Meningitis Caused by Multidrug Resistant *Acinetobacter baumannii*: an Emerging Threat for Neurosurgical Patients

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Abstract

Acinetobacter baumannii (A. baumannii) infection is a common clinical problem in critically ill patients, but it's still rare after neuro-surgical operation. We reported two cases of *A. baumannii* meningitis after neuro-srugical operation. Both two cases highlight the importance of repairing all dural tears and *A. baumannii* becomes an emerging threat for post-neurosurgical patients. The urgent need for increasing the awareness *A. baumannii* meningitis among the neuro-surgical wards cannot be over emphasized. (J Intern Med Taiwan 2014; 25: 436-445)

Key Words: *Acinetobacter baumannii*, Multidrug resistant, Meningitis, Neuro-surgical patient

Background

Acinetobacter baumannii (A. baumannii) has emerged as a significant nosocomial pathogen in hospitalized patients worldwide[1-2]. Although infections with *Acinetobacter* spp. occur infrequently, the incidence continues to increase. *Acinetobacter* spp. can cause a multitude of infections, including meningitis[3]. Mortality rates from 12% to 70% were reported from studies that evaluated Gram-negative bacillary meningitis[4,5]. Some authors had described the outbreaks of nosocomial postoperatively meningitis[6,7]. Also, *A. baumanii* meningitis after durotomy and after ventriculoperitoneal shunt insertion was reported[8,9]. After reviewing the literatures, the acinetobacter meningitis after neuro-surgical operation is actually not so rare. Also, multidrug resistance is a relatively common occurrence among these organisms, and the definition of multidrug resistance *A. baumanii* is according to Magiorakos's report in this study[10]. *A. baumannii* meningitis is a serious condition that yields high rates of mortality and morbidity[11-12].

In central Taiwan as well as the world, there was the emerging multidrug resistant *A. baumannii* meningitis[11]. Here, we reported first two cases of *A. baumannii* meningitis after neuro-surgical operation in our institute.

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Case one presentation

A 39 year-old healthy male visited to our emergency department because of accident trauma, and he presented with four limbs paralysis, and sensory loss. The cervical spinal injury was suspected, and he was admitted to surgical intensive care unit. Upon admission, he was afebrile, with a blood pressure of 120/80 mmHg. The magnetic resonance imaging (MRI) of the spine showed that abnormal bony alignment of the lower cervical spine due to grade II traumatic spondylolisthesis, C6 over C7 level, the mal-alignment bony structure and posterior disks protrusion cause severe C6/7 level central canal narrowing and deformity; the resultant ventral thecal sac and cord compression are also noted; there is focal high signal change seen on the T2WI in the C6/7 level; acute traumatic cord edematous change is compatible. The C6-7 fracture and subluxation with cord injury was impressed. The C6-7 dissectomy and anterior fusion with autollogous bone graft was performed on 4th admission day. His condition was stationary but he depended the ventilator because of respiratory failure. Fever occurred since 30th admission day, but the surgical site seemed no sign of local inflammation, urinalysis was normal, and his chest film did not have pneumonic patch. No obvious infectious focus was disclosed, lumbar puncture was performed to exclude the meningitis. The cerebral spinal fluid (CSF) examination revealed white cell count: 1120 /cmm, N/L: 83/15; protein 192 mg/dL (normal range 15-45 mg/dL); glucose: 2 mg/dL (normal range: 40-70 mg/dL). CNS infection was suspected, and the vancomycin 1000mg every 12 hours plus ceftazidime 2000mg every 8 hours was prescribed. *A. baumannii* was isolated on CSF culture three days later. The *A. baumannii* was identified with an API 20NE strip (BioMérieux, Durham, N.C.). We performed the susceptibility test of that *A. baumannii* stain. The results were only susceptible to carbapenem (imipenem-cilastatin and meropenem); and resistant to cefmetazole, cefotaxime, ceftazidime, cefepime, cefpirome, gentamicin, amikacin, ampicillin, amoxicillin-clavulanate, piperacillin, ciprofloxacin, and trimethoprim-sulfamethoxazole. We exchange to the imipenem-cilastatin 500mg every 6 hours. During the hospitalization, the serial microbiological studies showed no more *A. baumannii* growth in his follow-up sample. He received the 21-days imipenem-cilastatin. The serial follow-up laboratory data normalized. He was discharged on 63th admission days.

Case two presentation

A 32 year-old female presented with blurred vision progressively. She denied any discomforts before. She visited the ophthalmologist of our institute. The visual accurate was 0.2 (left eye), and 0.6 (right eye), but significant hemi-agnosia was disclosed on her visual filed examination. Optic neuropathy was suspected, and the brain MRI was arranged. The contrast enhanced and non-contrast MRI study of the brain showed the followings: One large tumor with intermediate T1 signal and high T2 signal, involving the sella turcica and suprasellar cistern. There is large cystic/necrotic part within the tumor. After contrast medium administration, the tumor shows strong enhancement. The tumor size is about 3.7 x 2.6 x 2.6 cm. The tumor compresses the optic chiasm upward. There is no evidence of brain infarction. The finding is consistent with pituitary macroadenoma. The trans-sphenoidal approach (left nostril) with partial removal of the tumor was arranged the 2nd admission day. The pathological results reported that the adenoma of the pituitary gland. On 1st post-operation day, she complained of mild rhinorrhea, vomiting, and dizziness. Brudzinski's sign and Kernig's sign were positive. The CSF examination revealed white cell count: 3220/cmm, N/L: 88/9; protein 999 mg/dL (normal range 15-45 mg/dL); glucose: 1 mg/dL (normal range:

40-70 mg/dL). The CSF leakage with infection was suspected. The vancomycin 1000mg every 12 hours plus ceftazidime 2000mg every 8 hours was prescribed. *A. baumannii* was isolated on CSF culture two days later. The *A. baumannii* was identified with an API 20NE strip (BioMérieux, Durham, N.C.). We performed the susceptibility test of that *A. baumannii* stain. The results were only susceptible to carbepenem (imipenem-cilastatin and meropenem); and resistant to cefmetazole, cefotaxime, ceftazidime, cefepime, cefpirome,gentamicin, amikacin, ampicillin, amoxicillin-clavulanate, piperacillin, ciprofloxacin, and trimethoprim-sulfamethoxazole. We exchange to the imipenem-cilastatin 500 mg every 6 hours accordingly. During the hospitalization, the serial microbiological studies showed no more *A. baumannii* growth in her follow-up samples. She received the 26-days imipenem-cilastatin. The serial follow-up laboratory data normalized. She was discharged on 35th hospitalized days. She was follow-up at outpatient department, and she recovered well.

Discussion

We reported first two cases of *A. baumannii* meningitis after neuro-surgical operation in our institute. Because *A. baumannii* meningitis has been rarely suggested as a cause of central nervous system infection, we conducted an evidence-based literature review with the keywords *"Acinetobacter baumannii"*, "meningitis", "operation", "central nervous system infection", "neuro-surgical operation", and "resistant". Only post-neurosurgical procedure and *A. baumannii* meningitis were enrolled. Fourty-nine patients with post-neurosurgical *A. baumannii* meningitis were reported worldwide (Table)[13-35]. The clinical manifestations of *A. baumannii* meningitis were variable. The crude mortality rate of *A. baumannii* bacteremia was 10.5% at our institute[11], but there is no data for mortality rate of *A. baumannii* meningitis at

Table 1. Literature review for predisposing factors and treatment of post-neurosurgical *Acinetobacter baumannii* Meningitis

Variable	Range
Overall patients numbers	49
Age, median (range)	38 (2 mo-74 years)
Sex, male (%)	26/49(53.1%)
Underlying disease (s) (%)	
SAH	18(36.7%)
HT	12(24.5%)
HC	10(20.4%)
MNGoma	6(12.2%)
Aneurysm	6(12.2%)
ICH	3(6.1%)
Choroid plexus papilloma	2(4.1%)
Medulloblastoma	1(2%)
Ependymoma	1(2%)
Artery dissection	1(2%)
BI	1(2%)
HTN	1(2%)
Subdural haematoma	1(2%)
Haemangioblastoma	1(2%)
Predisposing factors (%)	
EVD	40(81.6%)
VP shunt	5(10.2%)
Post-neurosurgical procedure[1]	4(8.2%)
ELD	4(8.2%)
Plastic meningeal prosthesis	2(4.1%)
Ommaya reservoir	1(2%)
Coil replacement	1(2%)
LP	1(2%)
Aneurysm clips	1(2%)
FATD, median(range), Days	15(1-82)
Final regimen (%)	
CMS monotherapy	30(61.2%)
CMS based combination	15(30.6%)
CAR[2] monotherapy	2(4.1%)
CAR[2] based combination therapy	7(14.3%)

Table 1. Continued

Variable	Range
DOEA, median(range), Days	27 (21-56)
Outcome, survival (%)	46/49(93.9%)

Notes
[1]Post-neurosurgical procedure included coil replacement, trans-sphenoidal biopsy.
[2]Carbepenem included meropenem and imipenem-cilastatin
The table were summarized from references[13-35].
Abbreviation: BI: Brain infarction; CAR: carbepenem; CMS, colistin methanesulfonate; DOEA, duration of effective antibiotics; ELD, external lumbar drain; EVD, external ventricular drainage; FATD: from admission to diagnosis; HT: head trauma; HTN, hypertension; ICH, intracerebral haemorrhage; LP, lumbar puncture; MNGoma: Meningioma; SAH, subarachnoid haemorrhage; VP, ventriculoperitoneal shunt.

our institute because of few cases. In last decade, Baltas's study for the post-traumatic meningitis reported 12 of 860 patients deveoped the complication after traumatic injury, and the infecting agents were Gram-negative bacilli in six patients (*Escherichia coli* in two, *Klebsiella pneumoniae* in two, and *Acinetobacter anitratus* in two)[36]. Since the decade, a remarkable increase in the incidence of nosocomial Gram-negative infections, especially *A. baumannii*, had been observed. These pathogens represented a substantial problem in clinical practice because of both susceptible to the immunocompromized hosts and the high resistance profile of most commonly used antibiotics[37]. These current two *A. baumannii* meningitis after neuro-surgical operation were testimony.

To study the possible predisposing factors, we summarized the literatures at Table and Appendix. The predisposing factors included external ventricular drain (44 patients), ventriculoperitoneal shunt (5 patients), plastic meningeal prosthesis (2 patients), Post-neurosurgical procedure (2 patients), Ommaya reservoir (1 patient), coil replacement (1 patient), and trans-sphenoidal biposy (1 patietn). Ninty-three percent among 48 patients (Fourty-six episodes) were survived. Here we reported two cases with *A. baumannii* meningitis post neuro-surgical operation, and they were survival. The possible source of those two cases with *A. baumannii* meningitis may be from either the device or the invasive procedures, or environment or the vicious cycle from the healthcare staff. And the *A. baumannii* went into the meningeal through the defect of the dural. Although many cases had been reported, it needed the further examination to prove this hypothesis.

One of the most striking features of acinetobacter species is their extraordinary ability to develop multiple resistance mechanisms against major antibiotic classes. In acinetobacter meningitis, the major problems confronting clinicians in intensive care units are related to the severity of acinetobacter nosocomial infections and to resistance to major antibiotic classes of these organisms[38]. Both of those two *A. baumannii* were multidrug-resistant strains, but we treated successfully with carbapenem. In order to study the treatment, we summarzed the literatures at Table. Colistin had been widely prescribed to treat multi-resistant *A. baumannii* meningitis in nowadays. Concerning the therapy of drug-resistant *A. baumannii* meningitis, Karaiskos reported intraventricular and intrathecal colistin represents the last resort treatment of MDR *A. baumannii* ventriculitis and meningitis, offering a unique, rather safe and successful mode of therapy[3]. Lu suggested that early initiation of appropriate antibiotic therapy is needed for those adult post-neurosurgical patients in this potentially fatal disease[39]. Those two cases with *A. baumannii* meningitis were successfully treated with intravenous carbapenem.

A. baumannii infection is a common clinical problem in critically ill patients, but it's still rare and severe after neuro-surgical operation. We reported two cases of *A. baumannii* meningitis after neurosrugical operation. The urgent need for increasing the awareness the *A. baumannii* meningitis among the neuro-surgical wards cannot be over emphasized.

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多重抗藥性包氏不動桿菌腦膜炎：神經外科病患術後的危機

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摘　要

包氏不動桿菌腦膜炎是在神經外科病患術後重要的感染症，我們描述了兩個案例。兩例都凸顯出神經外科病患手術時，腦膜會被剝開然後縫合，包氏不動桿菌趁虛而入感染為腦膜炎。在神經外科需要提防神經外科病患術後的包氏不動桿菌腦膜炎。

Appendix: Literature review for predisposing factors and treatment of post-neurosurgical *Acinetobacter baumannii* Meningitis

	Authors, year, country [Reference]	Age (years)/sex	Underlying disease(s)	Predisposing factors	FATD (Days)	Antimicrobial susceptibilitiesa	Final regimen	DOEA (Days)	CO
1	Fernandez- Viladrich et al., 1999, Spain[13]	16/M	Haemangioblastoma of 4th ventricle	EVD	16	Susceptible to CST and SUL; intermediate to TOB and IPM	TOB IV and CMS IV	NR	Cure
2	Fernandez- Viladrich et al., 1999, Spain[13]	34/F	SAH/HC	EVD	7	Susceptible to CST; intermediate to TOB	TOB IV and CMS IV	NR	Cure
3	Vasen et al., 2000, Argentina [14]	41/F	SAH/HC	EVD, aneurysm clips	8	Susceptible to CST	CMS IT	NR	Cure
4	Benifla et al., 2004, Israel [15]	49/F	Recurrent MNGoma, recurrent episodes of MNG	VP shunt externalised	82	Susceptible to CST and SUL	SAM and VAN IV, CMS IV	NR	Cure
5	Glesson T, et al, 2005, USA[15]	37/F	NR	Post-neurosurgical procedure	7	susceptibility to IPM, SAM	MEM,AMK, RIF, IV	21	Cure
6	Sueke et al., 2005, UK [16]	38/F	Sepsis, HC, HT	VP shunt externalised and removed, EVD	35	Susceptible to CST	CMS IV, CMS IT	28	Cure
7	Bukhary et al., 2005, Saudi Arabia [17]	23/F	MNGoma	EVD	13	Susceptible to CST	CMS IV	NR	Cure
8	Kasiakou et al., 2005, Greece [18]	28/M	HT, recurrent MNG	Plastic meningeal prosthesis, EVD	1st episode, 12	Susceptible to CST and AMK; intermediate to IPM and MEM	CMS, AMK and TEC, IV	21	Cure
9	Kasiakou et al., 2005, Greece (2nd episodes) [18]	28/M	HT, recurrent MNG	Plastic meningeal prosthesis, EVD	2nd episode, 69	Susceptible to CST and AMK; intermediate to IPM and MEM	CMS, AMK and TEC, IV	42	Cure
10	Charra et al., 2006, Morocco [19]	36/M	HT	EVD	8	Susceptible to CST	CMS IT	NR	Cure
11	Ng et al., 2006, Australia [20]	74/F	SAH/HC	EVD	8	MDR	CMS IV	NR	Cure
12	Ng et al., 2006, Australia[20]	56/F	SAH/HC	EVD	11	MDR	CMS IV	NR	Cure
13	Ng et al., 2006, Australia[20]	38/F	HT	EVD	40	MDR	CMS and AMK IV, CMS IV	NR	Cure
14	Ng et al., 2006, Australia[20]	26/M	ICH	EVD	13	MDR	CMS and AMK IV, CMS IT	NR	Cure
15	Ng et al., 2006, Australia[20]	4/M	Medulloblastoma	Post-neurosurgical procedure	10	MDR	CMS IT	NR	Cure

	Authors, year, country [Reference]	Age (years)/sex	Underlying disease(s)	Predisposing factors	FATD (Days)	Antimicrobial susceptibilitiesa	Final regimen	DOEA (Days)	CO
16	Al Shirawi et al., 2006, Saudi Arabia [21]	28/M	HT	EVD	28	Susceptible to CST	CMS IV	NR	Cure
17	Paramythiotou et al., 2007, Greece [22]	24/F	Ruptured aneurysm	EVD with Ommaya reservoir	7	Susceptible to CST	CMS IV	26	Cure
18	Paramythiotou et al., 2007, Greece[22]	20/M	HT	VP shunt	8	Susceptible to CST	CMS IV	20	Cure
19	Ho et al., 2007, Taiwan [23]	61/F	Recurrent MNGoma	ELD	34	Resistant to CB, FQ, AM and ATM	CMS IT and CMS IV	56	Cure
20	Lee et al., 2008, Taiwan [24]	78/M	SAH / HC	EVD	15	Susceptible to SUL and CST	CMS, MEM and SUL IV, CMS IV	NR	Cure
21	Hachimi et al., 2008, Morocco [25]	73/M	SAH / HC	EVD	8	Susceptible to AMK and CST	CMS IVR, AMK IV	NR	Cure
22	Dalgic et al.,2009. Turkey[26]	2 months/F	SAH, HC, recurrent MNG	EVD	70	Susceptible to CST	CMS IV	NR	Cure
23	López-Alvarez et al., 2009,Spain[27]	36/M	SAH, HC	EVD	26	Susceptible to CST	CMS IVR	NR	Cure
24	López-Alvarez et al., 2009,Spain[27]	57/F	SAH, HC	EVD, coil replacement	15	Susceptible to CST	CMS IV	NR	Cure
25	López-Alvarez et al., 2009,Spain[27]	43/F	SAH	ELD	15	Susceptible to CST	CMS IV	NR	Cure
26	Cascio , et al,. 2010, Italy[28]	36/M	HT	EVD	3	Susceptible to CST	CMS , IT	NR	Cure
27	Khawcharoenporn et al., 2010, Thailand[29]	72/M	HT	EVD	8	Resistant to CEP, FQ, AM, ATM, SUL,CB	CMS IT and CMS IV	NR	Death
28	Khawcharoenporn et al., 2010, Thailand[29]	46/M	MNGoma	EVD	30	Resistant to CEP, FQ, AM, ATM, SUL, CB	CMS IT and CMS IV	NR	Death
29	Khawcharoenporn et al., 2010, Thailand[29]	33/F	SAH	EVD	11	Resistant to CEP, FQ, AM, ATM, SUL, CB	CMS IT and CMS IV	NR	Cure
30	Khawcharoenporn et al., 2010, Thailand[29]	64/M	Medulloblastoma	EVD	28	Resistant to CEP, FQ, AM, ATM, SUL, CB	CMS IT and CMS IV	NR	Cure
31	Khawcharoenporn et al., 2010, Thailand[29]	22/M	HT	EVD	4	Resistant to CEP, FQ, AM, ATM, SUL, CB	CMS IT and CMS IV	NR	Cure

	Authors, year, country [Reference]	Age (years)/sex	Underlying disease(s)	Predisposing factors	FATD (Days)	Antimicrobial susceptibilitiesa	Final regimen	DOEA (Days)	CO
32	Khawcharoenporn et al., 2010, Thailand[29]	41/F	SAH	EVD	7	Resistant to CEP, FQ, AM, ATM, SUL, CB	CMS IT and CMS IV	NR	Cure
33	Khawcharoenporn et al., 2010, Thailand[29]	32/F	SAH	EVD	15	Resistant to CEP, FQ, AM, ATM, SUL, CB	CMS IT and CMS IV	NR	Cure
34	De Pascale et al., 2010, Italy[30]	42/M	Ependymoma 4th ventricle, HC	EVD	17	Susceptible to AM, TGC and CST (MIC < 0.5 μg/mL)	CMS, IV	30	Cure
35	Özdemir et al., 2010, Turkey[31]	3/F	Choroid plexus papilloma	ELD, followed by EVD	7	Susceptible to CST	MEM, SAM, AMK, CMS IV; RIF PO	35	Cure
36	Kim et al.,2011, Korea[32]	37/M	SAH	ELD, EVD, and LP	22	Resistant to CB, AM and FQ	CMS IV; RIF PO	NR	Cure
37	Patel et al., 2011, USA[33]	38/F	Artery dissection, CVA	EVD	1	Susceptible to TOB, TGC and CST	VAN, TGC, CMS, RIF IV; TOB IT	51	Cure
38	Wang et al., 2012, Taiwan[34]	31/M	HT,ICH	EVD	61	MDR	IPM, CMS, IV	55	Cure
39	Wang et al., 2012, Taiwan[34]	70/F	BI	VP shunt	55	MDR	IPM, SUL, CMS, IV	43	Death
40	Wang et al., 2012, Taiwan[34]	60/M	ICH	VP shunt	46	MDR	MEM, CMS, IV	37	Cure
41	Wang et al., 2012, Taiwan[34]	15/M	HC, HTN	EVD	74	MDR	MEM, CMS, IV	24	Cure
42	Karaiskos et al., 2013, Greece[35]	60/M	SAH, aneurysm	EVD	12	Susceptible to TGC and CST;	CMS, IV	21	Cure
43	Karaiskos et al., 2013, Greece[35]	26/M	HT, subdural haematoma	EVD	11	Susceptible to TGC and CST	CMS, IV	21	Cure
44	Karaiskos et al., 2013, Greece[35]	53/M	SAH, aneurysm	EVD	15	Susceptible to TGC and CST;	CMS	21	Cure
45	Karaiskos et al., 2013, Greece[35]	44/F	SAH, AVM	EVD	6	Susceptible to GEN and CST	CMS, IV	30	Cure
46	Karaiskos et al., 2013, Greece[35]	60/M	SAH, aneurysm	EVD	27	Susceptible to AMK and CST	CMS, IV	30	Cure.

	Authors, year, country [Reference]	Age (years)/sex	Underlying disease(s)	Predisposing factors	FATD (Days)	Antimicrobial susceptibilitiesa	Final regimen	DOEA (Days)	CO
47	Karaiskos et al., 2013, Greece[35]	62/F	SAH, aneurysm	EVD	77	Susceptible to TOB and CST	CMS, IV	21	Cure
48	This study	39/M	HT	EVD	30	susceptible to IPM	IPM, IV	21	Cure
49	This study	32/F	Choroid plexus papilloma	trans-sphenoidal biposy	2	susceptible to IPM	IPM, IV	26	Cure

Abbreviation : AM, aminoglycoside; AMK, amikacin; ATM, aztreonam; AVM, arteriovenous malformation; BI: Brain infarction; CAR: carbepenem; CAZ: ceftazidime; CB, carbapenem; CEP, cephalosporin; CIP, ciprofloxacin; CMS, colistin methanesulfonate; CNET, craniectomy; CNS, central nervous system; CNT, craniotomy; CO: clinical Outcome; CRO: ceftriaxone; CSF, cerebrospinal fluid; CST: colistin; CTX, cefotaxime; DOEA, duration of effective antibiotics; ELD, external lumbar drain; EVD, external ventricular drainage; F, female; FATD: from admission to diagnosis ; FQ, fluoroquinolone; GEN, gentamicin; HC, hydrocephalus; HT: head trauma; HTN, hypertension; ICH, intracerebral haemorrhage; IPM, imipenem-cilastatin; ITH/IVT, intrathecal / intraventricular; IV, intravenous; LP, lumbar puncture; M, male; MDR, multidrug-resistant; MDRAB, multidrug-resistant *Acinetobacter baumannii;* MEM, meropenem; MET, metronidazole; MIN, minocycline; MNG: meningitis; MNGoma:Meningioma; NR, not reported; PCN, penicillins; PO, per os; RIF, rifampicin; SAH, subarachnoid haemorrhage; SAM, ampicillin/sulbactam; SUL, sulbactam; TEC, teicoplanin; TET, tetracycline; TGC, tigecycline; TOB, tobramycin; TR, tumor resection; VAN, vancomycin; VP, ventriculoperitoneal shunt