Disseminated *Streptococcus anginosus* Infection with Empyema Thoracis in a Patient with Sarcoma

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*Streptococcus anginosus* is a member of the normal flora of the oral cavity and a pathogen of thoracic infection. However, disseminated infection that was identified from different body fluids at the same time has never been reported. We report a 52-year-old man with advanced pulmonary sarcoma who developed neutropenia, bronchopleural fistula and thoracic empyema after chemotherapy. Viridans group *Streptococcus* was isolated from both empyema and urine, which was confirmed as *S. anginosus* according to the biochemical reaction profiles and 16S rRNA gene sequencing results. The patient recovered uneventfully after tube drainage and treatment with imipenem. Disseminated *S. anginosus* infection should be considered as a possible pathogen in immunocompromised patients with empyema and can be rapidly identified by 16S rRNA gene sequencing. [J Formos Med Assoc 2006;105(9):760–764]

**Key Words:** disseminated, empyema thoracis, sarcoma, *Streptococcus anginosus*

**Case Report**

A 52-year-old man had right thigh sarcoma with lung and bone metastasis diagnosed in March 2004. On June 1, 2004, he was admitted for third-course chemotherapy with ifosphamide 5.4 g (3 g/m²) and etoposide 130 mg (75 mg/m²). The patient had not undergone any dental procedure recently. Four days after chemotherapy, he developed spiking fever, productive cough and progressive dyspnea. No frequency, urgency or dysuria was observed. Hemogram showed leukopenia, 210 white blood cells/mm³ (normal, 4000–11,000/mm³), anemia (hemoglobin, 7.4 g/dL; normal, 12.3–18.3 g/dL) and a low-borderline platelet count (118,000/mm³, normal, 120,000–320,000/mm³). Metabolic acidosis (arterial blood gas: pH, 7.375;
PCO₂, 26.2 mmHg; PO₂, 99 mmHg; HCO₃⁻, 15.5 mmol/L; under a non-rebreathing mask), hyperbilirubinemia (total bilirubin, 82.7 μmol/L; normal, 3.4–17 μmol/L), hyperammonemia (96 μmol/L; normal, 9–33 μmol/L) and elevated C-reactive protein (22.4 mg/dL; normal, <0.8 mg/dL) were also noted. He was treated for febrile neutropenia and nosocomial pneumonia with intravenous administration of cefepime (2 g/12 hr). However, profound septic shock and hypoxic respiratory failure developed and he was intubated and transferred to the intensive care unit (ICU). Chest X-ray showed a cavitory mass over the right upper lobe (RUL), multilobar consolidation and right loculated pleural effusion (Figure 1).

In the ICU, the patient was in a semicomatose state. Vital signs included temperature of 37.4°C, pulse rate of 140 beats/minute, respiratory rate of 30 breaths/minute and blood pressure of 100/60 mmHg under the administration of dopamine 25 μg/kg/minute. Physical examination showed dry skin turgor, icteric sclera and pale conjunctiva, decreased breathing sounds with coarse crackles over the right lower lung field and bronchial sounds over the right upper lung field. Other physical findings were unremarkable. Follow-up chest radiography showed progression of multiple lobar consolidation and development of right hydropneumothorax (Figure 2). Thoracocentesis of right pleural effusion yielded pus-like fluid with a pungent odor. Gram stain of the pleural effusion showed polymicrobial infection, which included numerous Gram-positive cocci in chains, Gram-negative bacilli and yeast. Tube thoracostomy was performed immediately, and air and pus were drained continuously. Antibiotics were then shifted to imipenem (500 mg every 6 hours) for mixed flora infection and better penetration. Four days later, the pleural effusion culture yielded group F Streptococcus, Fusobacterium necrophorum and Lactobacillus species, but the sputum culture yielded only Candida albicans. Urine culture yielded viridans group streptococci with a colony count of 1000 colonies/mL, although urinalysis did not disclose pyuria or hematuria despite the patient’s
neutropenic status. However, no pathogen was isolated from blood culture.

Chest computed tomography showed a huge mass with central necrosis over the RUL, a communication between the right main bronchus, right pleural cavity and right pneumothorax (Figure 3). Bronchoscopic study showed rupture of the right main bronchus that was 2 cm away from the carina. One-lung ventilation with left bronchial intubation was performed to improve persistent air leakage of the right pneumothorax and to avoid draining of massive necrotic tissue of the RUL tumor into the left bronchus. Nine days after intubation, tracheostomy was performed with the endotracheal tube directed to the left main bronchus. Right lung air leakage subsided soon after one-lung ventilation, but pus persistently drained from the right chest tube. Intermittent low grade fever and leukocytosis persisted under antibiotics, which impeded the progress of the weaning program. Open drainage from the right lower chest was performed. The patient became afebrile soon after open drainage and was smoothly weaned from the ventilator after 45 days.

The isolates from pleural effusion and urine samples were identified as group F Streptococcus (Oxoid, Unipath Limited, Basingstoke, England). The isolates grew well and had pinpoint colonies of beta-hemolysis on trypticase soy agar supplemented with 5% sheep blood. They were catalase-negative and Gram-positive cocci. Group F antigen reactions of the isolates were positive. The two isolates were identified as S. intermedius based on three commercial identification kits, including the API STREP, Phoenix System (Beckon Dickson, Cockeysville, MD, USA) and VITEK (99% identification) (bioMérieux Vitek, Inc., Hazelwood, MO, USA). However, the isolates showed negative reactions for α-glucosidase and hyaluronidase and positive reactions for β-N-acetylgalactosaminidase and β-N-acetylglucosaminidase. This profile was in accordance with the identification of S. anginosus. The 16S rRNA partial sequencing (1322 bp) analysis using the primer pair 8FPL (5′-AGAGTTTGATCTTGCTCAG-3′) and 1492 (5′-GGTACCCTTGTTACGACTT-3′) identified S. anginosus with identification of 99% (accession number AY691540).\textsuperscript{9,10} Antimicrobial susceptibility was performed using the E test (PDM EpiSimeter; AB Biodisk, Solna, Sweden), performed on Mueller–Hinton agar supplemented with 5% sheep blood agar (BBL Microbiology Systems, Cockeysville, MD, USA) in 5% CO\textsubscript{2} and ambient air at 35°C. The minimum inhibitory concentration (MIC) was 0.12 μg/mL for penicillin, 0.25 μg/mL for ceftaxime, 0.25 μg/mL for cefepime and 0.12 μg/mL for imipenem.

**Discussion**

Viridans group streptococci is comprised of a heterogeneous group of facultatively anaerobic, Gram-positive cocci that do not produce catalase or coagulase, and rarely produces beta-hemolysis on sheep blood agar.\textsuperscript{11} S. anginosus, S. constellatus and S. intermedius are commonly referred to as the S. milleri group (SMG).\textsuperscript{1,2,6,11} SMG strains are normal flora of the oral cavity and genitourinary tract.\textsuperscript{4} They are known for their association with purulent infection, which usually occurs after local disruption of the mucosal barrier, such as ulceration, perforation, inflammation and surgery.\textsuperscript{2,5,6} In addition, SMG has often been associated with
mixed infection, especially with anaerobic infection. Strains of *S. anginosus* are mainly beta-hemolytic and frequently present Lancefield group F antigens, although some strains may be of group A, C, or G, or are nongroupable. Previous research in the literature have demonstrated an association of *S. milleri* species with major surgery, surgical procedure involving the respiratory or digestive tract and nosocomial infection.

In a previous study, isolation of these organisms from empyema and lung abscesses was associated with a high mortality rate in those with malignant disease. Previous studies have also reported identification of SMG species in 0.7–40% of patients with culture-positive thoracic empyema. In Chen et al’s report, SMG accounted for 69.8% of thoracic empyema of viridans *Streptococcus* over a 10-year period. Only one isolate of *S. anginosus* was identified in this report. SMG was an important pathogen of thoracic empyema, but *S. anginosus* was not a common isolate. Although the isolation of *S. anginosus* from blood has been reported many times, isolation of *S. anginosus* from both urine and empyema has never been reported so far. In this case, *S. anginosus* was identified by sequencing analysis of 16S rRNA. The rRNA sequences of both isolates from urine and pleural effusion in our patient had a high degree (>99%) of similarity with the sequences of *S. anginosus*, which confirms that the isolates from both empyema and urine were of the same strain. By sequencing 16S rRNA, *Streptococcus* species infection was clearly identified, confirming disseminated infection of *S. anginosus*.

Confirmation of disseminated *S. anginosus* infection by cultures of thoracic empyema and urine and 16S rRNA gene sequence has not been previously reported. Hematogenous spread was the possible mechanism responsible for disseminated infection. Factors associated with disseminated infection in this case included immunocompromise, necrosis and cavitations of pulmonary sarcoma, aspiration of oral secretion and concomitant anaerobic infection.

Strains of group F *Streptococcus* were demonstrated to be susceptible to penicillin G. However, Farber et al showed that 9% of the group F streptococcal strains were highly resistant to penicillin G (MICs > 4 μg/mL). Furthermore, Fujiki et al reported that the number of intermediate or completely resistant strains against penicillin G was 33.3%. Clinically, infection caused by group F streptococci responds well to penicillin G and cephalosporins. In this case, the MIC for penicillin was 0.12 μg/mL. Possible explanations for the higher MIC in this case include nosocomial infection and previous use of antibiotics, which could have led to the selection of more resistant strains. Thoracostomy is often required for complete resolution of empyema. Our patient was treated with imipenem and concomitant tube thoracostomy. As a result, *S. anginosus* was not isolated from subsequent cultures.

In summary, this is an uncommon documented case of disseminated *S. anginosus* infection including thoracic empyema and urinary tract infection. The identification was confirmed by nucleotide sequencing of the 16S rRNA gene. Factors associated with the disseminated infection include an immunocompromised state, necrosis and cavitations of pulmonary sarcoma, aspiration and concomitant anaerobes infection. Treatment with imipenem led to a good recovery.

References


