Case Report

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A Case of Community-Onset Bacterial Meningitis due to Extended-Spectrum Beta-Lactamase Producing *Escherichia coli*

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Abstract

This is a case of community-onset bacterial meningitis caused by an extended-spectrum beta-lactamase-producing *Escherichia coli* that was resistant to ceftazidime, cefpirome, and aztreonam. Multidrug-resistant gram-negative bacilli, such as the *E. coli* in our study, are now spreading in many medical fields and may possibly become pathogens of community-onset meningitis. Our findings with this case and previously published reports indicate that empiric therapy with carbapenems may represent a suitable management option for future cases of meningitis due to gram-negative bacilli.

Keywords: Extended-spectrum beta-lactamase (ESBL); Meningitis; Carbapenem

Introduction

Bacterial meningitis is one of the several serious infectious diseases, which has high mortality rate [1]. It is well known that empiric antibiotic therapy is required because treatment must be initiated as soon as possible for the patient to survive the meningitis. The treatment guideline for bacterial meningitis also recommends that empiric antibiotic treatment should be initiated immediately [2].

Multidrug-resistant gram-negative bacilli (GNB) have become a major public health threat [3]. Beta-lactamase-producing GNB are particularly important pathogens because of their resistance to beta-lactam antibiotics. Extended-spectrum beta-lactamase (ESBL) is one of the major beta-lactamases, which can confer resistance to the fourth-generation cephalosporins. In some clinical fields, ESBL-producing GNB have begun to make the choice of empirical antibiotic regimens difficult. It has recently been reported that ESBL-producing GNB have become prevalent in the stools of healthy volunteers [4, 5].

Here, we report an adult hemodialysis patient with community-acquired bacterial meningitis due to ESBL-producing *Escherichia coli*. Community-acquired meningitis due to GNB in adult patients is rare, and particularly, meningitis due to ESBL-producing GNB has been reported in only a few cases [6, 7]. We also reviewed previously published reports to demonstrate the importance of ESBL-producing GNB in community-acquired meningitis.

Case Report

A 63-year-old Japanese man with fever and disturbance of consciousness was admitted to the emergency room of our hospital. The patient had previously been diagnosed with chronic renal failure and was initiated with artificial hemodialysis at the age of 55 years. The patient had also been diagnosed with choledocholithiasis and cholangitis at the age of 61 years. Endoscopic sphincterotomy and antibiotic treatment were performed at that time, at another hospital. After sphincterotomy, he was treated for cholangitis with levofloxacin twice before admission. On admission to our hospital, the patient's temperature was 39.0 °C, his heart rate was 124/min (regular), and he had a disturbance of consciousness (Glasgow Coma Scale; E4V4M6). He also had a stiff neck. His pupil size (diameter) was 2.5 mm/2.5 mm, and light reflex was positive in both eyes. There was no evidence of heart murmur or lung rale. There were no other abnormal findings. Chest/abdominal radiographs and brain computed tomography upon admission revealed normal findings. Blood tests revealed a white blood cell (WBC) count of 18,700 cells/μL and a C-reactive protein (CRP) level of 14.48 mg/dL; however, there were no other significant findings in the blood and urine tests indicating the focus

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Table 1. Drug Susceptibility Test of *E. coli* in Our Case

Drug	MIC (μg/mL)	Susceptibility
Ampicillin	> 16	R
Piperacillin	> 64	R
Amoxicillin-clavulanate	16	I
Cefazolin	>16	R
Cefotium	> 16	R
Cefotaxime	> 32	R
Ceftazidime	> 16	R
Cefpirome	> 16	R
Cefmetazole	≤ 4	S
Cefaclor	> 16	R
Cefcapene-pivoxil	> 1	R
Flomoxef	≤ 8	S
Cefoperazone-sulbactam	>16	R
Imipenem-cilastatine	≤ 1	S
Aztreonam	> 16	R
Gentamicin	> 8	R
Amikacin	≤ 4	S
Levofloxacin	> 4	R
Trimethoprim-sulfamethoxazole	≤ 2	S

MIC: minimum inhibitory concentration.

of infection. We also collected cerebrospinal fluid (CSF) on admission. The leukocyte count in the CSF was 6,420 cells/mm^3, with a predominance of polynuclear leukocytes.

The patient was diagnosed with meningitis. Blood was collected twice, once after admission and once before the administration of antibiotic agents, for culturing. Intravenous ceftriaxone (2 g every 12 h) and vancomycin (1 g after hemodialysis) were administered from the day of admission. Dexamethasone (10 mg every 6 h) was also administered.

Gram stain of the CSF was performed the day after admission, and GNB were detected. Two days after admission, blood and CSF cultures revealed ESBL-producing *E. coli* that was multidrug resistant (Table 1). We changed the antibiotic regimen from ceftriaxone and vancomycin to meropenem (1 g every 24 h). After the administration of meropenem, the patient's symptoms, including fever, neck stiffness, and disturbance of consciousness, improved gradually. His WBC count and CRP level also decreased. Six days after admission, the leukocyte count in his CSF was 146 cells/mm^3, and administration of dexamethazone was terminated. On day 21 after admission, the leukocyte count in his CSF was 123 cells/mm^3 and the patient's symptoms continued to improve. However, on day 24 after admission, the patient developed acute purulent cholangitis diagnosed by laboratory findings and abdominal ultrasonography, which resulted in his death, even though meropenem was administered.

Discussion

Community-onset meningitis due to ESBL-producing GNB has been rare [8]. Some neonatal cases, including outbreak case series, were reported because *E. coli* was one of the major pathogens responsible for meningitis in neonates. In contrast, only two cases of community-acquired meningitis due to ESBL-producing GNB have previously been reported

Table 2. Review of the Literature, Including the Present Case

Ref	Age	Gender	Background	Complication	Pathogen	Empiric therapy	Definitive therapy	Outcome
6	72	F	Diabetes mellitus	Vertebral osteomyelitis	*E. coli*	CTRX + Vanco	MEPM + GM	Cured
7	59	Un	Nothing	Mycotic aneurysm	*E. coli*	CTX + ABPC + GM	MEPM + CPFX	Died
our case	63	M	Chronic renal failure, post-endoscopic sphincterotomy	Acute pyogenic cholangitis	*E. coli*	CTRX + Vanco	MEPM	Died

Ref: reference; Un: unknown; CTRX: ceftriaxone; Vanco: vancomycin; MEPM: meropenem; GM: gentamicin; CPFX: ciprofloxacin.

in adult patients. Highlights of the previously documented cases of community-acquired meningitis due to ESBL-producing GNB, and of this case, are presented in Table 2.

In terms of pathogens, the major pathogen responsible for community-acquired meningitis has been *Streptococcus pneumonia*, which is isolated in about 58% of all cases [8]. In contrast, community-acquired meningitis caused by GNB has been rare. For instance, a previous report showed that *E. coli* was responsible for 2.5% of all pathogenic adult meningitis [9]. It was also reported that GNB could be the cause of meningitis in a few inpatients who were in an immunocompromised state [10]. However, as medicine has advanced, the number of immunocompromised outpatient hosts has increased. In addition, ESBL-producing GNB have now been reported to colonize not only inpatients but also outpatients, including healthy volunteers. All three cases of community-acquired meningitis due to ESBL-producing GNB (including ours) were published recently. These results demonstrate that ESBL-producing GNB may become important pathogens in meningitis, even in community-acquired cases.

In terms of treatment, all three cases were initially treated with third-generation cephalosporins. According to the guidelines, community-onset meningitis should be treated with the third-generation cephalosporins and vancomycin as empiric therapies [2]. The most common pathogen of bacterial meningitis in adults is *S. pneumoniae*, and some strains of *S. pneumonia* present in patients with meningitis are beta-lactam resistant, like penicillin-resistant *S. pneumonia* (PRSP). Therefore, third-generation cephalosporins and vancomycin are recommended as agents of empiric therapy. Even in cases of meningitis due to GNB, confirmed using Gram stain, third-generation cephalosporins are the recommended agents for empiric therapy and two of three cases were died [2]. However, these cases suggest that carbapenems may become the recommended agents of empiric therapy for meningitis due to GNB in the future.

In conclusion, ESBL-producing GNB are now becoming prevalent in many medical fields, even as pathogens of meningitis. In community-acquired cases as well, we should give special attention when choosing empiric antibiotics to treat meningitis cases in which GNB have been verified using Gram stain.

Authors' Contributions

The manuscript was prepared by YY under the supervision of YO. KS, IK and TK helped to draft the manuscript. All authors read and approved the final manuscript.

Conflict of Interest

None.

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