Case report

Successful treatment with doripenem of ventriculitis due to *Achromobacter xylosoxidans*

M.S. GELFAND and K.O. CLEVELAND

*From the Division of Infectious Diseases, Department of Medicine, University of Tennessee Health Science Center, Memphis, TN 38104, USA*

Address for correspondence to K.O. Cleveland, 1325 Eastmoreland Ave., Suite 460, Memphis, TN 38104, USA. email: kcleveland@uthsc.edu

Case report

A 29-year-old woman was admitted to our hospital with complaints of headache, dizziness and nausea. There was a history of spina bifida and placement of ventriculoperitoneal (VP) shunt in early childhood. One month prior to the current admission there was replacement of a VP shunt with a new system because of a mechanical malfunction. At that time there were no clinical signs of infection and cultures of the old shunt system and the cerebrospinal fluid (CSF) were negative.

On examination, temperature was 39.8°C, heart rate was 123, respiratory rate was 22 and blood pressure was 108/56 mmHg. Body weight was 60 kg. The neck was supple. The surgical sites of the VP shunt replacement showed no evidence of infection. Abdominal exam was unremarkable. Empiric intravenous (i.v.) piperacillin/tazobactam and vancomycin were begun.

Computed tomography (CT) of the abdomen showed a small area of fluid collection at the distal portion of the VP shunt. Cultures of the blood and urine were negative. Chest radiograph did not reveal infiltrates. The white blood cell (WBC) count was 14 100 cells/μl. Measurements of renal and hepatic function were normal. CT of the head with i.v. contrast showed right parieto-occipital VP shunt and no hydrocephalus.

CSF obtained via VP shunt reservoir showed WBC count of 22/mm³ with 70% neutrophils, glucose of 60 mg/dl, and protein of 20 mg/dl. CSF Gram stain showed rare Gram negative rods and the culture grew 2+ *Achromobacter xylosoxidans*. The isolate was resistant to cefotaxime, ceftriaxone, cefepime, ceftazidime, ciprofloxacin, levofloxacin, piperacillin/tazobactam, ticarcillin/clavulanate, gentamicin, tobramycin and amikacin, and was susceptible to imipenem with a minimal inhibitory concentration (MIC) of 2 mg/l (MicroScan, Dade Behring Inc., Sacramento, CA, USA). Additional testing of the isolate showed susceptibility to doripenem with a MIC of 1.5 mg/l and tigecycline with a MIC of 2 mg/l (Etest, AB bioMérieux, Durham, NC, USA).

On the second day of hospitalization, antibiotic therapy was changed to doripenem 500 mg i.v. infused over 60 min every 8 h and a single dose of 300 mg of i.v. tobramycin was given. On the third day of hospitalization, the VP shunt was removed and an external ventricular device (EVD) was placed. Culture of the VP shunt grew *A. xylosoxidans* with identical susceptibilities. The patient became afebrile and the WBC count normalized, but CSF obtained from the EVD on Days 4, 5 and 7 of doripenem therapy grew *A. xylosoxidans* with susceptibilities identical to those previously reported.

Magnetic resonance imaging of the head with gadolinium contrast showed no evidence of an intracranial abscess or fluid collection.

On Day 8 of hospitalization, the doripenem dose was increased to 1 gm i.v. every 8 h. Subsequent CSF cultures obtained on Days 10, 11, 12 and 13 of doripenem therapy were negative. On Day 15 of fielded analysis and interpretation of data were not done.
hospitalization, a ventriculopleural shunt system was placed. A course of 28 days of higher-dose doripenem therapy was completed. The patient experienced no myoclonus, seizure or other adverse effects attributable to doripenem.

Six months after placement of the ventriculopleural shunt, the patient has remained stable with no evidence of recurrent ventriculitis.

Discussion

*Achromobacter xylosoxidans* ventriculitis/meningitis is an unusual infection previously reported in neonates, HIV/AIDS and in association with neurosurgical procedures, trauma and epidural catheter.1-6 *Achromobacter* is a Gram negative rod routinely resistant to multiple classes of antibiotics including the cephalosporins, the earlier classes of penicillins, the fluoroquinolones, colistin and the aminoglycosides.7,8 *Achromobacter xylosoxidans* infections are usually treated with anti-pseudomonal penicillins, carbapenems or co-trimoxazole.8,9 Meropenem is the only carbapenem approved for CNS infections and is recommended in Gram negative meningitis.10 Imipenem is more likely to manifest epileptogenicity when used in meningitis.11 Imipenem failed in a patient with *A. xylosoxidans* neonatal meningitis reported by Manjra et al.7 and the isolate was tolerant to imipenem with MIC of 2 mg/l and minimal bactericidal concentration of 64 mg/l. Bactericidal activity is usually thought to be necessary for the cure of meningitis. While doripenem is not approved for the treatment of meningitis, we have previously successfully treated a patient with *Pseudomonas* ventriculitis with a regimen of high dose doripenem and tobramycin.12

Usual therapy of VP shunt infection includes removal of the infected shunt and administration of i.v. and/or intrathecal antibiotics.13 The choice of antibiotic therapy of *Achromobacter* ventriculitis is limited by the usual pattern of multiple antibiotic resistance.8 Anti-pseudomonal penicillins, co-trimoxazole and carbapenems have been used with variable success.4,5,7,9 Co-trimoxazole is inhibitory but not cidal against *A. xylosoxidans*.14 Meropenem is the only anti-pseudomonal carbapenem approved for the management of CNS infections. The isolate in our patient was resistant to piperacillin/tazobactam.

Doripenem is currently approved only for intra-abdominal and urinary tract infections with the usual dose of 500 mg i.v. every 8 h and is a standard formulary carbapenem in our hospital. We chose to increase the dose to 1 g every 8 h to approximate serum levels achieved with meropenem as the patient failed to show a microbiologic response to standard dose.15 The blood–brain-barrier penetration of doripenem is limited in the absence of inflammation, but no data are available in patients with ventriculitis.16 Carbapenems are recognized to have potential neurotoxicity, especially when used in patients with neurologic disorders and in high doses. Based on animal models and the results of clinical trials, doripenem may be less epileptogenic than other carbapenems.11,15 No neurotoxicity was observed in our patient.

With antimicrobial resistance limiting therapeutic options, increasingly treatment of CNS infections may leave clinicians in a therapeutic quandary. Additional future reports of clinical experiences in these situations will be helpful and may aid the healthcare provider in decision making.

Conflict of interest: None declared

References


