

World Journal of *Clinical Cases*

World J Clin Cases 2019 December 26; 7(24): 4172-4425



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Semimonthly Volume 7 Number 24 December 26, 2019

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The *WJCC* is now indexed in PubMed, PubMed Central, Science Citation Index Expanded (also known as SciSearch®), and Journal Citation Reports/Science Edition. The 2019 Edition of Journal Citation Reports cites the 2018 impact factor for *WJCC* as 1.153 (5-year impact factor: N/A), ranking *WJCC* as 99 among 160 journals in Medicine, General and Internal (quartile in category Q3).

RESPONSIBLE EDITORS FOR THIS ISSUE

Responsible Electronic Editor: *Ji-Hong Liu*
 Proofing Production Department Director: *Yun-Xiaojuan Wu*

NAME OF JOURNAL

World Journal of Clinical Cases

ISSN

ISSN 2307-8960 (online)

LAUNCH DATE

April 16, 2013

FREQUENCY

Semimonthly

EDITORS-IN-CHIEF

Dennis A Bloomfield, Bao-Gan Peng, Sandro Vento

EDITORIAL BOARD MEMBERS

<https://www.wjnet.com/2307-8960/editorialboard.htm>

EDITORIAL OFFICE

Jin-Lei Wang, Director

PUBLICATION DATE

December 26, 2019

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<https://www.wjnet.com/bpg/gerinfo/208>

ARTICLE PROCESSING CHARGE

<https://www.wjnet.com/bpg/gerinfo/242>

STEPS FOR SUBMITTING MANUSCRIPTS

<https://www.wjnet.com/bpg/GerInfo/239>

ONLINE SUBMISSION

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Postoperative multidrug-resistant *Acinetobacter baumannii* meningitis successfully treated with intravenous doxycycline and intraventricular gentamicin: A case report

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Author contributions: Wu X and Wang L contributed equally to this work; Wu X and Wang L designed and wrote the report; Ye YZ and Yu H reviewed the manuscript for its intellectual content and revised the entire work; all authors have read and approved the final manuscript.

Supported by The Shanghai Pujiang Program, No. 12PJ1401500.

Informed consent statement: The patient's family members provided written informed consent.

Conflict-of-interest statement: The authors have no conflicts of interest to declare.

CARE Checklist (2016) statement: The manuscript was prepared and revised according to the CARE Checklist (2016).

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Abstract

BACKGROUND

Multidrug-resistant *Acinetobacter baumannii* (MDRAB) has emerged as an increasingly important pathogen that causes nosocomial meningitis. However, MDRAB-associated nosocomial meningitis is rarely reported in children.

CASE SUMMARY

We report the case of a 1-year-old girl with a choroid plexus papilloma, who developed postoperative nosocomial meningitis due to MDRAB. The bacterial strain was sensitive only to tigecycline and colistin, and showed varying degrees of resistance to penicillin, amikacin, ceftriaxone, cefixime, cefotaxime, ciprofloxacin, levofloxacin, gentamicin, meropenem, imipenem, and tobramycin. She was cured with intravenous doxycycline and intraventricular gentamicin treatment.

CONCLUSION

Doxycycline and gentamicin were shown to be effective and safe in the treatment of a pediatric case of MDRAB meningitis.

Key words: *Acinetobacter baumannii*; Meningitis; Doxycycline; Gentamicin; Multidrug resistance; Case report

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Core tip: Multidrug-resistant *Acinetobacter baumannii* (MDRAB) is a troublesome pathogen owing to multidrug resistance. Postoperative nosocomial meningitis due to

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Manuscript source: Unsolicited manuscript

Received: September 18, 2019

Peer-review started: September 18, 2019

First decision: October 24, 2019

Revised: November 11, 2019

Accepted: November 23, 2019

Article in press: November 23, 2019

Published online: December 26, 2019

P-Reviewer: Cure E, Schwan WR, Yellanthoor RB

S-Editor: Zhang L

L-Editor: Wang TQ

E-Editor: Wu YXJ



Acinetobacter baumannii is rarely reported in children. Nosocomial meningitis due to MDRAB is fatal and its treatment is challenging because of the low blood-brain barrier permeability of antibiotic drugs. We describe the case of a child who developed post-neurosurgical meningitis due to MDRAB that was effectively treated by the combination of intravenous doxycycline and intraventricular gentamicin administration.

Citation: Wu X, Wang L, Ye YZ, Yu H. Postoperative multidrug-resistant *Acinetobacter baumannii* meningitis successfully treated with intravenous doxycycline and intraventricular gentamicin: A case report. *World J Clin Cases* 2019; 7(24): 4342-4348

URL: <https://www.wjgnet.com/2307-8960/full/v7/i24/4342.htm>

DOI: <https://dx.doi.org/10.12998/wjcc.v7.i24.4342>

INTRODUCTION

Acinetobacter baumannii (*A. baumannii*) is a Gram-negative bacterium that causes various nosocomial infections^[1,2]. Postoperative nosocomial meningitis due to *A. baumannii* is rarely reported in children. Treatment of *A. baumannii* infection is of concern due to the increasing prevalence of multidrug resistance^[3]. In this report, we present the case of a child who developed post-neurosurgical meningitis due to multidrug-resistant *A. baumannii* (MDRAB). The child was successfully treated with intravenous doxycycline and intraventricular gentamicin administration. This report also presents a systematic literature review concerning MDRAB-associated nosocomial meningitis in children.

CASE PRESENTATION

Chief complaints

A 1-year-old girl with head trauma was admitted to our hospital in November 2016. At four weeks after surgery, the patient was febrile and disturbance of consciousness was observed.

History of present illness

The patient fell off the bed and mild head trauma was suspected. Incidentally, a computed tomography (CT) scan of the head revealed an intracranial space-occupying lesion (Figure 1A). One week after the admission, the child underwent a brain tumor resection. Immunohistochemical staining of the specimens indicated a choroid plexus papilloma. On the fourth postoperative week, she suddenly developed an altered state of consciousness with febrile illness. External ventricular drainage was performed. During the course of the disease, the patient had no diarrhea, abdominal pain, nausea, vomiting, cold, or any other discomfort.

History of past illness

The patient had no medical history of chronic diseases such as diabetes, coronary and other heart diseases, infectious diseases such as hepatitis and tuberculosis, surgery, blood transfusion, trauma, and drug allergy. The patient's history of preventive inoculation was unknown.

Personal and family history

She was operated for a choroid plexus papilloma in November 2016. The rest of the personal and family history was unexceptional.

Physical examination upon admission

At admission, the patient showed stable vital signs; however, the skin on the right side of the forehead was swollen, approximately 5.5 cm × 4 cm in size. On the fourth postoperative week, she suddenly developed an altered state of consciousness and hypertonia of limbs, along with the disappearance of the direct and indirect pupillary light reflexes.

Laboratory examinations

Cerebrospinal fluid (CSF) examination showed a white blood cell count of 500/mm³. The patient was diagnosed with meningitis and intravenous administrations of

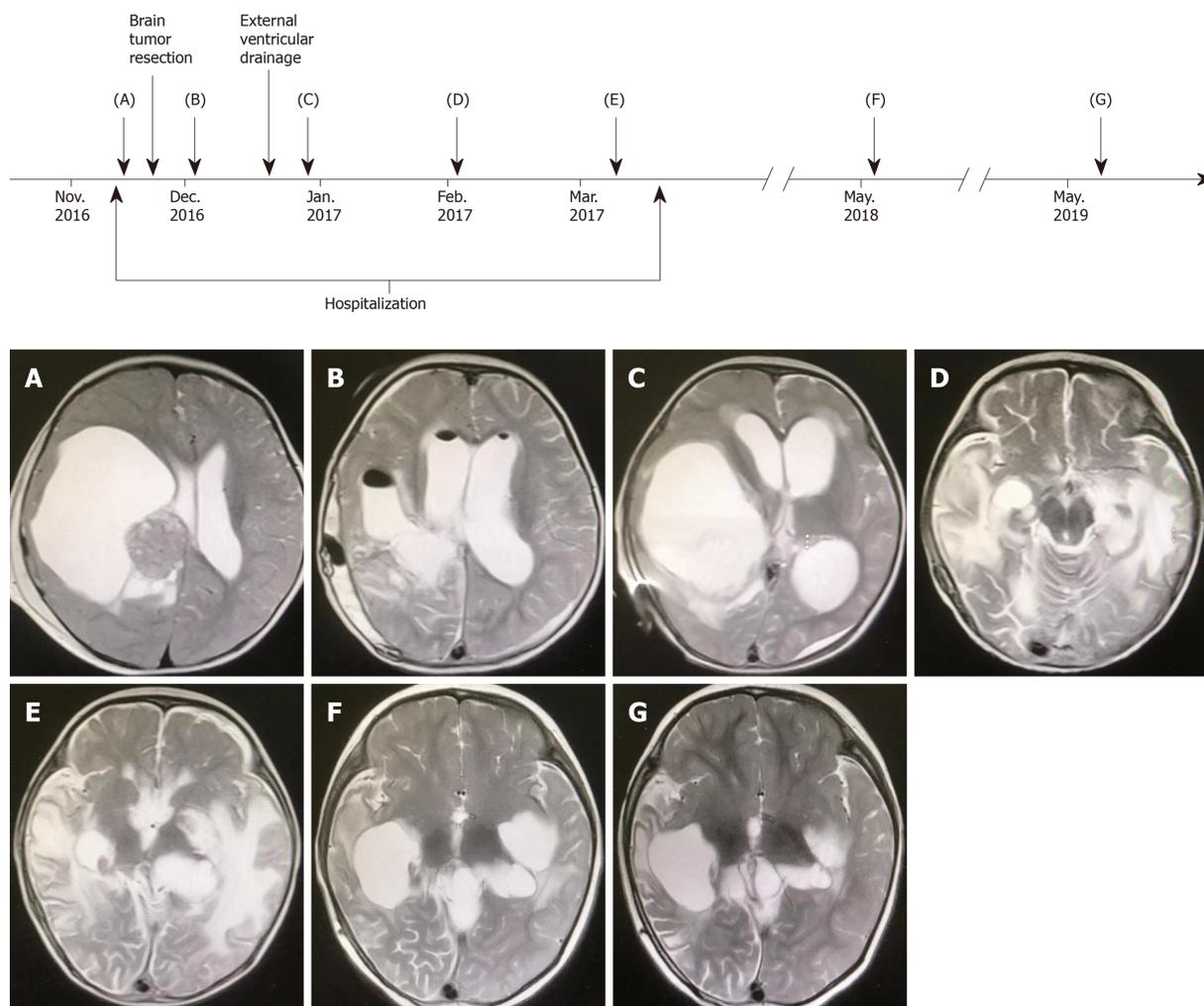


Figure 1 Computed tomography images. A: Computed tomography (CT) showed an intracranial space-occupying lesion; B-G: CT examination results during patient follow-up.

meropenem (120 mg/kg/d divided q8h) and vancomycin (60 mg/kg/d divided q6h) were initiated; however, the patient did not show any improvement. After 5 d, CSF analysis showed a white blood cell count of 40000/mm³, protein concentration of 573 mg/dL, and glucose concentration of 0 mmol/L. CSF culture was positive for *A. baumannii*, which was sensitive only to tigecycline and colistin while it showed varying degrees of resistance to penicillin, amikacin, ceftriaxone, cefixime, cefotaxime, ciprofloxacin, levofloxacin, gentamicin, meropenem, imipenem, and tobramycin.

FINAL DIAGNOSIS

Postoperative MDRAB meningitis.

TREATMENT

As colistin has severe side effects in children, the patient was started on tigecycline (2 mg/kg/d divided q12h). After 12 d of antibiotic therapy with tigecycline, the patient still had a fever. The CSF culture was positive for MDRAB. Doxycycline is known to be active against MDRAB and was administered to the patient following the failure of tigecycline (4 mg/kg/d divided q12h) and intraventricular gentamicin (2 mg/d, once daily) was administered. The patient became afebrile 6 d later. After 17 d, the CSF was found to be sterile. Doxycycline and gentamicin were administered for 8 wk. The clinical course of the patient is shown in [Figure 2](#).

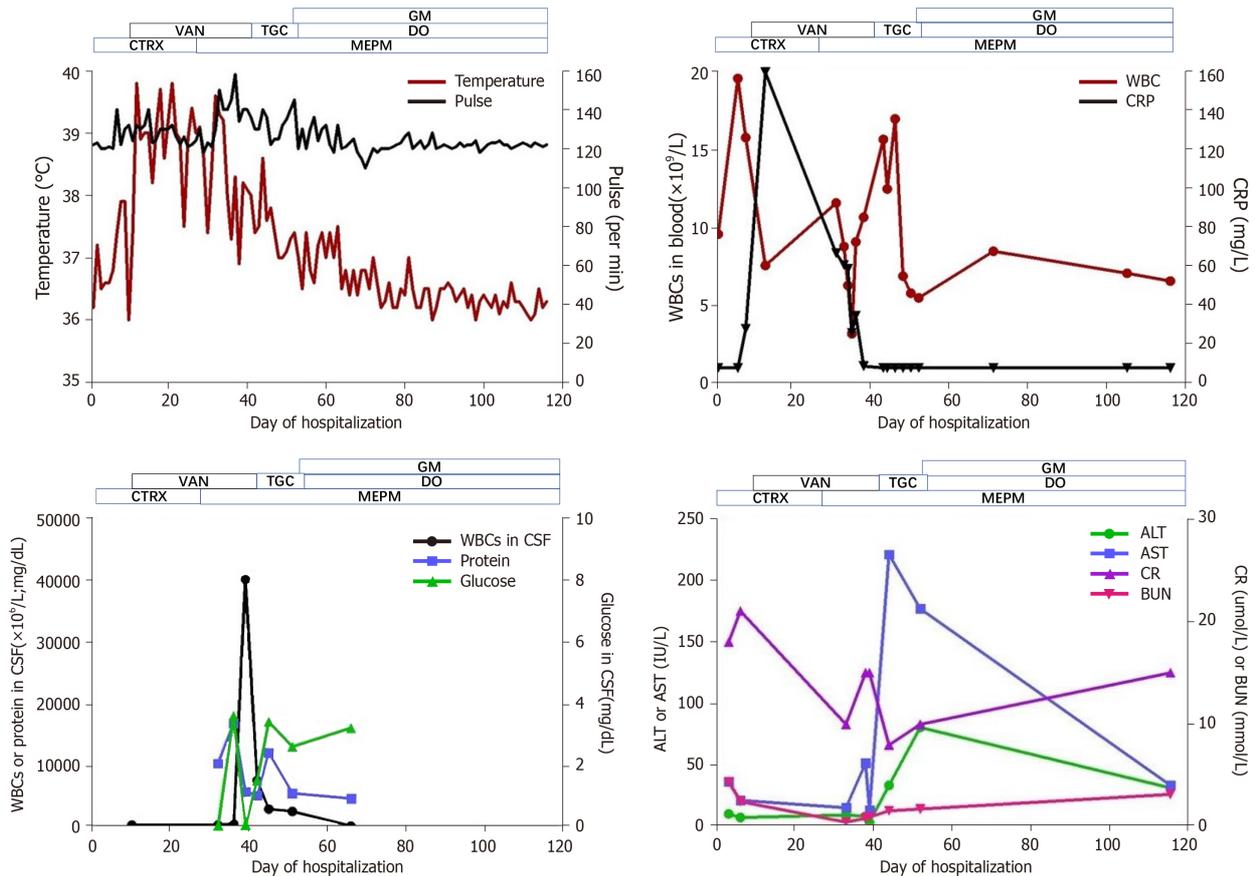


Figure 2 Clinical course of a 1-year-old patient with multidrug-resistant *Acinetobacter baumannii* meningitis. CTRX: Ceftriaxone (Rocephin); MEPM: Meropenem; VAN: Vancomycin; TGC: Tigecycline; DO: Doxycycline; GM: Gentamicin; WBC: White blood cell; CRP: C-reactive protein; CSF: Cerebrospinal fluid; ALT: Alanine aminotransferase; AST: Aspartate aminotransferase; BUN: Blood urea nitrogen; Cr: Creatinine.

OUTCOME AND FOLLOW-UP

There were no serious side effects of doxycycline and gentamicin treatment. The patient is now healthy and is receiving scheduled follow-up and her CT examination results remained normal at the subsequent two-year follow-up (Figure 1).

DISCUSSION

MDRAB is a troublesome pathogen in healthcare institutions owing to multidrug resistance, which is a threat to the current antibiotic era^[4]. Nosocomial meningitis due to MDRAB is fatal and its treatment is challenging because of the low blood-brain barrier permeability of antibiotic drugs^[5,6]. Thus, the choice of antibiotics is critical to the treatment of nosocomial MDRAB meningitis. It is also important to analyze the blood and CSF cultures before treatment initiation to avoid inappropriate antibiotic use. In the present case, CSF culture showed the presence of MDRAB that was sensitive only to tigecycline and colistin.

In the past, colistin had been used successfully against Gram-negative bacteria; however, its prescription decreased due to nephrotoxicity^[7]. Tigecycline is a broad-spectrum bacteriostatic compound of glycolcyclines, which is active against several multidrug-resistant pathogens as well as MDRAB^[8]. In our case, tigecycline was initially administered intravenously, but the patient did not respond to the treatment and continued to manifest typical signs of meningitis. The possible explanation of the therapeutic failure of intravenous tigecycline treatment could be attributed to its poor ability to penetrate through the blood-brain barrier. Thus, a combination of intravenous and intraventricular (IVT) antibiotic administration may be a therapeutic option to ensure sterilization of the CSF. Both doxycycline and tigecycline belong to the tetracycline class of antibiotics. Doxycycline was administered following the failure of tigecycline, known to be active against MDRAB. In our case, doxycycline was effective in the treatment of the CNS infection, which may be explained by an

increased doxycycline distribution in the CNS owing to the disruption of the blood-brain barrier, in inflammatory diseases like meningitis. However, further pharmacological studies are needed to confirm this observation. Moreover, the intraventricular gentamicin administration could effectively sterilize the CSF.

MDRAB has emerged as an increasingly important pathogen often associated with post-neurosurgical meningitis^[9]. In the literature, the number of pediatric cases with MDRAB meningitis is low. Data regarding the clinical characteristics, therapy, and treatment outcomes in pediatric cases are summarized in Table 1^[10-15]. Since active antibiotics including tigecycline and colistin diffuse poorly to the central nervous system, it is a challenge to treat patients *via* intravenous administration of these drugs. The IVT administration of these antibiotics is currently the only treatment option for MDRAB meningitis.

CONCLUSION

In conclusion, this case suggests that the combination of intravenous doxycycline and intraventricular gentamicin administration may be a potentially effective and safe therapeutic option for the treatment of childhood MDRAB meningitis.

Table 1 Clinical features of the reported series of multidrug-resistant *Acinetobacter baumannii* meningitis in children

Ref.	Age (yr)	Sex	Acinetobacter susceptibility	Final regimen(s)	Toxicity	Treatment outcome
Kaplan <i>et al</i> ^[10]	4	NR	Multidrug resistant	Cefotaxime and aminoglycoside IV, and colistin IVR	None	Cure
Ng <i>et al</i> ^[11]	4	Male	Multidrug resistant	Amikacin and colistin IV, and colistin IT	Chemical meningitis	Cure
Ozdemir <i>et al</i> ^[12]	3	Female	Colistin	Colistin and ampicillin-sulbactam IV, and colistin IT	None	Cure
	14	Female	Colistin	Meropenem and ampicillin-sulbactam IV, and rifampin PO	None	Cure
	1	Male	Colistin	Colistin and meropenem IV	None	Cure
Lee <i>et al</i> ^[13]	3	Male	Imipenem	Colistin IV	None	Cure
Ganjeifar <i>et al</i> ^[14]	6	Male	Doxycycline and rifampin	Colistin and rifampin IV, and colistin IVR	NR	Cure
Jiménez-Mejías <i>et al</i> ^[15]	14	Male	Colistin	Colistin IV	None	Cure

IT: Intrathecal; IV: Intravenous; IVR: Intraventricular; PO: Peroral; NR: Not reported.

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