**Globicatella sanguinis** Bacteremia in a Korean Patient

Kwangjin Ahn, Gyu Yel Hwang, Kap Jun Yoon, Young Uh

Department of Laboratory Medicine, Wonju Severance Christian Hospital, Yonsei University Wonju College of Medicine, Wonju, Korea

**INTRODUCTION**

*Globicatella sanguinis* was described in 1992 as a new genus and species when several isolates with phenotypically resemblance to *Streptococcus uberis* were characterized by Collins et al. [1]. *Globicatella* strains showed a negative leucine aminopeptidase (LAP) reaction and growth in the presence of 6.5% NaCl, totally opposite phenotypes of viridans streptococci [2,3]. Subsequently, a new species of the genus, *Globicatella sulfidifaciens*, was described, when several animal isolates from Belgium with resemblance to *G. sanguinis* were studied [4]. Although there was 99.2% similarity in 16S rRNA of *G. sulfidifaciens* to those of *G. sanguinis*, *G. sulfidifaciens* were classified as a new species based on differences in their whole cell protein patterns and biochemical profiles [4]. Until now, only 43 *G. sanguinis* isolates from clinical specimens and 14 case reports about bacteremia, meningitis or urinary tract infection have been reported [5]. To best of our knowledge, this is the second report of *G. sanguinis* bacteremia case identified by 16S rRNA gene sequencing and biochemical test in Korea [6].

**CASE REPORT**

A 76-year-old woman visited the orthopedic surgery department complaining of left knee joint pain. The patient had 2-year history of hypertension and 10-year history of rheumatoid arthritis, but did not take the medication regularly. The pain of left knee joint began to develop 10 years ago and the pain has become worse. The cause of the pain was due to the fluid retention in the joints, and the patient underwent continuous joint aspiration. Her knee pain did not improve with several procedures, so she was admitted to the hospital for the definite diagnosis. The patient was diagnosed with degenerative arthritis and admitted on October 17, 2017. On the day after admission, total left knee replacement was performed with elective surgery. On the 4th day after admission, deep wound aspirations were inoculated but there were no microorganisms. Until the 14th day of hospitalization, surgical site pain persisted and C-reactive protein and erythrocyte sedimentation rate were elevated to 7.70 mg/dL and 96 mm/h, respectively. Surgical site infection was diagnosed by reoperation. Flomoxef, an antibiotic used to pre-
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Table 1. Phenotypic characteristics of our isolate identified by commercial kits and *Globicatella* species previously reported

| Characteristics                  | Our isolate* | Previous study by | G. sanguinis | G. sulfidaciens |
|----------------------------------|--------------|-------------------|--------------|----------------|
|                                  |              | Facklam [3]†      | Shewmaker et al. [2]† | Collins et al. [1] | Previous study by Vandamme et al. [4] |
| Leucine aminopeptidase            | ND           | −                 | −            | ND             | ND             |
| Pyrrolidonylarylaminease          | ND           | +                 | V            | V              | +              |
| Growth in 6.5% NaCl              | −            | +                 | +            | +              | −              |
| Bile-esculin reaction            | −            | +                 | ND           | ND             | ND             |
| Esculin hydrolysis               | −            | +                 | ND           | ND             | +              |
| Voges-Proskauer reaction         | −            | −                 | ND           | ND             | −              |
| H2S production                   | −            | ND                | ND           | −              | +              |
| β-galactosidase                  | +            | ND                | ND           | ND             | +              |
| β-glucuronidase                  | −            | ND                | ND           | −              | +              |
| Hippurate hydrolysis             | −            | +                 | +            | +              | −              |
| Optochin resistance              | −            | ND                | ND           | ND             | ND             |
| Acidification                    |              |                   |              |                |                |
| Arginine                         | −            | −                 | ND           | ND             | ND             |
| Mannitol                         | −            | +                 | +            | +              | −              |
| Sorbitol                         | −            | V                 | V            | ND             | −              |
| Arabinose                        | −            | ND                | V            | ND             | −              |
| Lactose                          | −            | −                 | +            | ND             | −              |
| Maltose                          | +            | ND                | +            | ND             | +              |
| Sucrose                          | −            | ND                | +            | ND             | +              |
| Inulin                           | −            | ND                | ND           | −              | +              |
| Ribose                           | −            | ND                | ND           | +              | −              |

†+, positive; −, negative; †+, positive reactions ≥92%; †−, positive reactions ≤8%; †v, variable reactions positive in 9 to 91% of strains; †+†+, positive reactions ≥85%; †−, positive reactions ≤15%; †v, variable reactions positive in 16 to 84% of strains.

Abbreviation: ND, not done.
Sequencing was conducted using the Big Dye Terminator Cycle Sequencing kit (Applied Biosystems, Foster City, CA, USA) and ABI PRISM 3730 genetic analyzer (Applied Biosystems). All sequences were analyzed by using the basic local alignment search tool (BLAST, a genome database of the National Center for Biotechnology Information) and ribosomal database project (RDP). The 16S rRNA gene sequences from our isolate showed 99% similarity to G. sulfidifaciens and G. sanguinis, and the 16S rRNA gene sequences showed the highest similarity (99.74%) with G. sanguinis based on the analysis that uses the EzBioCloud database (www.ezbiocloud.net) (Fig. 1). For differential identification to Globicatella species level, the isolate was inoculated on triple sugar iron (TSI) agar and incubated at 35°C ambient air for 2 days. Since G. sulfidifaciens produce hydrogen sulfide when grown in TSI agar, the medium turns black when this bacterium grows [4]. As the isolate did not produce hydrogen sulfide, we finally confirmed it as G. sanguinis. No microorganisms were isolated on wound cultures at the 16th day after admission. Also vancomycin and levofloxacin treatment was discontinued because no more isolates were found in two additional blood cultures on 21st day and 23rd day after admission.

**DISCUSSION**

G. sanguinis could be misidentified with aerococci, streptococci, and enterococci due to their phenotypical resemblance [2]. The major differentiating characteristic between Globicatella and the aerococci is the cellular arrangement of the cells in the Gram stain. Globicatella forms chains while the aerococci form tetrads and clusters. The colonial morphology of Globicatella strains most closely resembles the viridans streptococci [2]. However, these strains are readily distinguished with a negative LAP and growth in the presence of 6.5% NaCl. The viridans streptococci are pyrroldonylarylamidase (PYR) negative and LAP positive and do not grow in the presence of 6.5% NaCl. The enterococci are PYR and LAP positive and grow at 10°C. None of the Globicatella isolates grew at 10°C or gave positive LAP reactions [2]. As Globicatella is rarely encountered in clinical microbiology laboratories, most laboratory personnel are not familiar with their phenotypic characteristics and identification. Moreover, Globicatella shows various biochemical reactions depending on strain [9] and Globicatella may not be included on the database of the commercial identification system [5]. As a result, the bacterium may be overlooked when isolated, reported as unidentified Streptococcus-like organisms, or misidentified as another species. Miller et al. [10] reported two cases of G. sanguinis infection and they used matrix-assisted laser desorption ionization time-of-flight mass spectrometry (MALDI-TOF MS). Identification scores were 2.26 and 2.22 respectively, which were high confidence identification. If our identification procedure contained MALDI-TOF MS, the blood culture report was finished early.

Our isolate was initially identified as S. pneumoniae by two commercial identification systems in spite of G. sanguinis and G. sulfidifaciens were included in VITEK 2 (bioMérieux) database. Lau et al. [9] reported that two isolates of Globicatella were optochin susceptible. However, Jain et al. [11] reported optochin resistance G. sanguinis. These reports suggested that G. sanguinis showed variable characteristics about optochin resistance. But in our case, there was discrepancy between opto-
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한국인에서 발생한 *Globicatella sanguinis* 균혈증 1예

연세대학교 원주의과대학 원주세브란스기독병원 진단검사의학교실
안광진, 황규열, 윤갑준, 이 영

*Globicatella sanguinis*는 드물게 균혈증, 뇌막염, 요로감염을 일으킬 수 있는 병원성 균종으로서 집락 형태가 유사한 *Streptococcus pneumoniae* 또는 비리단스 사슬알균으로 잘못 동정될 수 있다. 76세 여자 환자가 무릎관절 통증으로 입원하였으며 신행질환으로 고혈압과 뇌혈관질환이 있었다. 혈액배양에서 그람양성알균이 관찰되었으며 MicroScan 동정시스템(Beckman Coulter, USA)과 Vitek 2 동정시스템(bioMérieux, USA)에서 동일하게 *Streptococcus pneumoniae*로 동정되었으며, optochin 디스크감수성검사에서는 내성이었다. 원인 균종은 16S rRNA 염기순서분석과 황화수소생성검사에 의해 최종적으로 *G. sanguinis*로 확인되었다. 혈액을 포함한 무균체액에서의 *G. sanguinis*의 정확한 동정은 정확한 항균체감수성검사의 결과에 따라 적절한 항균제 선택에 중요하다. [Ann Clin Microbiol 2018;21:40-44]

교신저자 : 이 영, 26426, 강원도 원주시 일산로 20
연세대학교 원주세브란스기독병원 진단검사의학교실
Tel: 033-741-1592, Fax: 033-731-0506
E-mail: u931018@yonsei.ac.kr