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Original Article

Group B streptococcal bacteremia in non-pregnant adults

Po-Yen Huang, Ming-Hsun Lee, Chien-Chang Yang, Hsieh-Shong Leu

Division of Infectious Diseases, Department of Internal Medicine, Chang Gung Memorial Hospital, Taoyuan, Taiwan

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Background and Purpose: An increasing incidence of group B streptococcus (GBS) infection in non-pregnant adults has been noted in recent years. To understand the incidence, clinical characteristics, and outcome of GBS bacteremia in non-pregnant adults, we conducted a retrospective study at a tertiary teaching hospital in Taiwan.
Methods: This retrospective analysis included 94 non-pregnant adults (age ≥18 years) with GBS bacteremia hospitalized between January 2001 and December 2003.
Results: The incidence of GBS bacteremia increased from 0.16 cases/1000 admissions in 2001 to 0.30 cases/1000 admissions in 2003 (p=0.017, chi-squared test for trend). The mean age of patients was 64.7 ± 1.39 years. At least 1 underlying systemic disease was found in 81% of patients, with the most frequent being malignancy (43.6%), diabetes mellitus (42.6%), and liver cirrhosis (16%). The 2 major clinical syndromes were primary bacteremia (34%) and soft tissue infection (31.9%). The overall mortality rate was 20.2%. *Staphylococcus aureus* and *Klebsiella pneumoniae* were the 2 most common concurrently isolated bloodstream pathogens. Polymicrobial bacteremia, thrombocytopenia, and shock were independent risk factors for mortality in GBS bacteremia.
Conclusions: The increasing incidence of GBS bacteremia is noteworthy, especially among patients with invasive infections. These infections are also responsible for substantial mortality in elderly patients with underlying diseases. Susceptibility testing indicated that penicillin G remains the drug of choice for GBS bacteremia.

Key words: Adult, bacteremia; retrospective studies, risk factors, *Streptococcus agalactiae*

Introduction

Group B streptococcus (GBS, *Streptococcus agalactiae*) is an important cause of invasive infections in neonates and in the elderly with underlying or chronic diseases [1]. An increasing incidence of GBS infection in non-pregnant adults has been noted over the past decades [2-4]. Despite the decline in neonatal GBS infections, more than two-thirds of invasive GBS infections in the United States now occur in adults, most of which are unrelated to pregnancy [2]. Common presentations of GBS infections include skin and soft tissue infections, osteoarticular infections, pneumonia, and urosepsis [2]. Several chronic diseases, including liver cirrhosis, diabetes mellitus, stroke, breast cancer, decubitus ulcer, and neurogenic bladder, are associated with invasive GBS infections [5]. GBS causes substantial mortality and morbidity in non-pregnant adults, especially the elderly [6,7]. The mean age of non-pregnant adults with invasive GBS diseases is around 60 years, and the associated mortality rate is about 25% [2].

To study the trend in the incidence, as well as the clinical characteristics and risk factors for mortality in GBS bacteremia, we conducted a retrospective analysis of patients with GBS bacteremia admitted to Chang Gung Memorial Hospital-Linkou Medical Center between January 2001 and December 2003.

Methods

Patients and study design

We retrospectively reviewed medical charts of non-pregnant adults (age ≥18 years) with GBS bacteremia admitted to Chang Gung Memorial Hospital-Linkou Medical Center between January 2001 and December 2003. The first GBS bacteremic episode was included if the patient had multiple GBS bacteremic episodes during the study period. Patients with missing

Corresponding author: Dr. Hsieh-Shong Leu, Division of Infectious Diseases, Department of Internal Medicine, Chang Gung Memorial Hospital, 5 Fu-Shin St., Kweishan 333, Taoyuan, Taiwan.
E-mail: hsleu@adm.cgmh.org.tw

information on charts were excluded. Data on demographic characteristics, underlying systemic diseases, clinical presentations, specifically involved sites, bacteriology and related antimicrobial susceptibility testing, antimicrobial regimens, duration of hospital stay and outcomes were extracted for analysis. Diabetes mellitus was defined according to the American Diabetes Association guidelines [8]. Diagnosis of endocarditis was made according to the modified Duke criteria [9]. Bacteremia without a definite infection source was categorized as primary bacteremia. Polymicrobial bacteremia was defined as bloodstream infection caused by at least 2 bacteria species including GBS.

Renal insufficiency was defined as serum creatinine ≥1.6 mg/dL. Thrombocytopenia was defined as platelet count $\leq 100 \times 10^9$/L. Shock was defined as systolic blood pressure ≤90 mm Hg measured on the same day as the collection of blood specimens for culture. Mortality was defined as death due to all causes within 14 days after the emergence of bacteremia.

Laboratory identification

Identification of GBS was based on the recognition of Gram-positive cocci, absence of catalase production, beta-hemolysis on sheep blood agar plates, positive CAMP (Christie, Atkins, and Munch-Peterson) test, and latex agglutination with group-specific antiserum (Boule Diagnostics AB, Huddinge, Sweden). In total, 97 isolates were available for in vitro susceptibility testing using disk diffusion and broth microdilution methods, which were performed in accordance with National Committee for Clinical Laboratory Standards [10]. The tested antibiotics included penicillin G, cefuroxime, ceftriaxone and vancomycin. Penicillin-non-susceptible isolates were defined as a minimum inhibitory concentration (MIC) >0.13 μg/mL.

Statistical analysis

The results were analyzed using a commercially available software package (Statistical Package for the Social Sciences [SSPS] for Windows [Version 12.0; SPSS, Chicago, IL, USA]). Continuous variables were analyzed using Student's *t* test or Mann-Whitney *U* test. Binomial variables were analyzed using chi-squared or Fisher's exact test. Changes in incidence over time were analyzed using chi-squared test for trend. The potential risk factors for mortality in GBS bacteremia were assessed by univariate analysis. Variables with a 2-tailed *p* value <0.20 were then included in a forward, stepwise multiple logistic regression analysis to determine the independent risk factor(s) for mortality in GBS bacteremia. A 2-tailed *p* value <0.05 was considered statistically significant in the multivariate analysis and chi-squared test for trend.

Results

Initial episodes of GBS bacteremia in 97 patients during the study period were included. Episodes in 3 patients were excluded because of missing information, leading to inclusion of a total of 94 episodes in 94 patients in the analysis. The age of patients ranged from 22 to 89 years, with a mean of 64.7 ± 1.39 years. Forty eight (51.1%) patients were women. Episodes of GBS bacteremia occurred most frequently in adults aged more than 60 years (69.5%). At least 1 underlying medical disease was found in 77 (81.9%) patients, the most frequent being malignancy (43.6%), diabetes mellitus (42.6%), and liver cirrhosis (16%). Among the 22 female patients with malignancies, 12 (54.5%) had cervical cancer; 6 (31.6%) of 19 male patients with malignancies had head and neck cancer. The 2 major clinical syndromes were primary bacteremia (32/94 patients; 34%) and skin and soft tissue infection (30/94 patients; 31.9%) [Table 1].

Of the 4 cases of endocarditis, the mitral valve was affected in 3, and aortic valve in 1. All of these patients were febrile and treated with penicillin G. One patient also experienced splenic infarct. Eendocarditis caused by GBS was associated with intravenous drug use in 1 patient, who was treated with parenteral penicillin G for 15 days before being discharged against medical advice.

Susceptibility to penicillin was found in 98% of GBS isolates and all isolates were susceptible to cefuroxime, ceftriaxone, and vancomycin. Two penicillin-non-susceptible isolates (MIC = 0.5 μg/mL) were identified. A total of 20 isolates other than GBS were identified in concurrent blood cultures, including *Staphylococcus aureus* (n = 7), *Klebsiella pneumoniae* (n = 6), *Escherichia coli* (n = 4), *Acinetobacter baumanii* (n = 1), *Pseudomonas aeruginosa* (n = 1), and *Streptococcus anginosus* (n = 1).

The incidence of GBS bacteremia increased from 0.16 cases/1000 admissions in 2001 to 0.30 cases/1000 admissions in 2003 (p=0.017, chi-squared test for trend). Between the first half (January 1, 2001 to June 30, 2002) and second half (July 1, 2002 to December 31, 2003) of the study period, there were no significant differences in mean age (63.0 years vs 65.6 years, p=0.39), gender (male, 41.2% vs 53.3%, p=0.26),

Table 1. Demographic and clinical features of 94 non-pregnant adults with group B streptococcal bacteremia

Characteristics	No. of patients (%)
Male	46 (48.9)
Female	48 (51.1)
Polymicrobial bacteremia	17 (18.1)
Underlying disease[a]	
Malignancy	41 (43.6)
Diabetes mellitus	40 (42.6)
Liver cirrhosis	15 (16.0)
Immunosuppressive therapy[b]	3 (3.2)
Clinical syndrome	
Primary bacteremia	32 (34)
Skin and soft tissue infection[c]	30 (31.9)
Pneumonia	9 (9.6)
Peritonitis	7 (7.4)
Catheter-related infection[d]	5 (5.3)
Endocarditis	4 (4.3)
Septic arthritis[e]	3
Meningitis[e]	2
Urosepsis	3

[a]One patient might have more than 1 underlying disease.
[b]Steroid (2 cases) and cyclosporine (1 case).
[c]Cellulitis (22 cases), pyomyositis (3 cases), diabetic foot (2 cases), wound infection (2 cases), and psoas abscess (1 case).
[d]Dialysis shunt infection (3 cases), central catheter infection (1 case), and port-A-cath infection (1 case).
[e]One patient had concurrent meningitis and septic arthritis of knee.

hospital stay (19.5 ± 3.35 days vs 18.0 ± 2.38 days, p=0.53), polymicrobial bacteremia (11.8% vs 21.7%, p=0.23), and underlying diseases such as malignancy (47.1% vs 41.7%, p=0.61), diabetes mellitus (47.1% vs 40.0%, p=0.51), and liver cirrhosis (17.7% vs 15.0%, p=0.74).

There were 19 fatal cases, accounting for a mortality rate of 20.2%. Comparison of fatal cases with survivors revealed higher proportions of male patients (84.2% vs 40.0%, p=0.001), liver cirrhosis (42.1% vs 9.3%, p=0.002), polymicrobial bacteremia (52.6% vs 9.3%, p<0.001), renal insufficiency (47.4% vs 28.0%, p=0.052), thrombocytopenia (52.6% vs 14.7%, p=0.001), and shock (52.6% vs 4.0%, p<0.001) in fatal cases (Table 2). There was no significant difference in the mean time from the onset of symptoms to the initiation of effective antibiotic treatment (2.42 ± 0.53 days vs 2.47 ± 0.41 days, p=0.965) between fatal cases and survivors. Multivariate analysis revealed that shock [odds ratio (OR) = 22.67, 95% confidence interval (CI) = 2.91-176.70; p=0.005], thrombocytopenia (OR = 12.77, 95% CI = 2.15-75.99; p=0.005) and polymicrobial bacteremia (OR = 11.30, 95% CI = 1.65-77.21; p=0.013) were independent risk factors for mortality in GBS bacteremia.

Discussion

This study found an increasing number of cases of GBS bacteremia in non-pregnant adults in our institution during the study period, which parallels a global trend of increase in the incidence of GBS infections [2,3, 7,11]. The escalating incidence of GBS disease may be partly attributable to an expanding population of adults who are living longer with chronic debilitating diseases [2]. It is not clear whether the differences in virulence between serotypes has contributed to this trend. In comparison with younger adults, elderly persons (age ≥65years) are more likely to carry serotype V GBS

Table 2. Risk factors for mortality in 94 patients with group B streptococcal (GBS) bacteremia

Variable[a]	GBS bacteremia		Univariate	Multivariate analysis	
	Survived (n = 75)	Deceased (n = 19)	p	p	OR (95% CI)
Mean age (years)	65.2	62.7	0.481		
Male	30	16	0.001	0.572	
Underlying disease					
Malignancy	30	11	0.160	0.489	
Diabetes mellitus	32	8	0.965		
Liver cirrhosis	7	8	0.002	0.281	
Polymicrobial bacteremia	7	10	<0.001	0.013	11.30 (1.65-77.21)
Renal insufficiency	21	9	0.052	0.224	
Thrombocytopenia	11	10	0.001	0.005	12.77 (2.15-75.99)
Shock	3	10	<0.001	0.005	22.67 (2.91-176.70)
Hospital stay (days) [median]	14	7	0.002		

Abbreviations: OR = odds ratio; CI = confidence interval
[a]Refers to no. of cases unless stated otherwise.

[6,7,11], and to lack capsular polysaccharide-specific serum immunoglobulin G [12]. This might explain the substantial mortality and morbidity related to GBS infections in the elderly.

A variety of invasive GBS infections have been reported [2,7]. The clinical spectrum of the disease ranges from mild soft tissue infections to severe bacteremic infections coupled with septic shock. Primary bacteremia and soft tissue infections were the 2 most common clinical manifestations in this series, in accordance with previous reports [5,7,13]. Malignancies were the most commonly encountered underlying diseases, which is in sharp contrast to the finding that diabetes mellitus was the most frequently seen underlying disease in previous studies from Western countries [1-4,7] and Taiwan [13]. It is uncertain whether any specific factor (e.g., specific GBS strain) may have caused the high incidence of bacteremia in patients with malignancies in this series.

Cervical cancer was the predominant malignancy found in female patients in this series (12/22 cases; 63.2%), unlike previous studies which found breast cancer to be the predominant malignancy [3,7]. The low rate of regular Papanicolaou smear screening leading to a high incidence of cervical cancer in Taiwan may contribute to this phenomenon [14]. Head and neck cancer was the predominant malignancy among males (6 cases, 31.6%), which is in contrast to previous findings that prostate cancer was the most frequent malignancy in males with GBS infection [5,7]. This might be attributable to the high prevalence of betel quid use associated with head and neck cancers in Taiwan.

S. aureus and *K. pneumoniae* were the 2 leading concurrent bacterial isolates in GBS infection in this series, which is in agreement with previous reports [4, 5,7,13-15]. This finding is not surprising because diabetes mellitus is a very important underlying disease in this patient population, which predisposes patients to *K. pneumoniae* bacteremia [16]. In addition, the portals of entry in most patients with GBS infections were skin and soft tissue infections [4,5], which predispose patients to *S. aureus* bacteremia.

The overall mortality rate in this study was 20.2% (19 of 94 patients), which is comparable to previous reports ranging from 16.7% to 33.3% [13,15,17]. The high rate of susceptibility (97.9%) of isolates to penicillin G in this study confirms that it remains the drug of choice for GBS bacteremia in Taiwan. Similarly, high penicillin susceptibility rates in GBS were reported in other studies [6,7,13].

In conclusion, this study found an increasing incidence of GBS bacteremia in non-pregnant adults in our hospital during a recent 2-year peroid. GBS bacteremia mainly occurred in elderly persons with underlying diseases, such as malignancy, diabetes mellitus or liver cirrhosis. The overall mortality rate in GBS bacteremia is high and independently associated with polymicrobial bacteremia, thrombocytopenia, and shock. *S. aureus* and *K. pneumoniae* were 2 most frequently encountered concurrent blood isolates. In view of its increasing trend, continuous monitoring for GBS infection in groups of adults who are at high risk for mortality, and aggressive treatment of patients is needed.

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