

Lung Abscess and Bacteremia Caused by *Neisseria flavescens* and *Streptococcus sanguis* in Patient with Idiopathic Hypereosinophilic Syndrome

Ju Hyun Kong¹, Sung Hyun Shin¹, Su Eun Park¹, Hee Ju Park¹,
Jongyoun Yi², Shine Young Kim³, Seung Kook Son¹

Departments of ¹Pediatrics, ²Laboratory Medicine, Pusan National University School of Medicine, Yangsan,
³Department of Laboratory Medicine, Pusan National University Hospital, Busan, Korea

Neisseria flavescens has been rarely reported as a pathogen in the literature. We experienced a case of *N. flavescens* bacteremia and lung abscess co-infected with *Streptococcus sanguis* in patient with idiopathic hypereosinophilic syndrome. A 15-year-old boy was diagnosed with idiopathic hypereosinophilic syndrome complicated with pulmonary thromboembolism. He was given systemic steroids and thrombolytics. After 8 weeks of therapy, a lung abscess appeared on the plain chest radiograph. We treated him with empirical antibiotics and carried out surgical drainage. Two types of microorganisms were cultured from both blood and pus samples, obtained in the first

day of hospitalization. Pus was aspirated from the lung abscess with an aseptic technique. *Neisseria* species and *S. sanguis* were identified using traditional methods. To confirm the identity of the *Neisseria* species, we conducted further testing using 16S ribosomal ribonucleic acid sequencing whereupon *N. flavescens* was identified. This is the first case report of pulmonary infection caused by *N. flavescens*. We suggest that *N. flavescens* may act as a pathogen. (Korean J Clin Microbiol 2012;15:147-150)

Key Words: *Neisseria flavescens*, Sepsis, 16S ribosomal RNA sequencing

INTRODUCTION

Neisseria flavescens is one of the non-meningococcal and non-gonococcal *Neisseria* species that has infrequently caused meningitis, endocarditis, and sepsis [1]. Therefore they are distinguished from meningococcus or gonococcus and so called non-pathogenic *Neisseria*.

Although *N. flavescens* can colonize as a normal flora in the upper respiratory tract, an infection of the lower respiratory tract was never reported. However, we experienced a case of a lung abscess caused by *N. flavescens* with consequential bacteremia.

CASE REPORT

A 15-year-old boy was transferred to our center with complaints of cough, sputum, and progressive dyspnea for 4 days.

The plain chest radiograph showed pneumonic infiltration with pleural effusion in both lungs. The chest CT scan revealed patch consolidation on both lower lobes with pleural effusion and the thromboembolus within the left pulmonary artery. Thromboemboli were also detected in the portal vein and the left common iliac vein on the diagnostic work-up. Laboratory examinations showed a white blood cell count of 23,530/ μ L, segmental neutrophil of 56%, lymphocyte of 9.9%, eosinophil of 26.3% (6,630/ μ L), hemoglobin of 13.7 g/dL, platelet count of 77,000/ μ L, C-reactive protein of 11.4 mg/dL (reference range <0.5 mg/dL) and eosinophil cation protein >200 μ g/L (reference range, \leq 19 μ g/L). He was diagnosed as idiopathic hypereosinophilic syndrome (IHES) complicated with pulmonary thromboembolism [2]. He received systemic steroid therapy for IHES, thrombolytics and anti-coagulation therapy.

Hypereosinophilia was improved immediately after medication. Methylprednisolone was taken in doses of 2 mg/kg/day for 4 days and then prednisolone was used in doses of 1 mg/kg/day for a month. After 4 weeks of tapering periods, he had intermittent fever and cough over 2 days. The plain chest radiograph

Received 20 September, 2012, Revised 15 October, 2012

Accepted 17 October, 2012

Correspondence: Seung Kook Son, Department of Pediatrics, Pusan National University Children's Hospital, Pusan National University School of Medicine, 20, Geumo-ro, Mulgeum-eup, Yangsan 626-770, Korea. (Tel) 82-55-360-2180, (Fax) 82-55-360-2181, (E-mail) sonofs@naver.com

showed a shadow of a cavity with an air-fluid level (Fig. 1). He was diagnosed with lung abscess and hospitalized for antibiotics therapy and surgical drainage. We selected the antibiotics nafcillin and cefotaxime empirically.

Bacterial cultures of blood, urine, sputum, and pus drained from the abscess were carried out before antibiotics therapy. Two species of bacteria were cultivated from the blood and the pus obtained at the first day of hospitalization. These two were identified by conventional methods and the Vitek 2 system (BioMérieux, inc., Marcy-l'Etoile, France). One (gram-positive cocci) was identified as *Streptococcus sanguis*, and the other (gram-negative diplococci) as *Neisseria* species using Vitek 2 NH Identification Card. To confirm the identity of this isolate, 16S rRNA sequencing analysis was performed. InstaGene Matrix (Bio-Rad Laboratories, Hercules, CA, USA) was used to extract the bacterial genomic DNA, and the first 500 base pairs on the 5' end of the 16S rRNA gene were amplified and sequenced using MicroSeq 500 16S rDNA Bacterial Identification PCR and Sequencing Kits (Applied Biosystems, Foster City, CA, USA). The sequencing product was analyzed on a 3130 Genetic Analyzer (Applied Biosystems) according to the manufacturer's instructions. The resulting sequence was compared with sequences stored in GenBank (<http://www.ncbi.nlm.nih.gov/>). A GenBank BLAST search revealed that the 16S rRNA gene sequence of the isolate was 100% homologous with that of *N. flavescens* (GenBank Accession no. GU417548.1). This showed percent identity with >0.8% separation from other species that were listed up in the search (*Neisseria gonorrhea*, *Neisseria weaveri*, *Neisseria subflava*, etc.), and the isolate was



Fig. 1. Chest plain radiograph showing lung abscess.

confirmed to be *N. flavescens* [3].

After the antibiotics therapy, the clinical symptoms were improved. According to the results of the bacterial culture, we continued to use cefotaxime except for nafcillin. The sensitivity test of antibiotics was not performed because there was no protocol about the proper sensitivity test for *N. flavescens*. Subsequently the patient was discharged on the 37th day of hospitalization. On the second month of the follow-up he was in good condition without recurrence.

DISCUSSION

Neisseria is the genus characteristic of gram-negative diplococci. There are two well-known pathogenic organisms in the genus *Neisseria*, *N. gonorrhea* and *N. meningitidis*. These two organisms characterized the specific disease entity, respectively. *N. meningitidis* usually colonize in the nasopharynx of humans and sometimes invades into the bloodstream. Moreover, when invaded, it may cause bacteremia, meningitis, and severe meningococcemia. *N. gonorrhea* infects the genitourinary tract mucosa and rarely causes disseminated infection. While non-pathogenic *Neisseria* are commensal organisms living in the upper respiratory tract, and relatively few cases of infection were reported compared to pathogenic *Neisseria*.

Like other non-pathogenic *Neisseria*, *N. flavescens* has been rarely reported as a causative microorganism. The first case report of significant infection by this organism was of 14 cases of meningitis, which were a single epidemic in Chicago in 1928 [4]. Subsequently four other cases of meningitis were reported in 1957 [4]. The septicemia by this organism was reported first in 1968 [4]. It was a 20-year-old woman and her symptoms were discovered 7 days after dental surgery. And in 1984, more cases of meningitis and septicemia by *N. flavescens* were reported, which consisted of 15 cases of meningitis accompanied by septicemia and one case of septicemia [5]. After that, the first case of infectious endocarditis by *N. flavescens* was noted and reported in 1987 [6]. Infectious endocarditis was also observed in the case of a patient with narcotic addiction and reported in 1990 [7]. A case of septic shock was reported in 1990 which occurred in a pediatric patient [8]. Therefore, our report is one of the rare cases of the infection caused by *N. flavescens* especially in a pediatric patient, and also the first case report of the lung abscess, which is one of its resultant pulmonary infections.

N. meningitidis causes septicemia, sepsis, and meningitis by

invading into the blood stream [9]. In the present case, *N. flavescens* was found both in the abscess and blood. We predicted that *N. flavescens* caused localized pulmonary infection and then invaded into the bloodstream through the site.

In this context, the present case demonstrates several characteristic points. First, while, *N. flavescens* are commensal organisms, yet less virulent than the other pathogenic *Neisseria* species, it can potentially infect its host.

Second, *N. flavescens* not only cause sepsis, meningitis or infective endocarditis but it also locally infects the respiratory system. This would be more likely happened in patients who have underlying pulmonary problems or diseases. As with this case, the lung abscess occurred at the site, where pulmonary embolism and combined pneumonia was previously noticed. There are articles supporting this suggestion. One study revealed that the lower respiratory tract was non-sterile in patients with chronic obstructive pulmonary disease (COPD) and the increased number of microbial loads was related to acute exacerbation of COPD [10]. Another study showed common species identified in the lower respiratory tract of COPD patients, which included of *Neisseria* [11]. In comparison, the low respiratory tract of healthy subjects was relatively sterile [12]. Another study compared patients who had contracted cicatricial laryngeal stenosis after surgery with healthy subjects. The patients showed a significantly greater occurrence of staphylococci, *Neisseria* and *Candida* in the pharyngeal mucosa. What is more, they had a higher rate of dysbacteriosis, which was characterized by a predominance of *N. flavescens*, *Staphylococcus aureus*, alpha-hemolytic streptococcus, *Staphylococcus epidermidis* and *Candida* species [13].

Third, his illness could be influenced by immune suppression following the steroid therapy. The immune deficiency allows an extraordinary infection by a less virulent organism. Abscesses complicated in steroid therapy occur infrequently and have been reported as a case report, but it may be one of the important factors causing the infection.

In interpreting of the organism as a causative microorganism, it can be argued whether the identified organism is a

contaminant or not. In the present case, we believe that *N. flavescens* was a pathogen co-infected with *S. sanguis*, because same organisms were cultivated from both blood and pus simultaneously. The specimens were collected by an aseptic technique and the pus was attained by an aspiration through the chest wall not through the airway. The fact that *N. flavescens* was not a common colonizer of the skin also supports the contention that this microorganism was not a contaminant.

REFERENCES

1. Feder HM Jr and Garibaldi RA. The significance of nongonococcal, nonmeningococcal *Neisseria* isolates from blood cultures. *Rev Infect Dis* 1984;6:181-8.
2. Roufosse FE, Goldman M, Cogan E. Hypereosinophilic syndromes. *Orphanet J Rare Dis* 2007;2:37.
3. Clinical and Laboratory Standards Institute. Interpretive criteria for identification of bacteria and fungi by DNA target sequencing: Approved guideline. CLSI Document MM18-A. Wayne, PA; Clinical and Laboratory Standards Institute, 2008.
4. Wertlake PT and Williams TW Jr. Septicaemia caused by *Neisseria flavescens*. *J Clin Pathol* 1968;21:437-9.
5. Coovadia YM. *Neisseria flavescens* septicaemia with meningitis. A case report. *S Afr Med J* 1984;66:308-9.
6. Sinave CP and Ratzan KR. Infective endocarditis caused by *Neisseria flavescens*. *Am J Med* 1987;82:163-4.
7. Szabo S, Lieberman JP, Lue YA. Unusual pathogens in narcotic-associated endocarditis. *Rev Infect Dis* 1990;12:412-5.
8. Quintero Otero S, Rubio Quiñones F, Hernández Gonzalez A, Díaz Portillo J, García Martos P, Pantoja Rosso S. Septic shock caused by *Neisseria flavescens*. *An Esp Pediatr* 1990;33:64-5.
9. Melican K and Dumenil G. Vascular colonization by *Neisseria meningitidis*. *Curr Opin Microbiol* 2012;15:50-6.
10. Rosell A, Monsó E, Soler N, Torres F, Angrill J, Riise G, et al. Microbiologic determinants of exacerbation in chronic obstructive pulmonary disease. *Arch Intern Med* 2005;165:891-7.
11. Cabrera-Rubio R, García-Núñez M, Setó L, Antó JM, Moya A, Monsó E, et al. Microbiome diversity in the bronchial tracts of patients with chronic obstructive pulmonary disease. *J Clin Microbiol* 2012;50:3562-8.
12. Thorpe JE, Baughman RP, Frame PT, Wesseler TA, Staneck JL. Bronchoalveolar lavage for diagnosing acute bacterial pneumonia. *J Infect Dis* 1987;155:855-61.
13. Kovalyk AP and Govda AV. Characteristics of microflora of laryngeal mucosa in healthy subjects and patients with cicatricial stenosis of the larynx. *Vestn Otorinolaringol* 2010;17-20.

=국문초록=

특발성 호산구증가증 환자에서 발생한 *Neisseria flavescens*와 *Streptococcus sanguis* 중복감염에 의한 폐농양과 균혈증 1예

부산대학교 의학전문대학원 ¹소아과학교실, ²진단검사의학교실, ³부산대학교병원 진단검사의학과

공주현¹, 신성현¹, 박수은¹, 박희주¹, 이종윤², 김신영³, 손승국¹

*Neisseria flavescens*는 지금까지 감염원으로 보고된 예가 드문 균종이다. 저자들은 특발성 호산구 증가증으로 진단된 환자에서 *Streptococcus sanguis*와 중복 감염된 *N. flavescens* 균혈증과 폐농양 감염 증례를 경험하였다. 환자는 폐혈전색전증이 병발된 특발성 호산구증가증으로 진단된 15세 남아로 전신 스테로이드 치료 및 혈전용해제 치료를 받았다. 총 8주간의 스테로이드 치료 중에 폐농양이 발생하여 경험적 항생제 치료 및 배농을 시행하였다. 입원 1일에 시행한 혈액 배양 검사와 폐농양 천자를 통해 얻은 농 배양 검사에서 모두 동일한 두개의 균종이 배양되었다. 일반적인 균동정법에 의해 두 균종은 *Neisseria species*와 *S. sanguis*로 확인되었고, *Neisseria species*의 정확한 동정을 위해 16S ribosomal ribonucleic acid (16S rRNA) 염기서열분석을 시행하였고, *N. flavescens*로 확인되었다. 본 증례는 *N. flavescens*에 의한 폐감염에 대한 최초의 보고로서 *N. flavescens*가 병원균으로 작용할 수 있다는 것을 제시하여 준다. [대한임상미생물학회지 2012; 15:147-150]

교신저자 : 손승국, 626-770, 양산시 물금읍 금오로 20
부산대학교 의학전문대학원 부산대학교 어린이병원 소아청소년과
Tel: 055-360-2180, Fax: 055-360-2181
E-mail: sonofs@naver.com