

## Meningitis Due to Vancomycin-Resistant *Enterococcus faecium* Successfully Treated with Combined Intravenous and Intraventricular Chloramphenicol

We report a case of meningitis caused by vancomycin-resistant *Enterococcus faecium* (VREF) that was successfully treated with combined intravenous and intraventricular chloramphenicol, as follows. A 46-year-old man suffering from subarachnoid hemorrhage with intraventricular bleeding was admitted to the intensive care unit. On the 9th day, the patient underwent a craniotomy for clipping of an aneurysm. The patient developed a fever 10 days after surgery. Surgical wound tissue and cerebrospinal fluid (CSF) samples were examined, and for both samples, the culture grew *E. faecium* resistant to vancomycin, ampicillin, and quinolones; the cultured organism was also high-level gentamicin resistant and sensitive to linezolid, chloramphenicol, and quinupristin-dalfopristin.

A toilet of the surgical site was done, and intravenous chloramphenicol was administered (3 g/day). On the 6th day of therapy, VREF was cultured from a sample of CSF obtained by lumbar puncture. On the 12th day of chloramphenicol therapy, we performed an external drainage because of hydrocephalus, VREF was cultured from a surgical sample of CSF, and intraventricular chloramphenicol therapy was initiated (25 mg/day with a temporary occlusion for 60 min of the system after antibiotic instillation). Altogether, the patient completed 47 days of intravenous and 35 days of intraventricular administration of chloramphenicol. The evolution of CSF analysis is shown in Table 1. The patient suffered from a new episode of meningitis due to *Providencia stuartii* needing treatment with imipenem. Twenty-seven days after chloramphenicol therapy was halted (89th postsurgical day), the patient was discharged from the intensive care unit.

VREF isolates have emerged as significant nosocomial pathogens (9). Of the infections caused by VREF, meningitis represents a therapeutic challenge for several reasons, such as limited treatment options because of the frequent multidrug resistance of VREF and difficulty in reaching therapeutic drug concentrations in the CSF. VREF infection is associated with

considerable morbidity and mortality. In spite of its increasing importance as a human pathogen, VREF is an unusual etiologic agent of bacterial meningitis. Treatment is a major challenge because these organisms are usually resistant to multiple antibiotics. Therapeutic options include quinupristin-dalfopristin, linezolid, and daptomycin (5); chloramphenicol (5, 10); and investigational agents such as evernimicin (SCH27899) (13), oritavancin (LY333328) (7), dalbavancin (BI397) (1), and tigecycline (2). Meningitis due to VREF has been treated at several centers with various degrees of success. Linezolid and quinupristin-dalfopristin have been shown to be useful options for treating this infection (12, 15).

Although chloramphenicol is regarded as bacteriostatic against enterococci, it has a reported clinical efficacy of 53% for treatment of serious VREF infections (6), and successful treatment of meningitis due to VREF was communicated (10). The efficacy of chloramphenicol may be a result of the relatively low plasma drug concentration needed to inhibit susceptible organisms and its excellent diffusion into the CSF, as indicated by the average ratio of CSF:serum chloramphenicol concentration of 0.67 (range, 0.45 to 0.99) (3). In our patient, the initial treatment with intravenous chloramphenicol was unsuccessful, so we decided to begin intraventricular treatment. Intraventricular treatment of meningitis caused by multidrug-resistant bacteria has been reported by other authors (14). Some authors postulated the intrathecal use of chloramphenicol in patients suffering from infected CSF shunts (4, 8, 11), but no experience in treating VREF was communicated. We conclude that in cases of meningitis caused by VREF, intraventricular administration of chloramphenicol could be considered as an alternative treatment.

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TABLE 1. Clinical parameters and microbiology of CSF<sup>a</sup>

Parameter (unit)	Value or status on postsurgery day:								
	10	15	21	27	28	33	40	54	63
Dextrose in CSF (mg/dl)	61	ND	10	20	ND	41	34	26	62
Leukocyte in CSF (cells/ml)	1	ND	1,200	14	ND	8	8	120	ND
Protein in CSF (g/l)	0.19	ND	1.02	0.10	ND	0.17	0.19	0.92	1.52
Gram stain	(+C)	ND	(+C)	(+C)	ND	(+C)	(-)	(-)	(-)
CSF culture	VREF	ND	VREF	VREF	ND	VREF	PS	(-)	(-)
IV chloramphenicol	No	Init	Yes	Yes	Yes	Yes	Yes	Yes	No
IT chloramphenicol	No	No	No	No	Init	Yes	Yes	Yes	No

<sup>a</sup> ND, not done; (+)C, Gram-positive cocci; (-), negative; VREF, vancomycin-resistant *Enterococcus faecium*; PS, *Providencia stuartii*; IV, intravenous; IT, intrathecal; Init, initiated.

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