

Streptococcus suis Causes Septic Arthritis and Bacteremia: Phenotypic Characterization and Molecular Confirmation

Hanah Kim, M.D.¹, Sang Hoon Lee, M.D.², Hee-Won Moon, M.D.¹, Ji Young Kim, M.T.¹, Sun Hwa Lee, M.D.³,
Mina Hur, M.D.¹, and Yeo-Min Yun, M.D.¹

Departments of Laboratory Medicine¹ and Orthopedics², Konkuk University Medical Center, Seoul; Department of Laboratory Medicine³,
Neodin Medical Institute, Seoul, Korea

Streptococcus suis is a swine pathogen that causes meningitis, septicemia, pneumonia, and endocarditis. The first case of human *S. suis* infection was reported in Denmark in 1968, and since then, this infection with has been reported in many countries, especially in Southeast Asia because of the high density of pigs in this region. We report the case of a patient with septic arthritis and bacteremia caused by *S. suis*. Cases in which *S. suis* is isolated from the joint fluid are very rare, and to the best of our knowledge, this is first case report of *S. suis* infection in Korea. The identity of this organism was confirmed by phenotypic characterization and 16S rRNA sequence analysis. An 81-yr-old Korean woman who presented with fever, arthralgia, and headache was admitted to a secondary referral center in Korea. Culture of aspirated joint fluid and blood samples showed the growth of *S. suis* biotype II, which was identified by the Vitek2 GPI and API 20 Strep systems (bioMérieux, USA), and this organism was susceptible to penicillin G and vancomycin. The 16S rRNA sequences of the blood culture isolates showed 99% homology with those of *S. suis* subsp. *suis*, which are reported in GenBank. The patient's fever subsided, and blood and joint cultures were negative for bacterial growth after antibiotic therapy; however, the swelling and pain in her left knee joint persisted. She plans to undergo total knee replacement.

Key Words: *Streptococcus suis*, Arthritis, Bacteremia

INTRODUCTION

Streptococcus suis is a swine pathogen that causes meningitis, septicemia, pneumonia, and endocarditis [1]. The first case of human infection with *S. suis* was reported in Denmark in 1968 [2], and since then, this infection has been increasingly reported in many countries [3, 4]. Until now, more than 700 cases have been reported, and most of them have occurred in Southeast Asia because of the high density of pigs in this region [3]. Three outbreaks have occurred in China, and many patients have died [1]. *S. suis* infection in

humans has now become a great public concern worldwide. We report the case of a patient with septicemia and arthritis caused by *S. suis*. Cases in which *S. suis* is isolated from the joint fluid are very rare, and to the best of our knowledge, this is the first case report of *S. suis* infection in Korea. The identity of this organism was confirmed by phenotypic characterization and 16S rRNA sequence analysis.

CASE REPORT

An 81-yr-old Korean woman was admitted to Konkuk University Medical Center, a secondary referral center in South Korea; the patient had arthralgia of both knees, fever, headache, and neck stiffness for 4 days before admission. Physical examination indicated tenderness and swelling in the left knee and normal lung and heart sounds. Distal motor and sensory functions were also normal. Her blood was cultured and joint fluid was aspirated; she underwent empirical antibiotic therapy with intravenous administration of cefazolin (2 g every 8 hr). Initial laboratory studies showed the following results: Hb level, 15.0 g/dL; white blood cell (WBC) count, $12.8 \times 10^9/L$ (neutrophils, 81.1%; lympho-

Received: August 30, 2010

Manuscript No: KJLM-10-129

Revision received: January 13, 2011

Accepted: February 22, 2011

Corresponding author: Hee-Won Moon, M.D.

Department of Laboratory Medicine, Konkuk University Hospital, 4-12 Hwayang-dong,
Gwangjin-gu, Seoul 143-729, Korea

Tel: +82-2-2030-5583, Fax: +82-2-2030-5587, E-mail: hannasis@kuh.ac.kr

ISSN 1598-6535 © The Korean Society for Laboratory Medicine.

This is an Open Access article distributed under the terms of the Creative Commons Attribution Non-Commercial License (<http://creativecommons.org/licenses/by-nc/3.0>) which permits unrestricted non-commercial use, distribution, and reproduction in any medium, provided the original work is properly cited.

cytes, 12.9%; and monocytes, 5.8%); platelet count, $189 \times 10^9/L$; and C-reactive protein level, 7.30 mg/dL. Analysis of the cerebrospinal fluid (CSF) showed no red blood cells (RBCs); WBC count, 3/ μL ; protein level, 50.6 mg/dL; and glucose level, 71 mg/dL. Routine biochemical tests, including liver function tests and creatinine and glucose level determination, provided normal results. Joint fluid analysis showed that the RBC count was 1,500/ μL and WBC count was 76,800/ μL ; neutrophils were predominant among the WBCs (90%). The patient's chest radiograph showed no specific finding, and his knee joint radiograph showed severe osteoarthritis. Magnetic resonance imaging of the left knee joint showed a large amount of multiseptated joint effusion with heterogeneous signal intensity, which was suggestive of septic arthritis. The joint fluid was cultured on sheep blood agar and MacConkey agar, and blood was cultured in broth media at 37°C (BacT/Alert; bioMérieux; Durham, NC, USA); a CSF sample could not be obtained for culture. Gram-positive cocci were cultured from the blood and joint fluid. The colonies were small, grayish, and slightly mucoid, and no hemolysis occurred on the sheep blood agar plate. The isolated infectious agent was identified by both biochemical and molecular techniques as *S. suis* biotype II after 24 hr of incubation. The isolate was identified on the basis of its biochemical characteristics by using the automated Vitek2 system (bioMérieux; 99.0% probability) and the API 20 Strep system (bioMérieux;

99.7% probability). The biochemical profile of the isolate is summarized in Table 1. Antimicrobial susceptibility tests were performed using Mueller-Hinton agar with 5% sheep blood; the E test was performed for penicillin and disk diffusion methods were used for other antibiotics, according to the CLSI guidelines [5]. The isolates were susceptible to penicillin (minimum inhibitory concentration [MIC], 0.047 $\mu g/mL$), cefotaxime, vancomycin, and chloramphenicol and were resistant to erythromycin and clindamycin. The identity of the isolate was also confirmed by 16S rRNA sequencing. In brief, PCR of purified DNA was performed using a thermocycler (Applied Biosystems; Foster city, CA, USA) and primers targeting the 16S rRNA region. The primer pair used for amplification was 27F (5'-AGA GTT TGA TC[A/C] TGG CTCAG-3') and 1492R (5'-G[C/T]T ACC TTG TTA CGA CTT-3') [6]. This primer pair amplifies a 1,500-bp fragment of the 16S rRNA gene, which is highly conserved between different species of bacteria. The amplicons were purified, sequenced using the ABI PRISM Big-Dye Terminator Cycle Sequencing Kit (Applied Biosystems), and analyzed using the ABI PRISM 3730XL Analyzer (Applied Biosystems). The sequencing results indicated that the organism was *S. suis* strain ATCC 43765, with 99% identity. Subsequently, cefazolin was discontinued and replaced with intravenous administration of amoxicillin-clavulanate (1.2 g every 8 hr). The patient's fever subsided, and subsequent blood and joint fluid cultures were negative for streptococci and any other bacteria; however, the swelling and pain in her left knee joint persisted. She plans to undergo total knee replacement.

Table 1. Biochemical characteristics of isolates cultured from blood and reaction profiles of *Streptococcus suis* biotype II by API 20 Strep

| Characteristics | Present case | <i>S. suis</i> biotype II (%)* |
|------------------------------------|--------------|--------------------------------|
| Voges-Proskauer reaction | – | 0 |
| Bile-esculin hydrolysis | – | 70 |
| α -Galactosidase production | + | 91 |
| β -Glucuronidase production | + | 91 |
| β -Galactosidase production | – | 52 |
| LAP production | + | 100 |
| ADH production | + | 95 |
| Acidification | | |
| Mannitol | – | 3 |
| Lactose | + | 99 |
| Trehalose | + | 98 |
| Inulin | + | 63 |
| Raffinose | + | 93 |
| Starch | + | 99 |
| Glycogen | + | 96 |

*According to API 20 Strep insert.

Abbreviations: LAP, leucine aminopeptidase; ADH, arginine dihydrolase; +, positive reaction; –, negative reaction.

DISCUSSION

S. suis is an important pathogen that causes various diseases in pigs, including meningitis, septicemia, pneumonia, endocarditis, and arthritis [4]. Human infection with *S. suis* has been reported in many countries, and several outbreaks have occurred in China, which has raised great public concern regarding *S. suis* as an emerging pathogen [1]. *S. suis* infection in humans has mainly been reported in countries with high population densities of pigs. A matched case-control study on the risk factors for human infection in Sichuan Province, where outbreaks have occurred, indicated that slaughtering, cutting carcasses of, and processing sick or dead pigs are the main risk factors for *S. suis* infection in humans [7]. Factors such as occupational or household exposure to pigs or pork may not be considered as risk factors. In some cases reported in Hong Kong and Vietnam, the patients did not report any exposure to pork [8, 9]. In the

present case, the patient was from Chungcheong Province in South Korea; many pig farms were present around her house, but she was not specifically exposed to pigs or pork. Pork is the main type of meat in Korea, and housewives may come in contact with raw pork during cooking. A study has reported that *S. suis* was isolated from 55 of 406 palatine tonsillar samples of pigs in Korea [10]. *S. suis* causes a systemic infection in humans, and meningitis is the most common and serious clinical manifestation [2, 11]. Hearing loss is a frequent complication and has been reported in about half of the patients [3]. Bacteremia is also a common finding; a report on the outbreaks in China showed a high frequency of severe sepsis with high mortality rate [6]. Other clinical manifestations of *S. suis* infection include endocarditis, pyogenic arthritis, and peritonitis [12-15]. In the present case, the patient had arthritis and bacteremia, and joint fluid and blood culture showed the growth of *S. suis*. Although a CSF sample could not be obtained for culture, meningitis due to *S. suis* was suspected by her clinical features of severe headache and neck stiffness. However, the results of CSF analysis, such as WBC count and glucose and lactate levels, were not consistent with bacterial meningitis. A previous report on cases in Vietnam showed that *S. suis* is susceptible to penicillin, ceftriaxone, and vancomycin, and some strains are resistant to tetracycline (83.2% of the isolates), erythromycin (20%), and chloramphenicol (3.3%) [8].

This is the first case of human *S. suis* infection in Korea, and the identity of this organism was confirmed by 16S rRNA sequencing. Human infection by this organism can remain unrevealed because of incorrect identification, and infections with α -streptococci or viridans streptococci may be suggested. The majority of cases of *S. suis* human infection have been reported in Southeast Asia because of the high density of pigs in this region; *S. suis* infection may frequently occur in Korea, especially in rural areas with a high number of pig farms. Increased awareness about this emerging pathogen is needed for its detection and for prevention and treatment of diseases caused by this organism. Moreover, accurate identification of *S. suis* is essential, especially in cases where streptococci are isolated from the CSF, blood, or joint fluid.

Authors' Disclosures of Potential Conflicts of Interest

No potential conflict of interest relevant to this article was reported.

REFERENCES

1. Lun ZR, Wang QP, Chen XG, Li AX, Zhu XQ. *Streptococcus suis*: an emerging zoonotic pathogen. *Lancet Infect Dis* 2007;7:201-9.
2. Arends JP and Zanen HC. Meningitis caused by *Streptococcus suis* in humans. *Rev Infect Dis* 1988;10:131-7.
3. Wertheim HF, Nghia HD, Taylor W, Schultz C. *Streptococcus suis*: an emerging human pathogen. *Clin Infect Dis* 2009;48:617-25.
4. Staats JJ, Feder I, Okwumabua O, Chengappa MM. *Streptococcus suis*: past and present. *Vet Res Commun* 1997;21:381-407.
5. Clinical and Laboratory Standards Institute. Performance standards for antimicrobial susceptibility testing. Twentieth Information Supplement, M100-S20. Wayne, PA: Clinical and Laboratory Standards Institute, 2010.
6. Schuurman T, de Boer RF, Kooistra-Smid AM, van Zwet AA. Prospective study of use of PCR amplification and sequencing of 16S ribosomal DNA from cerebrospinal fluid for diagnosis of bacterial meningitis in a clinical setting. *J Clin Microbiol* 2004;42:734-40.
7. Yu H, Jing H, Chen Z, Zheng H, Zhu X, Wang H, et al. Human *Streptococcus suis* outbreak, Sichuan, China. *Emerg Infect Dis* 2006; 12:914-20.
8. Mai NT, Hoa NT, Nga TV, Linh le D, Chau TT, Sinh DX, et al. *Streptococcus suis* meningitis in adults in Vietnam. *Clin Infect Dis* 2008;46:659-67.
9. Ip M, Fung KS, Chi F, Cheuk ES, Chau SS, Wong BW, et al. *Streptococcus suis* in Hong Kong. *Diagn Microbiol Infect Dis* 2007;57:15-20.
10. Han DU, Choi C, Ham HJ, Jung JH, Cho WS, Kim J, et al. Prevalence, capsular type and antimicrobial susceptibility of *Streptococcus suis* isolated from slaughter pigs in Korea. *Can J Vet Res* 2001; 65:151-5.
11. Wangkaew S, Chaiwarith R, Tharavichitkul P, Supparatpinyo K. *Streptococcus suis* infection: a series of 41 cases from Chiang Mai University Hospital. *J Infect* 2006;52:455-60.
12. Doube A and Calin A. Bacterial endocarditis presenting as acute monoarthritis. *Ann Rheum Dis* 1988;47:598-9.
13. Voutsadakis IA. *Streptococcus suis* endocarditis and colon carcinoma: a case report. *Clin Colorectal Cancer* 2006;6:226-8.
14. Cheng AF, Oo KT, Li EK, French GL. Septic arthritis caused by *Streptococcus suis* serotype 2. *J Infect* 1987;14:237-41.
15. Vilaichone RK, Mahachai V, Nunthapisud P. *Streptococcus suis* peritonitis: case report. *J Med Assoc Thai* 2000;83:1274-7.