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CASE REPORT

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Group A Streptococcal Bacteremia following Streptococcal Pharyngitis in an Older Patient with Diabetes: A Case Report

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Group A streptococcus (GAS†) is responsible for a wide range of both invasive and noninvasive infections. Severe invasive group A streptococcal infection is associated with morbidity and mortality and has been linked to chronic medical conditions with skin and soft tissues involvement, and intravenous drug use (IVDU). Invasive diseases are, however, rare and have been recognized to affect the extremes of age (younger than 10 years of age and older than 74). We report a case of Group A streptococcus bacteremia following pharyngitis in a 76-year-old diabetic male with no history of IVDU. This report's main goal is to illustrate that chronic illnesses such as diabetes and congestive heart failure might predispose elderly patients to invasive diseases such as Group A streptococcus bacteremia.

INTRODUCTION

Group A streptococcus (GAS) is a gram-positive bacteria that causes infections ranging from mild skin infection to life threatening conditions such as toxic shock syndrome and sepsis. Mild GAS infections are more common in young children, whereas invasive disease such as bacteremia can affect children younger than 10 and adults older than 74. GAS is often associated with pharyngitis, which is diagnosed in large numbers of patients in the United States annually. Most cases of pharyngitis are viral pharyngitis. GAS is the most common bacterial etiology, accounting for 15 to 30 percent of cases in children and 5 to 20 percent in adults in the US [1]. The signs and symptoms of GAS overlap with other upper respiratory infections, making it a difficult clinical diagnosis.

To assist in diagnosis, the Centor score uses four signs and symptoms to estimate the probability of acute streptococcal pharyngitis in adults with a sore throat. Later it was modified to include age and was validated in 600 adults and children. The Modified Centor score includes five criteria: Absence of cough, swollen and tender anterior cervical nodes, temperature > 100.4°F, tonsillar exudates or swelling, and age. Each criterion is equivalent to 1 point, except for age 45 and older that is equivalent to -1, to reflect low incidence of acute streptococcal pharyngitis in older adults and the elderly [1]. Patients with a score of 2 or 3 require a rapid antigen detection testing (70 to 99 percent sensitivity and 90 to 99 percent specificity) or throat culture.

While pharyngitis is well known to be associated with GAS, invasive diseases such as bacteremia are rarely associated with GAS. A retrospective study conduct-

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†Abbreviations: GAS, Group A streptococcus; IVDU, Intravenous drug use; ABC, Active Bacterial Core Surveillance; DM, Diabetes mellitus; HIV, Human immunodeficiency virus; ICU, Intensive care unit; ARDS, Acute respiratory distress syndrome.

Keywords: Group A Streptococcal (GAS), pharyngitis, bacteremia, elderly patients

ed at the University Hospital La Fe in Valencia, Spain between 1994 and 2003 reported an annual incidence of GAS bacteremia ranging from 0.7 to 4.16 cases per 100,000 population [2]. In 1999, based on results of the Active Bacterial Core Surveillance (ABCs)/Emerging Infections Program network, a population-based surveillance system, the Centers for Disease Control and Prevention (CDC) estimates that the annual invasive GAS incidence was 3.5 cases per 100,000 population, yielding approximately 9,400 cases and 1,200 deaths in the United States that year [3]. Some of the associated diagnoses were cellulitis, necrotizing fasciitis, and bacteremia. In older individuals, underlying medical conditions were COPD, CHF, and venous insufficiency [2-5].

CASE PRESENTATION

This 76-year-old man with a history of poorly controlled diabetes (HA1c 9.2), congestive heart failure, hypertension, and hyperlipidemia developed a sore throat the evening before presentation. He went to a walk-in clinic the next morning for treatment of a sore throat. He was noted to have a negative rapid strep test but was given a prescription for penicillin. Several hours later he became very weak and was unable to walk. He then presented to the emergency room of the St. Raphael's campus of Yale New Haven Hospital.

In the emergency room his temperature was 102.7°F, pulse was 131 and respiration was 40. His blood pressure was 126/73 and oxygen saturation on room air was 96 percent. The patient complained of a sore throat, difficulty swallowing, hoarseness, and a cough. On physical examination, the patient was alert. He had no cervical lymphadenopathy, tenderness, or pharyngeal erythema. His lung exam revealed only diminished lung sounds at the bases. He was then evaluated by an otolaryngologist who performed a flexible fiber optic laryngoscopy. The exam showed mild edema and erythema of bilateral aryepiglottic folds extending down to involve the arytenoids and false vocal cords as well as mild post-cricoid edema. The remainder of the exam was insignificant except for bilateral lower extremities edema (baseline per patient and family).

The patient was treated with Dexamethasone as well as 1.5g of vancomycin hydrochloride, 1g of intravenous ceftazidime, and 600mg of Clindamycin. A rapid strep test was negative. A lower respiratory culture grew out beta-hemolytic streptococcus group A. A blood culture also grew out beta hemolytic streptococcus group A. The patient's original Centor score was 2 for tonsillar exudates and temperature > 100.4°F with a net score of 1 since 1 point was taken off for his age (> 45) per the modified Centor criteria.

The patient's antibiotic regimen was narrowed to 2g of intravenous ceftriaxone every 24 hours. The patient responded well to antibiotic therapy, and was discharged to a short-term rehabilitation unit to complete a 1-week course of IV ceftriaxone. He completed his treatment course without complications.

DISCUSSION

Group A streptococcal bacteremia is most commonly seen in the very young and in older adults [6-9]. In children, GAS bacteremia is often seen in patients with burns, varicella virus infections, malignancy, trauma, and immunosuppression [10,11]. In middle aged individuals, it is often seen in patients with intravenous drug abuse, as well as patients with HIV infections and postpartum infections [12,13]. In older patients, the most common sources of infection are cellulitis and/or soft tissue infections, pneumonia, necrotizing fasciitis, alcoholism, or iatrogenic causes associated with diagnostic or therapeutic invasive procedures [2,14,15].

Although GAS commonly causes pharyngitis, this condition is rarely associated with bacteremia [15]. In the 1930s, GAS was a common organism in bacteremia, and was frequently associated with infections of the throat, middle ear, and mastoid [16]. Beta hemolytic streptococci accounted for more than one-sixth of all bacteremic cases at Boston City Hospital in 1935 [9]. By 1955, due to the mass production of penicillin and other antibiotics, only 1 percent of bacteremic cases were due to GAS. The interest in GAS bacteremia decreased as a result. However, at the beginning of the 1970s, reports started to document the re-emergence of GAS bacteremia. [9,12]. The increase in incidence of GAS bacteremia coincided with a change in the M serotypes and the resurgence of serotypes M-1 and M-3 [17,18].

It is rare for pharyngitis in the post-antibiotic era to produce Beta hemolytic streptococcal bacteremia. In a study from Great Britain, 93 patients had positive Beta hemolytic streptococcal cultures from the respiratory tract, but none had bacteremia [19]. In her review, Choby et al., 2009 offers an approach to working up GAS pharyngitis. The risk for GAS pharyngitis is 5 to 10 percent with a score of 1, 11 to 17 percent with a score of 2, and over 50 percent with a score of 4 or higher [1]. Despite a Centor score of 1, our patient developed bacteremia and required inpatient care.

Unlike GAS, streptococcus G and streptococcus B have been associated with bacteremia, especially in the elderly. Streptococcus group G accounted for 15 percent of streptococcus-derived bacteremia cases, surpassing group A in frequency, from 1990 to 1999 at a community teaching hospital in Israel [20]. The majority of the patients were elderly men, with skin and soft tissue as the main portals of entry. Similarly, a retrospective study that

reviewed sixty-six adults over 70 years old with group B streptococcal bacteremia observed that a bedridden state was the one underlying condition that was highly associated with Group B streptococcal bacteremia [21]. A bedridden state is a risk factor for urinary tract infection and pneumonia and increases the probability for development of ulcers and other soft tissue infections. Soft tissue infections such as cellulitis and necrotizing fasciitis have been associated with group A, group B, and Group G streptococcal bacteremia [13,20,21].

Our patient presented with the rare feature of Group A streptococcal bacteremia associated with pharyngitis. Although GAS is the most common bacterial cause of acute pharyngitis, neither pharyngitis nor GAS are often associated with bacteremia. Clinicians must be aware that streptococcal infections can still produce invasive bacteremia in older adults, especially older adults living with chronic illnesses such as diabetes, congestive heart failure, and skin diseases.

Patients with diabetes mellitus (DM) develop more infections than patients without DM. It has been shown that both the humoral and the cellular immune system are affected in patients with diabetes [22]. The association between diabetes and development of GAS bacteremia suggests that immune suppression increases the risk for invasive GAS disease. Similarly, HIV infection and other immunosuppressive states have been associated with increased risk of GAS bacteremia [13].

The mechanism by which heart disease directly contributes to GAS bacteremia is not fully understood. However, heart failure has been long recognized as a risk factor for stasis ulcers [23]. We propose that stasis ulcers secondary to heart failure, similar to other soft tissue infections, can serve as point of entry for GAS, increasing the risk of GAS bacteremia in elderly patients with congestive heart failure.

CONCLUSIONS

Group A streptococcus (GAS) can cause a variety of infections and rarely can cause bacteremia, especially in the elderly with underlying conditions such as diabetes mellitus, heart failure, and soft tissue infections. The course of GAS bacteremia is rapid and requires prompt diagnosis and treatment. Untreated, GAS bacteremia can have serious consequences.

Patients with invasive GAS infection admitted to the intensive care unit (ICU) have significant morbidity and mortality. A prospective, population-based surveillance for invasive GAS infections conducted in Ontario from January 1992 to June 2002 reported development of Acute respiratory distress syndrome (ARDS) in 34 percent, hepatic dysfunction in 64 percent, and coagulopathy in 69 percent of patients with GAS bacteremia [24].

The overall mortality from GAS bacteremia ranges from 5 to 48 percent among adults [2,24,25]. The outcome of GAS bacteremia depends on certain host factors such as age and underlying chronic diseases. The rate of mortality is low in the pediatric population but increases in the elderly populations with underlying chronic diseases. A retrospective study conducted by Gauguet et al., 2015 reported an overall mortality of 2.3 percent for children, which is consistent with lower case fatality rates for children with bacteremia compared to adults [26].

In conclusion, elderly patients with underlying chronic illnesses such as diabetes, heart failure, and skin diseases are at increased risk for GAS bacteremia and are more likely to die from complications of GAS bacteremia.

REFERENCES

1. Choby BA. Diagnosis and treatment of streptococcal pharyngitis. Am Fam Physician. 2009;79(5):383-90.
2. Vallalta Morales M, Soriano Navarro CJ, Salavert Lleti M, Montero Alonso M, Perez Belles C, Lopez Aldeguer J, et al. Group A streptococcal bacteremia: outcome and prognostic factors. Rev Esp Quimioter. 2006;19(4):367-75.
3. Robinson KA, Rothrock G, Phan Q, Sayler B, Stefonek K, Van Beneden C, et al. Risk for severe group A streptococcal disease among patients' household contacts. Emerg Infect Dis. 2003;9(4):443-7.
4. Andersen MM, Ronne T. Group A streptococcal bacteraemias in Denmark 1987-89. J Infect. 1995;31(1):33-7.
5. Hoge CW, Schwartz B, Talkington DF, Breiman RF, MacNeill EM, Englender SJ. The changing epidemiology of invasive group A streptococcal infections and the emergence of streptococcal toxic shock-like syndrome. A retrospective population-based study. JAMA. 1993;269(3):384-9.
6. Woods WA, Carter CT, Stack M, Connors AF, Jr., Schlager TA. Group A streptococcal pharyngitis in adults 30 to 65 years of age. South Med J. 1999;92(5):491-2.
7. Davies HD, McGeer A, Schwartz B, Green K, Cann D, Simor AE, et al. Invasive group A streptococcal infections in Ontario, Canada. Ontario Group A Streptococcal Study Group. N Engl J Med. 1996;335(8):547-54.
8. Ben-Abraham R, Keller N, Vered R, Harel R, Barzilay Z, Paret G. Invasive group A streptococcal infections in a large tertiary center: epidemiology, characteristics and outcome. Infection. 2002;30(2):81-5.
9. McGowan JE, Jr., Barnes MW, Finland M. Bacteremia at Boston City Hospital: Occurrence and mortality during 12 selected years (1935-1972), with special reference to hospital-acquired cases. J Infect Dis. 1975;132(3):316-35.
10. Hidaka H, Kuriyama S, Yano H, Tsuji I, Kobayashi T. Precipitating factors in the pathogenesis of peritonsillar abscess and bacteriological significance of the Streptococcus milleri group. Eur J Clin Microbiol Infect Dis. 2011;30(4):527-32.
11. Begovac J, Kuzmanovic N, Bejuk D. Comparison of clinical characteristics of group A streptococcal bacteremia in children and adults. Clin Infect Dis. 1996;23(1):97-100.
12. Bernaldo de Quiros JC, Moreno S, Cercenado E, Diaz D,

Berenguer J, Miralles P, et al. Group A streptococcal bacteremia. A 10-year prospective study. Medicine (Baltimore). 1997;76(4):238-48.
13. Factor SH, Levine OS, Schwartz B, Harrison LH, Farley MM, McGeer A, et al. Invasive group A streptococcal disease: risk factors for adults. Emerg Infect Dis. 2003;9(8):970-7.
14. Nielsen HU, Kolmos HJ, Frimodt-Moller N. Beta-hemolytic streptococcal bacteremia: a review of 241 cases. Scand J Infect Dis. 2002;34(7):483-6.
15. Burkert T, Watanakunakorn C. Group A streptococcal bacteremia in a community teaching hospital--1980-1989. Clin Infect Dis. 1992;14(1):29-37.
16. Keefer CS, Ingelfinger FJ, Spink WW. Significance of hemolytic streptococcic bacteremia - A study of two hundred and forty-six patients. Archives of Internal Medicine. 1937;60(6):1084-97.
17. Colman G, Tanna A, Efstratiou A, Gaworzewska ET. The serotypes of Streptococcus pyogenes present in Britain during 1980-1990 and their association with disease. J Med Microbiol. 1993;39(3):165-78.
18. Cleary PP, Kaplan EL, Handley JP, Wlazlo A, Kim MH, Hauser AR, et al. Clonal basis for resurgence of serious Streptococcus pyogenes disease in the 1980s. Lancet. 1992;339(8792):518-21.
19. Barnham M. Bacteremia in Streptococcal Infections of the Throat. Journal of Infection. 1983;7(3):203-9.
20. Sylvetsky N, Raveh D, Schlesinger Y, Rudensky B, Yinnon AM. Bacteremia due to beta-hemolytic Streptococcus group G: increasing incidence and clinical characteristics of patients. Am J Med. 2002;112(8):622-6.
21. Trivalle C, Martin E, Martel P, Jacque B, Menard JF, Lemeland JF. Group B streptococcal bacteraemia in the elderly. J Med Microbiol. 1998;47(7):649-52.
22. Geerlings SE, Hoepelman AI. Immune dysfunction in patients with diabetes mellitus (DM). FEMS Immunol Med Microbiol. 1999;26(3-4):259-65.
23. Augey F, Pinet A, Renaudier P. [Heart failure and stasis ulcer: A significant association (prospective study of 100 cases)]. Ann Dermatol Venereol. 2010;137(5):353-8.
24. Mehta S, McGeer A, Low DE, Hallett D, Bowman DJ, Grossman SL, et al. Morbidity and mortality of patients with invasive group A streptococcal infections admitted to the ICU. Chest. 2006;130(6):1679-86.
25. Stromberg A, Romanus V, Burman LG. Outbreak of group A streptococcal bacteremia in Sweden: an epidemiologic and clinical study. J Infect Dis. 1991;164(3):595-8.
26. Gauguet S, Ahmed AA, Zhou J, Pfoh ER, Ahnger-Pier KK, Harper MB, et al. Group A streptococcal bacteremia without a source is associated with less severe disease in children. Pediatr Infect Dis J. 2015;34(4):447-9.