中文題目：使用 ceftazidime-avibactam 治療碳青黴烯類抗藥性肺炎克雷伯菌所致之院內感染腦膜炎：案例報告及文獻回顧

英文題目：Use ceftazidime-avibactam to treat nosocomial meningitis caused by carbapenem-resistant *Klebsiella pneumoniae*: a case report and literature review

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Introduction:

With the increasing use of carbapenems to treat multidrug-resistant (MDR) gram-negative bacteria (GNB), the emergence of carbapenem-resistant GNB has become a severe and imminent threat. Ceftazidime-avibactam (CAZ-AVI) is a novel combination of beta-lactam/beta-lactamase inhibitor active against carbapenem-resistant Enterobacteriaceae (CRE), except for metallo-β-lactamases (MBLs)-producing strains. It is approved for the treatment of complicated urinary tract infection (cUTI, including pyelonephritis), complicated intra-abdominal infection (cIAI), and hospital-acquired pneumonia (HAP, including ventilator-associated pneumonia (VAP)). However, there is seldom data for the use of CAZ-AVI in central nervous system (CNS) infection caused by CRE. Here we present a case of nosocomial meningitis caused by carbapenem-resistant *Klebsiella pneumoniae* (CRKP), successfully treated with CAZ-AVI in combination with intravenous amikacin and intraventricular colistin.

Case report:

A 40-year-old male with hypertension presented with acute onset left hemiplegia. The brain computed tomography (CT) revealed right thalamic hemorrhage and intraventricular hemorrhage. He underwent removal of hematoma and left external ventricular drainage (EVD) insertion, followed by ventriculo-peritoneal shunt (V-P shunt) implantation. During hospitalization, high spiking fever occurred due to catheter-associated urinary tract infection with MDR- *Escherichia coli* bacteremia. Antibiotic with meropenem was used for treatment. However, his consciousness deteriorated with pus discharge from the surgical site. Lumbar puncture disclosed a high opening pressure of 250 mmH_2O and a turbid cerebrospinal fluid (CSF). CSF analysis revealed an elevated cell count of 8320/uL with predominance of polymorphonucleocytes (PMN), low glucose level (<10 mg/dL) and an elevated protein level (341 mg/dL). Gram staining of the CSF found numerous GNB. Both the cultures from the pus and CSF yielded CRKP. The antimicrobial susceptibility testing showed susceptibility to cefmetazole, amikacin and CAZ-AVI. The CDC surveillance report for carbapenemase confirms the exhibition of *Klebsiella pneumoniae* carbapenemase (KPC). We used combination of intravenous CAZ-AVI and amikacin with intraventricular colistin to treat the patient. The V-P shunt was removed and the tip culture also yielded CRKP. His fever subsided after one week of combination therapy and the patient's consciousness level gradually improved. We kept the combination of CAZ-AVI and amikacin for 14 days after a negative CSF culture, with a total of 32 days of CAZ-AVI used.

Conclusion:

History of prior exposure to broad-spectrum antibiotic and invasive procedures increase the risk for colonization or infection of MDR organisms (MDROs). Nosocomial meningitis caused by MDROs leads to significant morbidity and

mortality. CRE meningitis is a clinical dilemma. In addition to the limited options for antimicrobial agent, there is also the issue of suboptimal concentration or lack of pharmacokinetic/pharmacodynamic (PK/PD) data regarding the blood-brain barrier penetration. Combination of intravenous meropenem and colistin, with intrathecal/intraventricular colistin, gentamicin or amikacin have been used in previous studies. CAZ-AVI has been reported to successfully treat meningitis caused by KPC-producing *Enterobacteriaceae*. As a promising treatment option for CRE CNS infections, further research is needed for the PK/PD data in dosing and intervals, and the optimal combination regimens. We present this case and share our experience with physicians in Taiwan.