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Short communication

Successful treatment of extensively drug-resistant *Acinetobacter baumannii* ventriculitis and meningitis with intraventricular colistin after application of a loading dose: a case series☆

Ilias Karaiskos[a], Lambrini Galani[a], Fotini Baziaka[a], Emmanouela Katsouda[b], Ioannis Ioannidis[c], Alexandros Andreou[c], Harry Paskalis[b], Helen Giamarellou[a,*]

[a] *6th Department of Internal Medicine, Hygeia General Hospital, 4 Erythrou Stavrou Str. & Kifissias Ave., Marousi 15123, Athens, Greece*
[b] *Intensive Care Unit, Hygeia General Hospital, Athens, Greece*
[c] *Department of Neurosurgery and Interventional Neuroradiology, Hygeia General Hospital, Athens, Greece*

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ABSTRACT

Treatment results of six post-neurosurgical ventriculitis and meningitis cases caused by extensively drug-resistant *Acinetobacter baumannii* after application of an intraventricular loading dose of 500 000 IU (40 mg) of colistin followed by a dose of 125 000–250 000 IU (10–20 mg) every 24–48 h plus parenteral colistin are reported. Simultaneous bacteraemia with an identical *Acinetobacter* strain was observed in three patients. The mean duration of treatment was 17.2 days (range 15–21 days) and the median time of sterilisation of cerebrospinal fluid was 2.5 days (range 1–5 days). All patients were cured, however one patient presented with chemical meningitis and one with chemical ventriculitis, conditions that clinically and biochemically resemble bacterial meningitis.

1. Introduction

Post-neurosurgical nosocomial meningitis has arisen as a significant category of bacterial meningitis in the hospital setting. *Acinetobacter baumannii* appears as the most frequent Gram-negative micro-organism implicated in the neurosurgery setting [1]. Therapeutic treatment is considered extremely challenging due to the fact that this pathogen possesses the aptitude to develop resistance easily to almost all conventional antimicrobial agents. Under these circumstances, colistin has been revived as a therapeutic regimen with great in vitro activity and excellent in vivo potency against *A. baumannii* [2]. However, recent pharmacokinetic data in humans indicate that penetration of colistin into the cerebrospinal fluid (CSF) is poor [3,4].

Consequently, intraventricular (IVT) administration of colistin appears to have a crucial role in the treatment of post-neurosurgical ventriculitis/meningitis caused by *A. baumannii* with multiple patterns of resistance.

Here we report six neurosurgical patients complicated with extensively drug-resistant (XDR) *A. baumannii* ventriculitis and meningitis, with concomitant bacteraemia in three of them, who were cured with IVT administration of colistin.

2. Patients and methods

2.1. Subjects

Patients admitted to the Intensive Care Unit (ICU) and the Department of Neurosurgery and Interventional Neuroradiology of Hygeia General Hospital (Athens, Greece), hospitalised between 1 January 2010 and 1 December 2012, were defined as case patients if they fulfilled the following criteria: (i) clinical evidence of central nervous system (CNS) infection; (ii) microbiological evidence in CNS infection; (iii) isolation of *A. baumannii* from CSF; and (iv) necessity of colistin administration via the IVT route.

For each patient, the following data were recorded retrospectively: age; sex; primary diagnosis; presence of foreign bodies; antimicrobial regimens prescribed; days from admission to diagnosis of meningitis; days for sterilisation of CSF; duration of intravenous (IV) and IVT/intrathecal (ITH) colistin treatment; toxicity; outcome; and follow-up (Table 1). Cure was defined as the absence of clinical and laboratory evidence of CNS infection on the day of discharge as well as at follow-up. The study was approved

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* Corresponding author. Tel.: +302106867377.
E-mail address: e.giamarellou@hygeia.gr (H. Giamarellou).

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Table 1
Clinical characteristics, treatment, outcome and toxicity profile of six cases of *Acinetobacter baumannii* (*A.b.*) ventriculitis/meningitis treated with intraventricular (IVT) colistin (CST).

Case	Age (years)/ sex	Underlying diagnosis	Current diagnosis	Foreign body	*A.b.* susceptibility	Time from hospitalisation to diagnosis (days)	Current regimens	IVT/ITH CST		IV CST dose (duration in days)	Time to CSF sterilisation (days)	Toxicity	Outcome
								Dosage	Duration (days)				
Case 1	60/M	SAH, aneurysm	Ventriculitis	EVD	Susceptible to TGC and CST (MIC < 0.5 μg/mL)	12	CST	IVT, 40 mg q24h 1st day, 20 mg q24h 2nd and 3rd days and 10 mg q48h for 12 days. ITH, 20 mg q48h for 4 days	19	Loading dose 480 mg followed by 360 mg q12h (21)	2	None	Cure; 22 months follow-up
Case 2	26/M	Head injury, subdural haematoma	Ventriculitis	EVD	Susceptible to TGC and CST (MIC ≤ 2 μg/mL)	11	CST	IVT, 40 mg q24h for 6 days, 20 mg q48h	21	240 mg q8h (21)	5	Chemical ventriculitis	Cure; 20 months follow-up
Case 3	53/M	SAH, aneurysm	Meningitis	EVD placed at onset of meningitis	Susceptible to TGC and CST (MIC ≤ 2 μg/mL)	15	CST	IVT, 40 mg q24h 1st day, 20 mg q24h 2nd and 3rd days, 20 mg q48h for 8 days. ITH, 20 mg q48h	21	Loading dose 480 mg followed by 360 mg q12h (21)	3	None	Cure; 18 months follow-up
Case 4	44/F	SAH, AVM	Ventriculitis	EVD	Susceptible to GEN and CST (MIC = 0.5 μg/mL)	6	CST	IVT, 40 mg 1st day, 10 mg q24h for 8 days. ITH, 10 mg q48h for 6 days	15	Loading dose 480 mg followed by 360 mg q12h (30)	3	Chemical meningitis	Cure; 14 months follow-up
Case 5	60/M	SAH, aneurysm	Ventriculitis	EVD	Susceptible to AMK and CST (MIC < 0.5 μg/mL)	27	CST	IVT, 40 mg 1st day, 10 mg q24h	15	360 mg q12h (30)	2	None	Cure. Died of septic shock due to KPC-producing *K.p.* bacteraemia
Case 6	62/F	SAH, aneurysm	Meningitis	EVD placed at onset of meningitis	Susceptible to TOB and CST (MIC = 0.5 μg/mL)	77	CST	IVT, 40 mg 1st day, 30 mg 2nd day, 10 mg q24h for 3 days, 10 mg q48h for 7days	12	240 mg q8h (21)	1	None	Cure; 5 months follow-up

ITH, intrathecal; IV, intravenous; CSF, cerebrospinal fluid; M, male; SAH, subarachnoid haemorrhage; EVD, external ventricular drain; TGC, tigecycline; MIC, minimum inhibitory concentration; q24 h, every 24 h; q48 h, every 48 h; q12 h, every 12 h; q8 h, every 8 h; F, female; AVM, arteriovenous malformation; GEN, gentamicin; AMK, amikacin; KPC-producing *K.p.*, *Klebsiella pneumoniae* carbapenemase-producing *K. pneumoniae*; TOB, tobramycin.