Case Report

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Spinal arachnoiditis followed by intrathecal tigecycline therapy for central nervous system infection by extremely drug-resistant *Acinetobacter baumannii*

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Abstract

In prior research, intrathecal tigecycline was successfully used to treat central nervous system infection by extensively drug-resistant *Acinetobacter baumannii*. However, little is known about its safe dose and adverse reactions. This study reports the case of a 28-year-old male patient who was diagnosed with central nervous system infection by extensively drug-resistant *A. baumannii* after the removal of a ventriculoperitoneal shunt. Intravenous and intrathecal tigecycline were administrated simultaneously. Spinal arachnoiditis was discovered after nine doses of intrathecal tigecycline. Spinal arachnoiditis was resolved after discontinuation of the antibiotic. This is the first report of an adverse reaction to intrathecal tigecycline. The case was complicated by spinal arachnoiditis, which obstructed the assessment of cerebrospinal fluid. The appropriate dose and administration schedule of intrathecal tigecycline remain to be determined.

Keywords

Tigecycline, adverse reaction, intrathecal therapy, *Acinetobacter baumannii*, extensively drug-resistant, central nervous system, infection

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Introduction

Central nervous system (CNS) infection by extensively drug-resistant *Acinetobacter baumannii* (XDRAB) is associated with high mortality. The current treatment of

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choice is colistin.[1] However, it was reported that 21.7% of patients experience neurotoxicity as an adverse reaction to this therapy.[2] Tigecycline has proven activity against XDRAB. However, because of its poor blood–brain barrier permeability, intravenous (IV) tigecycline is not recommended for treating CNS infection by XDRAB.[3] The intrathecal (IT) route is not routinely used to administer tigecycline. The first case report of IT tigecycline was presented in 2019.[4] This represents the second case report of IT tigecycline for the treatment of CNS infection.

Case report

A 28-year-old male patient presented with a high fever and rigidity in his extremities. He was discharged 1 month prior because of CNS infection. The patient was diagnosed with grade I astrocytoma in the third ventricle 2 years previously when he underwent ventriculoperitoneal shunting (VPS) to treat acute hydrocephalus. He did not recover from the coma (Glasgow coma score, E4V2M3) after the surgery.

Relapsed CNS infection was suspected. Empirical IV linezolid (Zyvox, 600 mg q12h, Pfizer, New York, NY, USA) and meropenem (Merrem, 2000 mg q8h, Dainippon Sumitomo Pharma Co., Ltd, Osaka, Japan) were used according to the previous admission information. The symptoms subsided on the seventh day. To prevent recurrent infection, the shunt was removed on the ninth day. The patient developed a high fever and seizure after the surgery. Lumbar puncture (LP) was performed, and an examination of cerebrospinal fluid (CSF) revealed leukocytosis ($22{,}592 \times 10^6$/L) accompanied by hypoglycorrhachia (0.11 mmol/L). CSF culture implied the presence of XDRAB that was only sensitive to colistin (minimum inhibitory concentration < 0.5 μg/mL) and tigecycline (minimum inhibitory concentration $= 2$ μg/mL). Therefore, IV tigecycline (Tygacil, 100 mg q12h, Pfizer) and cefotaxime/sulbactam (3000 mg twice daily) were applied.

IT tigecycline was administered simultaneously with IV tigecycline. LP was performed once daily. The L3/4 and L4/5 intervertebral spaces were chosen as the insertion sites alternatively. Five milligrams of tigecycline were diluted in saline to a total volume of 5 mL. After releasing 30 to 50 mL of CSF, the antibiotics were slowly injected using the withdraw/inject technique to achieve an even distribution. The patient was kept in the horizontal position for 4 to 6 hours.

IT tigecycline was discontinued after 7 days of persistently negative CSF cultures. The results of CSF analysis were improved (neutrophil cell count $= 1246 \times 10^6$/L, CSF glucose level = 2.88 mmol/L). In total, IV tigecycline was administered for 53 days, and nine doses of IT tigecycline were delivered. Dramatically, the patient's fever relapsed 10 days after the withdrawal of antibiotics. LP was performed, but no CSF was obtained. Non-enhanced lumbar magnetic resonance imaging (MRI) revealed a subdural T2-WI hyperintense sac located above the L1 level (Figure 1a). Spinal arachnoiditis (SA) was suspected, but the patients' family refused to allow the patient to undergo thoracic MRI. Thus, the extent of the lesion and its transverse section image were not accessible.

The patient's fever was ameliorated by 18 additional days of IV tigecycline administration. LP was not reattempted. CSF was sampled transcutaneously through the bulging right frontal surgical incision. The CSF test suggested that the CNS infection was resolved. Enhanced thoracic and lumbar MRI indicated that SA was resolved after 12 months of follow-up (Figure 1b).

All procedures performed in article were in accordance with the ethical standards of the local review board.

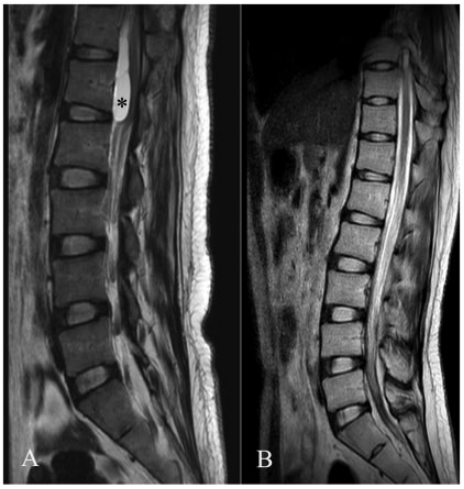

Figure 1. (a) Lumbar magnetic resonance imaging revealed a subdural sac (asterisk) compressing the conus medullaris and causing obstructive hydrocephalus. (b) The sac had disappeared after 12 months of follow-up.

Discussion

IT administration is a sophisticated technique for antibiotics with reduced blood-brain-barrier permeability. Deng et al.[4] successfully treated an XDRAB CNS infection by switching intraventricular tigecycline (4 mg twice daily) to IT tigecycline (4 mg once daily). However, little is known about the safe dose and treatment schedule of IT tigecycline.

SA usually presents with radiculopathy. In this case, because the patient was comatose, no obvious symptom or sign had been observed. The abnormality was identified only after the failure of LP. Although no special management was required, this obstructed the CSF examination, making it difficult to evaluate the stage of infection.

SA denotes inflammation of the pia-arachnoid and encapsulation of the nerve roots.[5] In this case, three pathophysiologic mechanisms should be considered, namely an adverse reaction to IT antibiotics, the complication of CNS infection, and injury caused by LP.

The safety of IT administration for various antibiotics such as vancomycin and amikacin has been established.[6–8] The most common complications of IT antibiotics are ventriculitis and seizure.[9] The adverse effects of IV tigecycline commonly involve the gastrointestinal tract, whereas those of IT tigecycline are unknown.[10] In this case, SA occurred rapidly after prolonged IT tigecycline administration, and this complication disappeared after treatment was halted. There was a possibility that the SA was the result of its toxicity and the subsequent reactive inflammation.

Mycotic[11] and tuberculous[12] CNS infection can have spinal involvement. The condition is mostly observed in immunocompromised patients with post-infectious inflammatory response syndrome in response to prolonged infection and the exudate.[13] However, most lesions present as extradural or leptomeningeal granuloma. Further, SA related to *A. baumannii* has not been described in the literature.

Repeated LP may cause chronic inflammation of the dura and arachnoid mater. Rarely, it can lead to intrathecal hematoma that presents as SA.[14,15] However, SA will develop at the puncture site in such cases, and it should present near the corresponding spinal level (L3–L5). In our case, the subdural sac was much higher than the site of puncture. In addition, SA displayed no relationship with the entrance pathway. It was extremely unlikely that SA resulted from direct injury caused by LP in this case.

To our knowledge, this is the first report of an adverse reaction to IT tigecycline. This case was complicated by SA that obstructed CSF assessment. The appropriate dose and treatment schedule of IT tigecycline remain to be determined.

Abbreviations

CNS = Central nervous system
CSF = Cerebrospinal fluid

IT = Intrathecal
IV = Intravenous
LP = Lumbar puncture
VPS = Ventriculoperitoneal shunting
XDRAB = Extensively drug-resistant *Acinetobacter baumannii*.

Authors' contributions

Zheng Wen-Jian interpreted the clinical findings. Shi Shang-Wen was a major contributor to writing the manuscript. Li Liang-Ming was the chief physician primarily managing the patient. All authors read and approved the final manuscript.

Availability of data and material

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Consent for publication

Consent was not required as there was no patient's private information in the paper.

Declaration of conflicting interest

The authors declare that there is no conflict of interest.

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