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Commentary

Emergence of *Escherichia coli* producing OXA-48-like carbapenemase in a patient with percutaneous transhepatic biliary drainage

Carbapenemase-producing Enterobacteriaceae are often multidrug-resistant (MDR) and pose serious problems for clinical treatment and infection control. Here, we report the first isolation of *Escherichia coli* producing OXA-48-like carbapenemase from a patient after percutaneous transhepatic biliary drainage (PTBD). The PTBD surgery was performed in India, and the bacteria were isolated at Teikyo University Hospital in Tokyo, Japan.

A 66-year-old man living in Kuwait was admitted to hospital in Mumbai, India, complaining of jaundice. He was diagnosed with intrahepatic cholangiocarcinoma and received PTBD to improve jaundice. He subsequently received anti-cancer chemotherapy in Kuwait and was later admitted to our hospital, Teikyo University Hospital, for further treatment. Upon admission to our hospital, the patient was diagnosed with obstructive jaundice and drug-resistant bacteria were detected in the bacterial culture from the tip of the PTBD tube. Ampicillin/sulbactam and amikacin combination therapy was used as infection prevention for only 1 day at the time of the PTBD exchange surgery because there were no symptoms of infection or inflammation. Subsequently, the patient received anti-cancer chemotherapy and was discharged after removal of the PTBD device.

The PTBD drain and peritoneal drain were collected for screening. To screen for extended-spectrum beta-lactamase (ESBL)-producing bacteria and carbapenem-resistant organisms (CRO), samples were cultured on CHROMagar ESBL/MDRA (Kanto Chemical, Tokyo, Japan) and BTB agar (Eiken Chemical, Tokyo, Japan) with a piperacillin/tazobactam (PIPC/TAZ, 100/10 μg) disc (Becton Dickinson, Franklin Lakes, NJ, USA) or an imipenem (10 μg) disc (Becton Dickinson, Franklin Lakes, NJ, USA). Isolates were identified with a MALDI biotyper (Bruker Daltonics, Billerica, MA, USA) and Vitek MS system (bioMérieux, Marcy l'Etoile, France). Susceptibility was defined according to breakpoints listed in the Clinical and Laboratory Standards Institute (CLSI) guidelines M100-S24. Testing was performed with a MicroScan WalkAway (Beckman Coulter, Brea, CA, USA).

A total of seven Gram-negative rod (GNR) species and three Gram-positive cocci (GPC) species were collected from the patient's peritoneal drain and PTBD drain (Table I). Of the GNR

Table I
Summary of bacterial isolates.

Sample	Gram stain	Species	Isolate number
Peritoneal drain	GNR	*Aeromonas hydrophila*	1
		Escherichia coli	2
		Klebsiella aerogenes	1
		Klebsiella pneumoniae	1
		Pseudomonas aeruginosa	1
	GPC	*Enterococcus casseliflavus*	1
		Enterococcus faecalis	1
		Streptococcus viridans	1
PTBD drain	GNR	*Escherichia coli*	3
		Klebsiella aerogenes	2
		Klebsiella oxytoca	1
		Klebsiella pneumoniae	3
		Pseudomonas aeruginosa	2
		Stenotrophomonas maltophilia	1
	GPC	*Enterococcus casseliflavus*	1
		Enterococcus faecalis	2
		Streptococcus viridans	2

GNR, Gram-negative rods; GPC, Gram-positive cocci; PTBD, percutaneous transhepatic biliary drainage.

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species, *Aeromonas hydrophila*, *E. coli*, *Klebsiella aerogenes*, *K. pneumoniae* and *Pseudomonas aeruginosa* were isolated from the peritoneal drain, and *E. coli*, *K. aerogenes*, *K. oxytoca*, *K. pneumoniae*, *P. aeruginosa* and *Stenotrophomonas maltophilia* were isolated from the PTBD drain. The GPC species *Enterococcus casseliflavus*, *E. faecalis* and a viridans streptococcus were isolated from both the peritoneal and PTBD drains.

Four of the 7 GNR species were PIPC/TAZ resistant; *E. coli*, *P. aeruginosa* and *S. maltophilia* showed an MDR phenotype. The antibiotic susceptibility profiles of these isolates are shown in Table II, along with the results of testing for carbapenemase and ESBL genes. Multiplex polymerase chain reaction (PCR) with a Cica Geneus genotype detection kit (Kanto Chemical, Tokyo, Japan) was used to identify the carbapenemase and ESBL genes.

Two E. coli strains were isolated from the peritoneal drain and three from the PTBD effluent, and all were piperacillin-tazobactam resistant. One of the two strains from the peritoneal drain was imipenem-intermediate resistant. All five strains had carbapenemase activity according to the carbapenem inactivation method and were positive for carbapenemase and extended-spectrum β-lactamase genes.

Infections associated with transhepatic biliary drainage devices have been reported previously [1]. *E. coli*, *P. aeruginosa*, *K. oxytoca*, *Hafnia alvei* and *E. faecium* have

Table II
Susceptibility profiles of multidrug-resistant Gram-negative bacteria

Species	*E. coli*	*S. maltophilia*	*P. aeruginosa*	*A. hydrophila*
Carbapenemase	OXA-48	ND	ND	ND
Extended-spectrum β-lactamase	CTX-M-1, TEM	ND	ND	ND
Antimicrobial agents				
Penicillins				
Piperacillin	**> 64**	**> 64**	**> 64**	**64**
Ampicillin/sulbactam	**> 16**	**> 16**	**> 16**	**> 16**
Amoxicillin/clavulanic acid	**> 16**	**> 16**	**> 16**	**16**
Piperacillin/tazobactam	**> 64**	**> 64**	**> 64**	**64**
Cephalosporins				
Cefazolin	**> 16**	**> 16**	**> 16**	**> 16**
Cefotiam	**> 16**	**> 16**	**> 16**	**> 16**
Cefotaxim	**> 2**	**> 2**	**> 2**	**> 2**
Ceftazidime	**> 16**	**> 16**	**> 16**	**> 16**
Ceftriaxone	**> 2**	**> 2**	**> 2**	**> 2**
Cefepime	**> 16**	**> 16**	**16**	2
Cefozopran	**> 16**	**> 16**	**> 16**	4
Cefmetazole	**> 32**	**> 32**	**> 32**	**> 32**
Cefpodoxime	**> 4**	**> 4**	**> 4**	**> 4**
Cefcapene	**> 2**	**> 2**	**> 2**	**> 2**
Flomoxef	**> 32**	**> 32**	**> 32**	**32**
Cephoperazon/sulbactam	**> 32**	**> 32**	**> 32**	**> 32**
Carbapenems				
Doripenem	1	ND	1	1
Imipenem	**2**	**> 8**	1	1
Meropenem	1	**> 8**	1	1
Monobactam				
Aztreonam	**> 16**	**> 16**	**16**	4
Fluoroquinolones				
Ciprofloxacin	**> 2**	**2**	**> 2**	1
Levofloxacin	**> 4**	1	**> 4**	0.5
Sitafloxacin	**> 2**	1	**> 2**	1
Aminoglycosides				
Gentamicin	2	**8**	4	2
Tobramycin	4	**8**	4	4
Amikacin	4	**> 32**	8	4
Tetracycline				
Minocycline	**> 8**	2	**> 8**	2
Polymyxin				
Colistin	2	ND	2	2
Other				
Fosfomycin	4	**> 16**	**> 16**	**16**
Trimethoprim/Sulfamethoxazole	**> 2**	2	**> 2**	2

Minimum inhibitory concentration (mg/L) values in bold represent resistant or non-susceptible strains. ND, not determined.

been isolated from blood cultures. Microorganisms including Enterobacteriaceae, *P. aeruginosa*, *Enterococcus* spp. and *Candida* spp., have been isolated from infected bile. *Aeromonas* spp. were isolated from a patient with sepsis who had transhepatic biliary devices [2]. However, these isolates were not reported to be drug-resistant. In the present study, we isolated a number of MDR GNR species from an infection associated with a transhepatic biliary drainage device, including OXA-48-producing *E. coli* and carbapenem-resistant *S. maltophilia*. To our knowledge, CRO and CPO (carbapenemase-producing organism) infections associated with PTBD devices have not been reported previously. *S. maltophilia* and *Aeromonas* spp. have intrinsic and inducible carbapenemases [3]. Such inducible CPOs should be further investigated to help prevent and control infections associated with transhepatic biliary drainage devices.

OXA-48-producing *E. coli* has been detected previously in patients hospitalised in India. For example, OXA-48-like-producing *E. coli* was isolated from patients who were transferred from India to France in 2011 [5]. Patients hospitalised in India are therefore at risk of infection or colonisation with OXA-48-producing Enterobacteriaceae [4]. OXA-48-like-producing Enterobacteriaceae have also spread throughout Turkey, Mediterranean countries and South Asia. The first OXA-48-producing Enterobacteriaceae reported in Japan were OXA-48-producing *K. pneumoniae* and *E. coli*, isolated from a patient with a medical history in Southeast Asia [6]. The OXA-48-like-producing *E. coli* isolates found in Japan and France, including those in the present study, were not resistant to carbapenems but were resistant to PIPC/TAZ [5,6]. Therefore, PIPC/TAZ may be useful for detecting carbapenem-sensitive CPOs. It is vital to continue to test for OXA-48-producing Enterobacteriaceae in hospitalised patients.

The results presented herein suggest that a medical history in India may be related to infection with a wide variety of MDR organisms. To reduce the spread of MDR organisms to low-prevalence countries like Japan, screening of all patients with a history of hospitalisation and travel abroad may be necessary. We suggest that medical staff consider contacting outpatients colonised with CPOs to help prevent the spread of MDR organisms.

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Declarations

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Competing Interests

No conflicts of interest associated with this manuscript.

Ethical approval

Not required.

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Satoshi Nishida[a,*], Miwa Asahara[b], Kentaro Nemoto[c], Shinobu Ishigaki[b], Taiji Furukawa[b], Keiji Sano[c], Yasuo Ono[a]

[a]*Department of Microbiology and Immunology, Teikyo University School of Medicine, Itabashi, Tokyo, Japan*

[b]*Department of Laboratory Medicine, Teikyo University Hospital, Itabashi, Tokyo, Japan*

[c]*Department of Surgery, Teikyo University School of Medicine, Itabashi, Tokyo, Japan*

* **Address Correspondence to:** Satoshi Nishida, Department of Microbiology and Immunology, Teikyo University School of Medicine, 2-11-1 Kaga, Itabashi, Tokyo, 173-8605, Japan. Tel.: +81 3 3964 3632; fax: +81 3 5375 5284.
E-mail address: nishida@med.teikyo-u.ac.jp (S. Nishida).

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