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Vancomycin Resistance due to *vanA* Gene Expression in an *Aerococcus viridans* Isolate: First Case in Korea

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Dear Editor,

Aerococcus viridans is a catalase-negative gram-positive coccus that appears in clusters, tetrads, or irregular arrangements [1]. This organism is generally considered as a contaminant in clinical cultures, but is also infrequently reported as a clinically significant isolate that causes endocarditis, bacteremia, spondylodiscitis, and urinary tract infections [2-5]. Although most *A. viridans* strains were susceptible to penicillin and other commonly used antibiotics, Uh *et al* [6] described a case of bacteremia caused by an *A. viridans* strain showing high resistance to penicillin, erythromycin, clindamycin, and ceftriaxone. In 2014, Zhou *et al* [7] reported a peritoneal dialysis-related infection caused by vancomycin-resistant *A. viridans* harboring the *vanA* gene. We report a case of a vancomycin-resistant *A. viridans* isolate obtained from an excisional biopsy wound. As far as we know, no study regarding vancomycin-resistant *A. viridans* has yet been published in Korea.

A 77-yr-old farmer visited the emergency room complaining of severe chills. Swelling in an external wound was observed on the inguinal areas where previous excisional biopsy was performed. He had recently been diagnosed as having colon adenocarcinoma and angioimmunoblastic T-cell lymphoma. On admission, his body temperature was 39.0°C. Hematological investigation revealed a hemoglobin level of 9.2 g/dL, white blood cell (WBC) count of 18.96×10^9/L (segmented neutrophils; 92.2%), and platelet count of 262×10^9/L. Serum C-reactive protein (CRP) level (14.36 mg/dL, reference range: <0.30 mg/dL) was elevated. Two aerobic and anaerobic blood culture sets were incubated in the BacT/Alert 3D system (bioMérieux, Durham, NC, USA). The mucus-like whitish aspirate from the wound was plated onto 5% sheep blood agar (BD Diagnostic Systems, Sparks, MD, USA), MacConkey agar (BD Diagnostic Systems), and fluid thioglycollate medium (BD Diagnostic Systems).

Some colonies grew on the 5% sheep blood agar after 24 hr aerobic incubation at 35°C; these colonies were identified as oxacillin-resistant *Staphylococcus hemolyticus* by VITEK 2 (bioMérieux, Marcy l'Etoile, France). No growth was detected in the blood cultures after five days of incubation. Thirteen days after hospital admission, chemotherapy for lymphoma was initiated. Although WBC count and CRP level were within reference ranges at that time, mucus-like discharge from the wound remained, and CRP started to rise steadily. *A. viridans* and *S. hemolyticus* were repeatedly simultaneously isolated from wound cultures. The identification probability of *A. viridans* by VITEK 2 was 98%. Antimicrobial susceptibility test by a MicroScan MICroSTREP plus panel (Beckman Coulter, Brea, CA, USA) showed that *A. viridans* was susceptible to tetracycline, but resistant to vancomycin, penicillin, cefotaxime, ceftriaxone, sulfamethoxazole/tri-

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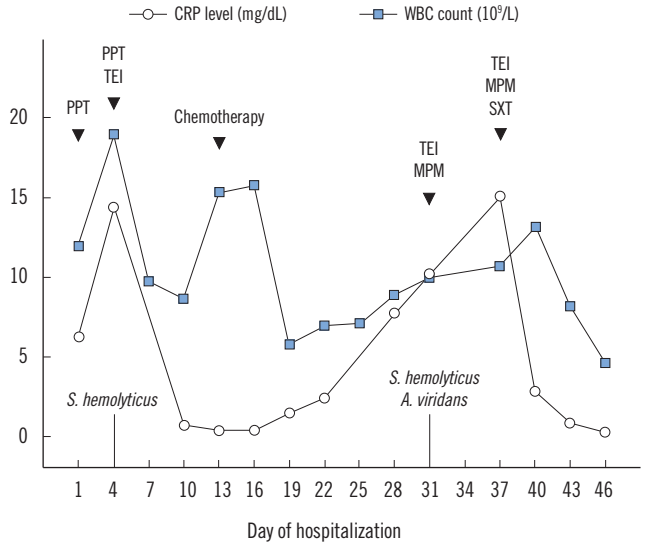

Fig. 1. Changes in white blood cell count and C-reactive protein level during hospitalization.
Abbreviations: CRP, C-reactive protein; MPM, meropenem; PPT, piperacillin/tazobactam; SXT, sulfamethoxazole/trimethoprim; TEI, teicoplanin; WBC, white blood cell.

methoprim, meropenem, and levofloxacin.

To confirm the species identification and antimicrobial susceptibilities, 16S rRNA sequence analysis, minimal inhibitory concentration (MIC) determination for vancomycin (Daewoong Lilly, Seoul, Korea) and teicoplanin (Narion Merrell Dow, Seoul, Korea), and PCR to detect *vanA* and *vanB* genes were performed. MICs were performed by using the broth microdilution method according to CLSI guidelines [8]. PCR amplification of 16S rRNA was performed by using primers 16SF (5′-TAA YAC ATG CAA GTC GAR CG-3′) and 608R (5′-TAT TAC CGC GGC TGC TGG CA-3′), and sequencing was conducted by using the Big Dye Terminator Cycle Sequencing kit (Applied Biosystems, Foster City, CA, USA) and an ABI PRISM 3730 genetic analyzer (Applied Biosystems). All sequences were analyzed by using the basic local alignment search tool and ribosomal database project. The 450-bp 16S rRNA gene sequence from our isolate showed 100% similarity to and 99% query coverage with several *A. viridans* strains (GenBank accession no. KR140225.1, LN998006.1, EU169542.1). The primers and PCR procedure for amplification of *vanA* and *vanB* genes were previously described [9]. Each DNA product was tested by using gel electrophoresis, where *vanA* gene was conclusively detected. *A. viridans* showed a high degree of resistance to vancomycin (<128 μg/mL) and teicoplanin (64 μg/mL), indicating potential acquisition of the *vanA* gene.

The physician added sulfamethoxazole/trimethoprim to teicoplanin and meropenem combination therapy. Consequently, exudate lessened, and WBC count and CRP level also decreased (Fig. 1).

It is difficult to distinguish simple colonization from real infection when *A. viridans* is identified in a wound specimen. However, we paid attention to our *A. viridans* isolate because this patient struggled with chemotherapy before *A. viridans* was isolated and because the resistance may spread to other gram-positive cocci through transfer of *vanA* from *A. viridans* [10].

Authors' Disclosures of Potential Conflicts of Interest

No potential conflicts of interest relevant to this article were reported.

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