Case Report

# Management of Intracranial Ventriculitis caused by Multidrug Resistant Acinetobacter Baumannii: Case Report and Literature Review

**K Simfukwe, Y Zhou, G Han,[1] L Wang, J Liu[3]**

*[1]Department of Neurosurgery Second Military Medical University, Shanghai Changhai hospital, Shanghai 200433, China*

*[2]Department of Neurosurgery, Stroke center, Shanghai Changhai hospital, Shanghai 200433, China*

*[3]Department of Neurosurgery, Second Military Medical University, Department of Health Statistics, Shanghai Changhai hospital, Shanghai 200433, China*

## ABSTRACT

***Background:*** We report a case of a male patient in our hospital who developed associated multidrug-resistant Acinetobacter baumanii (MDRAB) intracrainial ventriculitis and treated using intraventricular (IVT)plus intrathecal(IT) colistin.

***Objective:*** The purpose of our case report is to show case the effectiveness and safety of using intraventricular (IVT) plus intrathecal(IT) colistin in the management of potentially fatal MDRAB associated intracrainial ventriculitis.

***Materials and methods*:** Patient was diagnosed with MDRAB after developing associated symptoms and conducting cerebral spinal fluid(CSF) culture and sensitivity analysis. Colistin 250,000 IU once daily administered via intraventricular plus intrathecal routes for 14 days was prescribed.

***Result*:** Cerebrospinal fluid was collected on the 14th day post commencement of colistin and sterilization was attained.

***Conclusion*:** Colistin is a potentially effective and safe therapy for the treatment of MDRAB intracrainial ventriculitis.

## INTRODUCTION

Neurosurgery patients who after cranial-cerebral procedures have a high risk of suffering from intracrainial ventriculitis caused by *Acinetobacter baumannii* (AB) and get potentially fatal consequence.[1] Nosocomial intracrainial ventriculitis caused by AB has a high rate of mortality due to limited penetration of antibiotics through the blood–brain–barrier (BBB). Literature review report a high mortality rate ranging from 71.4% to 72.7% in neurosurgical patients with AB associated intracrainial ventriculitis.[2] In a separate study by Chen *et al*, in which 13 patients had a carbapenem-resistant isolate, mortality from AB meningitis was 30% (four of 13 patients died) compared with 29.4% (20 of 68 patients) from other causes of Gram-negative meningitis.[3] Timely recognition and effective treatment of intracranial ventriculitis caused by AB, has been of concern due to high motility rates. In this case report, we document a case of a patient with intracranial ventriculits secondary to nosocomial AB who was timely diagnosed and effectively treated using intraventricular and intratheacal colistin.

**Corresponding author**:
Dr. Keith Simfukwe
Second Military Medical University,
Department of Neurosurgery,
No.168 Changhai Road, Yangpu District,
Shanghai, China, 200433

***Keywords:*** Acinetobacter baumannii, colistin, ventriculitis, intraventricular, intrathecal.

## CASE REPORT

We report a case of a male adult patient who presented with a history of unconsciousness after being involved in a road traffic accident (RTA). Neurosurgical assessment showed a Glasgow Coma Score (G.C.S) of 10/15; pupils were 2mm in size and reacting sluggishly to light. Radiological examination showed a left frontal-temporal-occipital acute subdural hematoma with some midline shift to the right, left parietal epidural hematoma, multiple brain contusion and multiple scalp fractures (Image 1). An emergency left temporal craniectomy was performed. The patient was later admitted in the neurosurgical intensive care unit. Poor wound healing accompanied with cerebral spinal fluid leakage from the incision scar developed ten (10) days after the operation was performed. The patient became febrile with the hyperpyrexia peak at 39c and lethargic. Blood samples from central venous catheter and arterial line, including tracheal aspirate, bronchial alveolar lavage, and urine spacemen's were collected for analysis in our laboratory. The specimen results were found to be inappreciable. While awaiting results for CSF culture and sensitivity, the patient was empirically started on vancomycin plus meropenum. However, the general condition of the patient got worse with fluctuating high grade fevers. A repeat Computer Tomography (CT) scan was conducted. The CT scan images reviled the patient developed communicating hydrocephalus with severe cerebral oedema (image 2). The patient underwent repeat surgery and ventricular drainages were placed. The CSF was turbid (Image 3) and had neutrophil pleocytosis, yielded multidrug resistant Acinetobacter baumannii (MDRAB). MDRAB was resistant to all the antibiotics examined in the laboratory by disk diffusion susceptibility test, including carbapenems, cephalosporins, fluoroquinolones, aminoglycosides, and aztreonam. It was however sensitive only to colistin.

Once the organism was identified, parenteral therapy was discontinued and intrathecal (IT) plus intraventricular (IVT) colistin was commenced. The intraventricular colistin was given via an external ventricular drain (EVD), which was clamped for 1 h and released. Intrathecal colistin was given via lumbar puncture. An intraventricular and intrathecal dose 250,000 IU daily once daily for 14 days. The patient became afebrile at 72 h after the beginning of intrathecal plus intraventricular colistrin. CSF cultures performed daily became negative after 5 days of intrathecal therapy. On day 10, CSF culture

**Image 1**

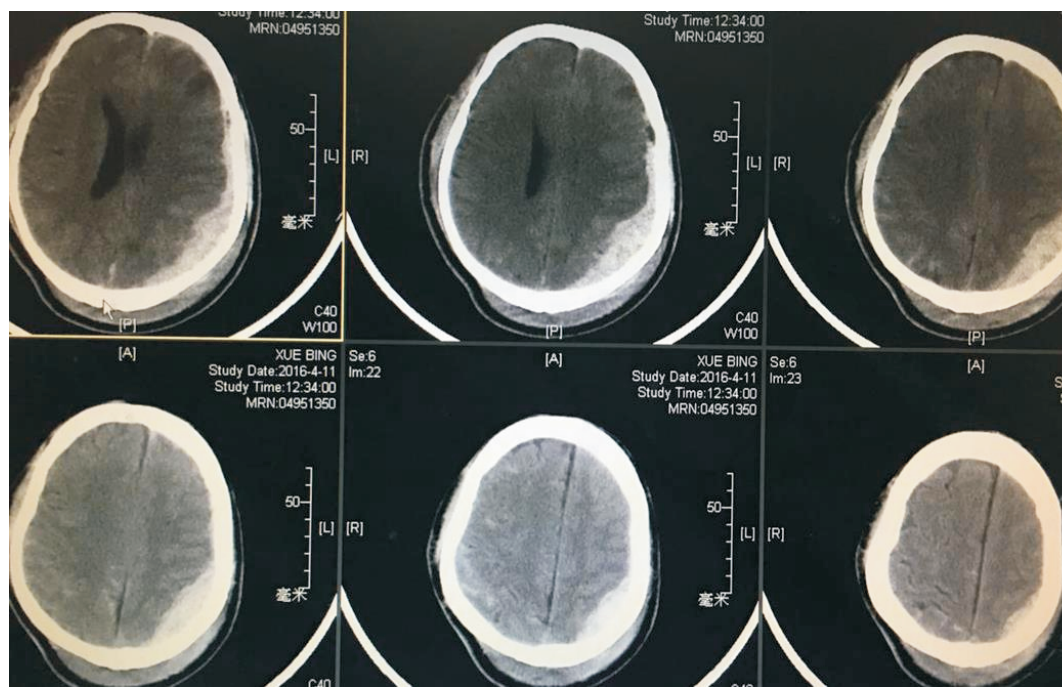

**Image 2**

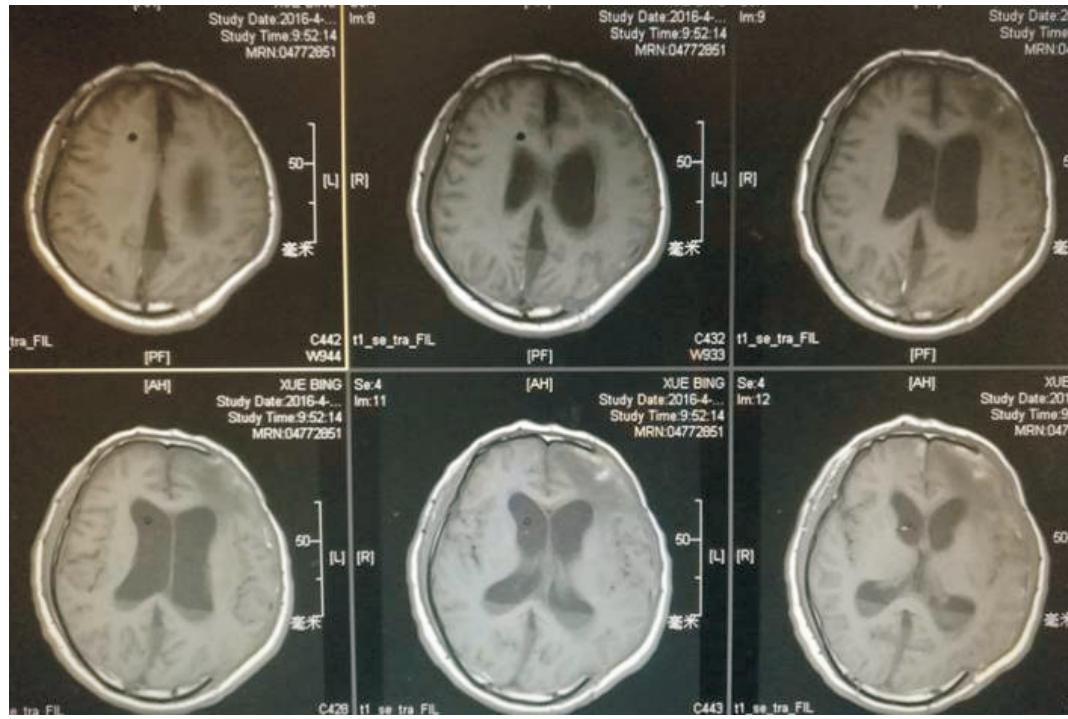


**Image 3**

continued to be sterile, the CSF WBC count had further decreased and hence the therapy stopped on day 14. At discharge, the patient adequately obeyed command, conversed normally and opened eyes spontaneously. No complications or side effects were observed during the treatment. Renal functions were normal.

PubMed data base was used to examine the various relevant published cases from the period 2000 January to 2016. Key terms used were polymyxins OR plomyxin OR colistin AND meningitis OR ventriculitis OR intrathecal OR intrathecal ventriculitis OR meningitis AND acinetobacter AND "2000"[CDAT]: "3000"[CDAT].

**Table 1. Literature review of successfully treated MDR AB patients**

| Auther year country | age | Primary diagnosis | External device | Aceneto bacter baumanii | Initial drug used | Finial regimen | Dosage of intrathecal colistin | toxicity | outcome |
|---|---|---|---|---|---|---|---|---|---|
| Schiaroli et al 2015[4] | M/71 | Oligodendroglima, CSF rhinorrhea | EVD | MDR | Vancoycin 750mg, imipenum iv 500mg | Colistrin 4.5IU,over 30 BID, rifampicin 600mg<br>Teicoplanin 600mg | Colistrin 4.5IU,over 30 BID, rifampicin 600mg Teicoplanin 600mg | non | cured |
| Karaiskos et al 2013[3] | M/60 | SAH,aneurysm | EVD | MDR | Colistrin IVT, 40mg q24h 1st day,20mg q24h and 10mg ,q48h fo r 12 days, ITH 20mg q48h for 4 da y | colistrin | Loading dose 3 480mg followed by 360mg q12h | Non | cured |
| | M/26 | SDH | EVD | MDR | Colistrin,IVT,40mg,q24h for 6 days,20mg q48 | colistrin | Loading dose 3 480mg followed by 360mg q12h | non | cured |
| | M/56 | SAH, aneurysm meningitis | EVD | MDR | Colistrin IVT 40mg q24 1st day,20mg q24h | Loading dose 480mg followed by 360 mg | | non | cured |
| | M/44 | SAH,AVM Ventriculitis | EVD | MDR | Colistrin IVT, 40mg 1st day,10mg q24h or 8 days.ITH 10mg q48h for 6 day | colistrin | Loading dose 3 480mg followed by 360mg q12h | Chemical meningitis | cured |
| | M/60 | SAH, aneurysm ventriculitis | EVD | MDR | Colistrin,IVT,40mg 1st day, 10mg q24h<br>15d | colistrin | 360mg q12h (30) 2d | non | cured |
| | M/62 | SAH, aneurysm meningitis | EVD | MDR | Colistrin, IVT,40mg,1st day<br>30mg 2nd day,10mg q24h for 3 days, 10mg q48h for 7days | colistrin | 240mg q8h | non | cured |
| Rastogi S et al 2013 | M/52 | Cranio facial trauma | EVD | MDR | cefazolin | Colistrin<br>2.5mg/kg/day | | non | cured |
| Shrestha GS[2] | M/75 | SDH Ventriculitis | EVD | MDR | Vancomycin<br>ceftazidim | Colistrin , Tigecycline | Colistin 2000,000 IU | Renal disfunction | Sterile csf<br>died |
| Moosavian M[1] | M/20 | Gun shot wound abdomen through back | EVD | MDR | meropenem, vancomycin and amikaci ne | colistin | | Colistin resistant strains | Sterile csf |

AVM - Arteriovenous malformation SAH-Subarachnoid hemorrhage SDH- Subdural heamatoma EVD - External ventricular drain, MDR – Multidrug resistant CSF – Cerebral spinal fluid, MDRAB- Multidrug Resistant Acenetobacter Baumanii

**Table 1 References**


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## DISCUSSION

*Acinetobacter baumannii* is a Gram-negative organism reported worldwide as a cause of health-care-associated infections, particularly in neurosurgery intensive care units (ICUs).[4] MDRAB intracrainial ventriculitis offers a difficult therapeutic problem owing to the limited penetration of antibiotics through the BBB.[5] Colistin is an old polymyxin antibiotic developed in 1959. Due to its potential nephrotoxicity, it has been seldom used in clinical practice in the past decades. Due to its infrequent application, this drug has turned out to be an effective tool for the treatment of MDRAB infection. The re-emergence of colistin has provided an option for the treatment of MDRAB associated intracrainial ventriculitis.

The intravenous route of administration use is commonly used rather than intrathecal plus intraventricular, due to colistin's potential side effects such as nephrotoxicity.[6] However, intraventricular or intrathecal administration of colistin can be a life-saving intervention for patients with intracrainial ventriculitis caused by MDR gram-negative organisms not responding to intravenous colistin.[7] Recent studies have shown administration of colistin directly into the CNS appears to be successful and well tolerated.[8] Review of the literature suggests a minimum intrathecal dose of 125,000 IU daily as suggested by the guidelines of Infectious Disease Society of America and may possibly increase to 250,000 IU daily.[9]

A series of reviews published cases of successful treated MDR AB patients (Table 1). Patel *et al* reported in their study that the prolonged combination therapy with intraventricular colistin and tobramycin plus intravenous colistin, rifampin, and vancomycin led to the resolution of a persistent central nervous system infection caused by MDRAB.[10] Karaiskos *et al*, in their case study indicated that direct administration of colistin into the CSF was effective and well tolerated in the treatment of AB meningitis of patients.[11]

A larger case study was done by Guardado *et al* in which 22 cases of nosocomial postsurgical meningitis due to *A. baumanii* were reported.[12] They used a combination of intravenous and intrathecal colistin and proved that it was a safe and useful option for the treatment of AB meningitis in each of their patients.

Death was reported in an isolated case due to nephrotoxicity, even though CSF sterility was achieved.[13] The toxicity is dose-dependent and reversible on discontinuation of the treatment.[8] Concomitant administration of other potential nephrotoxic agents (such as diuretics, aminoglycosides or vancomycin) increases the likelihood of nephrotoxicity.[8] Additionally older and more severely ill patients are at higher risk for nephrotoxicity and it further independently predicts higher mortality.[14]

In our patient, post-operative intracrainial ventriculitis associated with extensively drug-resistant AB was conclusively diagnosed based on the following criteria ; (a) culture from the patients CSF samples ,(b) the patients clinical symptoms , and (c) marked improvement of clinical symptoms after commencement of intraventricular plus intrathecal colistin. An intraventricular plus intrathecal dose of 250,000 IU daily once daily for 14 days was administered. The improvement of the patient's general status and inflammatory symptoms proved that IV intraventricular plus intrathecal colistin is effective in treating intracrainial ventriculitis caused by extensively multidrug-resistant AB strains.

## CONCLUSION

This case study reaffirms the successful treatment of MRAB by use of intraventricular plus intrathecal colistin. Following the successful treatment of our first patient using colistin and improvement of clinical symptoms, we strongly agree with the authors in the literature review, who advocate for the use of IVT/IT colistrin in treating MRAB associated intracranial ventriculitis.[11] Colistin is a potentially effective and safe therapy for the treatment of multidrug-resistant *A. baumannii* intracranial ventriculitis .

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