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ORIGINAL ARTICLE

Clinical manifestations and bacteriological features of culture-proven Gram-negative bacterial arthritis

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KEYWORDS

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septic arthritis

Abstract *Background/Purpose:* To investigate the clinical manifestations and bacteriological features of culture-proven, Gram-negative bacterial arthritis.

Methods: This study was conducted at the Chi Mei Medical Center, a 1300-bed teaching hospital located in southern Taiwan. Patients with synovial fluid cultures positive for Gram-negative bacilli (GNB) during the period January 2009 to May 2014 were identified from the hospital's computerized microbiology database.

Results: During the study period, a total of 48 patients with culture-confirmed, GNB septic arthritis were identified. In the majority of patients ($n = 33$, 68.8%), the knee was the most commonly involved joint. The most common causative pathogen was *Pseudomonas* spp. ($n = 16$, 33.3%), followed by *Escherichia coli* ($n = 13$, 28.1%). Among the 29 clinical isolates of Enterobacteriaceae, eight (27.6%) were resistant to ceftriaxone and six (20.7%) were resistant to ceftazidime. Three *E. coli* isolates and three *Klebsiella pneumoniae* isolates were extended-spectrum beta-lactamase producers ($n = 6$, 20.7%). Among the nonfermenting GNB (NFGNB), 21.1% were resistant to ceftazidime, 21.1% were resistant to ciprofloxacin, 26.3% were resistant to piperacillin-tazobactam, and 15.8% were resistant to imipenem. The overall mortality rate was 10.4%, and the significant risk factors for death were concomitant

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bacteremia [odds ratio (OR): 14.6, 95% confidence interval (CI): 1.9–115.2, $p = 0.011$] and liver cirrhosis (OR: 20.0, 95% CI: 2.4–169.9, $p = 0.006$).

Conclusion: Approximately 25% of cases of septic arthritis were due to GNB and resistance to commonly used antimicrobial agents was common. Liver cirrhosis and concomitant bacteremia were significant risk factors for death.

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Introduction

Septic arthritis is inflammation of a joint due to bacterial, mycobacterial, or fungal infection.¹ Without appropriate treatment, septic arthritis can lead to the irreversible destruction and dysfunction of the joint. The reported incidence ranges from four to 29 cases per 100,000 person-years.² Gram-positive bacteria are the most common causative pathogens, with *Staphylococcus aureus* and *Streptococcus pneumoniae* being the most frequently isolated.^{3–6} Septic arthritis is less commonly caused by Gram-negative bacilli (GNB), accounting for only 14–19% of septic arthritis cases.^{7,8}

Treatment of septic arthritis requires appropriate antibiotics and drainage. The initial use of antibiotics should be based on knowledge of the epidemiology of the causative bacterium and its drug-resistance pattern; however, little is known about the bacteriology and associated antibiotic-resistance patterns of GNB causing septic arthritis.^{4,8} The aim of this study was to investigate the clinical manifestations of patients with septic arthritis due to GNB and to evaluate the bacteriology and antibiotic-resistant patterns of GNB.

Methods

Hospital setting and patient selection

This study was conducted at the Chi Mei Medical Center, a 1300-bed hospital in southern Taiwan. All patients with synovial fluid cultures positive for GNB during the period from January 2009 to May 2014 were retrospectively identified from the computerized database of the microbiology department. Information was collected on age, gender, and underlying conditions including the history of immunosuppressant drug use, diabetes mellitus, liver cirrhosis, end-stage renal disease, and malignancy. Infections were classified as health care-associated infections in patients who acquired the disease during the course of treatment for other conditions within a health care setting. Otherwise, septic arthritis was classified as community acquired. Polymicrobial infections were diagnosed in patients from whom GNB isolates in addition to other pathogens were isolated from synovial fluid specimens. Immunocompromised status was diagnosed in patients with liver cirrhosis, diabetes mellitus, end-stage renal disease, or active cancer. Concomitant bacteremia was diagnosed in patients whose blood cultures were positive for the same species yielded from synovial fluid. In-hospital mortality was

defined as death from all causes during hospitalization. The data were collected on a routine basis, and the analysis was performed retrospectively. Therefore, no informed consent was required, and the Institutional Review Board of the Chi Mei Medical Center specifically waived the need for informed consent when it approved the study.

Bacterial isolates and antimicrobial susceptibilities

All isolates were identified by conventional methods and the susceptibilities of the isolates to a battery of antimicrobial agents were determined using the disk diffusion method as described by the Clinical and Laboratory Standards Institute.

Statistical analysis

Continuous variables are expressed as means \pm standard deviations and were compared using the Wilcoxon rank sum test or Student independent t test, as appropriate. Categorical variables were compared using the Chi-square test or Fisher's exact test. A p value <0.05 was considered to indicate statistical significance. All statistical analyses were performed with the statistical package SPSS for Windows (version 19.0, SPSS Inc., Chicago, IL, USA).

Results

Patient demographics and clinical characteristics

Of the 194 patients with culture-confirmed septic arthritis identified during the study period, 48 (24.7%) had septic arthritis caused by GNB species. The clinical characteristics of all patients with culture-proven septic arthritis are summarized in Table 1. We found that arthritis due to Gram-positive cocci (GPC) was more likely to develop in patients with end-stage renal disease, diabetes mellitus, and prosthetic joints ($p < 0.05$), and that *S. aureus* was the most prevalent GPC species.

Of the patients with arthritis due to GNB, 30 (62.5%) were ≥ 65 years of age. The knee was the most commonly involved joint ($n = 34$, 70.8%), followed by hip ($n = 8$, 16.7%), ankle ($n = 4$, 8.3%), elbow ($n = 1$, 2.1%), and shoulder ($n = 1$, 2.1%). Only one (2.1%) patient had multiple joint involvement (bilateral shoulders). More than half of the infections developed in prosthetic joints, and most (24/26) of the prosthetic joint infections developed within 6 months after joint surgery. Seven (14.6%) patients had

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