Journal of Infection (2017) 74, 450—455

BIA
British Infection Association

www.elsevierhealth.com/journals/jinf

Effect of underlying immune compromise on the manifestations and outcomes of group A streptococcal bacteremia

Kathleen A. Linder [a], Leen Alkhouli [b], Mayur Ramesh [b], George A. Alangaden [b], Carol A. Kauffman [a,c], Marisa H. Miceli [a,*]

[a] *Division of Infectious Diseases, Department of Internal Medicine, University of Michigan Health System, USA*
[b] *Henry Ford Health System, USA*
[c] *Veterans Affairs Ann Arbor Healthcare System, USA*

Accepted 16 February 2017
Available online 22 February 2017

KEYWORDS
Streptococcus pyogenes;
Group A *Streptococcus*;
Bacteremia;
Necrotizing fasciitis;
Toxic shock syndrome;
Immunosuppression

Summary *Background:* Group A streptococcal bloodstream infection is the most common presentation of invasive group A streptococcal disease. We sought to determine the impact of immunosuppression on severity of disease and clinical outcomes.
Methods: This retrospective review of 148 patients with at least one positive blood culture for *Streptococcus pyogenes* from 1/2003 to 3/2013 compared immunocompromised patients with those with no immunocompromise in regards to development of severe complications and mortality.
Results: Twenty-five patients (17%) were immunocompromised; 123 were not. Skin and soft tissue infection occurred in 60% of immunocompromised vs. 38% of non-immunocompromised patients, $p = .04$. Necrotizing fasciitis and septic shock were significantly more common in immunocompromised patients, $p < .0001$ and .028, respectively. Mortality at 30 days was 32% in immunocompromised patients vs. 16% in non-immunocompromised patients, $p = .05$.
Conclusion: Patients who are immunocompromised are more likely to develop necrotizing fasciitis and septic shock as complications of group A streptococcal bacteremia and have a higher mortality rate than patients who are not immunocompromised.

* Corresponding author. Division of Infectious Diseases, University of Michigan Medical School, 3120 Taubman Center, 1500 E. Medical Center Dr. SPC 5378, Ann Arbor, MI 48109-5378, USA.
E-mail address: mmiceli@med.umich.edu (M.H. Miceli).

http://dx.doi.org/10.1016/j.jinf.2017.02.006
0163-4453/

Introduction

Infections caused by Group A *Streptococcus* present a broad range of manifestations, from localized pharyngitis and skin infections to invasive disease, including bacteremia, necrotizing fasciitis and toxic shock syndrome. Bacteremia is documented in 41—72% of cases of invasive infection and is associated with higher mortality than localized infections.[1—4] Bacteremia may be primary without an obvious source or secondary to infection in specific organ systems.

Predisposing factors for group A streptococcal bacteremia noted in other reports include HIV infection, intravenous drug use, heart disease, cancer, obesity, and diabetes.[1,2,5—8] It does not appear that solid organ transplant recipients, hematopoietic cell transplant recipients, or patients with hematological malignancies are at greater risk for development of group A streptococcal bacteremia. In fact, multiple surveys from cancer centers and transplant units have only rarely noted group A *Streptococcus* as a cause of bacteremia in these populations.[9—17] However, we noted that our immunocompromised patients who developed group A streptococcal bacteremia appeared to have more severe complications and poorer outcomes. We report our experience over a decade with immunocompromised and non-immunocompromised patients who developed group A streptococcal bacteremia.

Methods

Patients and setting

This retrospective study was conducted at the Henry Ford Health System, a 900-bed tertiary care center in southeastern Michigan. We identified all patients who had at least one blood culture yielding group A *Streptococcus* between January 2003 and March 2013. The Henry Ford Health System Institutional Review Board approved this study.

Demographic data, underlying illnesses, clinical presentation, laboratory data and 30-day outcomes were collected. Treatment of group A streptococcal bacteremia was with intravenous penicillin G or a third or fourth generation cephalosporin; vancomycin was given in patients who were intolerant of beta-lactam antibiotics. Surgical debridement was performed at the discretion of the Surgery Service.

Definitions

Patients were stratified into either immunocompromised or non-immunocompromised groups. The immunocompromised group included patients who had HIV infection with CD4 count <200 cells/μl, solid organ or hematopoietic cell transplant, hematological or solid tumor malignancy treated with chemotherapy in the preceding 90 days, collagen vascular disease treated with immunosuppressive agents in the preceding 90 days, or high dose corticosteroid therapy (equivalent of $\geq$.3 mg/kg/day of prednisone) given for at least 3 weeks prior to the diagnosis of group A streptococcal bacteremia.

Statistical analysis

Statistical analysis determined associations between group A streptococcal bacteremia and predisposing risk factors, as well as clinical presentation and outcome in the immunocompromised and non-immunocompromised groups. Chi square test was used for categorical variables and Student's t-test or Wilcoxan rank sum test were used for continuous variables.

Results

Patients and demographics

A total of 151 cases of group A *Streptococcus* bacteremia were identified during the study period. Of these 151 patients, 3 were excluded because clinical data were not available. The ages of the 148 patients in the study ranged from 24 days to 93 years, and 52% were male. Eight patients (5%) were below the age of 18 and 47 patients (32%) were $\geq$65 years of age. The number of cases of group A streptococcal bacteremia seen each year appeared relatively stable over the decade from 2003 to 2013, with the exception of a slight increase in the number of cases seen in 2007 (Fig. 1).

A total of 25 patients were immunocompromised (17%). The most common immunocompromising conditions were solid organ transplant in 8 (5 kidney, 3 liver) and solid tumors treated with chemotherapy in 8. In the immunocompromised group, only one (4%) was under the age of 18 and 9 (36%) were $\geq$65 years of age, compared with 6% and 31%, respectively for the non-immunocompromised group. Except for immunosuppressive conditions, underlying illnesses and risk factors were similar in both groups (Table 1). Forty-nine patients in the non-immunocompromised group (40%) had no known predisposing risk factors for group A streptococcal bacteremia.

Source and end-organ involvement

A source for bacteremia or associated end organ infection was identified in 116 patients (78%) (Table 2). The remaining 32 patients (22%) had primary bacteremia with no specific source identified; this occurred no more frequently in the immunocompromised group than in the non-immunocompromised group. Skin and soft tissue infections in 62 patients (42%) were the most common source or end organ involved, occurring in 15 (60%) patients in the immunocompromised group and 47 (38%) patients in the non-immunocompromised group, $p = .04$. Pneumonia/empyema was noted in 3 (12%) in the immunocompromised group and 17 (14%) in the non-immunocompromised group. Other infections (gynecologic, osteoarticular, and intra-abdominal) were less commonly associated with bacteremia, and all but one of these occurred in the non-immunocompromised cohort.

Complications and outcomes

Complications of group A streptococcal bacteremia, specifically necrotizing fasciitis and septic shock, were