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Case Report

Post-neurosurgical meningitis caused by acinetobacter baumannii: case series and review of the literature

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Abstract: Background: Acinetobacter baumannii (A. baumannii), a gram-negative bacterium, has now become an important hospital pathogen, which causes various serious nosocomial infections worldwide. Bacterial meningitis is a common complication after neurosurgical operation, and the percentage of A. baumannii meningitis is growing, especially the one resisting multiple drugs. Method: We retrospectively reviewed the cases with postoperative A. baumannii meningitis (PABM) in the First Affiliated Hospital of Wenzhou Medical University from January 2013 to October 2014. And we retrieved the PubMed for cases with PABM and reviewed them. Result: Five cases were included in our retrospective study. Two cases with sensitive A. baumannii and one with multidrug-resistant acinetobacter baumannii (MRAB) were cured, and other two with MRAB died. Conclusion: Intraventricular or intrathecal colistin could be a treatment to the MRAB.

Keywords: Acinetobacter baumannii, postoperative meningitis, colistin

Introduction

Acinetobacter baumannii (A. baumannii) is a gram-negative bacillus of the acinetobacter. Infection caused by A. baumannii becomes more and more common in hospital worldwide, due to it possessing multiple mechanisms of drug resistance [1]. It is an opportunistic pathogen that can be detected on human skin and in human tracts connected with the outside world. Thus A. baumannii easily causes serious infection of critical patients, such as the one with pneumonia, septicemia, meningitis, etc. [2, 3].

The patients after craniocerebral operations in neurosurgery have a high risk to suffer from bacterial meningitis caused by A. baumannii and get potentially fatal consequences. The meningitis caused by A. baumannii is well recognized and has been described by many doctors worldwide. Most of case reports about the meningitis were associated with external ventricular drainage (EVD), cerebrospinal fluid (CSF) leaking, or head trauma [4-6]. Here we reported five cases of PABM in the same neurosurgical intensive care Unit.

Materials and methods

We performed a retrospective clinical study of PABM in neurosurgery during the period between 1 January 2013 and 31 October 2014. During this period, A. baumannii was isolated from the CSF of five patients treated at the First Affiliated Hospital of Wenzhou Medical University.

When the patient's symptoms or signs disappeared, clinical cure was considered [5]. Bacteriologic cure was considered when A. baumannii was not found in CSF during therapy for two successive cultures [7]. A patient was considered to be cured for both clinical cure and bacteriologic cure. At the same time, death was considered to be related to meningitis when the patient died during treatment for meningitis with no other obvious explanation for death.

Results

There were five cases of nosocomial A. baumannii meningitis over the study period (four males and one female). All patients received broad-spectrum antibiotics prior to their infections. Three patients were cured and two patients died of the serious meningitis.

Case 1: A 35-year-old man without any medical history was admitted to the hospital because of the thalamus and brainstem hemorrhage breaking into the ventricles. Cerebral arteriography was performed that demonstrated a Moyamoya disease, and two EVDs were implanted into both sides. The right EVD was removed on day 16 and the left one on day 31. On day 30 of hospitalization, his condition worsened, fever appearing (peak 39.7°C) with narcosis. CSF analysis was performed and revealed a WBC count of 1240×10^6/L with 98% polymorphonuclear leukocytes and 1% lymphocytes, a glucose concentration of 1.1 mmol/L, a protein level of 2470 mg/L and chloride of 112 mmol/L. CSF culture yielded A. baumannii just resisting Aztreonam and Ceftriaxone and sensitizing to other antibiotics. Recurrent hydrocephalus was detected, brain CT images showed ventriculomegaly, so another EVD was re-implanted into the right ventricle and an OMMAYA reservoir sac was implanted to left ventricle. 12 days later, the EVD was removed. Linezolid 0.6 g, meropenem 1 g, Ciprofloxacin 100 ml and Fosfomycin 8 g 12 hourly were administrated successively for 12 days. On day 46 and 48 of hospitalization, CSF culture yielded sterile, but functional recovery was poor despite rehabilitation. The patient was discharged on day 53 to a rehabilitation centre and he fully recovered after 2 months in there.

Case 2: A 57-year-old man with a medical history of hypertension was admitted to the neurosurgical intensive care unit (NSICU) because of the thalamus hemorrhage breaking into the ventricles. The patient had another medical history of diabetes. On day 2, an OMMAYA reservoir sac was implanted and tracheotomy was performed. Linezolid and Augmentin were directly applied as prior antibiotics. On day 7 of hospitalization, because of fever (peak 38.4°C), a CSF tap was performed and revealed a WBC count of 360×10^6/L with 98% polymorphonuclear leukocytes and 2% lymphocytes, a glucose concentration of 1.1 mmol/L, a protein level of 2173 mg/L and chloride of 113 mmol/L. Ceftriaxone and Betamipron were added into therapeutic regimen. On day 16, sputum and CSF culture yielded MRAB, which were only sensitive to Tobramycin. So Tobramycin, ceftriaxone, linezolid and minocycline were administrated. On the 15th day of treatment, CSF culture yielded sterile. On day 34 of hospitalization, the patient was discharged.

Case 3: A 5-year-old boy with medulloblastoma required craniotomy in hospital. On day 4 of hospitalization, intracranial tumor resection was performed without an EVD. Because of intracranial pressure increasing, the operation of lumbar continuous drainage of fluid was performed on day 13 and the drainage tube was removed 7 days later. On day 16, because of the hyperpyrexia (peak 39.2°C), CSF analyses revealed a WBC count of 560×10^6/L with 96% polymorphonuclear leukocytes and 4% lymphocytes, a glucose concentration of 2.2 mmol/L, a protein level of 2413 mg/L and chloride of 118 mmol/L. At the same time, CSF and blood culture yielded sensitive A. baumannii. Subsequently, after 3 days of meropenem and linezolid administrated, repeated cerebrospinal fluid cultures were negative. On day 28 of hospitalization, the patient was discharged with improved clinical symptoms.

Case 4: A 41-year-old man was admitted to the NSICU because of subarachnoid hemorrhage (SAH). Cerebral arteriography was performed to demonstrate right vertebral dissecting aneurysm and anterior communicating aneurysms. Endovascular aneurysm and parent artery embolization was performed when he was admitted to hospital immediately. On day 3, the patient underwent a tracheotomy. On day 18, sputum culture yielded A. baumannii. On day 30, ventriculo-peritonal shunt operation was performed. Because of ardent fever (peak 39.5°C), intravenous Tazocin 4.5 g 8 hourly and Meropenem 0.5 g 6 hourly were commenced. On day 40, MRAB was isolated from CSF and EVD, which was only sensitive to Sulfamethoxazole. CSF analysis revealed a WBC count of 41600×10^6/L with 97% polymorphonuclear leukocytes, a glucose concentration of 1.1 mmol/L, a protein level of 3000 mg/L and chloride of 103 mmol/L. Intravenous Sulperazone and Sulfamethoxazole were commenced for 17 days, and intravenous Norvancomycin for 14 days. On day 58 of hospitalization, the patient died from the serious intracranial infection.

Table 1. Published cases of A. baumannii meningitis treated with colistin.

Reference	Age/sex	Dosage	Route	Outcome
Benifla et al., 2004 [16]	49/F	3.2 mg q24 h for 17 days	IVT	Cured
Bukhary et al., 2005 [17]	23/F	10 mg q12 h for 21 days	IVT	Cured
Kasiakou et al., 2005 [18]	28/M	Episode 1: 1.6 mg for 3 weeks; Episode 2: 3.2 mg q24 h for 42 days	IVT	Cured
Berlana et al., 2005 (2 cases) [19]	U	Patient 1: 10 mg q12 h for 8 days; Patient 2: 20 mg q24 h for 10 days	IVT	One cured, one died
Ng et al., 2006 (5 cases) [20]	74/F	5 mg 1st day and10 mg q24 h for 18 days	IVT	Cured
	56/F	5 mg 1st day and10 mg q24 h for 3 days	IVT	Cured
	38/F	5 mg 1st day and10 mg q24 h for 12 days	IVT	Cured
	26/M	5 mg 1st day and 10 mg q24 h for 6 days	IT	Cured
	4/M	1 mg q24 h 1st day, 2 mg q24 h 2nd and 3rd day, then 4 mg q24 h for 13 days	IT	Cured
Al Shirawi et al., 2006 [21]	28/M	3.2 mg q24 h for 28 days	IT	Cured
Motaouakkil et al., 2006 [22]	36/M	5 mg q24 h 1st day, 10 mg q24 h for 21 days	IT	Cured
Ho et al., 2007 (2 episodes) [23]	68/F	Episode 1: 1.6 mg q24 h 1st day, 3.2 mg q24 h 2nd, 4.8 mg q24 h 3rd day, 2.4 mgq 24 h 4th day, then 4.4 mg q48 h for 13 days. Episode 2: 6.4 mg q24 h for 12 days	IT	Cured
Hachimi et al., 2008 [24]	73/M	5 mg q24 h 1st day, 10 mg q24 h for 21 days	IVT	Cured
Pascale et al., 2009 [25]	42/M	75 000 IU every 24 hours for 3 days, 150 000 IU every 24 hours for 22 days	IT	Cured
Antonio Cascio et al., 2010 [4]	36/M	10 mg q24 h for 10 days	IT	Cured
Karaiskos et al., 2013 (6 cases) [6]	60/M	IVT, 40 mg q24 h 1st day, 20 mg q24 h 2nd and 3rd days and 10 mg q48 h for 12 days. IT, 20 mg q48 h for 4 days	IVT, IT	Cured
	26/M	40 mg q24 h for 6 days, 20 mg q48 h for 15 days	IVT	Cured
	53/M	IVT, 40 mg q24 h 1st day, 20 mg q24 h 2nd and 3rd days, 20 mg q48 h for 8 days. IT, 20 mg q48 h for 10 days	IVT, IT	Cured
	44/F	IVT, 40 mg 1st day, 10 mg q24 h for 8 days. IT, 10 mg q48 h for 6 days	IVT, IT	Cured
	60/M	40 mg 1st day, 10 mg q24 h for 14 days	IVT	Cured
	62/F	40 mg 1st day, 30 mg 2nd day, 10 mg q24 h for 3 days, 10 mg q48 h for 7 days	IVT	Cured

M, male; F, female; U, unknown; IVT, intraventricular; IT, intrathecal; IU, international units.

Case 5: A 65-year-old woman with a medical history of hypertension was admitted to the NSICU because of right basal ganglia hemorrhage. The patient had a medical history of diabetes. On the day of admission, an OMMAYA reservoir sac was implanted to left frontal and an EVD removed 8 days later to right ventricle. On day 4, the patient underwent a tracheotomy. After intracranial operation, sulperazone was commenced to prevent infection for 20 days. On day 23, the OMMAYA was removed. On day 24 of hospitalization, the patient presented with fever (peak 39.0°C) accompanied with altered mental status. CSF analyses revealed a WBC count of 1880×10^6/L with 95% polymorphonuclear leukocytes and 2% lymphocytes, a glucose concentration of 1.1 mmol/L, a protein level of 2158 mg/L and chloride of 109 mmol/L. CSF culture yielded MRAB resisting to β-lactam, quinolones and sulfonamides antibiotics. And we administrated tobramycin, imipenem and tazocin for 5 days. Then CSF culture yielded not only MRAB, also klebsiella pneumonia and pseudomonas aeruginosa. Thus, vancomycin, tobramycin, fosfomycin, cefoperazone and meropenem were successive and combined to treat the meningitis for 23 days. However, repeated CSF cultures were all positive during this period with symptoms getting worse and signs becoming more obvious. The patient died from serious intracranial infection on day 53 of hospitalization.

Literature review and discussion

Intracranial infections including ventriculitis and meningitis caused by A. baumannii in the neurosurgery setting have been challenging situations [8, 9]. The percentage of intracranial infection caused by A. baumannii in postoperative infection continuously increased in recent years.

Meningitis developing within 3 months after neurosurgery is defined as "post-neurosurgical meningitis" [10]. Post-neurosurgical A. baumannii meningitis was diagnosed after meeting following criteria: (1) A. baumannii was cultured from the cerebrospinal fluid (CSF) of a patient; (2) CSF changed in white cells increasing, protein elevating, glucose decreasing, etc.; (3) the patient had at least one symptom or sign without other apparent causes: fever (≥38°C), headache, vomiting, confusion, irritability or meningeal irritation; (4) the patient underwent an operation procedure of neurosurgery within 3 months [7]. A patient was considered to be cured when both symptoms and signs disappeared and the CSF was sterile.

In this report, we reported 5 cases with infection of A. baumannii after craniocerebral operation, and 3 of them were infected by MRAB. Two patients with MRAB died during treatment. Thus, the mortality of postoperative meningitis with MRAB was high. Reducing the death rates and improving cure rates was very important and urgent clinically.

There were various antibiotics clinically used to treat the infection. Carbapenems used to be the empirical drugs for choice [11]. However, more than 30% of A. baumannii strains were resistant to at least three kinds of antibiotics in many general hospitals. And MRAB generally resisting to fluoroquinolones and carbapenems gradually increased in recent years [12]. At present, more and more reports about postoperative infections with A. baumannii in neurosurgery cured by intraventricular (IVT) or intrathecal (IT) colistin were published in various journals around the world.

Colistin was introduced in clinical use from 1950s, and abrogated in 1980s due to serious renal toxicity and neurovirulence. However, colistin was found to be effective for the multidrug resistance (MDR) and extensive drug resistance (XDR) Gram-negative bacteria, including the Acinetobacter [9, 13].

Maartens et al. compared colistin with carbapenems and tobramycin, and found that colistin was still effective for A. baumannii in resistance of other antibiotics, and no difference in renal toxicity was revealed among these antibiotics [14]. Rolain et al. indicated that colistin worked through modifying the negative charges of outer membrane's in Gram-negative bacteria [15].

We retrieved the cases of PABM treated with colistin in PubMed, and reviewed them as **Table 1**. And we found that IVT or IT colistin was one optional way to treat the postoperative meningitis with sensitive or resistant A. baumannii.

Disclosure of conflict of interest

None.

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