

Case Report

Successful treatment of multidrug resistant *Acinetobacter baumannii* meningitis

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Abstract

Background: *Acinetobacter baumannii* is a major cause of nosocomial infections in many hospitals and appears to have a propensity for developing multiple antimicrobial resistance rapidly.

Cases: We report two cases with post-surgical meningitis due to multidrug resistant *A. baumannii* which were successfully treated with high-dose intravenous meropenem therapy.

Conclusions: Multidrug resistant *Acinetobacter spp.* in intensive care units are a growing concern. High-dose meropenem is used in the treatment of these infections.

Key Words: *Acinetobacter baumannii*, Post-surgical meningitis, High dose meropenem.

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Introduction

A. baumannii is a major cause of nosocomial infections in worldwide. The infection caused by *Acinetobacter* is difficult to control due to multidrug resistance, which limits therapeutic options in critically ill and debilitated patients, especially those in intensive care units [1]. We report two cases of post-surgical meningitis due to multidrug resistant *A. baumannii* occurring in patients admitted in the same neurosurgical intensive care unit of Pamukkale University Hospital, Turkey. Upon institution of therapy with high doses of meropenem, the patients experienced successful clinical and microbiological outcomes.

Case 1

A 52-year-old man developed meningitis due to *A. baumannii* 4 days after placement of a ventriculostomy catheter for management of post traumatic left temporal lobe hemorrhage. Prior to the development of meningitis, the hospital course was significant for ventilator-associated pneumonia and receipt of multiple courses of broad-spectrum antibiotics. Seven days later, cerebrospinal fluid (CSF) was turbid and its examination revealed neutrophil pleocytosis. *A.*

baumannii was isolated from the culture of the CSF. The following antimicrobial agents were tested and the microorganism was resistant to ampicillin, amoxicillin/clavulanic acid, cephalothin, ceftriaxone, cefixime, ceftazidime, cefuroxime, cephalexin, ciprofloxacin, ofloxacin, fosfomycin, trimethoprim-sulphamethoxazole, aztreonam, tetracycline, piperacillin-tazobactam, piperacillin, amikacin, tobramycin, and gentamicin except carbapenems. The therapy with intravenous meropenem (daily total dose 6 grams) was started and the extraventricular drainage system was removed. CSF cultures became sterile at the fourth day of the treatment. High-dose intravenous meropenem therapy continued 21 days. Laboratory results of CSF are shown in Table 1.

Case 2

A 62-year-old woman was admitted to Pamukkale University Hospital because of cerebellar hematoma and aspiration pneumonia. A ventriculostomy catheter was used on the patient for management of cerebellar hematoma. Post-operatively, her fever persisted and she developed convulsions and deterioration in the level of consciousness. The hospital course was

significant for aspiration pneumonia, bloodstream infection, and receipt of multiple courses of broad-spectrum antibiotics. Multidrug resistant *A. baumannii* was isolated from the CSF. The following antimicrobial agents were tested and the microorganism was resistant to ampicillin, amoxicillin/clavulanic acid, cephalothin, ceftriaxone, cefixime, ceftazidime, cefuroxime, cephalexin, ciprofloxacin, ofloxacin, fosfomicin, trimethoprim-sulphamethoxazole, aztreonam, tetracycline, piperacillin-tazobactam, piperacillin, amikacin, tobramycin, and gentamicin except carbapenems. Diagnosis was accepted as hospital acquired meningitis due to *A. baumannii*. The therapy with intravenous meropenem (daily total dose 6 grams) was started and continued 21 days. The ventriculostomy catheter was removed on the 32nd day of her hospitalization and the CSF remained sterile from *A. baumannii* throughout the rest of the hospitalization. Laboratory results of CSF are shown in Table 1.

Table 1. Laboratory results of CSF.

Day of treatment	CSF [cell/mm ³]		Type of CSF cells		Microorganism		Meropenem Treatment
	Case 1	Case 2	Case 1	Case 2	Case 1	Case 2	
1 st day	1940	-	PMNL*	PMNL+ erythrocyte	<i>A.baumannii</i>	<i>A.baumannii</i>	6 gr/day
3 rd day	2000	-	PMNL	PMNL+ erythrocyte	<i>A.baumannii</i>	<i>A.baumannii</i>	6 gr/day
4 th day	90	-	PMNL	PMNL+ erythrocyte	-	<i>A.baumannii</i>	6 gr/day
5 th day	450	-	PMNL+ Lymphocyte	PMNL+ erythrocyte	-	<i>A.baumannii</i>	6 gr/day
6 th day	100	-	Lymphocyte	-	-	<i>A.baumannii</i>	6 gr/day
7 th day	250	-	PMNL+ Lymphocyte	-	-	<i>A.baumannii</i>	6 gr/day
10 th day	10	30	PMNL+ Lymphocyte	-	-	<i>A.baumannii</i>	6 gr/day
14 th day	0	-	-	-	-	-	6 gr/day

Discussion

Acinetobacter species are aerobic gram negative coccobacilli that have emerged as important opportunistic pathogens, especially among debilitated patients. *A. baumannii* can be a causal agent of diseases such as pneumonia, bacteremia, meningitis, soft tissue and urinary tract infections associated with high mortality [2]. Jover Saenz *et al.* [3] reported that the overall annual incidence of nosocomial infections by multiresistant pathogens was 4.0 per 1,000 patients admitted. *A. baumannii* showed the highest incidence, particularly in the intensive care units (15.4 per 1,000 patients admitted).

A. baumannii is a bacterium that appears to have a propensity for developing multiple antimicrobial resistance [1]. Because of frequent

resistance to aminoglycosides, fluoroquinolones, ureidopenicillins and third-generation cephalosporins, carbapenems are important agents for managing *Acinetobacter* infections. Carbapenem resistance has been reported with many outbreaks of *Acinetobacter spp.* Many of these strains remain susceptible only to polymyxin, a toxic peptide antibiotic. The rapid evolution of drug resistance has severely limited the options for effective therapy for infections caused by this pathogen [2]. The mortality rate of patients with *A. baumannii* was significantly higher than that of patients without infection [4]. Vivek *et al.* [2] found that *Acinetobacter* species accounted for 10% of Gram negative isolates and from these isolates only half of *Acinetobacter* species were susceptible to carbapenems; 11 hospitals had at least one isolate resistant to carbapenems. Other *Acinetobacter* susceptibility rates were as follows: polymyxin, amikacin, ampicillin/sulbactam, ceftazidime and ciprofloxacin. Yaman *et al.* [5] reported that meropenem was the most effective antibiotic against gram negative organisms (89%); this was followed by imipenem (87.2%) and piperacillin/tazobactam.

In many adults with acute bacterial meningitis, *Acinetobacter spp.* were found to be responsible for approximately 10% of Gram negative bacillary and 4% of all nosocomial meningitis [6]. Post-neurosurgical meningitis is a serious complication. When this disease is caused by a multidrug-resistant *A. baumannii*, the management of such a case is challenging. When the infection involves the meninges, the choice of an antibiotic is further limited by the blood-brain barrier. There are differences between the CSF concentrations of meropenem and imipenem. The diffusion of both drugs into the healthy meninges is very low (1-10%); however, when the meninges become inflamed, the diffusion increases. For imipenem this rate is about 15%, but for meropenem it is increased up to 45-50%. Adverse effects, especially neurotoxicity, are lower in meropenem usage than in imipenem. For these reasons meropenem treatment is suggested for cases of meningitis. The recommended dosage is 6 grams per day [7]. In our cases, meropenem therapy was given due to *A. baumannii* meningitis and there was a clinical and laboratory response in a few days. In our cases CSF remained free of *A. baumannii* throughout the rest of the

hospitalization. Our case reports are limited in that we were unable to conduct molecular analysis so we did not determine whether the strains were the same or not.

In conclusion, in the last two decades *Acinetobacter baumannii* has emerged as a major relevant world nosocomial pathogen. Post-neurosurgical meningitis is a serious complication when multidrug resistant *A. baumannii* are isolated. In our cases we presented the potential utility of high-dose meropenem for meningitis due to resistant *A. baumannii*. New antibiotics and new therapeutic strategies are needed to combat this multidrug resistant pathogen.

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Conflict of interests: The authors declare that they have no conflict of interests.