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Clinical and Microbiological Characteristics of Bacteremia Caused by *Eggerthella*, *Paraeggerthella*, and *Eubacterium* Species at a University Hospital in Taiwan from 2001 to 2010

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We describe 16 patients with bacteremia caused by *Eggerthella lenta* ($n = 7$), *Paraeggerthella hongkongensis* ($n = 3$), *Eubacterium limosum* ($n = 4$), *Eubacterium callanderi* ($n = 1$), and concomitant *Eubacterium limosum*/*Eggerthella lenta* ($n = 1$). Nine (56%) patients had polymicrobial bacteremia. The overall 60-day mortality rate was 19%, and all deaths occurred in patients with *E. lenta* bacteremia.

Eubacterium and *Eggerthella* species are Gram-positive, non-spore-forming, obligately anaerobic rods that previously belonged to the *Eubacterium* genus. *Eggerthella* species were reclassified as belonging to a novel genus because of their distinct 16S rRNA sequence (4). *Eggerthella hongkongensis* was reclassified as *Paraeggerthella hongkongensis* gen. nov., comb. nov. based on 16S rRNA sequencing (19). *Eubacterium* and *Eggerthella* species are common gastrointestinal commensals and have been implicated as the cause of intra-abdominal infections and bacteremia (8). They have been isolated from various human sites, including the gastrointestinal tract, the female genital tract, the oral cavity, the thoracic cavity, and the prostate (8).

Correct identification of *Eggerthella*, *Paraeggerthella*, and *Eubacterium* to the species level is difficult with conventional phenotypic methods (12). The patterns of acid produced in peptone-yeast extract glucose broth can be used to differentiate *Eggerthella* and *Eubacterium* from other closely related genera, such as *Propionibacterium*, *Bifidobacterium*, *Lactobacillus*, and *Actinomyces* (4). Furthermore, other newer genera closely related to *Eubacterium* and *Eggerthella* species, such as *Atopobium*, *Slackia*, and *Solobacterium*, were also associated with bacteremia (5, 6, 7, 15, 18). Even with biochemical and fermentation reactions, the subspecies of *Eubacterium* cannot be reliably differentiated (4, 8). Furthermore, newer subspecies of *Eggerthella*, *Paraeggerthella*, and *Eubacterium* are not included in the databases of commercial rapid identification systems.

Patients with laboratory-documented *Eubacterium* bacteremia during the period from January 2001 to December 2010 at the National Taiwan University Hospital, a 2,500-bed tertiary medical center in northern Taiwan, were included in the analysis. Disease severity was evaluated by the Pittsburgh bacteremia score (14). Healthcare-associated bacteremia was defined as infections that were acquired during the course of receiving treatment for other conditions within a health care setting. Community-associated bacteremia was defined as infections that were acquired outside the hospital setting (9, 10).

All *Eubacterium* isolates were initially identified by conventional methods and were reidentified using partial sequencing of the 16S rRNA gene as previously described (11, 17). The results were compared with published sequences in the GenBank database using the BLASTN algorithm. Based on the results of partial sequencing of 16S rRNA genes, *Eggerthella lenta* bacteremia was diagnosed in seven patients, *Eubacterium limosum* bacteremia in four, *Paraeggerthella hongkongensis* bacteremia in three, *Eubacterium callanderi* bacteremia in one, and concomitant *Eubacterium limosum* and *Eggerthella lenta* bacteremia in one patient (Table 1).

The MICs of 16 antimicrobial agents (except daptomycin) were determined using the agar dilution method according to Clinical and Laboratory Standards Institute (CLSI) guidelines with *Brucella* agar supplemented with 5 μg/ml hemin, 1 μg/ml vitamin K1, and 5% laked sheep blood (2). For daptomycin susceptibility assay, the broth microdilution method was performed. *Brucella* broth (BBL Microbiology Systems) supplemented with hemin (5 μg/ml), vitamin K1 (1 μg/ml), lysed horse blood (5%), and calcium (50 μg/ml) was used (2). *Clostridium difficile* ATCC 700057 and *Bacteroides fragilis* ATCC 25285 were used as quality control strains. The MIC data of the 17 agents against the 17 isolates are shown in Table 2. According to 2010 CLSI breakpoints (1), all 17 isolates were susceptible to ampicillin-sulbactam, metronidazole, imipenem, and meropenem, while 82%, 88%, and 88% of the isolates were susceptible to moxifloxacin, cefmetazole, and piperacillin-tazobactam, respectively. In contrast, 71% of the isolates were resistant to penicillin. *Eggerthella* species showed the highest rate of resistance to clindamycin (63%).

The details of the 16 patients are depicted in Table 1. The majority of infections were community acquired. Almost half of the patients (44%) presented with abdominal symptoms. The most common immunocompromised status was malignancy ($n = 6$, 38%). Gynecologic malignancy was noted in two patients. None of the patients had gastrointestinal tract malignancy. Nine (56%) patients had polymicrobial bacteremia. The most common con-

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TABLE 1 Clinical features of 16 patients with *Eggerthella*, *Paraeggerthella*, or *Eubacterium* bacteremia

Characteristic	Patients [no. (%) or as indicated] with:					
	E. lenta [7 (44)]	*P. hongkongensis* [3 (19)]	*E. limosum* [4 (25)]	*E. callanderi* [1 (6)]	*E. lenta* and *E. limosum* [1 (6)]	Total [16 (100)]
Age [yr; median (range)]	56 (51–93)	49 (32–73)	76 (26–81)	44	66	58.5 (26–93)
Gender						
No. male/no. female	4:3	2:1	2:2	0:1	0:1	8:8
Abdominal symptoms	2 (29)	1 (33)	3 (75)	0	1	7 (44)
Healthcare associated/community acquired	2 (29)/5 (71)	1 (33)/2 (67)	0/4 (100)	1 (100)/0	1 (100)/0	5 (31)/11 (69)
Underlying health status						
Steroid usage	2 (29)	0	0	1 (100)	0	3 (19)
Diabetes mellitus	1 (14)	0	1 (25)	0	0	2 (13)
End-stage renal disease	2 (29)	0	0	0	0	2 (13)
Recent chemotherapy	1 (14)	0	0	1 (100)	0	2 (13)
Malignancies	3 (43)	0	1 (25)	1 (100)	1 (100)	6 (38)
Gynecologic malignancy	1 (14)	0	0	0	1 (100)	2 (13)
Gastrointestinal disease	1 (14)	1 (33)	3 (75)	0	1 (100)	6 (38)
Abdominal operation within 4 weeks	0 (0)	1 (33)	1 (25)	0	0	2 (13)
Polymicrobial bacteremia	3 (43)	1 (33)	4 (100)	0	1 (100)	9 (56)
Pitt bacteremia score (mean ± SD)[a]	2.85 ± 3.67	2 ± 3.46	1 ± 1.1	3	0	2.06 ± 2.86
Initial antibiotic treatment						
Penicillins	2 (29)	0	2 (50)	1 (100)	1 (100)	6 (38)
Carbapenems	0 (0)	2 (67)	0	0	0	2 (13)
Cephalosporins	4 (57)	0	1 (25)	0	1 (100)	6 (38)
Vancomycin	0	1 (33)	0	0	0	1 (6)
Metronidazole	1 (14)	0	0	0	0	1 (6)
All-cause mortality at:						
14 days	1 (14)	0	0	0	0	1 (6)
30 days	1 (14)	0	0	0	0	1 (6)
60 days	3 (43)	0	0	0	0	3 (19)

[a] Disease severity at bacteremia onset.

comitant polymicrobial pathogens were *Bacteroides* species, including four cases of bacteremia due to *Bacteroides caccae* and two due to *B. fragilis*, and three cases were due to *Escherichia coli*. Other pathogens associated with polymicrobial bacteremia included coagulase-negative staphylococci, *Clostridium clostridioforme*, *Staphylococcus aureus*, and *Klebsiella pneumoniae*. The overall 60-day mortality rate was 19% ($n = 3$), and all deaths occurred in patients with *E. lenta* bacteremia. The cause of mortality was directly attributed to profound shock due to monomicrobial *E. lenta* bacteremia in one patient. The Pitt bacteremia score was 6 in this patient. The other two patients, with concomitant multiple comorbidity conditions (one patient had gastrointestinal bleeding, biliary tract infection, and venous thrombosis, and one had nasopharyngeal and tongue cancer), subsequently developed clinical deterioration during the episode of *E. lenta* bacteremia and died of repeated nosocomial infections and multiorgan failure. The Pitt bacteremia scores of these two patients with fatal outcomes were 0 and 8.

Bacterial species in the *Eubacterium* and *Eggerthella* genera are common gastrointestinal commensals (3, 8). Previous reports, therefore, focused on associated gastrointestinal diseases as the disease mechanism (8, 16). In our series, about half of the patients presented with abdominal symptoms. Two patients had gynecological malignancies. This may highlight the importance of the female reproductive tract as another potential portal of entry, since the vaginal tract has also been reported to be a natural human habitat of *Eubacterium* and *Eggerthella* species (8).

In our series, *E. lenta* was isolated primarily from patients with significant comorbidities, and it is likely that the preexisting disease state of the patient allowed the organism to gain access to the bloodstream. *P. hongkongensis* is a novel species first discovered in blood from four bacteremic patients in Hong Kong (8, 19). Our study also supports the idea that *P. hongkongensis* may be the second-most-common *Eggerthella* species causing bacteremia (8).

In one case series including 29 clinical isolates of *E. lenta*, all were susceptible to clindamycin, piperacillin, and imipenem (13). In the study by Lau et al., all 10 *Eggerthella* and *Paraeggerthella* isolates were susceptible to penicillins and metronidazole (8). In our study, there was a high rate of resistance to penicillin, as defined by CLSI breakpoints (1). In the present study, novel antibiotics, including doripenem, tigecycline, and daptomycin, all showed low MICs against *Eggerthella*, *Paraeggerthella*, and *Eubacterium* species.

In summary, *Eggerthella*, *Paraeggerthella*, and *Eubacterium*

TABLE 2 Antimicrobial susceptibilities of 17 blood isolates of *Eggerthella*, *Paraeggerthella*, and *Eubacterium* species

Isolate no. (bacterial species)	MIC (susceptibility)[a]																
	PEN	SAM	CMZ	FLO	TZP	MEM	DOR	MOX	NEM	CLI	VAN	LIN	MET	FID	IMI	TIG	DAP
1 (*E. lenta*)	2 (R)	4 (S)	16 (S)	16	32 (S)	0.5 (S)	0.25	0.25 (S)	0.12	>32 (R)	1	0.5	1 (S)	0.015	1 (S)	0.12	0.25
2 (*E. lenta*)	2 (R)	4 (S)	16 (S)	8	32 (S)	0.5 (S)	0.25	0.25 (S)	0.25	>32 (R)	1	1	1 (S)	0.06	1 (S)	0.12	0.25
3 (*E. lenta*)	2 (R)	4 (S)	16 (S)	16	32 (S)	0.5 (S)	0.25	0.25 (S)	0.5	>32 (R)	1	1	2 (S)	0.03	1 (S)	0.12	0.5
4 (*E. lenta*)	2 (R)	4 (S)	16 (S)	16	32 (S)	0.5 (S)	0.25	4 (I)	2	2 (S)	2	1	2 (S)	0.06	1 (S)	0.25	0.25
5 (*E. lenta*)	4 (R)	4 (S)	32 (I)	16	32 (S)	0.5 (S)	0.25	0.25 (S)	0.5	>32 (R)	2	1	2 (S)	0.25	1 (S)	0.25	0.25
6 (*E. lenta*)	4 (R)	4 (S)	32 (I)	16	64 (I)	0.5 (S)	0.25	0.5 (S)	0.5	1 (S)	2	1	2 (S)	0.12	1 (S)	0.25	0.25
7 (*E. lenta*)	1 (I)	4 (S)	16 (S)	8	32 (S)	0.5 (S)	0.25	>32 (I)	>32	>32 (R)	2	1	2 (S)	0.06	0.5 (S)	0.12	0.25
8 (*E. lenta*)	1 (I)	4 (S)	16 (S)	8	32 (S)	0.5 (S)	0.25	0.25 (S)	0.25	0.5 (S)	0.5	1	2 (S)	0.015	1 (S)	0.12	0.25
9 (*P. hongkongensis*)	0.5 (S)	4 (S)	8 (S)	8	32 (S)	0.5 (S)	0.25	0.25 (S)	0.5	4 (I)	1	1	2 (S)	0.12	0.5 (S)	0.06	0.25
10 (*P. hongkongensis*)	2 (R)	4 (S)	16 (S)	16	64 (I)	0.5 (S)	0.25	4 (I)	1	4 (I)	2	1	4 (S)	0.12	1 (S)	0.25	0.25
11 (*P. hongkongensis*)	0.5 (S)	2 (S)	8 (S)	8	16 (S)	0.5 (S)	0.25	0.25 (S)	2	4 (I)	2	1	4 (S)	0.25	0.5 (S)	0.12	0.25
12 (*E. limosum*)	2 (R)	0.12 (S)	0.5 (S)	0.25	0.03 (S)	0.03 (S)	0.03	2 (S)	1	2 (S)	1	2	0.12 (S)	32	0.06 (S)	0.06	0.06
13 (*E. limosum*)	2 (R)	0.25 (S)	2 (S)	1	0.12 (S)	0.06 (S)	0.06	2 (S)	1	2 (S)	2	2	0.25 (S)	32	0.12 (S)	0.06	0.12
14 (*E. limosum*)	2 (R)	0.5 (S)	1 (S)	1	0.25 (S)	0.03 (S)	0.06	2 (S)	1	2 (S)	2	4	0.25 (S)	32	0.12 (S)	0.12	0.25
15 (*E. limosum*)	2 (R)	0.12 (S)	1 (S)	0.5	0.06 (S)	0.03 (S)	0.03	2 (S)	2	2 (S)	2	2	0.12 (S)	32	0.12 (S)	0.12	0.12
16 (*E. limosum*)	1 (I)	0.25 (S)	2 (S)	1	0.12 (S)	0.03 (S)	0.12	2 (S)	1	>32 (R)	2	4	0.12 (S)	16	0.12 (S)	0.06	0.12
17 (*E. callanderi*)	4 (R)	0.5 (S)	2 (S)	1	0.25 (S)	0.03 (S)	0.12	2 (S)	2	4 (I)	2	4	0.25 (S)	32	0.12 (S)	0.12	0.25

[a] MICs are in μg/ml. PEN, penicillin; SAM, ampicillin-sulbactam; CMZ, cefmetazole; FLO, flomoxef; TZP, piperacillin-tazobactam; MEM, meropenem; DOR, doripenem; MOX, moxifloxacin; NEM, nemofloxacin; CLI, clindamycin; VAN, vancomycin; LIN, linezolid; MET, metronidazole; FID, fidaxomicin; IMI, imipenem; TIG, tigecycline; DAP, daptomycin; S, susceptible; I, intermediate; R, resistant (according to CLSI MIC interpretive breakpoints) (1).

species can cause invasive human infections in immunocompromised hosts. More than 50% of the infections were polymicrobial, so that these organisms participated in bacteremias in patients with leaky guts or diseased female reproductive tract. *Eggerthella lenta* bacteremia is associated with significant mortality and morbidity. Ampicillin-sulbactam, metronidazole, carbapenems, tigecycline, and daptomycin all possess low MICs against species of these three genera.

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