A Brain Abscess Due to Multiply-Resistant Enterobacter cloacae Successfully Treated with Meropenem

Sir—Brain abscess due to Enterobacteriaceae in children is rare and is mostly seen as a complication of neurosurgical procedures or trauma to the head [1]. Antibiotic treatment of this condition is known to be difficult. Third-generation cephalosporins have been used with success; however, some gram-negative rods (Enterobacter, Citrobacter, and Serratia) have become resistant because of production of derepressed type 1 β-lactamase [2, 3]. Emergence of resistance was associated with higher mortality and with prior administration of third-generation cephalosporins [2, 3]. We describe the successful use of meropenem (ICI 194660, Zeneca Pharmaceuticals, Cheshire, United Kingdom) for medical management of a child with a brain abscess due to multiply-resistant Enterobacter cloacae.

A 7-year-old boy with acute lymphoblastic leukemia that was diagnosed in May 1986 had been in remission after receiving chemotherapy. The disease relapsed in his testis in June 1993; orchidectomy was performed and induction therapy was started. During therapy the patient developed a sore throat and a fever; he was treated initially with amoxicillin and later with cefazidine. Throat cultures yielded E. cloacae, which was susceptible to cefazidine. Fecal cultures 1 week later also yielded E. cloacae. After recovery the patient was sent home with oral ciprofloxacin (15 mg/[kg·d]) for selective gut decontamination before his next cycle of chemotherapy. One month later he was admitted with headache, seizures, and hemianopia, but he did not have a fever or a history of trauma. Physical examination revealed increased intracranial pressure with papilledema.

The patient’s WBC count was 6.9 × 10⁹/L, and the erythrocyte sedimentation rate was 92 mm/h. Examination of CSF disclosed pleocytosis with a WBC count of 32/mm³ and a protein level of 130 mg/dL; gram staining was negative. CT of the head revealed a large mass process in the left occipital region, which suggested lymphoma or an abscess. Because surgery was not considered to be urgent, empirical therapy was started with cefazidime (100 mg/kg), amphotericin B (1 mg/kg), and amoxicillin (100 mg/kg). After 14 days without improvement in the patient’s condition, a diagnostic puncture of the cerebral lesion was performed, which revealed an abscess. Gram stains showed many leukocytes but no microorganisms. After 3 days, broth cultures yielded a multi-resistant Enterobacter cloacae. Cefazidime therapy may have contributed to induction of β-lactamase and multiple resistance. Alternative agents to treat infections by β-lactamase-producing Enterobacter species include imipenem-cilastatin, ciprofloxacin, aminoglycosides (amikacin), and trimethoprim-sulfamethoxazole. However, these agents are not suitable for use in children with cerebral infections because of side effects [4] and because sufficient high concentrations can not be reliably achieved in brain tissue.

Meropenem, a new carbapenem with comparable activity to that of imipenem/cilastatin, has been reported to be useful in the treatment of meningitis in adults [5, 6] and children [7] and does not show neurotoxicity. Meropenem is not hydrolyzed by repressed chromosomal β-lactamases of E. cloacae and is therefore a suitable alternative therapy for infections by multiply-resistant organisms that are difficult to treat.

Because of the reported neurotoxicity of imipenem/cilastatin [4], we requested a supply of meropenem from Zeneca Pharmaceuticals on a compassionate-use basis. Meropenem was given intravenously at a dose of 1.5 g thrice daily (120 mg/kg) for 6 weeks. Within 1 week the headache subsided and the patient recovered. No side effects were noted. At the end of treatment the patient was clinically and radiologically cured.

Our patient was colonized with E. cloacae before the cerebral abscess developed. We speculate that an unrecognized bacteremia from the throat or the intestine might have seeded the brain. Cefazidime therapy may have contributed to induction of β-lactamase and multiple resistance. Alternative agents to treat infections by β-lactamase-producing Enterobacter species include imipenem-cilastatin, ciprofloxacin, aminoglycosides (amikacin), and trimethoprim-sulfamethoxazole. However, these agents are not suitable for use in children with cerebral infections because of side effects [4] and because sufficiently high concentrations can not be reliably achieved in brain tissue.

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References