The Laryngoscope

Case Report

Supraglottitis Due to Group B Streptococcus in an Adult With IgG4 and C2 Deficiency: A Case Report and Review of the Literature

Vinayak Nagaraja, MBBS; Thomas E. Stewart, MBBS; Stuart G. Mackay, MBBS, FRACS; Derek W. Glenn, MBBS, FRANZCR; Denis Wakefield, DSc, MD; Craig S. Boutlis, MBBS, FRACP, PhD

Acute supraglottitis is a medical emergency as it can rapidly lead to airway compromise. With routine pediatric immunization for *Hemophilus influenzae* serotype b, supraglottitis is now more prevalent in adults, with a shift in the causative organisms and a change in the natural history of this disease. Here, we present a case of supraglottitis due to group B streptococcus that occurred in an adult with previously undetected immunoglobulin 4 (IgG4) and complement protein C2 deficiency.

Key Words: Immunology, larynx, *Streptococcus agalactiae*, supraglottitis, group B streptococcus.

***Laryngoscope*, 00:000–000, 2014**

INTRODUCTION

Acute supraglottitis, defined as inflammation of the epiglottis with or without adjacent supraglottic structures, is a potentially life-threatening condition that requires prompt and accurate assessment and management of the airway.[1] Airway narrowing may reach its peak within a few hours of symptom onset and lead to upper airway obstruction. Epiglottitis was previously a more common pediatric emergency, but the advent of the *Haemophilus influenzae* serotype b vaccine has caused a marked reduction in its rate in children.[2] *Streptococcus agalactiae*, or group B streptococcus (GBS), is a leading cause of infection in newborns, pregnant women, and older persons with chronic medical illness. In addition to maternal cervicovaginal colonization and neonatal infection, GBS causes invasive infections in adults.[3] However, GBS is a rare cause of supraglottitis.[4–6] Herein, we report a case of GBS supraglottitis that occurred in a 41-year-old male whom we had initially presumed to be immunocompetent. Subsequent testing demonstrated that he was deficient in immunoglobulin G4 (IgG4) and complement protein C2, with corresponding decrease in total complement activity (CH100).

From the Prince of Wales Hospital (V.N.), Sydney, New South Wales, Australia; Division of Surgery (T.E.S., S.G.M.), Wollongong Hospital, Wollongong, New South Wales, Australia; St. George Hospital (D.W.G.), Sydney, New South Wales, Australia; School of Medical Sciences (D.W.), University of New South Wales, Sydney, New South Wales, Australia; and the Graduate School of Medicine (C.S.B.), University of Wollongong, Wollongong Hospital, Wollongong, New South Wales, Australia.

Editor's Note: This Manuscript was accepted for publication July 18, 2014.

The authors have no funding, financial relationships, or conflicts of interest to disclose.

Send correspondence to Craig Steven Boutlis, MBBS, Adjunct Appointment, Graduate School of Medicine, University of Wollongong, and Head of Infectious Diseases, Department of Infectious Diseases, Wollongong Hospital, 348 Crown St., Wollongong, NSW, Australia 2500. E-mail: craig.boutlis@sesiahs.health.nsw.gov.au

DOI: 10.1002/lary.24874

CASE REPORT

A 41-year-old male presented to our emergency department with a 1-day history of fever, rigors, sore throat, and progressive odynophagia associated with dysphonia after returning from a business trip to Singapore. He had previously been admitted to the hospital twice with community-acquired pneumonia 16 and 5 years prior. On the first occasion he required intensive care admission for invasive ventilation. He had also undergone tonsillectomy as a child. There were no regular medications, and he had received all recommended childhood vaccinations. He denied any systemic disease, smoking, substance abuse, or drinking. There was no stridor or signs of upper airway obstruction, and oxygen saturation was 95% on room air. Vital signs were within normal ranges. He had palpable cervical lymphadenopathy, and direct fiberoptic laryngoscopy performed by an otolaryngologist demonstrated markedly edematous and erythematous false vocal cords, aryepiglottic folds, and epiglottis.

After a set of blood cultures, he received intravenous (IV) administration of normal saline, dexamethasone, ceftriaxone and flucloxacillin. A chest radiograph revealed no abnormal findings. Laboratory data showed leukocytosis of 32.9×10^9/L (normal range $3.5–11.0 \times 10^9$/L) with a neutrophilia and left shift and a C-reactive protein of 332 mg/L (normal range <5 mg/L). Other blood tests were in normal ranges. Ultrasound of the neck did not reveal any additional abnormalities. He underwent a computed axial tomography (CT) scan of the neck with IV contrast. This was consistent with the clinical finding of supraglottitis, and excluded an abscess (Fig. 1). Within 24 hours of incubation, a blood culture grew GBS that was sensitive to penicillin. Treatment was continued with IV antibiotics and oral corticosteroids for a total of 9 days in the hospital. He was switched to oral amoxycillin at discharge and completed

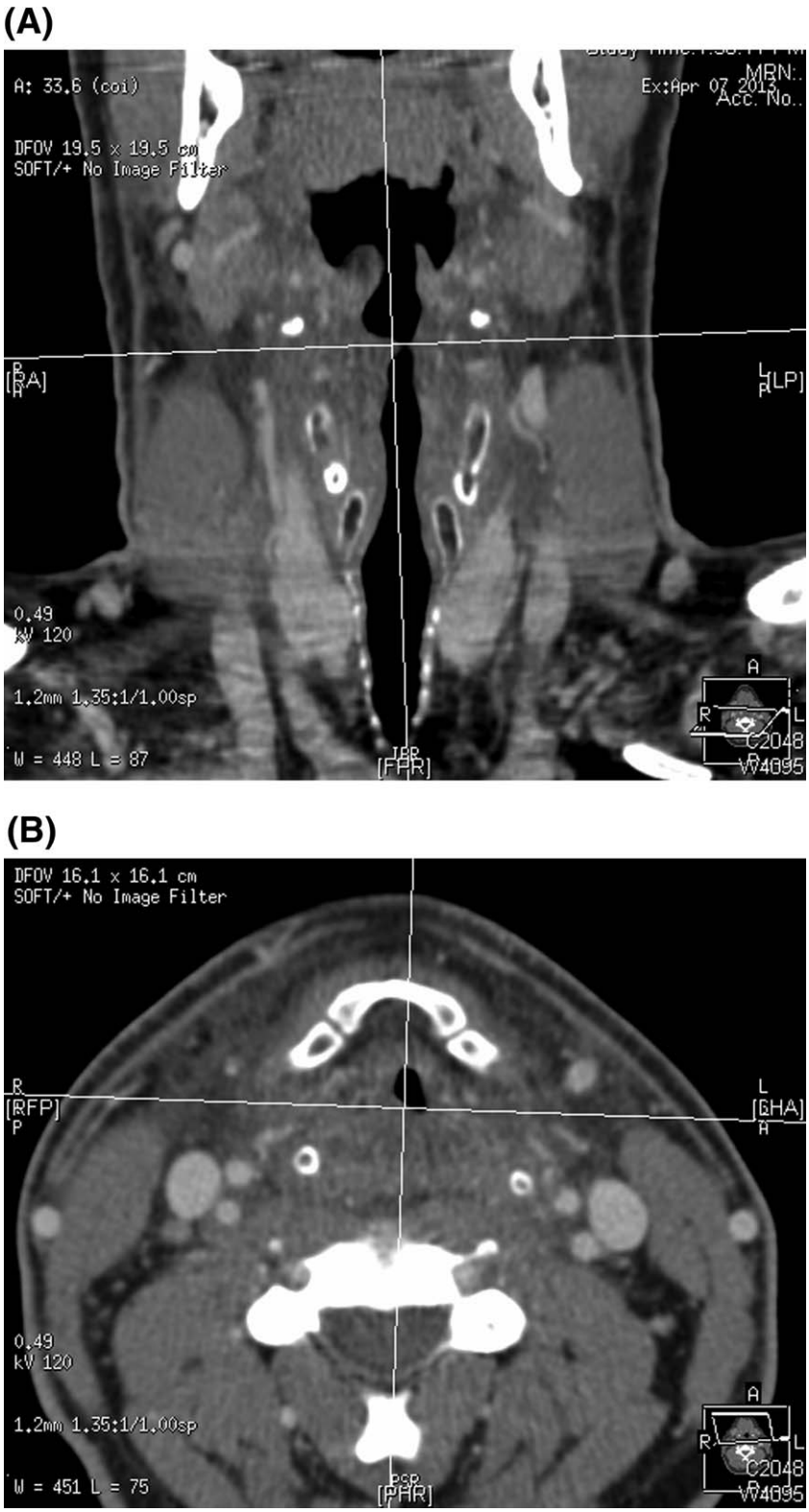

Fig. 1. (A) Coronal computed tomography image of the neck showing extensive laryngeal and supraglottic edema associated with narrowing of the airway, extending from the level of the cricoid cartilage to the epiglottis. (B) Axial computed tomography image of the neck showing extensive laryngeal and supraglottic edema associated with narrowing of the airway, extending from the level of the cricoid cartilage to the epiglottis.

4 more weeks of this treatment. He recovered fully and remained asymptomatic after being off treatment for 12 months. Because of the unusual presentation, an immunodeficiency screen was performed after recovery. This revealed: normal fasting blood sugar; normal serum electrophoresis, an isolated low IgG4 level (0.02 mg/mL, normal range 0.03–2.01 mg/L) but normal total IgG, markedly low CH100 assay (<266 units/mL, normal range 392–1019 units/mL); and very low C2 level (<3.2 mg/L, normal range 14–25 mg/L). C3 and C4 levels

TABLE I.
Literature Review of *Streptococcus agalactiae* Invasive Upper Airway Infections.

Author	Year	Diagnosis	
Lipson et al.[4]	1986	Supraglottitis	3.5-month-old female infant
Ridgeway et al.[5]	1984	Epiglottitis with abscess	Adult with diabetes mellitus
Young et al.[6]	1996	Epiglottitis	11-week-old male infant
Sapunar et al.[17]	2008	Retropharyngeal phlegmon	47-year-old diabetic male
Chivite and Carratala[16]	1998	Retropharyngeal abscess	49-year-old male
Kelly and Isaacman[15]	2002	Retropharyngeal cellulitis	2.5-month-old female infant
Lo et al.[18]	2001	Retropharyngeal abscess	3-year-old male child

were normal. Human immunodeficiency virus serology was negative. He also underwent a CT scan of the abdomen that was unremarkable.

DISCUSSION

GBS is a polysaccharide-encapsulated[7–9] Gram-positive coccus that commonly colonizes the human genital and gastrointestinal tracts, and the upper respiratory tract in young infants.[10,11] Oropharyngeal colonization has been described as occurring in 4% to 8.4%[12,13] of healthy nonpregnant adults and of 4.4% of girls and 7% of boys with diabetes.[14] It is an increasingly recognized cause of bacteremia without a focus, as well as a causative organism in soft tissue infections and other focal infections in nonpregnant adults.

GBS is a rare cause of supraglottitis or epiglottitis, and the literature so far has described only three cases, two in children and one case of epiglottitis in an adult with diabetes.[4–6,] Other invasive upper airway infections caused by GBS in adults have included retropharyngeal cellulitis[15] and abscesses[16–18] (Table I). Bizaki et al.[19] performed a retrospective review of 308 cases of supraglottitis in Finnish adults. *Streptococcus* species were the leading causative microorganisms (most commonly *Streptococci* [unspecified] followed by *Streptococcus pneumoniae*, *Streptococcus pyogenes*, and *Streptococcus milleri*), but GBS was not specifically described. Blood cultures were taken in 155 cases and Streptococci were cultured in 66.67% of the positive cultures. Other contributing microbes were *Candida* species, Staphylococci, and *Pseudomonas* species.

A case-control study compared patients with invasive GBS infections to patients hospitalized for other illnesses.[20] On multivariate analysis, the odds ratio (OR) was highest for the following independent risk factors: cirrhosis (OR 9.7), diabetes mellitus (OR 3.0), stroke (OR 3.5), breast cancer (OR 4.0), decubitus ulcer (OR 4.0). and neurogenic bladder (OR 4.6). Nosocomial infection, which accounted for 22% of these cases, was associated strongly with central venous line placement (OR 30.9) and less strongly with diabetes, congestive heart failure, and seizure disorder. Although deficiencies of complement have been commonly associated with invasive infections involving polysaccharide-encapsulated bacteria, we are only aware of three previous cases involving GBS, all less than 3 years of age.[21,22] IgG4 deficiency has also been associated with recurrent pyogenic infections due to encapsulated bacteria,[23,24] but it is relatively common in the normal population and usually asymptomatic.[23] Thus, it is plausible that this patient's demonstrated immunodeficiency predisposed him to GBS infection; however, given the fairly benign nature of this immunodeficiency, it is also possible that the two events were coincidental.

CONCLUSION

The present case appears to be only the second case of GBS-related epiglottitis or supraglottitis in an adult and the first due to GBS in an adult with IgG4 and C2 deficiency. We highlight this unusual presentation and wish to increase awareness of this infection among otolaryngologists and infectious diseases physicians alike.

BIBLIOGRAPHY

1. Riffat F, Jefferson N, Bari N, McGuinness J. Acute supraglottitis in adults. *Ann Otol Rhinol Laryngol* 2011;120:296–299.
2. Frantz TD, Rasgon BM. Acute epiglottitis: changing epidemiologic patterns. *Otolaryngol Head Neck Surg* 1993;109:457–460.
3. Edwards MS, Baker CJ. Group B streptococcal infections in elderly adults. *Clin Infect Dis* 2005;41:839–847.
4. Lipson A, Kronick JB, Tewfik L, Mills EL. Group B streptococcal supraglottitis in a 3-month-old infant. *Am J Dis Child* 1986;140:411–412.
5. Ridgeway NA, Perlman PE, Verghese A, Berk SL. Epiglottic abscess due to group B Streptococcus. *Communication. Ann Otol Rhinol Laryngol* 1984;93:277–278.
6. Young N, Finn A, Powell C. Group B Streptococcal epiglottitis. *Pediatr Infect Dis J* 1996;15:95–96.
7. Jennings HJ, Katzenellenbogen E, Lugowski C, Kasper DL. Structure of native polysaccharide antigens of type Ia and type Ib group B Streptococcus. *Biochemistry* 1983;22:1258–1264.
8. Jennings HJ, Rosell KG, Katzenellenbogen E, Kasper DL. Structural determination of the capsular polysaccharide antigen of type II group B Streptococcus. *J Biol Chem* 1983;258:1793–1798.
9. Wessels MR, Benedi WJ, Jennings HJ, Michon F, DiFabio JL, Kasper DL. Isolation and characterization of type IV group B Streptococcus capsular polysaccharide. *Infect Immun* 1989;57:1089–1094.
10. Schrag SJ, Zywicki S, Farley MM, et al. Group B streptococcal disease in the era of intrapartum antibiotic prophylaxis. *N Engl J Med* 2000;342:15–20.
11. Zangwill KM, Schuchat A, Wenger JD. Group B streptococcal disease in the United States, 1990: report from a multistate active surveillance system. *MMWR CDC Surveill Summ* 1992;41:25–32.
12. van der Mee-Marquet N, Fourny L, Arnault L, et al. Molecular characterization of human-colonizing Streptococcus agalactiae strains isolated from throat, skin, anal margin, and genital body sites. *J Clin Microbiol* 2008;46:2906–2911.
13. Green SL, Nodell CC, Porter CQ. The prevalence and persistence of group B streptococcal colonization among hospital personnel. *Int J Gynaecol Obstet* 1978;16:99–102.
14. Nowakowska M, Jarosz-Chobot P. Streptococcus group B (GBS)—characteristic, occurrence in children and adolescents with type 1 diabetes mellitus. *Pol J Microbiol* 2004;53:17–22.

15. Kelly CP, Isaacman DJ. Group B streptococcal retropharyngeal cellulitis in a young infant: a case report and review of the literature. *J Emerg Med* 2002;23:179–182.
16. Chivite D, Carratala J. Retropharyngeal abscess caused by Streptococcus agalactiae. *Clin Infect Dis* 1998;27:1320–1321.
17. Sapunar ZJ, Cabello VA, Godoy RE. Retropharyngeal phlegmon caused by a group B Streptococcus in a diabetic patient: report of one case [in Spanish]. *Rev Med Chil* 2008;136:351–355.
18. Lo WT, Lien YH, Wang CC, Chu ML. Retropharyngeal abscess caused by group B Streptococcus in a previously healthy child. *Infection* 2001;29: 289–290.
19. Bizaki AJ, Numminen J, Vasama J-P, Laranne J, Rautiainen M. Acute supraglottitis in adults in Finland: review and analysis of 308 cases. *Laryngoscope* 2011;121:2107–2113.
20. Jackson LA, Hilsdon R, Farley MM, et al. Risk factors for group B streptococcal disease in adults. *Ann Intern Med* 1995;123:415–420.
21. Jonsson G, Truedsson L, Sturfelt G, Oxelius VA, Braconier JH, Sjoholm AG. Hereditary C2 deficiency in Sweden: frequent occurrence of invasive infection, atherosclerosis, and rheumatic disease. *Medicine (Baltimore)* 2005;84:23–34.
22. De Witt CC, Ascher DP, Winkelstein J. Group B streptococcal disease in a child beyond early infancy with a deficiency of the second component of complement (C2). *Pediatr Infect Dis J* 1999;18:77–78.
23. Ochs HD, Stiehm E.R, Winkelstein JA, et al. Antibody deficiencies. In: Ochs HD, Stiehm ER, Winkelstein JA, eds. *Immunologic Disorders in Infants and Children*. 5th ed. Philadelphia, PA: Elsevier; 2004:356–426.
24. Hill SL, Mitchell JL, Burnett D, Stockley RA. IgG subclasses in the serum and sputum from patients with bronchiectasis. *Thorax* 1998;53:463–468.