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Bacteremia caused by antimicrobial resistant *Campylobacter* species at a medical center in Taiwan, 1998–2008

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Summary *Objectives:* This study was intended to delineate the clinical and microbiological characteristics of patients with bacteremia caused by *Campylobacter* species.
Methods: Twenty-four patients with *Campylobacter* bacteremia were treated at the National Taiwan University Hospital from 1998 to 2008. All isolates from the 24 patients were confirmed to the species level by multiplex PCR (*cad*F, *hip*O and *asp* gene) and 16S RNA gene sequencing.
Results: Bacteremia was caused by *Campylobacter coli* in 15 (62.5%) patients, *Campylobacter fetus* in 6 (25%), and *Campylobacter jejuni* in 3 (12.5%). Of the 24 patients, 16 were male. The major underlying conditions included chronic renal insufficiency (41.7%), liver cirrhosis (37.5%), malignancy (33.3%), and previous abdominal surgery (33.3%). The most common infections were intra-abdominal infection (54.2%), followed by primary bacteremia (41.7%), and cellulitis (4.2%). The mean Pittsburgh bacteremia score was 2.5 (range, 0–9). During the bacteremic episodes, six (25%) patients developed septic shock. Third-generation cephalosporins were administered to 12 (50%) patients as empirical therapy. All-cause mortality was 4.2% at 14 days and 12.5% at 30 days. The majority of the isolates were resistant to third-generation

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cephalosporins and quinolones, with minimum inhibitory concentration (MIC_{90}) values of 32 mg/L for cefotaxime, 128 mg/L for ceftriaxone, and 32 mg/L for both ciprofloxacin and levofloxacin. All isolates possessed a *par*C mutation (Arg-139-Gln) and 15 exhibited an additional *gyr*A mutation (Thr-86-Ile). Among these isolates, 20.8% were susceptible to erythromycin ($MIC \leq 0.5$ mg/L).

Conclusion: Bacteremia caused by antimicrobial resistant *Campylobacter* species is alarming although the mortality rate is low.

Introduction

Campylobacter is a genus of Gram-negative, non-spore-forming, motile bacteria with a characteristic spiral or corkscrew-like appearance. *Campylobacter* species are recognized as one of the major causes of bacterial enteritis in the developed world, and *Campylobacter jejuni* is the most common causative pathogen.[1–3] A number of studies have demonstrated that *C. jejuni*, *Campylobacter fetus*, and *Campylobacter coli* can result in bacteremia in patients with underlying illness, such as liver cirrhosis and HIV infection.[4–10] Moreover, other rare *Campylobacter* species were also reported to cause bacteremia, such as *Campylobacter lari*, *Campylobacter insulaenigrae*, and *Campylobacter upsaliensis*.[11] However, the presentations and severity of diseases and distributions of *Campylobacter* species differed among those studies, which might reflect differences in the epidemiology and virulence of *Campylobacter* in different regions.[3–10]

Quinolone resistance emerged among *Campylobacter* species and might increase the duration of diarrhea and limit the utility of quinolone,[12–15] but one study questioned the clinical significance of quinolone resistance.[16] Enteritis caused by *Campylobacter* is normally self-limiting, and patients usually recover without antimicrobial therapy. In contrast, physicians usually prescribe systemic antimicrobial agents for patients with *Campylobacter* bacteremia. However, the susceptibilities of *Campylobacter* isolates vary and susceptibility testing of *Campylobacter* species is not routinely performed in most laboratories.[9] Therefore, clinicians need to choose antimicrobial therapy based on historical local susceptibility patterns, which might change with time.

In our previous report on bacteremia due to *Campylobacter* species during 1991—1999 at the National Taiwan University, resistance rates of macrolides and quinolone among *Campylobacter* isolates were high.[6] In order to delineate the *Campylobacter* species causing bacteremia and its clinical presentations of patients, we conducted a retrospective analysis of all cases of *Campylobacter* bacteremia diagnosed at the National Taiwan University Hospital (NTUH) from 1998 through 2008. Antibiotic susceptibility patterns of different species were also analyzed.

Materials and methods

Patients and setting

Patients with *Campylobacter* bacteremia were identified by review of the laboratory records of the NTUH from January 1998 to December 2008. The hospital is a 2500-bed university-affiliated hospital in Taipei that provides both primary and tertiary medical care. The medical records of patients with *Campylobacter* bacteremia were retrospectively reviewed. The following data were systematically extracted: demographic characteristics, clinical manifestations associated with bacteremia, underlying conditions, severity of bacteremia by Pittsburgh bacteremia score,[17] empirical and definite antimicrobial agents, and mortality within 30 days. Appropriate antimicrobial therapy was defined as therapy with antimicrobial agents to which the isolates were susceptible *in vitro*.

Laboratory methods

Blood cultures were processed using the BACTEC blood culture system (Becton Dickson, Sparks, MD, USA), and Gram-negative bacteria demonstrating a curved or spiral-shaped appearance that reacted positively to oxidase and catalase were preliminarily identified as *Campylobacter* species using conventional biochemical methods.[18] The isolates were subcultured onto CAMPY BAP agar plates (BBL Microbiology System, Cockeysville, MD, USA) after incubation for 48 h in a microaerobic atmosphere (5% O_2, 10% CO_2, 85% N_2) at 25 °C, 37 °C, or 42 °C. Isolates that grew well at 42 °C but not at 25 °C and that were resistant to cephalothin (30-μg disk diffusion method) were identified as either *C. jejuni* or *C. coli*. These thermophilic *Campylobacter* isolates were considered to be *C. jejuni* if they were positive for hippurate hydrolysis and *C. coli* if they were negative for hippurate hydrolysis.[1] *C. fetus* was identified if the isolate grew at 25 °C but not at 42 °C and was susceptible to cephalothin (30-μg disk diffusion method).

The isolates were further confirmed to the species level by multiplex PCR (*cad*F, *hip*O and *asp* gene) and 16S rRNA gene sequencing as previously described.[18,19] The 16S rRNA gene sequencing data (907 bp) of these isolates were deposited to GenBank and the accession numbers of the submitted nucleotide sequences were reported.

Antimicrobial susceptibility testing

Minimum inhibitory concentrations (MICs) of 15 antimicrobial agents were determined using the agar dilution method as previously described.[20] Mueller-Hinton agar plates with 5% of sheep blood (BBL Microbiology System) was used for susceptibility testing. The antimicrobial agents used for susceptibility testing were obtained from their corresponding manufacturers. The MICs were read after 48 h of incubation in a microaerobic atmosphere (5% O_2, 10% CO_2, and 85%