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Review

Post-neurosurgical multidrug-resistant *Acinetobacter baumannii* meningitis successfully treated with intrathecal colistin. A new case and a systematic review of the literature

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SUMMARY

Introduction: Post-neurosurgical nosocomial meningitis has become an important subgroup of bacterial meningitis in the hospital setting. The increase in meningitis caused by multidrug-resistant (MDR) *Acinetobacter baumannii* has resulted in a significant reduction in available treatment options.
Case report and literature review: We report the case of a 36-year-old man with a complex craniofacial trauma, who developed a nosocomial meningitis due to MDR *A. baumannii* that was cured by intrathecal colistin. The case is contextualized among all the published cases of Acinetobacter meningitis treated with topical colistin found through a MEDLINE search of the literature. To date, including the present case, eight reported cases of Acinetobacter meningitis have been treated with colistin administered by an intrathecal route and 24 by an intraventricular route. The daily dose of colistin used ranged from 1.6 mg every 24 h to 20 mg every 24 h in adult patients. The median time necessary to obtain cerebrospinal fluid sterilization was 4.1 days, and treatment was always successful even if in two cases Acinetobacter meningitis relapsed. Toxicity probably or possibly related to the topical administration of colistin was noted in five out of the 32 patients.
Conclusions: Topical colistin can be an effective and safe treatment for MDR Acinetobacter meningitis.

Introduction

Neurosurgical patients have a high risk of developing nosocomial meningitis, with potentially lethal consequences. The widespread use of antibiotics may have altered the epidemiology of post-neurosurgical meningitis in recent years.[1,2] During the past three decades, *Acinetobacter baumannii* has emerged as an infectious agent of importance in hospitals worldwide, due to its ability to tolerate desiccation and to accumulate diverse mechanisms of resistance.[3]

We report the case of a neurosurgical patient who developed meningitis due to multidrug-resistant (MDR) *A. baumannii* that was cured by intrathecal colistin, and contextualize it among all the published cases of Acinetobacter meningitis treated with intrathecal or intraventricular colistin found through a MEDLINE search of the international literature from 1950 to date.

Case report

A 36-year-old man was admitted to the intensive care unit (ICU) with a complex craniofacial trauma resulting from a recreational fireworks blast. The injuries involved the anterior skull base with exposure and severe damage to the dura mater and brain, loss of orbital contents, cerebrospinal fluid (CSF) leak, and soft tissue and facial skin loss. On admission, the patient was comatose with a Glasgow coma scale score of 7/15. He was intubated under sedation, and ventilation and oxygenation were supported by mechanical ventilation.

An urgent craniotomy was performed for the evacuation of hematomas, debridement of cortical contusions, and repair of the

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dura mater. At this time, a lumbar drainage was inserted to maintain a low CSF pressure and facilitate healing.

Perioperative antibiotic chemoprophylaxis with cefazolin was started, and considering the patient's condition, it was prolonged. On the third day after surgery the patient presented with remittent fever (peak 38.8 °C), but no source of infection could be found on physical examination and imaging studies. Laboratory examinations revealed a white blood cell (WBC) count of 14.1×10^9/l with 72% neutrophils and 23% lymphocytes. Cultures of blood, central venous catheter, arterial line, tracheal aspirate, bronchial alveolar lavage, and urine were drawn and subsequently found to be negative. Results of urinalysis were unremarkable. Pending the culture results, the patient was empirically treated with intravenous meropenem and teicoplanin. The patient's CSF was clear with a glucose concentration of 16 mg/dl, a protein level of 380 mg/dl, and a WBC count of 300×10^6/l, with 95% polymorphonuclear leukocytes and 5% lymphocytes. Gram staining of the CSF revealed no organisms.

Three days later, a culture of CSF yielded *A. baumannii*. The bacteria were identified by morphology, Gram stain, and reactions with the Vitek 2 GNI card (bioMérieux-Vitek). It was resistant to all the antibiotics examined in the laboratory by disk diffusion susceptibility test, including carbapenems, cephalosporins, fluoroquinolones, aminoglycosides, and aztreonam, and sensitive only to colistin. Susceptibility to sulbactam and tigecycline was not tested.

Once the organism was identified, parenteral therapy was discontinued and intrathecal colistin 10 mg/day was started. The colistin dose was diluted in 2 ml of sterile normal saline and given through the lumbar drainage after removal of a greater or equal volume of CSF. After each dose, the lumbar drainage was clamped for 1 h and released.

The patient became afebrile at 48 h after the beginning of intrathecal colistin. CSF cultures performed daily became negative after 5 days of intrathecal therapy and on that day the CSF WBC count had decreased to 100×10^6/l. On day 10, CSF culture continued to be sterile, the CSF WBC count had further decreased to 8×10^6/l, and hence the lumbar drainage was removed and the therapy stopped. No complications or side effects were observed during the treatment. Renal function was stable. The patient's clinical status progressively improved and the maxillofacial surgery team began the orbitocranial reconstruction. After one month, the patient was discharged from the hospital with moderate neuropsychological consequences. The patient has been followed up for two years, with no evidence of relapse or CSF leak.

The clinical data for our patient are summarized in the last row of Table 1.

Literature review and discussion

For the review of published cases, a PubMed search was performed combining the terms (polymyxins OR polymyxin OR colistin) AND (meningitis OR ventriculitis OR intrathecal OR intra thecal OR intraventricular OR intra ventricular OR intraspinal OR intracerebral) AND (Acinetobacter OR Achromobacter) for the period January 1950 to April 2009; references were also checked for relevant articles, including review papers.

A study was considered eligible for inclusion in the systematic review if it reported data on the clinical effectiveness and/or safety of intraventricular or intrathecal colistin for the treatment of patients with meningitis caused by MDR Acinetobacter.

Our search identified 45 potentially relevant articles. After a scrupulous analysis of all studies, 18 articles describing 33 episodes of Acinetobacter meningitis occurring in 31 patients on all five continents, published between the years 1990 and 2009, were further evaluated together with our patient data. Data regarding the clinical characteristics, therapy, and outcome of these patients are shown in Table 1.[4–22] Of note, not one paper reporting cases of Acinetobacter meningitis treated intraventricularly or intrathecally was excluded; in all these cases the authors considered the Acinetobacter as MDR.

In some papers the term 'intrathecal' was improperly used for cases treated intraventricularly. In this review the patients were classified according to the way in which they were actually treated, independently of the way the authors used the terms. Furthermore, we used the term 'topical colistin' to refer to both means of administration, intrathecal and intraventricular.

In one patient, the species involved was *Acinetobacter calcoloaceticus*;[6] in all the others *A. baumannii*. In two patients, other bacteria were also isolated from the CSF cultures: methicillin-resistant *Staphylococcus aureus* and *Enterobacter cloacae* in one patient and *Staphylococcus epidermidis* in the other.[7,13] In two patients, probably due to predisposing factors, meningitis episodes due to other bacteria also occurred.[7,10] Most of the patients (27/32) included in the reviewed studies were adults, and for adult patients for which this information was available, the mean age was 42.9 ± 18 years. Of the three children, two were 4 years old and one 16 years old.[4,5,13]

In all the patients, meningitis was secondary to neurosurgical procedures for the management of various central nervous system (CNS) diseases, often resulting from a head injury. Colonization of a ventriculoperitoneal (VP) shunt with Acinetobacter was considered as the source of the infection in two patients.[7,8]

Minimum inhibitory concentration (MIC) values for colistin and/or other antibiotics were reported in only two cases.[18,21] Strains with intermediate resistance to carbapenems were reported in two cases.[5,10] Intravenous carbapenems were initially used in nine patients. In none of the articles were strains tested for their ability or inability to form a biofilm. Colistin was administered intraventricularly by external ventricular drainage (EVD) or by an externalization of a VP shunt in 24 cases,[4,5,7,9–11,13,14,17–21] and intrathecally by an external lumbar drainage or by lumbar puncture in seven patients (eight including the present case).[6,8,12,13,15,16]

Even though colistin was the only antibiotic to which the organism was susceptible in many cases, topical colistin was used from the beginning of therapy in only four cases.[5,6,12,15] Monotherapy with topical colistin was the final therapeutic regimen in eight cases,[6,9,12–14,21] and combination of systemic and topical colistin in 13 cases.[8,11,16,17,20] In one patient, intrathecal colistin was combined with intravenous rifampin.[15] In the remaining episodes, various combinations of topical colistin with systemic and/or topical antibiotics of other categories were administered. There was considerable variability in the daily dose and dosing scheme of colistin administered by the intrathecal or intraventricular route in the reviewed studies. In adults and in the 16-year-old boy, the daily dose of colistin ranged from 1.6 mg every 24 h to 20 mg every 24 h. In the 4-year-old child treated intrathecally, the colistin dose was 1 mg on the first day increasing to 4 mg on the fourth day, continued for 13 days.[13] In six out of the eight cases treated intrathecally and in four out of the 24 cases treated intraventricularly, the first dose was half of the daily dose. In all the cases treated intrathecally and in 11 out of 24 cases treated intraventricularly, topical colistin was administered in a single daily dose, in the other patients it was administered in two divided doses. The duration of treatment also varied greatly, approximately ranging from 3 to 42 days. In the cases where therapy lasted less than 7 days, this was due to the death of the patient or for the occurrence of side effects.[13,18]

In all the cases, CSF cultures became negative during treatment with topical colistin. The median time necessary to obtain CSF sterilization was 4.1 days (range 1–15 days), and all the episodes

Table 1
Clinical characteristics, therapy and outcome of patients with *Acinetobacter spp* meningitis treated with intraventricular or intrathecal colistin[a]

Authors, year, country (notes) [Ref.]	Age/sex	Primary diagnosis	Foreign bodies	Acinetobacter susceptibility	Initial regimens used	Final regimen	Dosage of intrathecal colistin (colistimethate)[b]	Toxicity	Outcome (comment)
Kaplan and Patrick, 1990, USA [4]	4/NR	Meningitis	EVD	MDR	None	Cefotaxime and aminoglycoside IV, colistin IVR	20 unspecified doses	None	Cure
Fernandez-Viladrich et al., 1999, Spain (2 cases) [5]	16/M	Hemangioblastoma	EVD	Susceptible only to colistin and sulbactam; intermediate to tobramycin and imipenem	Meropenem, tobramycin and, sulbactam IV; tobramycin IVR	Tobramycin IV and colistin IVR	5 mg q12h for 19 days	None	Culture-negative after 2 days Cure Died of cardiac arrest 40 days later
	34/F	SAH and hydrocephalus	EVD	Susceptible only to colistin; intermediate to tobramycin	None	Tobramycin IV and colistin IVR	5 mg q12h, increased to 10 mg q12h after the 5th day, for 3 weeks	None	Culture-negative after 6 days Cure Follow-up 4 months
Vasen et al., 2000, Argentina [6]	41/F	SAH and hydrocephalus	Aneurysm clip, EVD	Susceptible only to colistin	None	Colistin IT	5 mg 1st day and 10 mg q24h remaining 20 days	None	Culture-negative after 1 day Cure Follow-up 6 weeks
Benifla et al., 2004, Israel (*Staphylococcus aureus* was also isolated in one of the cultures) [7]	49/F	Recurrent meningioma, recurrent episodes of meningitis	VP shunt	Susceptible only to colistin and sulbactam	Ceftriaxone IV, co-amoxiclav IV and meropenem IV, ampicillin/sulbactam and vancomycin	Ampicillin/sulbactam and vancomycin IV, Colistin IVR	3.2 mg q24h for 17 days	None	Culture-negative after 6 days Cure Follow-up 4 years
Sueke et al., 2005, UK [8]	38/F	VP shunt infection and hydrocephalus	VP shunt, EVD	Susceptible only to colistin	Colistin IV, gentamicin IT	Colistin IV, colistin IT	4 mg q24h, then increased to 8 mg for one dose, then 6 mg q24h and finally 6 mg q12h	Seizure immediately after administration of the 8 mg dose	Cure (Authors do not report total duration of therapy and follow-up)
Bukhary et al., 2005, Saudi Arabia [9]	23/F	Meningioma, posterior fossa craniotomy and upper cervical laminectomy	EVD	Susceptible only to colistin	Imipenem, ciprofloxacin, moxifloxacin and colistin IV	Colistin IVR	10 mg q12h for 21 days	None	Culture-negative after 7 days Cure

Kasiakou et al., 2005, Greece (2 episodes) [10]	28/M	Head trauma, recurrent meningitis	Plastic meningeal prosthesis, EVD	Susceptible only to colistin and amikacin; imipenem and meropenem intermediate	Amikacin, colistin and teicoplanin IV. For the second episode: meropenem, ciprofloxacin, teicoplanin, and colistin IV	Colistin, amikacin and teicoplanin, IVR and IV for both the episodes	1.6 mg for 3 weeks, and for the second episode: 3.2 mg q24h for 42 days	None	Cure One other episode of Acinetobacter meningitis occurred after 40 days Cure Follow-up 1 year
Berlana et al., 2005, Spain (2 cases) [11]	NR	NR	EVD	MDR not further specified	NR	Colistin IV, colistin IVR	10 mg q12h for 8 days	None	Cure
	NR	NR	EVD	MDR not further specified	NR	Colistin IV, colistin IVR	20 mg q24h for 10 days	None	Culture-negative Cure The patient died later of unreported causes
Charra et al., 2006, Morocco [12]	36/M	Craniocerebral trauma	EVD	Susceptible only to colistin	None	Colistin IT	5 mg 1st day and 10 mg q24h remaining 21 days (22 days total)	None	Culture-negative after 2 days Cure
Ng et al., 2006, Australia (5 cases; *Staphylococcus epidermidis* was also isolated in one of the CSF cultures of the first case) [13]	74/F	SAH with obstructive hydrocephalus	EVD	MDR not further specified	Vancomycin and amikacin IV	Colistin IVR	5 mg 1st day and 10 mg q24h for 18 days	None	Culture-negative after 14 days Cure A myocardial infarction resulted in death on day 32
	56/F	SAH with obstructive hydrocephalus	EVD	MDR not further specified	Amikacin and colistin IV	Colistin IVR	5 mg 1st day and 10 mg q24h for 3 days	Not specified neurological disorders	Culture-negative after 3 days The patient survived and was transferred to a nursing home
	38/F	Closed head injury	EVD	MDR not further specified	Vancomycin, meropenem and amikacin IV	Colistin and amikacin IV, colistin IVR	5 mg 1st day and 10 mg q24h for 12 days	Chemical ventriculitis	Culture-negative after 4 days Cure
	26/M	Intracerebral hemorrhages	EVD	MDR not further specified	Colistin and amikacin IV	Colistin and amikacin IV, colistin IT	5 mg 1st day and 10 mg q24h for 6 days	Chemical meningitis	Culture-negative after 1 day Cure
	4/M	Medulloblastoma requiring craniotomy		MDR not further specified	Colistin and amikacin IV	Colistin IT	1 mg q24h 1st day, 2 mg q24h 2nd and 3rd day, then 4 mg q24h for 13 days	Chemical meningitis	Culture-negative after 3 days Cure

Table 1 (*Continued*)

Authors, year, country (notes) [Ref.]	Age/sex	Primary diagnosis	Foreign bodies	Acinetobacter susceptibility	Initial regimens used	Final regimen	Dosage of intrathecal colistin (colistimethate)[b]	Toxicity	Outcome (comment)
Al Shirawi et al., 2006, Saudi Arabia [14]	28/M	Craniocerebral trauma	EVD	MDR not further specified	Meropenem, ciprofloxacin and vancomycin IV	Colistin IVR	3.2 mg q24h for 28 days	None	Culture-negative after 3 days Cure Follow-up NR
Motaouakkil et al., 2006, Morocco [15]	36/M	Craniocerebral trauma	EVD	MDR not further specified	None	Rifampin IV, colistin IT	5 mg q24h 1st day, 10 mg q24h for 21 days	None	Culture-negative after 2 days Cure
Paramythiotou et al., 2007, Greece [21]	24/F	Ruptured aneurysm of the middle cerebral artery.	EVD with Ommaya reservoir	Susceptible only to colistin (MIC $<0.5\ \mu g/ml$)	Colistin IV	Colistin IVR	10 mg q24h for 20 days		Culture-negative after 15 days Cure
Ho et al., 2007, Taiwan (2 episodes) [16]	68/F	Recurrent meningioma, Emergent craniectomy and duraplasty	External lumbar drainage	MDR including carbapenems, cephalosporins, fluoroquinolones, aminoglycosides and aztreonam	Meropenem and sulbactam IV and then colistin IV	Colistin IT and colistin IV for both the episodes	1.6 mg q24h 1st day, 3.2 mg q24h 2nd, 4.8 mg q24h 3rd day, 2.4 mg q24h 4th day, then 4.4 mg q48h for 13 days. Second episode: 6.4 mg q24h for 12 days	None	Culture-negative after 2 days The 2nd episode occurred when the dose was reduced to 4.4 mg q48h Culture-negative 1 day after the 6.4 mg q24h dose Cure Follow-up 6 months
Rodriguez Guardado et al., 2008, Spain (8 adult patients) [17]	NR	NR	EVD	MDR not further specified	NR	Colistin IV, colistin IVR	10 mg q12 h for 21 ± 4.4 (mean $\pm$ SD) days	None	Cure
Lee et al., 2008, Taiwan [18]	78/M	SAH and obstructive hydrocephalus	EVD	Susceptible only to sulbactam and colistin (MIC $\leq 0.2\ \mu g/ml$)	Meropenem and sulbactam IV	Colistin, meropenem and sulbactam IV, colistin IVR	5 mg q24h for 4 days		Culture-negative after 2 days Cure The patient died of hypoxemia secondary to respiratory distress syndrome 4 days later
Hachimi et al., 2008, Morocco [19]	73/M	SAH and obstructive hydrocephalus	EVD	Susceptible only to colistin and amikacin	None	Colistin IVR, amikacin IVR	5 mg q24h 1st day, 10 mg q24h for 21 days	None	Culture-negative after 3 days Cure

									The patient died of *Pseudomonas aeruginosa* septic shock and pneumonia
Hekimoglu Sahin et al., 2008, Turkey [20]	30/M	Craniocerebral trauma	EVD	MDR not further specified	Colistin IV	Colistin IVR, colistin IV	5 mg q24h for 21 days	None	Cure
Present case	36/M	Craniofacial trauma. Emergent craniectomy and duraplasty	External lumbar drainage	Susceptible only to colistin (MIC <0.5 μg/ml)	Meropenem and teicoplanin IV	Colistin IT	10 mg q24h for 10 days	None	Culture-negative after 5 days
									Cure
									Follow-up 2 years

CSF, cerebrospinal fluid; EVD, external ventricular drainage; F, female; IU, international units; IT, intrathecal; IV, intravenous; IVR, intraventricular; M, male; MIC, minimum inhibition concentration; MDR, multidrug resistant; NR, not reported; q12 h, every 12 h; q24 h, every 24 h; q48 h, every 48 h; SAH, subarachnoid hemorrhage; VP, ventriculoperitoneal.

[a] The term intrathecal was used only if the drug was actually administered into the subarachnoid space, independently of the way the authors reported this in the original papers.

[b] In many cases the dose was converted from international units (IU) to milligrams (mg) for comparison purposes (conversion 1 mg = 12 500 IU).

could be considered cured, even if in two cases Acinetobacter meningitis relapsed. In one patient with recurrent episodes of meningitis, *A. baumannii* reappeared in the CSF 40 days after microbiological cure.[10] In another patient, *A. baumannii* reappeared in the CSF when the colistin dose was reduced.[16] Both the patients were successfully retreated, one with a combination of antibiotics, including intraventricular colistin, and the other with intrathecal and IV colistin.

Five patients died of causes not related to meningitis or its treatment.[5,11,13,18,19]

Toxicity probably or possibly related to the topical administration of colistin was noted in five patients: in three cases, a reversible ventricular or meningeal irritation was reported, manifested by neurological symptoms/signs and an increase in the cell count in the CSF, despite negative cultures. In one case, unspecified neurological disorders appeared after four days of intraventricular treatment, making it necessary the discontinue treatment;[13] and in the other case, an episode of seizure immediately after the administration of an 8 mg intrathecal dose made it necessary to reduce the colistin dose.[8]

Characteristics of the patients grouped on the basis of the route of colistin administration are compared in Table 2. Within the limits of a statistical analysis performed on groups of scattered cases, we tried to analyze the numeric differences. The daily dosage and the total amount of colistin administered were higher in patients treated intraventricularly (*t*-test, $p = 0.05$ and $p = 0.03$, respectively). The time for culture sterilization was shorter in the subgroup treated intrathecally (*t*-test, $p = 0.05$). Side effects occurred more frequently in the subgroup treated intrathecally (Chi-square, $p = 0.11$). No relapse was observed in the eight patients in which topical colistin (four patients treated intrathecally and four patients treated intraventricularly), was the only microbiologically active drug.

In only seven of the retrieved papers were data on the management of external drainage catheters and shunts clearly reported, and in only one case was the patient's EVD replaced with a drain at a new site due to minimal clinical response and little change in the CSF cultures.[8]

Acinetobacter spp is a Gram-negative coccobacillus that, during the past three decades, has emerged from an organism of questionable pathogenicity to an infectious agent of importance in hospitals worldwide.[3] The organism's ability to tolerate desiccation and to accumulate diverse mechanisms of resistance favor its long-term persistence in ICUs, where skin carriage may persist for weeks/months and the Acinetobacter-colonized hands of the staff may be responsible for patient-to-patient spread. Environmental contamination and contamination of medical equipment may also play an important role in the transmission of *A. baumannii* in healthcare institutions.[1,3]

Bacterial meningitis caused by *A. baumannii* constitutes around 10% of Gram-negative and 4% of nosocomial meningitis.[23] The mortality rate of patients with neurosurgery-related Gram-negative meningitis is about 33%.[24] The mortality rate in patients with Acinetobacter meningitis treated only parenterally (without a topical administration of colistin) is about 27%.[25] Only five out of the 32 (15.6%) patients we considered in our review died, and for none of them was the death considered to be related to meningitis or its treatment.

The presence of multiresistance and the poor penetration of many drugs through the blood–brain barrier have forced the use of topical therapies, initially with aminoglycosides and more recently with colistin. The combination of topical and intravenous amikacin has been associated with a survival rate of less than 60%.[17,26,27]

Colistin (polymyxin E) is available in vials containing one million units corresponding to 80 mg of colistimethate (1 mg = 12 500 IU). There is much uncertainty surrounding the penetration of

Table 2
Characteristic of the patients grouped on the base of the route in which colistin was administered[a]

	Intrathecal	Intraventricular
Patients, *n*	8	24
Cases in which topical colistin was the only microbiologically active drug	4/8	4/24
Age, mean ± SD (median; 25th % case; 75th % case; range), years	35 ± 19 (36; 26; 41; 4–68)	39.5 ± 22.1 (34; 24; 56; 4–78)
Children (<5 years old)	1	1
Colistin dosage, mean ± SD (median; 25th % case; 75th % case; range), mg	8 ± 3.3 (10; 6.4; 10; 2.2–12)	13.5 ± 7.3 (18.5; 5; 20; 1.6–20)
Mean duration ± SD (median; 25th % case; 75th % case; range)	14.6 ± 5.7 (13; 11; 21; 6–21)	18.9 ± 7.9 (21; 17; 21; 3–42)
Total amount, mean ± SD (median; 25th % case; 75th % case; range)	118.4 ± 88.4 (78.4; 56; 210; 28.6–210)	249 ± 161 (200; 105; 420; 20–420)
Chemical meningitis or ventriculitis	2/8	1/24
Other side effects	Seizure, 1 case	Unspecified neurological disorder, 1 case
Time for culture sterilization, mean ± SD (median; 25th % case; 75th % case; range)	2.1 ± 1.3 (2; 1; 2.5; 1–5)	6.2 ± 4.8 (4; 3; 6; 2–15)
Death	0/8	5/24
Relapse	1/8	1/24

[a] The term intrathecal was used only if the drug was actually administered into the subarachnoid space, independently of the way the authors reported this in the original papers.

colistin into the CSF, and its use only by intravenous route is not recommended for the treatment of Acinetobacter meningitis.[25]

The manufacturer does not suggest intrathecal administration; however, administration into the CNS is associated with a favorable outcome in a considerable proportion of patients. Falagas et al. have summarized the evidence regarding the intrathecal and intraventricular use of polymyxins in an excellent systematic review of the literature.[28] Treating CNS infections with topical colistin alone will avoid the significant renal toxicity associated with the intravenous route of administration.

Guidelines published by the Infectious Diseases Society of America (IDSA) in 2004, suggest that the intraventricular dosage of colistin should be 10 mg every 24 h.[29] However, it should be mentioned that, to the best of our knowledge, no antimicrobial agent has been approved by the Food and Drug Administration (FDA) for intrathecal or intraventricular use.

It should be remembered that CSF volumes of distribution of neurosurgical patients vary considerably, thus varying the therapeutic dose. EVD rates are widely variable—in those with excessive drainage, topical antibiotics will be diluted more, and conversely if drainage is minimal, higher levels and possibly greater toxicity may result.[13] We, as did most of the authors of the collected papers, clamped the drainage for 1 h to deal with the problem of excessive drainage. Furthermore, attention should be paid to the volume in the drainage pipe; after the antibiotic administration, the drainage tube should be filled with saline solution to avoid that part of the infused drug not reaching the subarachnoid space.

From the analysis of the retrieved cases, data are insufficient to establish whether only colistin through a topical route or a combination of topical colistin and intravenous colistin is more advantageous to treat Acinetobacter meningitis. We believe that the only rationale for adding intravenous colistin would be an attempt to sterilize the possible site of infection or colonization.

Interestingly, Motaouakkil et al. used the combination of intravenous rifampin and topical colistin.[15] Rifampin has an excellent CSF penetration.[30] Colistin and rifampin appeared to be an effective and safe combination therapy for severe human infections due to MDR *A. baumannii*.[31] However, insufficient data exist to recommend this association for the treatment of MDR Acinetobacter meningitis.

Topical administration of colistin is currently withheld as a last treatment option for MDR Acinetobacter meningitis, probably due to the doctor's fear of side effects. In fact, topical colistin was well tolerated, reversible chemical meningitis being the most common form of toxicity reported and irreversible toxicity not reported in any study.

We believe that topical colistin should be initiated without delay. From the analysis of the retrieved papers, data are too scarce to yield a meaningful analysis of shunt management. However, considering the possibility of biofilm-forming strains,[32] shunt removal may be an important adjunct to treatment of post-neurosurgical Acinetobacter meningitis in patients with ventricular shunts.[25]

We think that when feasible, in cases of meningitis or ventriculitis, especially if external devices are implanted, the intraventricular route should be preferred to the intrathecal route, for at least the following two reasons: (1) For a drug administered intrathecally, it is more difficult to obtain a high concentration in the ventricular system; in fact, the CSF circulates from the ventricular system to the cerebellomedullary cistern and then down the spinal cord. (2) From the analysis of the reviewed cases, as shown in Table 2, chemical ventriculitis and meningitis occurred in one case out of 24 patients (4.2%) treated intraventricularly and in two out of eight cases (25%) treated intrathecally.

Data are insufficient to determine whether the strategy of a reduced first dose adopted by many authors, probably to test for tolerability, is meaningful or not. Neither can conclusions be drawn regarding the duration of topical colistin treatment. Even if the CSF sterilization was obtained after fewer than 5 days of therapy in 75% of the reported cases, we think that when possible, the recommendations of IDSA should be followed, and that antimicrobial therapy be continued until CSF culture results remain negative for 10–14 consecutive days before a new CSF shunt (if necessary) is placed.[29]

In conclusion, our case along with the available evidence suggests that topical colistin can be an effective and safe treatment for the management of MDR Acinetobacter meningitis.

Conflict of interest: No conflict of interest to declare.

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