBCs 290/μL (62% neutrophils, 33% lymphocytes, and 5% monocytes). Gram staining revealed 1+ PMN cells and 1+ RBCs. Ventricular fluid aspirated at CHLA revealed an RBC count of 30/μL and a WBC count of 95/μL (37% neutrophils, 29% lymphocytes, and 34% monocytes). Cultures of ventricular fluid aspirates obtained from ventriculoperitoneal shunts at both hospitals yielded nontypeable *H. influenzae* that was β-lactamase negative. Results of a culture of a CSF specimen obtained by lumbar puncture and of blood culture from the outside hospital were negative. The patient was treated intravenously with a 14-day course of cefotaxime with documented susceptibility of the isolate to that antibiotic. Results of repeated cultures of ventricular fluid from the patient’s ventriculoperitoneal shunt after 1 week of cefotaxime therapy were negative, and the patient’s condition improved clinically.

Three days after the patient was discharged, she was readmitted for evaluation of abdominal pain and reported fever (temperature, 101.5°F) at home. She was not vomiting, nor had she diarrhea. Augmentin therapy had been started 2 days earlier for treatment of otitis media. Findings on physical examination were remarkable for a temperature of 38.2°C, right tympanic membrane with effusion, and a distended abdomen with diffuse tenderness but normoactive bowel sounds throughout. Laboratory studies revealed a CBC with a WBC count of 12.8 × 10^9/L with 62% neutrophils, 34% lymphocytes, and 4% monocytes. Intravenous therapy with ampicillin, gentamicin, and metronidazole was started, and the patient was evaluated for a possible surgical abdomen. During observation, her abdominal pain subsided, and findings on abdominal ultrasound were unremarkable, with no evidence of appendicitis. The patient’s pain recurred, however, on hospital day 2. A CT scan of the abdomen was then performed and revealed a pseudocyst at the distal end of the ventriculoperitoneal shunt. The pseudocyst was drained under CT guidance after the patient had received two intravenous doses of each antibiotic. Culture of the fluid was negative for aerobic, anaerobic, fungal, and viral growth. Abdominal pain subsided markedly after drainage.

Analysis of a CSF specimen from lumbar puncture on hospital day 2 revealed an RBC count of 2/μL and a WBC count of 5/μL. Gram staining revealed no organisms. Culture of the CSF revealed recurrence of infection with >100 colonies of nontypeable, β-lactamase-negative *H. influenzae*, also susceptible to cefotaxime. CT scan of the head revealed no anatomical defects in the paranasal sinuses, and a culture of blood drawn on admission was negative. The patient underwent ventriculoperitoneal shunt revision on hospital day 5; all subsequent CSF cultures were negative. Her hospital course was complicated by malfunction of the newly revised ventriculoperitoneal shunt: she developed emesis and became irritable on hospital day 15. Head CT revealed an increase in the size of the ventricles bilaterally. The ventriculoperitoneal shunt reservoir was replaced that day, and marked improvement was noted. Results of repeated cultures of CSF remained negative for bacterial growth.

Most CSF shunt infections are caused by normal skin flora and most commonly by *Staphylococcus* species, with the majority of cases associated with the surgical procedure of shunt placement itself. In this case, however, disease occurred 3 years after the patient’s only revision. Delayed infections that occur >1 year after surgery are associated with gram-negative bacilli, suggesting that inoculation occurred some time after the surgery. Bowel perforation is thought to be a possible predisposing event for these cases, especially when multiple organisms are isolated and include gram-negative enteric bacteria and anaerobes. Another possibility involves the ascent of bacteria from the gastrointestinal tract without overt abdominal infection [5].

Nontypeable *H. influenzae* is considered part of the normal respiratory flora and is an unusual cause of invasive disease. However, when invasive disease does occur, it is usually seen in elderly patients with significant underlying disease, immunocompromised patients, or premature neonates [6]. In the absence of evidence of
any anatomic defect that could predispose this patient to invasive disease due to this unlikely pathogen, a history of suspected immuno
deficiency, or evidence of bloodstream infection, it is unclear what mechanism underlies this patient’s infection. Although non-
typeable *H. influenzae* is rarely found in the gastrointestinal tract [1], given this patient’s abdominal complaints and pseudocyst formation, the most likely source of her infection is her gastrointestinal tract. Studies suggest that certain nontypeable *H. influenzae* strains possess one or more virulence factors capable of mediating bloodstream invasion or resistance to host immune defenses [6]. Whether the nontypeable *H. influenzae* isolated in our case with recurrent ventriculoperitoneal shunt infection possesses such virulence determinants remains to be determined.

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Herpes Simplex Virus Encephalitis: Chronic Progressive Cerebral Magnetic Resonance Imaging Abnormalities in Patients Despite Good Clinical Recovery

Herpes simplex virus encephalitis (HSVE) is a life-threatening encephalitis. Cranial MRI is sensitive in the detection of morpho-
logical abnormalities in acute HSVE. We aimed to prospectively study MRI changes in patients with HSVE, who were treated early in the course of the disease, and continued the studies for up to 6 months following onset of symptoms.

All patients (five male, one female) had received acyclovir (three doses daily, 10 mg/kg of body weight) for at least 14 days. HSV DNA in the CSF was confirmed by PCR assay, done as described recently [1]. Patients were clinically assessed daily during hospitalization and 6 months later. MRI and neuropsychological assessment [2–4] were done on admission, at discharge, and at 6 months.

Clinical symptoms during acute disease were recorded as mild (no impairment of consciousness, minor cognitive dysfunction), moderate (focal neurological signs, disoriented, or stuporous), and severe (comatose, severe dysfunction after short-term recovery) [1]. Magnetic resonance images were obtained (1.0 T; Picker-Vista; Cleveland) with the following sequence parameters: proton density, T2-weighted spin echo (SE) (repetition time [TR], 2400 ms; echo time [TE], 20 ms, 80 ms, respectively); T1-weighted SE (TR, 560 ms; TE, 20 ms). MRI was done before and after administration of gadopentetate dimeglumine, 0.2 mmol/kg of body weight. Mild MRI changes were defined as abnormal areas without space-occupying effect in <30% of characteristic locations (temporal lobe, cingulate gyrus, frontobasal lobe). Moderate changes involved <50% of the described areas, but >30% with an occasional space-occupying effect. Severe findings involved >50% and showed a space-occupying effect.

Neurological and neuropsychological assessment. On admission, two patients were graded as mildly impaired (Glasgow coma scale [GCS] 14), two patients had moderate clinical and neuropsychological findings (GCS 9, 10), and two were graded severe (GCS 7, 8). At discharge, MRI of five of six patients revealed improve-
ment. All patients were significantly improved after 6 months.

Cranial MRI findings. Abnormalities on admission and at dis-
charge from hospital were graded as mild (in 2/6), moderate (in 3) and normal (in 1). After 6 months, MRI findings were moderate (in 5) and normal (in 1). Two patients had progressive abnormalities (figure 1). One of these was clinically mildly impaired and the other moderately impaired at 6 months. Because both showed significant clinical improvement, repeated CSF analysis was not done.

Kapur et al. [5] described a positive correlation between long-
term cognitive impairment and involvement of limbic structures on MRI. Consistent with that, in five patients we found abnormali-
ties in limbic structures and neuropsychological impairment. In two patients we found chronic progressive MRI changes despite clinical improvement. The histological background of these find-
ings is not known. One may hypothesize that these changes repre-
sent relapsing or chronic HSVE [6]. However, relapsing, chronic HSVE is characterized by clinical deterioration and is therefore unlikely. Progressive changes after early antiviral treatment may be secondary to tissue damage not directly mediated by the virus. Evidence for such secondary immune-mediated tissue damage comes from experimentally induced HSVE [7]. Clinicians should be aware of the possibility of chronic progressive MRI changes in HSVE despite clinical improvement and antiviral therapy.

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