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ORIGINAL ARTICLE

Clinical analysis of *Enterobacter* bacteremia in pediatric patients: A 10-year study

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Background: Enterobacter species has emerged as an important pathogen of nosocomial bacteremia. The purpose of this study is to review the clinical characteristics of bacteremia in pediatric patients.
Materials and methods: We reviewed retrospectively the medical records of patients (under the age of 18 years) having *Enterobacter* bacteremia who were treated at Taipei the Veterans General Hospital from January 2001 to June 2011.
Results: In total, 853 positive blood cultures were obtained from 620 patients during the study period. Among them, 96 episodes of *Enterobacter* bacteremia were found in 83 patients, accounting for 11.3% of all bacteremia. Eighty-two cases (98.8%) were nosocomial infections. Most of the cases were neonates (62 cases, 74.7%) and premature infants (51 cases, 61.5%). The common sources of bacteremia were the respiratory tract (53.0%), followed by intravascular catheter (10.8%), multiple sources (10.8%), and the gastrointestinal tract (8.4%). The overall case fatality rate was 18.1%, with the highest rate being reported among premature infants. The factors responsible for the deaths were leukocytosis and a higher median number of underlying diseases.
Conclusion: Based on the findings of the present study, it can be concluded that *Enterobacter* species are probably an important pathogen of nosocomial bacteremia in premature neonates. The number of underlying diseases should be considered a major factor influencing the prognosis.

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Introduction

Nosocomial bloodstream infections are important causes of morbidity and mortality worldwide. *Enterobacter* species, which are the normal members of the flora of the gastrointestinal tract, are significant pathogens for a variety of infections, such as pneumonia, urinary tract infections, wound infections, and bacteremia, especially in nosocomial infections.[1–3] In healthy children, *Enterobacter* species rarely cause any disease; however, in patients with underlying diseases, especially in premature patients, they are frequent pathogens involved in bacteremia.[3–5] Several risk factors of *Enterobacter* bacteremia are known, such as gastrointestinal disease, life-threatening infections, malignancies, prematurity, use of a central venous catheter, ventriculostomy, use of a ventriculoperitoneal shunt catheter, prolonged antibiotic therapy, parenteral nutrition, and immunosuppressive therapy.[6] According to a large-scale survey conducted in the USA, *Enterobacter cloacae* accounted for 3.9% of all nosocomial bloodstream infections.[4] At the same time, a significant increase was observed in the antimicrobial resistance rates of *E. cloacae*. We conducted a retrospective study in order to review the clinical characteristics and antimicrobial susceptibility of *Enterobacter* bacteremia in pediatric patients.

Materials and methods

We reviewed retrospectively the medical records of patients under the age of 18 years, whose blood cultures yielded *Enterobacter* species, treated at the Taipei Veterans General Hospital between January 2001 and June 2011. Data were collected on age, sex, abnormal clinical findings [fever, poor activity, leukocytosis, leukopenia, and high C-reactive protein (CRP) level], underlying illness, and type of infection. The presence of the following comorbid conditions was also documented: parenteral nutrition, corticosteroid use, immunosuppressant use, and invasive procedures.

Definitions

Enterobacter bacteremia was defined as the presence of *Enterobacter* species in one or more positive blood cultures collected during the hospitalization of these patients with corresponding clinical conditions. Only the first episode of *Enterobacter* bacteremia in each patient was considered as "one patient". Nosocomial infection was defined as an infection occurring after 72 hours of admission. Otherwise, bacteremia was considered to be community acquired. Polymicrobial bacteremia was defined as the isolation of multiple pathogens from the same culture (the same bottle of blood culture) or from different cultures (different bottles) but at the same time.

The source of infection was determined as one of the following: respiratory tract, intestinal, biliary tract, urinary tract, surgical wounds, intravascular catheter, or multiple or unknown sources, based on clinical signs and symptoms (e.g., fever, leukocytosis, leukopenia, poor activity, and high CRP level) of infection and organisms cultured from these possible sources. Bacteremia was considered to have originated from the lungs when a ventilator was used for a prolonged time or radiologic evidence of new-onset or progressing pneumonia was found with concomitant isolation of *Enterobacter* species from blood or sputum. Bacteremia of unknown origin was defined as bacteremia for which there was no documented distal source.

Empirical antibiotic treatment was considered appropriate when all isolated pathogens were susceptible to at least one of the administered agents and it was administered prior to the time of positive blood culture. However, empirical therapy was considered inappropriate when the isolate was nonsusceptible to the antimicrobial agents(s) administered or the patients were not prescribed antimicrobial agents on the day of the onset of bacteremia.[7] Recovery was defined as improvements in patients' clinical condition, such as becoming afebrile and having stable vital signs after the initiation of antibiotic therapy. Morbidity was considered when the patients had long time sequels which were directly related to bacteremia, despite appropriate antibiotic treatments. The case fatality rate was defined as the number of deaths among patients with bacteremia. Death was not considered directly because of other conditions being apparently documented as the cause of death; otherwise, the death was attributable to the bacteremia. Nonparametric data were expressed as median and range.

Microbiology

Blood samples of around 0.5—1.0 mL were collected under sterile conditions from peripheral punctures and injected directly into Baxtar blood culture bottles. These bottles were then incubated in BACTEC 9240, which is designed for the rapid detection of bacteria and fungi in clinical cultures of blood (Becton Dickinson Diagnostic Instrument Systems, Sparks, MD, USA), at 35.5°C. Antimicrobial susceptibility tests were carried out using the MicroScan AutoSCAN-4 data management system (Dade MicroScan Inc., West Sacramento, CA, USA).

Statistical analysis

Univariate analysis was performed to identify the possible risk factors associated with death attributable to *Enterobacter* bacteremia. The Mann—Whitney *U* test, independent samples *t* test, and Fisher's exact test were used as appropriate. Statistical analysis was performed using IBM SPSS version 19 (SPSS Inc., Chicago, IL, USA). A p value of <0.05 was considered statistically significant.

Results

During the 10-year retrospective study period, 853 positive blood cultures were obtained from 620 pediatric patients. The most common pathogens of bacteremia were yeast, *Staphylococcus aureus*, and *Staphylococcus epidermidis*; *Enterobacter* ranked fourth, accounting for 11.3% of all types of bacteremia. *E. cloacae* was the most common species, accounting for 78 episodes (81.3%); followed by *Enterobacter aerogenes*, for 11 episodes (11.5%); *Enterobacter sakazakii*, for four episodes (4.2%); and