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Variables determining mortality in patients with *Acinetobacter baumannii* meningitis/ventriculitis treated with intrathecal colistin

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ABSTRACT

Aim: To examine the variables associated with mortality in patients with *Acinetobacter baumannii*-related central nervous system infections treated with intrathecal colistin.
Materials and methods: This multi-centre retrospective case control study included patients from 11 centres in Turkey, as well as cases found during a literature review.

Only patients with CNS infections caused by multidrug-resistant or extensively drug-resistant *Acinetobacter baumannii* treated with intrathecal colistin were included in this study. The variables associated with mortality were determined by dividing the patients into groups who died or survived during hospitalisation, and who died or survived from *Acinetobacter* meningitis.
Results: Among the 77 cases enrolled in the study, 35 were found through a literature review and 42 were cases from our centres. Forty-four cases (57.1%) were male and the median age was 48 years (range: 20–78 years). Thirty-seven patients (48%) died during hospitalisation. The variables associated with increased all-cause mortality during hospitalisation included old age (odds ratio, 1.035; 95% confidence interval (CI), 1.004–1.067; $p = 0.026$) and failure to provide cerebrospinal fluid sterilisation (odds ratio, 0.264; 95% confidence interval, 0.097–0.724; $p = 0.01$). There is a trend (P = 0.062) towards higher mortality with using of meropenem during meningitis treatment. Fifteen cases (19%) died from meningitis. There were no significant predictors of meningitis-related mortality.
Conclusions: The mortality rate for central nervous system infections caused by multidrug-resistant or extensively drug-resistant *Acinetobacter baumannii* is high. Old age and failure to provide CSF sterilisation are associated with increased mortality during hospitalisation.

1. Introduction

Acinetobacter baumannii is a non-enteric Gram-negative bacillus with low virulence characteristics. As the prevalence of nosocomial

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infections caused by this bacterium is increasing, it is becoming an important concern [1]. The patients that most commonly develop central nervous system (CNS) infections associated with *A. baumannii* are those that have undergone brain surgery and external ventricular drainage via a catheter [2]. Compared with other bacteria, the ability of *A. baumannii* to develop resistance against antibiotics that are in current use is quite high; thus, this bacterium ranking among the most frequent causes of hospital-acquired infections [3]. Only a limited number of antibiotics are effective against this bacterium, and no new antibiotics are expected to be introduced in the short term. In recent years, colistin, which was previously abandoned due to its toxic effects, started being used again for resistant *A. baumannii* infections [4]. The clinical effectiveness of colistin against various infections, including CNS infections, is not known since it has not been subject to drug development trials and has not been evaluated in comparative clinical studies. It has been suggested that intravenous colistin does not penetrate well into the cerebrospinal fluid (CSF) [5,6]. Therefore, intrathecal or intraventricular administration of colistin has become an increasingly common method for the treatment of multidrug-resistant (MDR) or extensively drug-resistant (XDR) *A. baumannii*-related CNS infections [7–17].

However, our knowledge concerning these methods of administering colistin is limited due to a lack of randomised controlled studies on the subject, and by the fact that the available studies are case reports and case series including low numbers of cases [7–17]. The aim of this study was to examine the variables associated with mortality in *A. baumannii*-related CNS infections treated with intrathecal colistin.

2. Materials and methods

This multi-centre retrospective case control study included patients drawn from 11 centres in Turkey. Information from electronic patient files between 2001 and 2015 was reviewed, with eligible patients included on that basis. The literature was also reviewed to identify cases suitable for inclusion in this study. Patients treated with intrathecal colistin due to MDR or XDR *A. baumannii*-related CNS infections were included. Presence of nosocomial meningitis/ventriculitis was determined in accordance with the definition of the Center for Disease Control [18]. According to this definition, fulfilment of one of the following criteria, in a patient with a fever above 38 °C and an *A. baumannii* infection identified from the CSF, is considered a CNS infection: (1) number of leukocytes in CSF > 10/mm^3, (2) CSF protein levels > 45 mg/dL, or (3) CSF glucose level < 40 mg/dL. MDR and XDR *A. baumannii* were defined in accordance with the literature [19]. Cases with CNS infections caused by *Acinetobacter* that were susceptible to cefepime, ceftazidime, carbapenem, and trimethoprim-sulfamethoxazole, all of which have good CSF penetration and can be used to treat meningitis, as well as cases with CNS infections caused by non-*Acinetobacter* Gram-negative bacilli, were excluded from the study. The following data were extrapolated from the patients' files: general characteristics (age, gender, and underlying diseases), source of infection, CSF pre-treatment characteristics (number and type of cells, and glucose and protein levels), blood culture results, dose and duration of intrathecal colistin, dose and duration of intravenous colistin, antibiotics used before and concomitant with intrathecal colistin, duration of stay in the intensive care unit, time from hospitalisation until development of meningitis, reason of death, time from initiation of meningitis treatment until death, whether CSF sterilisation was achieved, and time until CSF sterilisation.

To identify cases in the literature with CNS MDR and XDR *A. baumannii* infections, a comprehensive search of the PubMed database was performed, of papers published since 2000. Only English language publications were searched for, using the following terms: multidrug-resistant, extensively drug-resistant, CNS, *A. baumannii*, ventriculitis, intrathecal, meningitis, intraventricular, colistimethate, colistin, review, case report, and mortality. The references of each article were reviewed to prevent inclusion of duplicate cases. In total, 11 articles were found, which included 35 cases eligible for inclusion.

The variables associated with mortality were identified by dividing the patients into groups who died or survived during hospitalisation, and who died or survived from *Acinetobacter* meningitis. To ensure that deaths were related to meningitis, all of the following criteria had to be present [20]: (1) lack of improvement of clinical and laboratory indicators of inflammation after treatment, (2) lack of two consecutive negative CSF cultures, and (3) no disorder apart from meningitis that could lead to death. Unless two consecutive CSF cultures were obtained from a case, discontinuation of meningitis-related treatment before death was included among the inclusion criteria.

2.1. Statistical analysis

The SPSS software package (ver. 17.0; SPSS Inc., Chicago, IL, USA) was used for all statistical analyses. Categorical variables were expressed as a number and percentage and non-normally distributed constant variables were expressed as the median (minimum-maximum). The Kaplan-Meier method and uni- or multi-variable Cox regression analysis were used to determine the independent variables associated with mortality. A P value < 0.05 was considered to indicate statistical significance (Fig. 1).

3. Results

3.1. Case characteristics and risk factors

Seventy-seven meningitis cases, caused by XDR or MDR *Acinetobacter* and treated with intrathecal colistin, were included in this study. In total, 35 cases from the literature and 42 cases from our centres were included. Forty-four patients (57.1%) were male and the median age was 48 years (range: 20–78 years).

The source of CNS infection was determined to be intraventricular catheters (35, 45.5%), lumbar catheters (9, 11.7%), open head trauma (2, 2.6%), neurosurgical intervention (30, 39%) (Ventriculoperitoneal shunt operation in 3 cases), and hematogenous spread during *A. baumannii* sepsis (1, 1.2%). *A. baumannii* was observed in the blood of 12 (15.5%) patients.

3.2. CSF examination results

The median number of leukocytes in CSF was 2739/mm^3 (range: 10–16,000/mm^3), the median polymorphonuclear leucocytes ratio was 86% (range: 44–100%), the median glucose level was 26 mg/dL (range: 1–122 mg/dL) mg/dL, and the median protein level was 510 mg/dL (range: 53–3373 mg/dL).

3.3. Information regarding treatment

Prior to developing meningitis, 32 (47.1%), 27 (39.7%), 7 (10.3%), 6 (8.9%), 4 (5.4%) and 32 (47%) patients were treated with carbapenems (meropenem and imipenem), cephalosporins (cefazolin, ceftriaxone, cefepime, ceftazidime, and cefuroxime), piperacillin-tazobactam, quinolones (ciprofloxacin and levofloxacin), aminoglycosides (amikacin and gentamicin), and drugs effective against Gram-positive cocci (vancomycin, teicoplanin, and linezolid), respectively.

A median of 10 mg/day (range: 3–40 mg/day) of intrathecal colistin was used for a duration of 16 days (range: 2–47 days).

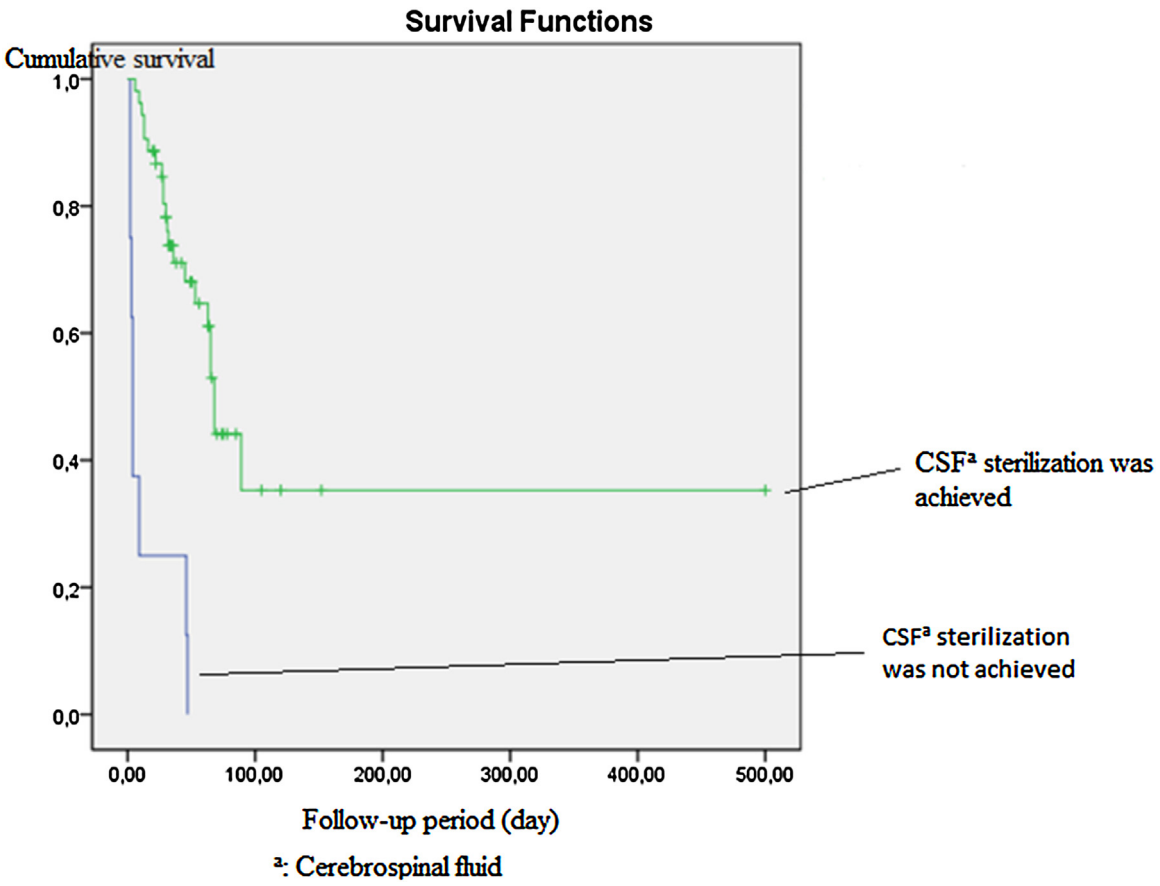

Fig. 1. Kaplan–Meier curve of the effect of providing cerebrospinal fluid sterilisation on mortality.

Sixty-three (81.8%) cases were treated with 418 mg/day (range: 240–720 mg/day) of intravenous colistin for 20 days (range: 2–47 days) in addition to intrathecal colistin treatment. Intrathecal colistin treatment was administered using intraventricular and lumbar catheters in 71 (92.2%) and 6 (7.8%) cases, respectively. Patients with *A. baumannii* bacteraemia also received intravenous colistin.

3.4. Outcome

Twenty-seven (64.3%) patients from our centres, and ten (28.6%) patients from the literature, died ($P = 0.002$). Of all patients, 37 (48%) died during hospitalisation (Table 1). Univariate analysis revealed that patients who died during hospitalisation were older, had a lower CSF sterilisation rate, and a higher rate of use of meropenem with intrathecal colistin (Table 2). In a multivariate analysis, older age and failure to provide CSF sterilisation were independently associated with mortality (Table 2). Although not statistically significant, mortality was high in patients receiving meropenem during meningitis treatment ($p = 0.062$). Fifteen cases (19.2%) died due to meningitis. No variables were associated with meningitis-related mortality (Table 3).

4. Discussion

A. baumannii is as an opportunistic microorganism known to cause health-related infections [21]. XDR and MDR *A. baumannii*-related meningitis has been increasingly reported in recent years, particularly in patients who had undergone brain surgery and were treated with intraventricular or intralumbar catheters [7–16,22,23]. As these patients generally stay in the intensive care unit due to severe underlying diseases, and receive broad-spectrum antibiotics for various infections, they are at risk of developing XDR and MDR *A. baumannii*-related CNS infections. In a previous study, the use of cephalosporins, carbapenems, penicillin, quinolones, and aminoglycosides for various infections was reported in 63%, 44%, 31%, 31%, and 25% of patients, respectively, prior to the development of *A. baumannii*-related CNS infections [8]. Consistent with the literature, the rate of use of carbapenems and cephalosporins for any infection prior to CNS infection was high in our study.

Only two studies have previously reported all-cause mortality rates in patients with MDR or XDR *A. baumannii*-related meningitis, of 13% and 16%, respectively [7,8]. Mortality was higher among the cases that we included from our country compared with those obtained from the literature. In a previous study on *Acinetobacter*-related meningitis, an APACHE II score > 19, use of intrathecal colistin, old age, high number of leukocytes in the CSF, and non-removal of a foreign body (intraventricular catheter, intralumbar catheter, or ventriculoperitoneal shunt) from the CNS were the variables associated with all-cause mortality [7,8,24]. In our study, the APACHE II instrument was not used, but old age, which is one of the most important variables in the APACHE II scoring system, was an independent variable associated with mortality. Due to the retrospective nature of our study, we were unable to examine the effects of early removal of foreign bodies from the CNS.

Colistin and carbapenem combination therapy did not affect survival in patients with *A. baumannii* infections susceptible to colistin only [25]. However, a previous *in vitro* study suggested that colistin-sulbactam, colistin-meropenem, and colistin-meropenem-sulbactam combinations had synergistic effects when time-kill curves were examined for a case that developed *A. baumannii*-related meningitis susceptible to colistin only [9]. In our study,

Table 1
Characteristics of patients with meningitis caused by multidrug-resistant *Acinetobacter baumannii*.

	Survival (n = 40, 52%)	Non-survival (n = 37, 48%)
Age (years)	42.5 (20–69)	53 (23–78)
Gender (males, n)	23 (57.5)	21 (56.8)
Source of infection (n)		
Ventricular drainage catheter	17 (42.5)	18 (48.6)
Lumbar catheter	7 (17.5)	2 (5.4)
Open head trauma	2 (5)	0 (0)
Neurosurgical intervention	13 (32.5)	17 (45.9)
Sepsis	1 (2.5)	0 (0)
Underlying CNS disease (n)		
Cerebrovascular disease	17 (42.5)	10 (27)
CNS tumour	6 (15)	9 (24.3)
Hydrocephalus	1 (2.5)	0 (0)
Arteriovenous malformation	0 (0)	2 (5.4)
Number of pre-treatment CSF leukocytes/mm^3	2739 (10–16000)	2500 (90–8900)
Pre-treatment CSF neutrophils (%)	86 (44–100)	86 (70–100)
Pre-treatment CSF glucose level (mg/dL)	26 (2–107)	26 (1–112)
Pre-treatment CSF protein level (mg/dL)	515 (67–2362)	505 (53–3373)
Presence of concomitant *Acinetobacter baumannii* bacteraemia	5 (14.3)	7 (21.2)
Intrathecal colistin dose (mg/day)	10 (3–40)	10 (5–40)
Intrathecal colistin treatment duration (days)	19 (3–40)	14 (2–47)
Intravenous colistin dose (mg/day)	418 (240–720)	410 (300–720)
Intravenous colistin treatment duration (days)	21 (7–40)	20 (2–47)
Concomitant parenteral antibiotic treatment for meningitis (n)		
Tigecycline	3 (7.5)	3 (8.1)
Sulbactam	9 (25.7)	6 (18.2)
Meropenem	7 (20)	21 (63.6)
Rifampicin	2 (5.7)	3 (9.1)
Achievement of CSF sterilisation (n)	31 (100)	22 (73.3)
Time from intrathecal colistin treatment initiation to CSF sterilisation (days)	5 (1–48)	6 (1–32)
Treatment in intensive care unit (n)	37 (92.5)	35 (94.6)

CNS, central nervous system; CSF, cerebrospinal fluid.

Table 2
Results of uni- and multivariate Cox-regression analyses of variables associated with all-cause mortality in patients with multidrug-resistant *Acinetobacter baumannii*-related infections treated with intrathecal colistin.

	Univariate analysis			Multivariate analysis		
	Odds ratio	95% confidence interval	*P*-value	Odds ratio	95% confidence interval	*P*-value
Age	1.026	1.005–1.049	0.017	1.035	1.004–1.067	0.026
CSF sterilisation achievement with treatment	0.121	0.05–0.290	0.0001	0.264	0.097–0.724	0.010
Use of meropenem during meningitis treatment	2.404	1.167–4.951	0.017	2.387	0.956–5.964	0.062

CSF, cerebrospinal fluid.

the combined use of meropenem or sulbactam and colistin had no effect on the mortality rate of our patients. This might be attributable to the fact that the synergistic effects of these antibiotics *in vitro* are less pronounced in clinical practice compared to the effects of other factors. Moreover, a CSF penetration ratio as low as 1–33% may also result in a lack of effect of sulbactam on mortality [1,26]. There is a trend towards higher mortality with using of meropenem during meningitis treatment in our Study. This may be due to that the clinician may have preferred to use meropenem in critically ill patients. An *in vitro* and an *in vivo* animal study investigating rifampicin use in combination with colistin suggested a synergistic action against *Acinetobacter*-related infections [27,28]. However, studies performed on cases with ventilator-associated pneumonia caused by *A. baumannii* and sepsis yielded controversial results on the synergistic effects of colistin-rifampicin combinations [29]. The use of rifampicin appeared to have no effect on mortality in our study, which might be attributed to the small number of patients treated with this agent. In some of our cases, *A. baumannii* was susceptible to tigecycline, for which it was administered in combination with colistin in some patients. However, the use of tigecycline in combination with colistin did not have an effect on mortality, which we attribute to the weak dispersion of tigecycline in CSF.

According to the Infectious Disease Society of America guidelines, intraventricularcolistin should be administered at a dose of 10 mg/day for 21 days in meningitis cases caused by aerobic Gram-negative bacilli [30]. In the literature, no standard dose has been established for resistant *A. baumannii*-related meningitis; the median dosage range is 12 mg/day (range: 3–40 mg/day) [9–15,22,23]. A previous study including few patients demonstrated that the dose of intrathecal colistin did not affect mortality [8]. However, no randomised controlled studies have assessed the effects of intrathecal colistin dose on mortality and the dose was not associated with mortality in our study.

Various intrathecal colistin treatment durations have previously been reported for *Acinetobacter* related meningitis [9–15,22,23]. In our study, we were unable to investigate the effects of treatment duration on mortality, because in many cases the treatment period was cut short due to patient death. We showed that *A. baumannii* bacteraemia concomitant with *Acinetobacter*-related meningitis had no effect on mortality rate, which might be due to the fact that all of the *Acinetobacter*bacteraemia cases received intravenous colistin. However, no conclusions can be drawn regarding this association, as only a small number of patients had bacteraemia. In our study, CSF sterilisation was achieved in all surviving patients, but only in 73.3% of those who died. These results suggest that a lack of CSF sterilisation with treatment may lead to increased mortal-

Table 3
Characteristics of patients with multidrug-resistant *Acinetobacter*-related meningitis treated with intrathecal colistin.

	Gender	Age (years)	CSF[a] sterilisation time (days)	Underlying disease	Cause of meningitis	Time between hospitalisation and meningitis development	Antibiotics used 1 month prior to meningitis treatment	Intrathecal colistin dose (mg/day)	Intrathecal colistin treatment duration (days)	Intravenous colistin dose (mg/day)	Intravenous colistin treatment duration (days)	Cause of death	Time between meningitis treatment initiation and death (days)	Duration of stay in intensive care unit	Susceptibility of bacterium to antibiotics other than colistin	Concomitant *A. baumannii* bacteraemia
Case 1	M[b]	21	7	,0	Lumbar catheter	4	Ampicillin/sulbactam, Tigecycline, Colistin	10	14	14	300	–	–	0	–	–
Case 2	M[b]	23	None	,0	Brain surgery	11	N	10	28	14	450	–	–	0	–	–
Case 3	F[c]	72	None	SVD[d]	Ventricular catheter	2	N	10	9	9	450	Meningitis	9	0	–	–
Case 4	M[b]	24	None	,0	Brain surgery	15	Meropenem, Vancomycin	10	21	21	300	–	–	1	Gentamicin, Tigecycline	–
Case 5	M[b]	54	8	,0	Ventricular catheter	6	Ceftriaxone	10	11	18	450	–	–	23		–
Case 6	F[c]	24	3	Brain tumor	Ventricular catheter	81	Meropenem, Ciprofloxacin, Linezolid	10	21	21	450	–	–	135	Gentamicin, Amikacin	Yes
Case 7	M[b]	62	None	SVD[d]	Brain surgery	24	Piperacillin/tazobactam, Moxifloxacin, Clarithromycin	10	14	26	300	–	–	79		–
Case 8	F[c]	51	9	,0	Brain surgery	9	Ceftriaxone, Meropenem, Linezolid	10	20	7	300	–	–	3	Levofloxacin, Tigecycline	–
Case 9	M[b]	26	16	,0	Brain surgery	14	Rifampicin, Linezolid	10	28	28	300	–	–	50	Gentamicin	–
Case 10	M[b]	55	12	,0	Brain surgery	35	Meropenem, Cefoperazone/sulbactam, Tigecycline, Linezolid, Amikacin	10	19	30	450	–	–	51	Gentamicin, Tigecycline	–
Case 11	M[b]	23	None	,0	Head trauma	0	Ceftriaxone, Metronidazole, Meropenem, Vancomycin	10	10	14	450	–	–	14	Amikacin, Tigecycline	Yes
Case 12	F[c]	47	1	,0	Ventricular catheter	16	N	10	12		–	–	–	37	Gentamicin	–
Case 13	M[b]	24	None	Brain tumor	Brain surgery	30	Linezolid, Amphotericin-B, Colistin, Caspofungin, Daptomycin	10	21	21	300	–	–	50	–	–
Case 14	F[c]	58	None	SVD[d]	Brain surgery	19	Ceftriaxone, Vancomycin, tigecycline, Colistin	10	25	33	300	–	–		Gentamicin, Tigecycline	–
Case 15	M[b]	31	3	,0	Brain surgery	7	Meropenem	10	21		–	–	–		Tigecycline	Yes
Case 16	M[b]	43	None	SVD[d]	Brain surgery	2	N	10	16	24	300	,-	–		Gentamicin, Tigecycline	–
Case 17	F[c]	47	None	,0	Ventricular catheter		vankomycin, Meropenem, Cefepime, Fluconazole, Linezolid	10	47	47	300	Meningitis	47	60	Gentamicin	–
Case 18	F[c]	65	6	Brain tumor	Lumbar catheter	29	Ceftazidime, Vancomycin, Meropenem	10	11	11	450	Other disease out of meningitis	11	37	Gentamicin, Amikacin	–
Case 19	M[b]	73	None	,0	Ventricular catheter	9	Cefazolin, Piperacillin/tazobactam	10	2	2	450	Meningitis	2	14	Amikacin	–
Case 20	M[b]	33	4	,0	Brain surgery	41	Doripenem, Imipenem, Colistin	10	8	26	300	Meningitis	9	66	Gentamicin, Tigecycline	Yes
Case 21	F[c]	56	None	,0	Ventricular catheter	18	Meropenem, Vancomycin	10	23	15	450	Meningitis	24	12	–	–

Table 3 (*Continued*)

	Gender	Age (years)	CSF[a] sterilisation time (days)	Underlying disease	Cause of meningitis	Time between hospitalisation and meningitis development	Antibiotics used 1 month prior to meningitis treatment	Intrathecal colistin dose (mg/day)	Intrathecal colistin treatment duration (days)	Intravenous colistin dose (mg/day)	Intravenous colistin treatment duration (days)	Cause of death	Time between meningitis treatment initiation and death (days)	Duration of stay in intensive care unit	Susceptibility of bacterium to antibiotics other than colistin	Concomitant *A. baumannii* bacteraemia
Case 22	F[c]	58	15	,0	Ventricular catheter	16	Cefazolin, Meropenem, Vancomycin	10	7	31	450	Other disease out of meningitis	31	25	Gentamicin, Amikacin	–
Case 23	F[c]	28	3	,0	Ventricular catheter	12	Cefazol, Ceftriaxone	10	10	13	450	Meningitis	13	24	Gentamicin, Amikacin	–
Case 24	M[b]	60	3	SVD[d]	Brain surgery	17	Meropenem	10	10	6	300	Meningitis	10	1	–	–
Case 25	F[c]	55	5	Brain tumor	Brain surgery	28	Meropenem, Ceftriaxone, Tigecycline	10	6	16	450	Other disease out of meningitis	16	36	Tigecycline	–
Case 26	M[b]	62	8	,0	Brain surgery	48	Meropenem, Trimethoprim/sulfamethoxazole, Ciprofloxacin, Vancomycin, Tigecycline	10	25	25	450	Other disease out of meningitis	28	95	Amikacin, Levofloxacin, Tigecycline	–
Case 27	M[b]	62	None	,0	Ventricular catheter	8	Cefazol, Meropenem, Vancomycin	10	3	3	450	Meningitis	3	5	Amikacin	–
Case 28	M[b]	23	2	Brain tumor	Brain surgery	28	Piperacillin/tazobactam, Linezolid, Meropenem	10	21	21	450	Other disease out of meningitis	45	67	–	–
Case 29	F[c]	36	None	,0	Ventricular catheter	14	Ceftriaxone, Meropenem, Vancomycin, Colistin	10	21	21	300	Other disease out of meningitis	53	50	Tigecycline	–
Case 30	F[c]	63	None	Brain tumor	Brain surgery	16	Vancomycin, Ceftazidime, Tigecycline, Colistin, Linezolid, Rifampicin	10	13	14	300	Meningitis	14	31	–	Yes
Case 31	F[c]	52	None	,0	Brain surgery	12	Cefazol, Cefepime	10	4	4	450	Meningitis	4	21	Amikacin	Yes
Case 32	M[b]	47	None	,0	Ventricular catheter	14	Ceftriaxone, Cefoperazone/sulbactam, Vancomycin, Meropenem, Linezolid	10	28	14	300	Meningitis	46	61	Tigecycline	Yes
Case 33	M[b]	30	None	Brain tumor	Brain surgery	2	Meropenem, Vancomycin	10	21	21	300	Other disease out of meningitis	150		–	–
Case 34	M[b]	42	3	SVD[d]	Brain surgery	9	Meropenem	10	30	20	450	Other disease out of meningitis	30	44	–	–
Case 35	M[b]	26	None	SVD[d]	Brain surgery	12	Meropenem, Vancomycin	10	20	28	450	Meningitis	28	32	–	–
Case 36	M[b]	50	None	,0	Brain surgery	21	Cefuroxime, Ceftriaxone, Ciprofloxacin, Meropenem, Colistin	10	3	15	450	Meningitis	14	30	–	Yes
Case 37	M[b]	62	4	,0	Brain surgery	12	Meropenem, Linezolid, Vancomycin, Cefoperazone/sulbactam	10	16	19	450	Other disease out of meningitis	65	92	Amikacin, Tigecycline	–
Case 38	F[c]	58	15	,0	Ventricular catheter	25	Meropenem, Linezolid	10	32	28	300	Other disease out of meningitis	36	56	–	–
Case 39	M[b]	53	None		Brain surgery	18	Ceftriaxone, Meropenem, Vancomycin	10	3	27	450	Other disease out of meningitis	41	34	Gentamicin	–
Case 40	F[c]	53	None	SVD[d]	Ventricular catheter	5		10	16	22	300	Other disease out of meningitis	33	40	Tigecycline	Yes
Olgu 41	M[b]	28	6	Brain tumor	Brain surgery	29	Piperacillin/tazobactam, Meropenem, Vancomycin	10	15	15	450	Other disease out of meningitis	27	60	Gentamicin, Amikacin	–
Case 42	F[c]	48	1	Brain tumor	Brain surgery	8	Piperacillin/tazobactam, Meropenem, Linezolid	10	17	32	300	Other disease out of meningitis	89	99	Tigecycline	–

[a] Cerebrospinal fluid.
[b] Male.
[c] Female.
[d] Serebrovascular diseases.

ity. However, cultures of CSF samples taken under the antibiotic pressure would not indicate a microbiological cure. If we take odds ratios in multivariate analysis into account,CSF sterilization seems to have more effect on mortality than age.

In conclusion, we demonstrated that MDR and XDR *A. baumannii*-related CNS infections treated with intrathecal colistin are associated with a high risk of mortality, which is further increased by old age and failure to achieve CSF sterilisation.

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