Published in final edited form as: *Scifed J Cardiol.* 2018; 2(4): .

# **Group B Streptococcal Tricuspid Endocarditis: Case Report and Systematic Review**

Perry Wengrofsky\*,1, Ghassan Mubarak1, Nabila Khondakar1, Syed Haseeb1, David Landman2, Suzette Graham-Hill3, Angelina Zhyvotovska1, and Samy I McFarlane1

<sup>1</sup> Department of Internal Medicine, State University of New York, Downstate Medical Center, Brooklyn, N.Y., USA-11203

<sup>2</sup>Department of Internal Medicine, Division of Infectious Disease, Kings County Hospital Center, Brooklyn, N.Y., USA-11203

<sup>3</sup>Department of Internal Medicine, Division of Cardiovascular Disease, Kings County Hospital Center, Brooklyn, N.Y., USA-11203

#### **Abstract**

Infective Endocarditis (IE), the microbial infection of the endocardial surface, is categorized by anatomy, microbiology, and valve nativity. Infective endocarditis generally affects older adults, and more commonly presents as a Left-sided IE (LSIE) affecting the mitral or aortic valves. Right-sided IE (RSIE) typically affects younger patients with less pre-existing valvular disease. RSIE is also more commonly associated with intravenous drug use (IVDU) and intra-cardiac instrumentation, such as pacemakers or defibrillators. While *Staphylococcus aureus* is the most common microorganism responsible for both LSIE and RSIE, *Streptococcos agalactiae*, or Group B Streptococcus (GBS), accounts for a very small percentage of IE, and, in such instances, rates of tricuspid endocarditis are dramatically lower than LSIE. GBS endocarditis usually affects patients with particular comorbidites, such as diabetes mellitus (DM) and cirrhosis. We present a case of GBS tricuspid endocarditis in a female patient without the typical risk factors for GBS endocarditis. We also present a systematic review of case reports and case series of GBS tricuspid endocarditis highlighting the risk factors, presentation and clinical characteristics, as well as up-to-date outcomes, and mortality rates of GBS endocarditis, a potentially fatal disease entity.

#### **Keywords**

Group B Strep;	Streptococcus agal	<i>lactiae</i> ; Tricuspid	Valve Endocarditis	

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<sup>\*</sup>Corresponding author: Perry Wengrofsky, Department of Internal Medicine, State University of New York, Downstate Medical Center, Brooklyn, N.Y., USA-11203. Samy.mcfarlane@downstate.edu; Tel: 917-219-2325.

## Introduction

Infective Endocarditis (IE) is a microbial infection of the endocardial surface. It is classified based on disease activity, recurrence, whether verified by diagnostic studies (definite or possible), by anatomy (left-sided involving aortic and/or mitral valve, or right-sided involving tricuspid and/or pulmon ic valve), by whether the valve is a native valve IE (NVE) or a prosthetic valve IE (PVE), and by microbiology: the causative organism [1]. The mean age is nearly 60 years, and IE most commonly involves the mitral and aortic valves, either individually or with concurrent bivalvular disease; right-sided IE, however, comprises approximately 5–21% of all IE cases [1, 2].

RSIE patients are historically younger with less underlying medical conditions and valvular disease. IVDU represents the greatest risk factor for right sided IE cases [2, 3]. *Staphylococcus aureus, Streptococcus* spp. and *Enterococcus* spp. are responsible 70–80% of LSIE and RSIE case. *Staph. aureus* is the predominant organism in RSIE in IVDU and non-IVDU cases alike [2–4]. Among 90% of RSIE cases involve the tricuspid valve, generally arising in patients with a history of IVDU, cardiac implantable electronic devices (CIED), or chronic indwelling venous access lines [5].

A survey of IE cases in the United States from 1998–2009 demonstrated that *Strep* spp. accounted for 24.7% of IE cases in the United States, and *Streptococcos agalactiae*, commonly referred to as GBS, accounted for 1.3% of all cases, a rate similar to the 1.7% seen in Spain from 1979–1998 [6, 7]. GBS endocarditis accounts for less than 18% of all adult invasive GBS disease, and while GBS endocarditis historically affected postpartum women colonized with GBS, it is now becoming a recognized, albeit rare, etiology of IE among older nonpregnant adults, male and female alike [8]. Along with pregnancy-associated GBS endocarditis, adult invasive GBS disease is associated with chronic medical conditions such as DM, cirrhosis, breast cancer, and neurogenic bladder [9, 10].

We present the case of a 59-year-old female with no significant past medical history who was found to have tricuspid valve GBS endocarditis. We also present a systematic review of the existing cases and literature on GBS endocarditis, and highlight important differences in patient characteristics, clinical findings, and outcomes depending on the affected valve.

#### **Case Presentation**

A 59-year-old female with no past medical history presented with complaints of sweats, chills, weakness, and cough for a few weeks in mid-January. She originally presented to our emergency department two weeks prior with complaints of cough, and was discharged with a suspected upper respiratory tract infection. On the day prior to this presentation, the patient noted the development of sudden onset sharp R buttock pain and redness. At presentation, patient was febrile with a rectal temperature of 102.0 F, and hypotensive to 85/55. Exam revealed bibasilar rales, a 2/6 systolic murmur best heard at heart base, and warmth and tenderness of the right hip and thigh.

Initial laboratory testing was significant for leukocytosis of 19.6/nL, 86.6% neutrophils, hemoglobin of 6.8/nL, high-sensitivity C-reactive protein of 298.69 mg/L, and erythrocyte

sedimentation rate of 98 mm/h. Initial chest X-ray (CXR) was unremarkable. Blood cultures were obtained, broad-spectrum antibiotics were initiated with vancomycin and piperacillintazobactam (zosyn). The patient's vital signs and hemoglobin responded to volume resuscitation and packed RBC (pRBC) transfusion. Computed tomography (CT) of the abdomen, pelvis, and right lower extremity revealed trace bilateral pleural effusions, pulmonary interstitial edema, and diffuse subcutaneous edema over the right thigh extending to the right lateral gluteal region.

Blood cultures obtained on admission grew GBS. Repeat CXR revealed new Right Middle Lobe (RML) and Left Lower Lobe (LLL) infiltrates. Antibiotics were switched from vancomycin and zosyn to ceftriaxone. Magnetic Resonance Imaging (MRI) of the spine was negative for osteomyelitis or epidural abscess, and CT chest revealed filling defects consistent with pulmonary embolism in the apical segment of Right Upper Lobe (RUL) pulmonary artery and anterior mediastinal basilar artery of LLL, and a wedge-shaped opacification of the LLL concerning for pulmonary infarction.

This array of findings led to concern for IE. The patient was switched back to vancomycin and zosyn. A Transthoracic Echocardiography (TTE) was performed and it revealed moderate Tricuspid Regurgitation (TR) but no echocardiographic evidence of vegetation on any of the valves (Figure 1). Repeat CT chest was remarkable for persistent bilateral pulmonary emboli in segmental and sub segmental branches of the RUL, Left Upper Lobe (LUL), and LLL, and progressive multifocal alveolar airspace disease, concerning for multiple Septic Pulmonary Emboli (SPE).

Patient underwent Transesophageal Echocardiography (TEE), which revealed Right Atrium (RA) and Right Ventricle (RV) dilation with severe TR, TV annulus dilation, and a mobile  $1.9\times1.4$  cm hypodensity consistent with vegetation (Figure 2). Patient was transitioned back to ceftriaxone, and was evaluated by the cardiothoracic surgery team. The patient underwent repeat TTE which showed continued evidence of endocarditis. Since the patient did not have recurring fevers and did not show signs of heart failure, medical management was deemed the best management strategy. Ergo, the patient completed a 6-week course of IV antibiotics.

# Systematic Review

#### **Materials and Methods**

**Sources of Data**—Search terms used for retrieval of case reports and cases series from PubMed, Springer Link, and Science Direct included "Group B Streptococcal Endocarditis" and "Group B Streptococcal Tricuspid Endocarditis". Case reports and series published between January 1, 1986 and October 1, 2018 were included. The retrieval was supplemented by literature tracing to collect any relevant articles as comprehensively as possible. English language case reports and series available via the library at SUNY Downstate Medical Center or through inter-library loan were included in the analysis.

#### **Inclusion and Exclusion Criteria**—Inclusion criteria were as follows:

(1) Individual case reports, case series, case reports with accompanying review.

- (2) The patients in the cases were older than 18 years of
- (3) Study results could be either quantitive representation of the rates or frequency of specified clinical characteristics, or a qualitative representation of specified clinical characteristics.

Exclusion criteria were as follows:

- (1) Non-English language articles or articles without an available full text version.
- (2) Articles that contained data that significantly overlapped with that of another published report.

# Results

Review of case reports and series [7, 10–24] revealed 24 cases of GBS tricuspid endocarditis (Table 1), demonstrated a female predominance (17:7 female: male), an average age of approximately 39, and a morality rate of 12.5%.

GBS tricuspid endocarditis shows an asymmetrical gender distribution in favor of women, with gender specific mean ages of approximately 35 and 48 for females and males, respectively.

Males with GBS tricuspid endocarditis had higher rates (6/7) of having a predisposing medical comorbidity or a history of IVDU, and were considerably older than their female counterparts [7, 11, 20, 21].

The average female with GBS tricuspid endocarditis was considerably younger than our patient. Over half (8/17) of the females in the review had a recent OBGYN event, such as childbirth or abortion, or a predisposing condition associated with invasive GBS infection such as alcoholism and diabetes, or IVDU with or without a previous episode of endocarditis. One female patient had an implanted cardiac pacemaker [10, 12–24]. SPE was documented in 54.1% (13/24) of cases, and surgical intervention was performed in 37.5% (9/24) of cases [10–13, 19–21, 24].

### **Discussion**

While GBS endocarditis has been documented in previous case reports and case series, involvement of the tricuspid valve, particularly in patients without a history of IVDU or other predisposing medical conditions and risk factors, remains uncommon. Although there have not been dedicated reviews examining clinical characteristics, outcomes, and mortality rates of GBS endocarditis by affected valves, mortality rates of GBS endocarditis have declined over time, from greater than 80% in the early 1940s to less than 40% in the 1980s and 1990s [7, 20]. The mitral valve historically remains the predominant valve affected in GBS endocarditis. The rates of GBS endocarditis have steadily increased among men, and the distribution has shifted towards adults in the sixth decade of life [7, 9, 20]. The average age of adult patients with GBS endocarditis is similar to that of patients with GBS Bacteremia of other etiologies [25–28].

Prenatal screening for maternal GBS colonization has been overwhelmingly successful in reducing neonatal GBS infections such as meningitis. Pregnancy- associated invasive GBS disease in the mother, however, can manifest as puerperal sepsis or Bacteremia without a focus, endometritis or chorioamnionitis without fetal demise, pneumonia, and IE [29]. Despite the association between GBS, pregnancy and a recent OBGYN event with GBS tricuspid endocarditis, pregnancy associated IE still more commonly presents as a LSIE. Meanwhile, RSIE in the setting of pregnancy is more likely to be caused by a staphylococcal species [30]. IVDU is a well-known risk factor and potential source of microbiologic introduction in the pathogenesis of IE, and the predominant organism is *Staph. Aureus*; the tricuspid valve, in isolation or in combination with another valve, is the most commonly affected valve [2, 31, 32]. While CIED have been associated with endocarditis, CIED associated endocarditis remains rare, with *Staph. aureus* and other staphylococcal species [33] as the most common causative agents.

This analysis of the different predisposing medical, social and obstetric conditions that is associated with IE of all valves—specifically GBS IE—highlights the diverse pathopshiological processes behind GBS tricuspid endocarditis and illuminates the types of patients that should be considered for broader endocarditis workup in the setting of GBS Bacteremia. While the Duke Criteria utilizes microbiologic, echocardiographic, and clinical information in the diagnosis of IE, the history and physical exam in IE can be highly variable. Local and systemic symptoms may be connected to or may be completely unrelated to the implicated valve or possible underlying source of infection [2, 34, 35]. GBS Bacteremia, one of the major Duke criteria for diagnosis of GBS endocarditis of the tricuspid or any other valve, can be from a primary infection of the tricuspid valve, resulting from a direct venous or right heart portal of entry, such as in IVDU, central venous catheterization or hemodialysis access, or the Bacteremia may be from a secondary infection such as from a distant primary source: the urinary tract, respiratory tract, and soft tissue, etc. [8, 25, 36, 37].

In our patient, the presence of unilateral buttock pain and associated CT imaging suggestive of a soft tissue infectious process raises suspicion for a potential soft tissue source with secondary venous seeding of the tricuspid valve. However, the temporal relationship between the symptomology of fevers, chills, and weakness for a few weeks preceding the acute onset of buttock pain raised suspicions of paradoxical systemic arterial seeding from the tricuspid valve. This theory is further reinforced by the chest imaging findings consistent with SPE and infarction. RSIE is typically associated with SPE, and LSIE is typically associated with arterial seeding of septic emboli affecting the brain, spleen, limbs, intestines, and bones [37–39]. SPE was seen in over 50% of GBS tricuspid endocarditis, and while no studies have analyzed the microbiologic patterns of SPE in RSIE, previous work has shown that the most common organisms seen in SPE, in the setting of endocarditis and other primary sources of infection, were staphylococcal species, most prominently Staph. aureus [38, 40].

Despite the associations between RSIE and SPE, clinical evidence of non-pulmonary septic embolization in the setting of suspected GBS endocarditis should not preclude the possibility of tricuspid valve involvement. Antibiotic therapy in previous case reports of

GBS tricuspid endocarditis, when indicated, was quite variable with changes in antibiotic trends depending on the year of treatment, with the main agents being  $\beta$ -lactam antibiotics such as a penicillin or cephalosporin [7, 10–19, 21–24]. Current guidelines endorsed by the Infectious Disease Society of America for GBS IE, recommend treatment with penicillin or ceftriaxone for 4–6 weeks, or vancomycin for those patients who are unable to tolerate a βlactam; additionally, gentamicin can be added for the first two weeks of treatment due to the increased resistance to penicillin among GBS and other strains of β-hemolytic streptoccocal species [41]. Early surgery in IE of all valves has been shown to lower mortality, and studies examining surgical outcomes specifically of tricuspid valve IE, either valvular replacement or repair, have shown lower morbidity and mortality and overall similar long-term survival [42–44]. While there are not well defined surgical indications in tricuspid endocarditis, surgery should be considered in the presence of TV vegetations > 20 mm and recurrent SPE with or without concurrent right heart failure, cultures growing microorganisms like fungi that are difficult to eradicate, persistent Bacteremia for at least 7 days despite appropriate antibiotic therapy, and right heart failure secondary to severe TR that responds poorly to diuresis [5, 45, 46].

In summary, we presented a case of GBS tricuspid endocarditis in a female patient without the typical comorbid predisposing medical conditions and risk factors for GBS endocarditis. Systematic review of the previous literature on GBS endocarditis demonstrated the rarity of GBS endocarditis affecting the tricuspid valve. There is a lack of concrete recommendations for the initial evaluation and medical and surgical management in a patient with suspected endocarditis in the setting of GBS Bacteremia. Further studies are needed to elucidate appropriate strategies for echocardiographic testing, both TTE and TEE, in a patient with unexplained GBS Bacteremia, and the timing of and indications for specific surgical interventions.

# Acknowledgement

This work is supported, in part, by the efforts of Dr. Moro O. Salifu M.D., M.P.H., M.B.A., M.A.C.P., Professor and Chairman of Medicine through NIH Grant number S21MD012474.

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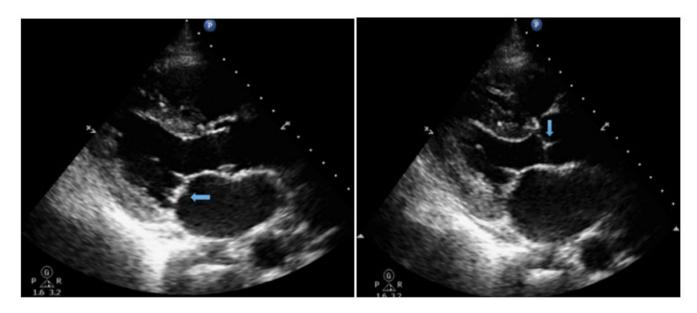
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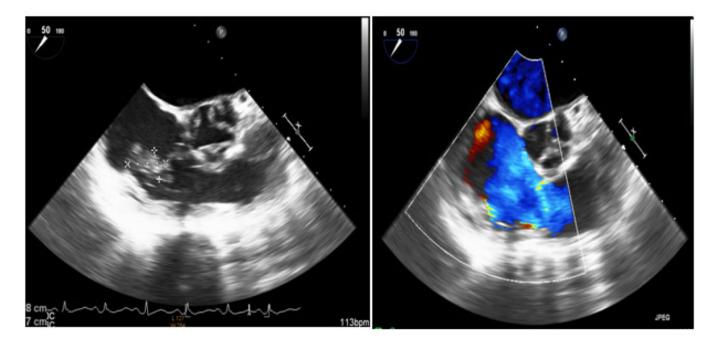
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**Figure 1:**TTE without Evidence of Vegetations on the MV (Left, Blue Arrow) or the AV (Right, Blue Arrow)



**Figure 2:** TEE Demonstrating TV Vegetation (Left) and Associated TR (Right)

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Table 1:

Literature Review - Demographics, Patient History, Clinical Findings, Outcome

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Age (years), Sex	Presenting Complaint	IVDU	Recent OBGYN	History of Valve or Cardiac Disease	Additional PMH	Antibiotic Therapy	SPE	Surgery	Outcome	Reference
22, F	4 day history of fever, chills, substemal chest pain with coughing, greenish sputum	Y	N	Tricuspid Endocarditis	N	Pen, Gent	Y	Z	Death	22
32, F	1 week of fever, nonproductive cough, L knee and back pain	Y	N	Tricuspid Endocarditis	N	Pen, Gent	IN	Z	Recovery	22
18, F	1 week persistent fevers despite recent antibiotics	N	Abortion	N	N	Pen, Gent	IN	N	Recovery	23
36, F	IN	Z	Pap smear	Z	N	Pen, Gent	N	Y	Recovery	24

M - Male, F - Female, IVDU - intravenous drug use, Y - Yes, N - No, OBGYN - obstetrics/gynecology (recent obstetric/gynecologic event or procedure), PMH - past medical history, CHF - congestive heart failure, SSS - sick sinus syndrome, PPM - permanent pacemaker, IHD - ischemic heart disease, EtOH - alcohol abuse, DM - diabetes mellitus, Pen - penicillin, Gent - gentamicin, Vanc - vancomycin, Rif - rifampin, Amp - ampicillin, Amox - amoxicillin, NI - not indicated, NA - not applicable