Case Report
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Intractable Post-traumatic Brain Abscess Caused by *Klebsiella pneumoniae* with Extended-Spectrum β-Lactamase Phenotype

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Abstract

Extended-spectrum β-lactamase-producing *Klebsiella pneumoniae* (ESBL-KP) has increasingly been isolated in meningitis and ventriculitis episodes, which antimicrobial therapy is challenging to physicians as extremely limited treatment options and difficulty to maintain effective drug concentration in the cerebrospinal fluid. We report a patient who experienced 2 stages of post-traumatic intracranial infections form initial Staphylococcal brain abscesses to second stage of ESBL-KP ventriculitis. Flomoxef followed by prolonged meropenem therapy failed to rescue the patient, highlighting an urgent need to develop a more effective therapeutic strategy for this difficult-to-treat infection.

Keywords: Brain abscess; Extended-spectrum β-lactamase; *Klebsiella pneumoniae*; Meningitis; Ventriculitis

Introduction

Klebsiella pneumoniae is a relatively common cause of nosocomial meningitis, for which neurosurgery is the main risk factor [1]. Extended-spectrum β-lactamase producing *K. pneumoniae* (ESBL-KP) has increasingly been isolated in meningitis and ventriculitis episodes [2]. Nonetheless, the mortality rates in patients with spontaneous meningitis were usually higher than those in patients with post-traumatic or postoperative meningitis [1,3]. We herein reported a delayed-type traumatic brain abscess caused by an ESBL-KP strain, which was difficult to treat.

Case Presentation

A 73-year-old man was first admitted to the hospital on July 1, 2013, due to traumatic brain injury with skull bone fracture, left frontotemporoparietal subdural hematoma and left temporal contusion hemorrhage. The patient underwent craniectomy for removal of hematoma. He denied history of diabetes mellitus. Thereafter, the patient had experienced 2 stages of intracranial infections.

First stage: Staphylococcal brain abscess

On August 27, 2013, he was re-admitted to the hospital due to left temporal brain abscess with focal compression of ventricle (Figure 1A), of which stereotactic aspiration of pus and blood cultures all yielded coagulase-negative *Staphylococcus* species. He was discharged after cefpirome plus fosfomycin therapy for about one month. On October 2, 2013, he was re-admitted to remove left temporal abscess (Figure 1B). He was discharged after vancomycin plus fosfomycin therapy for about 4 weeks. But, he was soon re-admitted for high fever. Brain CT (Figure 1C) showed hydrocephalus but cerebrospinal fluid (CSF) culture yielded no growth of bacteria. Antimicrobial therapy with vancomycin plus fosfomycin was given for one week. Thereafter, ventricular peritoneal shunt was inserted. CSF was clear without bacterial growth. Ceftazidime plus fosfomycin were used for additional 2 weeks.

Second stage: ESBL-KP brain ventriculitis

On November 28, 2013, high fever flared up during the same hospital episode. Blood and CSF cultures yielded *K. pneumoniae* strains with same antibiogram of resistance to ceftazidime and ceftriaxone, but remained susceptible to gentamicin, amikacin, ciprofloxacin, flomoxef, ertapenem

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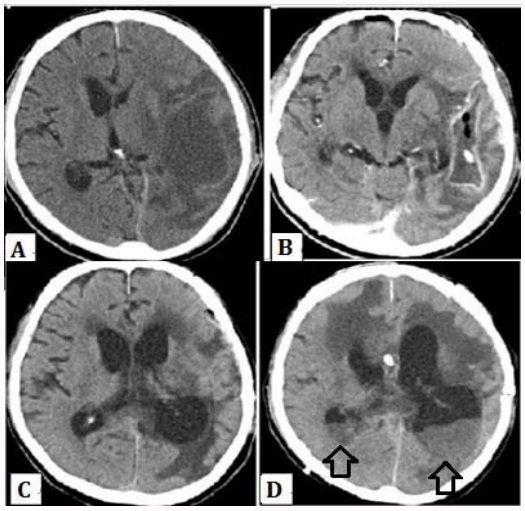

Figure 1: Brain CT showing left temporal abscess (A), residual left temporal abscess (B), hydrocephalus (C), and ventriculitis with fluid-fluid levels (arrow) in the bilateral lateral ventricles (D).

and meropenem, which were confirmed ESBL phenotype (ESBL-KP). Then, the patient still had fever and seizure developed. Brain CT showed worsening hydrocephalus with ventriculitis (Figure 1D), so ventricular peritoneal shunt was revised and was irrigated by normal saline with gentamicin solution. The CSF obtained at surgery was purulent with a white blood cell (WBC) count of 48,200/μL, which culture also yielded ESBL-KP. Antibiotic therapy was thus changed to flomoxef (2gm every 8 hours) for one week followed by meropenem (1gm every 8 hours) due to a difficult-to-treat infection. On December 30, 2013, the followed-up CSF was some turbid with a WBC count of 722/μL, which culture still yielded ESBL-KP with the same antibiogram to previous isolates without changing the resistance profile. The patient died 2 weeks later even after a total of 5 weeks of meropenem therapy had been administered.

Microbiological study

The first isolated CSF ESBL-KP strain was non-K1/K2 capsule serotype and was negative for common virulence factors, such as hypermucoviscosity phenotype, plasmid-borne *rmpA*, *rmpA2* and chromosomal *rmpA* genes [4]. The virulence profiles was in consistent with our previous report that post-craniotomy *K. pneumoniae* isolates were significantly less virulent than primary meningitis isolates, except for similar serum resistance capability [3].

Discussion

Staphylococcal species have been the most common pathogen, accounting for 27.6% of adult bacterial meningitis in Taiwan, followed by *Klebsiella* species (13.8%) as the second common etiology [5]. In contrast to community-acquired bacterial meningitis by virulent *K. pneumoniae* strains, nosocomial meningitis of *K. pneumoniae* is usually by less-virulent strains and mortality is quite low [3]. However, we reported a delayed-onset post-traumatic brain infection caused by ESBL-KP, albeit less-virulent in nature, which was difficult to treat despite surgical intervention and broad-spectrum antibiotic therapy. Because, resistance to carbapenems did not develop during the course of therapy, the intractable course of our case might be attributed to inadequate CSF concentration of antibiotic versus the multi-drug resistance of ESBL-KP. Alternatively, several methods might be hopefully to achieve a successful outcome in combat such a serious ESBL-KP brain meningitis by either (1) intravenous colistin in combination with a higher dosage of meropenem (2gm every 8 hours); (2) intraventricular administration of colistin and off-label tigecycline; or (3) combined intravenous and intraventricular administration of tigeycline [2,6,7]. Combination of colistin and tigecycline has been reported to be highly synergistic against ESBL-KP isolates in an *in-vitro* study [8].

Conclusion

We report a patient who experienced 2 stages of post-traumatic intracranial infections form initial *Staphylococcal* brain abscesses to second stage of ESBL-KP ventriculitis. Flomoxef followed by prolonged meropenem therapy failed to rescue the patient. There is an urgent need to develop a more effective therapy to overcome such a difficult-to-treat and life-threatening intracranial infection caused by ESBL-KP.

Ethical Approval

The study and waiver from the inform consent process were approved by the Institutional Review Board (IRB) of the Chi Mei Medical Center, Tainan city, Taiwan (IRB Serial number 10603-013).

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