



Group B Streptococcal Infective Endocarditis: Report of 19 Cases of Definite Endocarditis from a Single Medical Center and Review of the Literature

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Abstract

Introduction: Infection due to Group B *Streptococcus* (GBS) has historically been associated with pregnant women and neonates. Recently GBS bacteremia has been reported more frequently in patients >65 years of age with multiple comorbid conditions. GBS Endocarditis (GBSE) is unusual. In a recent multinational cohort study of patients with definite infective endocarditis, GBS was the etiology in 95 of 4,794 patients (2.0%). We recently encountered 2 elderly patients with acute GBSE. These encounters prompted us to review the experience with GBSE at our institution from 2002 to 2019 to define the current epidemiology of GBSE in the 21st century.

Methods: This was an IRB-approved Quality Improvement project. We reviewed the medical records of all patients with GBS bacteremia from July 1, 2002 to June 30, 2019 and report the incidence, epidemiology, symptoms, comorbid conditions, treatment and outcome for patients with GBSE. We compare these data to previously published series of patients with GBSE in the medical literature.

Results: During the study period, there were 258 episodes of GBS bacteremia. 19 patients (7.4%) had definite infective endocarditis. 11 patients were women (58%); 8 patients were men (42%). There were no puerperal or postpartum cases. Ages ranged from 46 to 85 years (mean = 67.5). 13 of 19 patients (68%) were ≥ 64 years. 17/19 patients had multiple comorbidities. The average age adjusted Charlson comorbidity index was 4.6. 7/19 patients were compromised hosts: Cirrhosis (2), multiple sclerosis (1), multiple myeloma (1), non-Hodgkin's lymphoma (1), colon cancer/chemotherapy (1), end-stage kidney disease (1). Patients usually presented with acute/subacute onset of non-specific symptoms such as fever, chills, fatigue and malaise. Cardiac valve involvement: 9 mitral (8 native, 1 prosthetic); 4 aortic (3 native, 1 prosthetic); 1 tricuspid (1 native); 1 mitral + tricuspid (1 native); 1 aortic + pulmonic (1 native); 3 pacemakers. 5/19 patients (26%) required surgical intervention. All 19 patients received infectious disease consultation and appropriate antimicrobial therapy. 5/19 patients (26%) died from complications of GBSE.

Conclusion: GBS bacteremia and endocarditis are currently diseases of older adults. Neonatal, puerperal and postpartum cases are rare. Endocarditis is infrequent, presents with non-specific manifestations, is seen in patients with multiple comorbid conditions, and has a high mortality rate (26%) despite appropriate antimicrobial, universal infectious disease consultation and appropriate surgical intervention. Internists, family practitioners, emergency physicians and surgeons must be aware of the change in epidemiology of GBS bacteremia and endocarditis. Most severe GBS infections now occur in the elderly and have a high mortality rate.

Keywords: *Streptococcus agalactiae*; Group B streptococcus; Endocarditis; Bacteremia

Introduction

Until the mid-twentieth century, Group B streptococcal bacteremia was a disease primarily seen in puerperal women and neonates. However, series of adult patients with *Streptococcus agalactiae* bacteremia began to appear in the literature in 1977 [1]. We previously reported our experience with 132 adults with GBS bacteremia and reviewed the literature from 1977 to 2013 [2]. A subset of our original 132 bacteremia patients with infective endocarditis numbered 13 patients (9.8%).

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In 2 recently published studies of patients with definite infective endocarditis, GBS was the etiologic agent in 39 of 1,280 (3.0%) episodes in one study [3] and in 95 of 4,794 (2.0%) episodes in another [4]. We recently cared for two elderly patients with GBSE and decided to review our experience with this disease and compare our experience to that of other GBSE series reported in the literature.

Materials and Methods

This study was approved by the Summa Health (Akron, Ohio) Institutional Review Board as a quality improvement project. We reviewed the medical records of all adult patients (≥ 18 years of age) from whom *Streptococcus agalactiae* (Group B *Streptococcus*) was isolated from blood culture specimens at our institution from July 1, 2002, to June 30, 2019. Summa Akron City Hospital is a 577-bed hospital affiliated with the Northeast Ohio Medical University and hosts 12 Accreditation Council for Graduate Medical Education-approved residency programs and several fellowship programs. Group B *Streptococcus* was identified by standard microbiologic methods [5]. Each chart was reviewed and the following information was recorded: Age, sex, date of occurrence, source of infection, comorbid conditions, echocardiographic data, antimicrobial therapy, presence or absence of surgical intervention, and outcome. Infective endocarditis was diagnosed using the modified Duke criteria [6]. Only patients with definite endocarditis by these criteria were included in the analysis. PubMed and Google Scholar searches were performed using the following key words/phrases or combinations thereof: *Streptococcus agalactiae*, Group B *Streptococcus*, invasive disease, infective endocarditis, bacteremia, bacterial endocarditis. Articles were reviewed and the reference lists of these articles were used to identify other series of patients with GBSE. The data from all GBSE articles with a series of GBSE patients with individually extractable patient information was assembled and compared to our study data. Single case reports of GBSE and series of GBSE patients without individually extractable patient information were not included in this review [7,8].

Results

Source of bacteremia

During the 18-year study period, there were 258 episodes of GBS bacteremia. Skin and soft tissue infection was the most common cause of GBS bacteremia (81 episodes) followed by bone and joint infection (47 episodes), primary bacteremia (31 episodes), and infective endocarditis (26 episodes). The sources of GBS bacteremia are shown in Table 1. Of the 26 episodes of infective endocarditis, 19 were definite endocarditis and 7 were probable endocarditis. We will review the 19 patients with definite endocarditis in detail.

Infective endocarditis

Definite endocarditis was diagnosed in 19 of the 258 episodes of GBS bacteremia (7.4%). Data from our patients with definite GBSE are summarized in Table 2. There was an average of 1.1 episodes/year of GBSE over the 18-year study period and the occurrence of GBSE was equally distributed throughout the study period with 9 patients in first 9-year period (2002 to 2010) and 10 patients in the second 9-year period (2011 to 2019). 11 patients were women (58%) and 8 patients were men (42%). Patients' ages ranged from 56 to 85 years with a mean of 67.5 years. 13 of the 19 patients (68%) with GBSE were 64 years of age or older. 3 of the 19 patients had polymicrobial bacteremia: Methicillin-resistant *Staphylococcus aureus* (2 patients) and viridans streptococcal (1 patient) bacteremia. 17 of 19 patients

Table 1: Site of *Streptococcus agalactiae* Bacteremia -258 Episodes.

Site of Bacteremia	No. Episodes	Percentage
Skin and Soft Tissue	87	33.7
Bone and Joint	47	18.2
Primary (Spontaneous)	31	12
Endocarditis	26	10.1
Pneumonia	21	8.1
Urinary Tract Infection/Pyelonephritis	16	6.2
Obstetric/Gynecologic	6	2.3
Spontaneous Bacterial Peritonitis	5	1.9
Vascular Catheter Infection	5	1.9
Meningitis	3	1.2
Vascular Graft Infection	3	1.2
Endophthalmitis	2	0.8
Epidural Abscess	2	0.8
Psoas Abscess	2	0.8
Pancreatic-Biliary Infection 0	2	0.8
TOTAL	258	10

Table 2: Characteristics of 19 Patients with Definite *Streptococcus agalactiae* Infective Endocarditis.

Parameter	Number	Percentage
Episodes of GBS Bacteremia	258	100%
Episodes of Definite GBS Endocarditis	19	7%
Women/Men	11/8	58%/42%
Charlson Age-Adjusted Co-Morbidity Index	4.6	NA
Compromised Hosts*	7/19	37%
Surgical Intervention**	5/19	26%
Mortality	5/19	26%

Notations: NA: Not Applicable; *Compromised Hosts: Cirrhosis (2), Multiple Sclerosis (1), Multiple Myeloma (1), Non-Hodgkin's Lymphoma (1), Colon Cancer (1), End-Stage Kidney Disease (1); **Bio-prosthetic Mitral Valve Placement (2); Prosthetic Mitral Valve Re-Do (1); Pacer/Defibrillator Extraction (2)

had multiple comorbid conditions at presentation: 7 of 19 patients were compromised hosts: Cirrhosis (2), multiple sclerosis (1), multiple myeloma (1), non-Hodgkin's lymphoma (1), colon cancer on chemotherapy (1), end-stage kidney disease (1). The average age-adjusted Charlson comorbidity index was 4.6 [9,10]. All but 2 patients presented with acute onset of illness. This was similar to the experience of Ivanova-Georgieva et al. who found left-sided GBS endocarditis was a clinical mimic of left sided *Staphylococcus aureus* endocarditis [8]. Valvular involvement in GBSE was as follows: Mitral valve only in 9 (8 native, 1 prosthetic); aortic valve only in 4 (3 native, 1 prosthetic); tricuspid valve only in 1 (1 native); multiple valves in 2 (1 patient with aortic and pulmonic valves; 1 patient with mitral and tricuspid valves); pacemaker endocarditis in 3 patients. Overall, the mitral valve was involved in 10 of 19 patients (53%) and the aortic valve in 5 of 19 patients (26%). Tricuspid valve was involved in 2 patients (11%) and the pulmonic valve in 1 patient (5%). Surgical intervention was required in 5 of 19 patients (26%): 2 patients with surgical pacer extraction; 1 patient with a replacement of a previously placed bioprosthetic mitral valve; and 2 patients with new bio-prosthetic mitral valves. All 19 patients were seen in consultation by an infectious disease specialist and all received the appropriate type and length of antimicrobial therapy.

Table 3: *Streptococcus agalactiae* Endocarditis -Review of Literature.

Year	First		No.	Study	Age in Yrs.	Gender	Valves Affected					Surgery	Antibiotics	Outcome
Published	Author	Site	Pts.	Years	(Mean/Range)	(F/M)	Mitral	Aortic	Tricuspid	Aortic + Mitral	Other	Yes/No	Yes/No	R/D
1977	Reid [1]	Scotland	13	1965-1974	67.9/32-85	4/9	6	2	0	4	1	ND	12/1	9/4
1985	Backes [11]	USA/MN	5	1970-1983	50.4/18-72	2/3	1	4 (1P)	0	0	0	0/5	4/1	4/1
1986	Gallagher [12]	USA/OH	7	1980-1984	56.1/35-73	2/5	3 (1P)	2 (1P)	1	1	0	1/6	7/0	1/6
1987	Scully [16]	USA/NY	12	1974-1985	60.3/62-81	6/6	2	4 (1P)	4	1	1	2/10	11/1	7/5
1989	Pringle [13]	Scotland	5	1975-1998	48.6/28-63	2/3	2	3 (1P)	0	0	0	3/2	5/0	2/3
2002	Sambola [15]	Spain	30	1975-1998	56.8/22-83	17/13	15 (3P)	8 (1P)	2	4	1	12/18	30/0	16/14
2003	Rollan [14]	Spain	9	1996-2002	66.0/47-84	3/6	4	2	1	2	0	6/3	9/0	4/5
2010	Siciliano [17]	Brazil	6	2000-2006	49.3/20-78	2/4	1	4 (2P)	0	1 (MP)	0	5/1	6/0	4/2
This Series	Patel	USA/OH	19	2002-2019	67.5/46-85	8/11	9 (1P)	4 (1P)	1	0	5	5/14	19/0	14/5
Total	All	All	106	1965-2019	60.0/20-85	57 (54%/46%)	43 -41%	33 -31%	9 -8%	13 -12%	8 -8%	34/59 (37%/63%)	103/3 (97%/3%)	61/45 (57%/43%)

Abbreviations: F: Female; M: Male; P: Prosthetic valve; MP: Mitral Prosthesis; ND: No Data; R: Recovered; D: Died

Literature Review

In our literature review, we found 8 published series of GBSE patients with a range of 5 to 30 patients published between 1977 and 2010 and present these with our patients in Table 3 [11-17], of these 106 patients, ages ranged from 20 to 85 years with a mean of 60.0 years. There were 57 women (54%) and 49 men (46%). The mitral valve was the most commonly involved valve followed by aortic, and tricuspid valves respectively. 13 patients (12.3%) had multi-valvular endocarditis. 103 of 106 patients (97%) received initial antimicrobial agents that would be effective against GBS. 34 of 93 evaluable patients (37%) required surgical intervention. 45 of 106 patients (42%) died.

Discussion

In the United States, a rare disease is defined as a condition that affects fewer than 200,000 people [18]. This definition was created by the Congress in the Orphan Drug Act of 1983. In the European Union, a rare disease is defined as one that affects fewer than 1 in 2,000 people [19]. By either standard, GBSE is rare. In our 577-bed institution, we had an average of 1.06 cases/year for 18 years of the study. Nine patients were seen in the first 9 years and 10 patients in the second 9 years so there was no increase in incidence of GBSE during the study period. Patients generally had acute to subacute endocarditis although some patients had longer duration of symptoms before diagnosis. The clinical picture was similar to that of *Staphylococcus aureus* endocarditis and Ivanova-Georgieva et al. have written that the two diseases seemed indistinguishable with similar presentations, complications and mortality [8]. 13 of our 19 patients (68%) were ≥ 64 years and 17/19 patients had multiple comorbidities with the average age + adjusted Charlson comorbidity index = 4.6. Seven of 19 patients were compromised hosts.

Since this began as a QI project, we expected to find some issues in management that might help us improve the care of GBSE patients. However, all patients were seen by an Infectious Disease specialist; all received appropriate type and length of antimicrobial therapy; and all that required surgical intervention (without contraindications) had such intervention. Therefore, our next avenue of approach will be to look for different ways in which to improve outcomes and somehow improve upon our 26% mortality rate. Potential avenues for

improvement in outcome and survival include: (1) Earlier suspicion for and diagnosis of GBSE with resultant earlier antimicrobial therapy; (2) A push for more aggressive surgical intervention especially in the patients who might have relative but not absolute contraindications for surgery; (3) An evaluation of methods to prevent some cases of GBS bacteremia since bacteremia is the sine qua non for the development for infective endocarditis; (4) Earlier diagnosis and treatment of conditions causing GBS bacteremia.

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