
**High-level cephalosporinase-producing Enterobacter cloacae meningitis in a newborn**

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*Enterobacter cloacae* is an uncommon cause of meningitis. The organism is known to mutate to produce large amounts of cephalosporinase able to hydrolyze third-generation cephalosporins [1], which are often thought to be responsible for the selection of such resistant mutants.

A newborn female, born at full term by vaginal delivery, was admitted to the neonatal intensive care unit with a lumbar meningomyelocele. Apgar scores were 10 and 10 at 1 and 5 min, respectively. Physical examination revealed an active neonate with only bladder dysfunction. No signs of neonatal infection were noted, and the serum C-reactive protein (CRP) level was less than 10 mg/L.

Surgical closure of the meningomyelocele was performed 2 days later (day 3). Preoperative smears of the meningomyelocele were obtained for bacteriologic culture, and scanty *Staphylococcus haemolyticus, Escherichia coli* and *Enterobacter cloacae* were isolated. Postoperatively, the patient became subfebrile. The peripheral white blood cell count was 10,760/mm³, including 63% polymorphonuclear leukocytes and 21% lymphocytes, and serum CRP increased to 37 mg/L on day 4 and then to 99 mg/L on day 5. The antibiotic susceptibilities of the *Enterobacter cloacae* is shown in Table 1. Therapy was initiated on day 5 with ceftaxime and vancomycin given intravenously (50 mg/kg 6-hourly and 10 mg/kg 12-hourly, respectively).

Eight days after surgery, the patient had a rectal temperature between 38 and 39°C, and developed vomiting, a stiff neck and convulsions. She developed severe apnea and brachycardia which required mechanical ventilation. Serum CRP levels remained increased at 196 mg/L on day 11, when we replaced vancomycin with fosfomycin (100 mg/kg 12-hourly). On day 12, cerebrospinal fluid cultures yielded *Enterobacter cloacae*. Cerebrospinal fluid (CSF) contained 1094 nucleated cells/mm³ (86% neutrophils, 14% monocytes). This isolate was susceptible in vitro to carbapenems, ceftazime, ciprofloxacin, fosfomycin and aminoglycosides but was shown to produce high-level, derepressed cephalosporinase. In order to verify that the two *Enterobacter cloacae* isolates were clonally related, pulsed-field gel electrophoresis was performed on intact DNA preparations, as previously described for *S. aureus* [2], except that lysostaphin was not added (Figure 1). The results indicated that the two isolates were related. The second strain was therefore considered to be a resistant mutant of the previous strain. This prompted us to replace ceftaxime with imipenem (50 mg/kg three times daily). However, the infant developed ventricular dilatation, and on day 15 a ventricular external shunt was put in place. At this time, the CSF white cell count was 230/mm³, with 98% polymorphonuclear leukocytes, the protein content was 439 mg/mL and no glucose was found in the CSF. *Enterobacter cloacae* was isolated from further CSF cultures.

On day 17, because of poor CSF concentrations of imipenem (day 17, 1 mg/L; day 18, 0.1 mg/L) and according to previously published data [3], ceftaxime (37.5 mg/kg every 6 h) was substituted and on day 19 amikacin (7.5 mg/kg every 12 h) was added. The in vitro bactericidal activity of this combination was

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The usual treatment of a CSF infection due to a Gram-negative organism is a third-generation cephalosporin used alone. Thus, we chose cefotaxime but, as described in the literature, including four cases of enterobacter meningitis [4,5], the Enterobacter cloacae developed resistance by overproduction of a derepressed type 1 β-lactamase after mutation [6,7]. Cefepime is highly resistant to hydrolysis by this periplasmic β-lactamase, in part because of the low affinity of this enzyme for the drug [8,9] and in part because of the extremely rapid penetration of this drug into the periplasmic space.

The efficacy of cefepime in the treatment of bacterial meningitis has been previously demonstrated in experimental animals models [10,11] and in infants with non-enterobacter meningitis [3].

In our case, cefepime in combination proved for the first time its usefulness in readily penetrating the CSF, achieving high local concentrations and thus sterilizing the CSF by ensuring local bactericidal activity. The use of cefepime as first-line therapy might have prevented the selection of a resistant mutant.

Acknowledgments
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References
4. Heusser MF, Patterson JE, Kuritzis AP, Eshberg SC, Baltimore A, Baltimore RS. Emergence of resistance to multiple beta-lactams...

**Mollaret meningitis with orolabial herpes and large lysed ghost cells**

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Mollaret's meningitis is a benign aseptic meningitis of unclear etiology characterized by headache, meningism, malaise, and fever, which recurs at intervals ranging from weeks to months [1]. Signs and symptoms of meningeal irritation appear acutely, in association with fever and pleocytosis of mononuclear cells. These episodes last for 2–5 days, or occasionally longer, and remit spontaneously. Five to 15 attacks may occur, separated by symptom-free intervals of weeks to months. Transient neurologic abnormalities may be present during the attacks, but they disappear after the acute illness. The diagnosis of Mollaret's meningitis is made only after other recognized causes of recurrent lymphocytic meningitis have been excluded.

A 7-year-old girl with Mollaret's meningitis, a rarely reported disease in childhood, presented with the major clinical aspects, laboratory findings and the ghost cells in cerebrospinal fluid (CSF), which are known as hallmarks of Mollaret's meningitis (Figure 1). The child presented with a 5-day history of fever, headache, nausea, vomiting and meningism. Previously, she had had three similar episodes. She had no history of head injury or recent dental work. She had ruptured herpetic vesicles on her mouth and lips, a stiff neck, and positive Kernig's and Brudzinski's signs.

The first CSF examination in August 1997 revealed a normal opening pressure, 180 white blood cells/mm³ (95% polymorphonuclear cells), protein 175 mg/dL, glucose 21 mg/dL, chloride 129 mmol/L, IgG 37.4 mg/dL, IgM 5.78 mg/dL, and IgE 13 IU/mL, serum IgG level 1230 mg/dL, IgM 120 mg/dL, IgE 456 IU/mL, and IgG index 0.54, blood urea nitrogen 39 mg/dL, glucose 97 mg/dL, total protein 6.3 g/dL, alanine aminotransferase 20 IU/L, aspartate aminotransferase 18 IU/L, Na+ 124 mmol/L and K+ 6 mmol/L. After 4 days, lumbar punctures revealed only 40 leukocytes (most of them were mononuclear cells) and many special types of large cell that have been called 'endothelial', per cubic millimeter. After 36 h, the last lumbar punctures revealed only 30 leukocytes and no ghost cells per cubic millimeter. Other laboratory tests showed the following: hemoglobin 11 g/dL, hematocrit 40%, leukocytes 40 000/mm³, platelets 157 000/mm³. Peripheral blood smear showed 93% neutrophils, 7% lymphocytes, polychromasia, and erythrocyte sedimentation rate 105 mm/h. Urinalysis showed no specific findings. CRP (+ + +), ASO 50 Todd Units, Latex RF

*Figure 1* Mollaret's large mononuclear cells in the CSF of our patient (HE X 40).