

Streptococcus suis Meningitis with Bilateral Sensorineural Hearing Loss

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Streptococcus suis infection is an emerging zoonosis in Asia. The most common disease manifestation is meningitis, which is often associated with hearing loss and cochleovestibular signs. *S. suis* infection in humans mainly occurs among risk groups that have frequent exposure to pigs or raw pork. Here, we report a case of *S. suis* meningitis in a 67-yr-old pig carcass handler, who presented with dizziness and sensorineural hearing loss followed by headaches. Gram-positive diplococci were isolated from cerebrospinal fluid (CSF) and blood cultures and showed gray-white colonies with α -hemolysis. *S. suis* was identified from CSF and blood cultures by using a Vitek 2 system (bioMérieux, France), API 20 STREP (bioMérieux), and performing 16S rRNA and *tuf* gene sequencing. Even after receiving antibiotic treatment, patients with *S. suis* infection frequently show complications such as hearing impairment and vestibular dysfunction. To the best of our knowledge, this is the first case of *S. suis* meningitis in Korea. Prevention through public health surveillance is recommended, especially for individuals who have occupational exposures to swine and raw pork.

Key Words: *Streptococcus suis*, Meningitis, Hearing loss, Korea

INTRODUCTION

Streptococcus suis is an important swine pathogen associated with a wide range of diseases in pigs. The upper respiratory tract, genital, and alimentary tracts are the natural habitats of the pathogen in pigs [1]. *S. suis* is mainly transmitted to human beings by cutaneous contact with infected pigs or raw pork, especially when the skin has cuts and abrasions [2]. Human infection presents predominantly as acute meningitis or arthritis, but may also present with pneumonia, endophthalmitis, endocarditis, and fatal septicemia. Patients with *S. suis* meningitis can develop permanent hearing loss [1, 3, 4]. Since the first human case was reported in Denmark in 1968, over 700 cases have been reported worldwide;

most are from the European and Asian countries [2, 5]. Here, we report the first case of *S. suis* meningitis in Korea.

CASE REPORT

Sixty seven-year-old man, working as a pig carcass handler, present-ed with hearing difficulty and dizziness followed by nausea and headache for 5 days. He had a history of hypertension and diabetes mellitus. On admission, his temperature was 35.1°C, blood pressure was 86/65 mm Hg, pulse rate was at 61 beats per min, and respiratory rate was 19 breaths per min. Although he was alert and oriented, physical examination revealed neck stiffness and limb and gait ataxia. Laboratory investigation showed a leukocyte count of 10,190/mm³ with 90% polymorphonuclear cells and a platelet count of 87,000/mm³. The serum C-reactive protein level (30.0 mg/dL) and erythrocyte sedimentation rate (45 mm/hr) were elevated. The coagulation profile showed a slightly prolonged prothrombin time (15.5 sec, international normalized ratio 1.22) and elevated D-dimer levels (11.53 μ g/mL). The serum glucose level was 257 mg/dL, and the serum creatinine level had increased to 1.69 mg/dL. The patient's cerebrospinal fluid (CSF) was turbid and had 2,350 leukocytes/ μ L (polymorphonuclear cells, 81%), he had a protein concentration of 349.9 mg/dL, and a glu-

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cose concentration of 10 mg/dL (serum glucose level of 257 mg/dL). Therefore, bacterial meningitis was immediately suspected. After performing CSF analysis and 2 sets of peripheral blood cultures, empirical antibiotic treatment with intravenous ampicillin, ceftriaxone, and vancomycin was initiated.

Computed tomographic (CT) scans of the head and temporal bone showed normal results. However, magnetic resonance imaging (MRI) of the brain showed abnormal enhancement of the leptomeninges in both the cerebral hemispheres (Fig. 1). Pure-tone audiometry showed profound bilateral sensorineural hearing loss.

On day 2 at the hospital, aerobic bottles of both blood culture sets grew gram-positive diplococci after 8 hr of incubation

in the BacT/Alert 3D system (bioMérieux Inc; Durham, NC, USA). CSF samples cultured in the thioglycollate broth also grew the same organisms (Fig. 2). Subinoculation on sheep blood agar plates was performed for both the CSF and blood cultures. After 24 hr of incubation at 35°C in the presence of 5% CO₂, we observed small gray-white colonies that showed catalase negativity, optochin resistance, and α-hemolytic activity. After prolonged incubation for 48 hr, large colonies were visible and the α-hemolysis was more pronounced (Fig. 3). This organism was identified as *S. suis* biotype II using the Vitek 2 Gram-Positive Identification (GPI) card (probability, 99.0%; which represents excellent identification [ID]); (bioMérieux; Marcy-l’Etoile, France) and the API 20 STREP (profile code 4771473, % ID 99.7%, T index

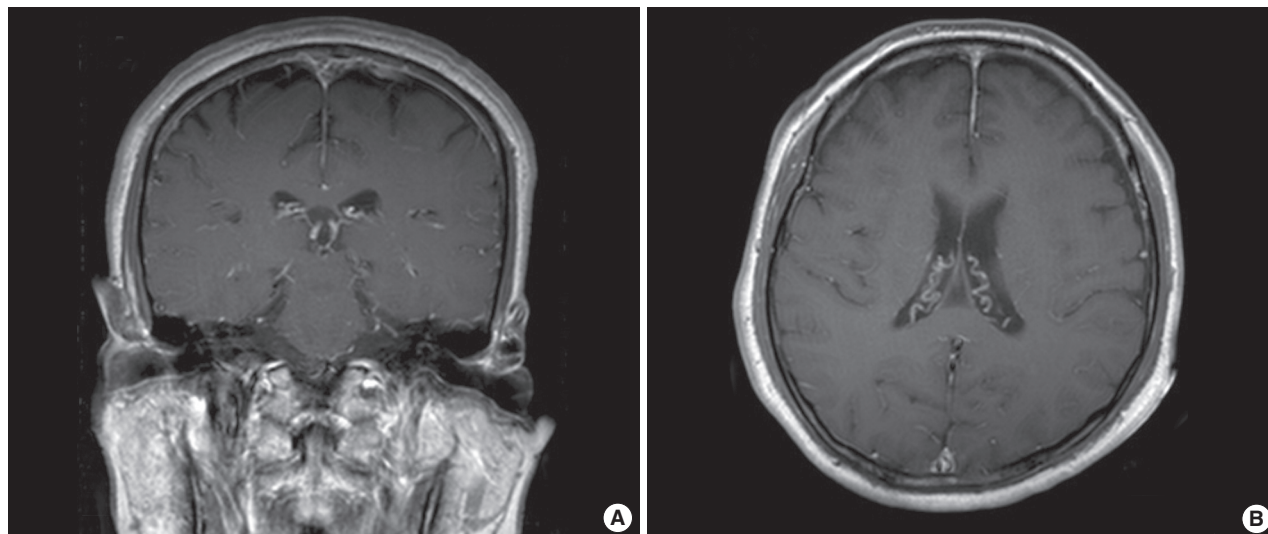


Fig. 1. Brain MRIs. T1 weighted gadolinium enhanced axial (A) and coronal (B) images reveal diffuse leptomeningeal enhancement in both cerebral hemispheres.

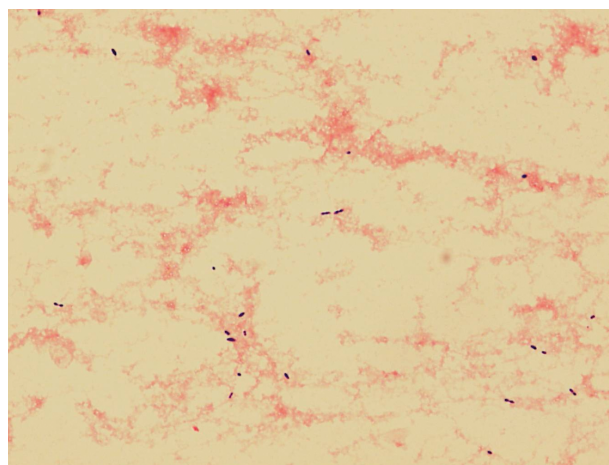


Fig. 2. Gram stain of *Streptococcus suis* of cerebrospinal fluid showed Gram positive diplococci under a light microscope ($\times 1,000$).

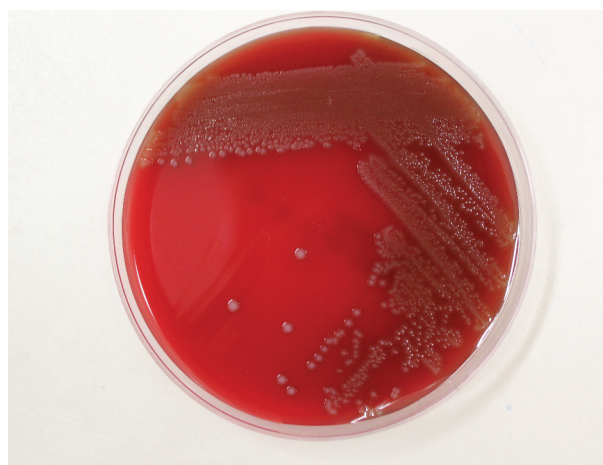
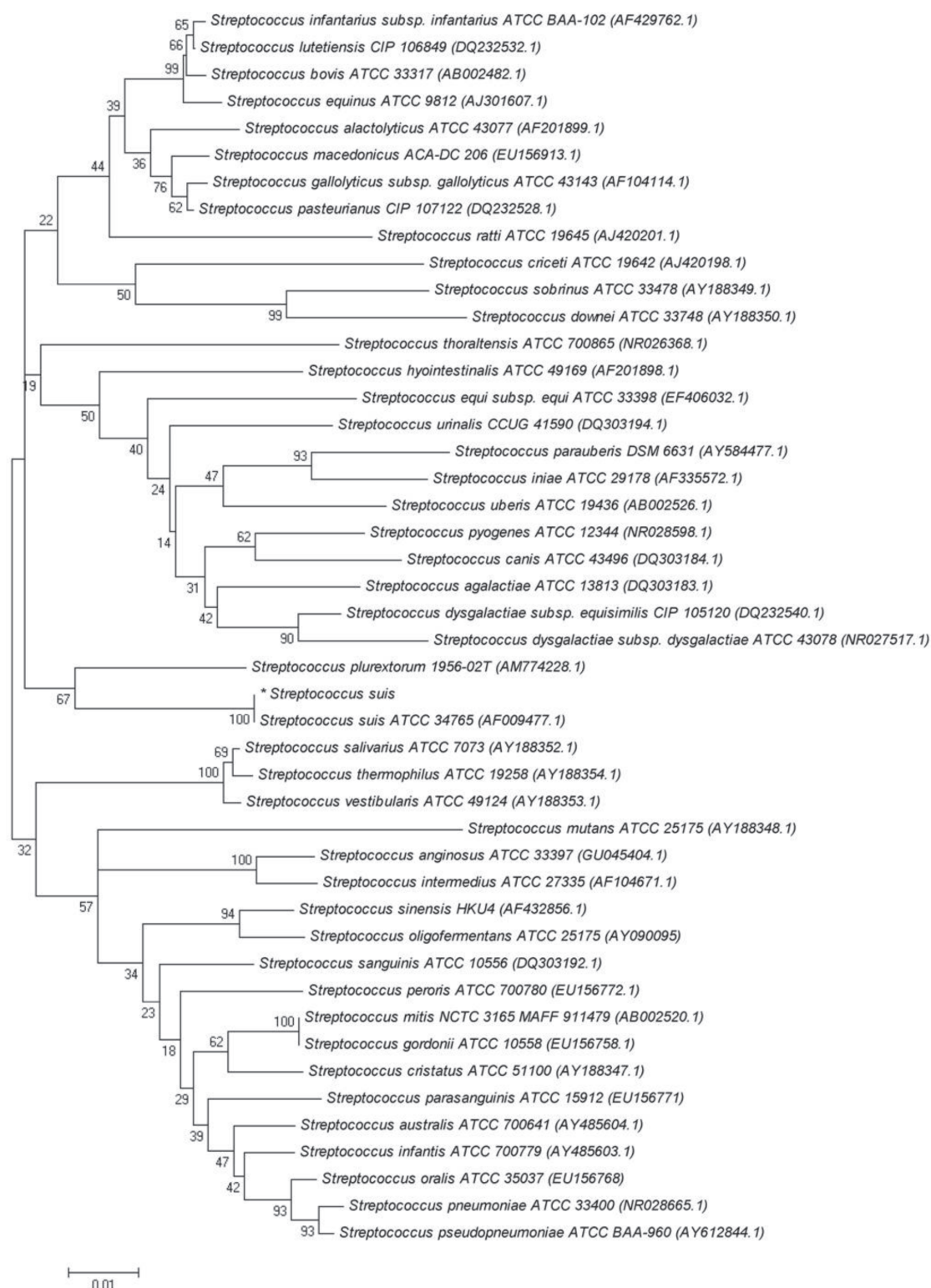


Fig. 3. Gray-whitish, α-hemolytic colonies of *Streptococcus suis* on sheep blood agar plate at 35°C in the presence of 5% CO₂ after 24 hr incubation.



A

Fig. 4. Molecular phylogenetic tree constructed by neighbor-joining method using the 16S rRNA (A) and *tuf* gene (B) sequences of our *S. suis* isolate and various *Streptococcus* species. Reference sequences were from the type strains of the species and accession numbers are given in parentheses. All names and accession numbers are given as cited in the GenBank database. (Continued to the next page)

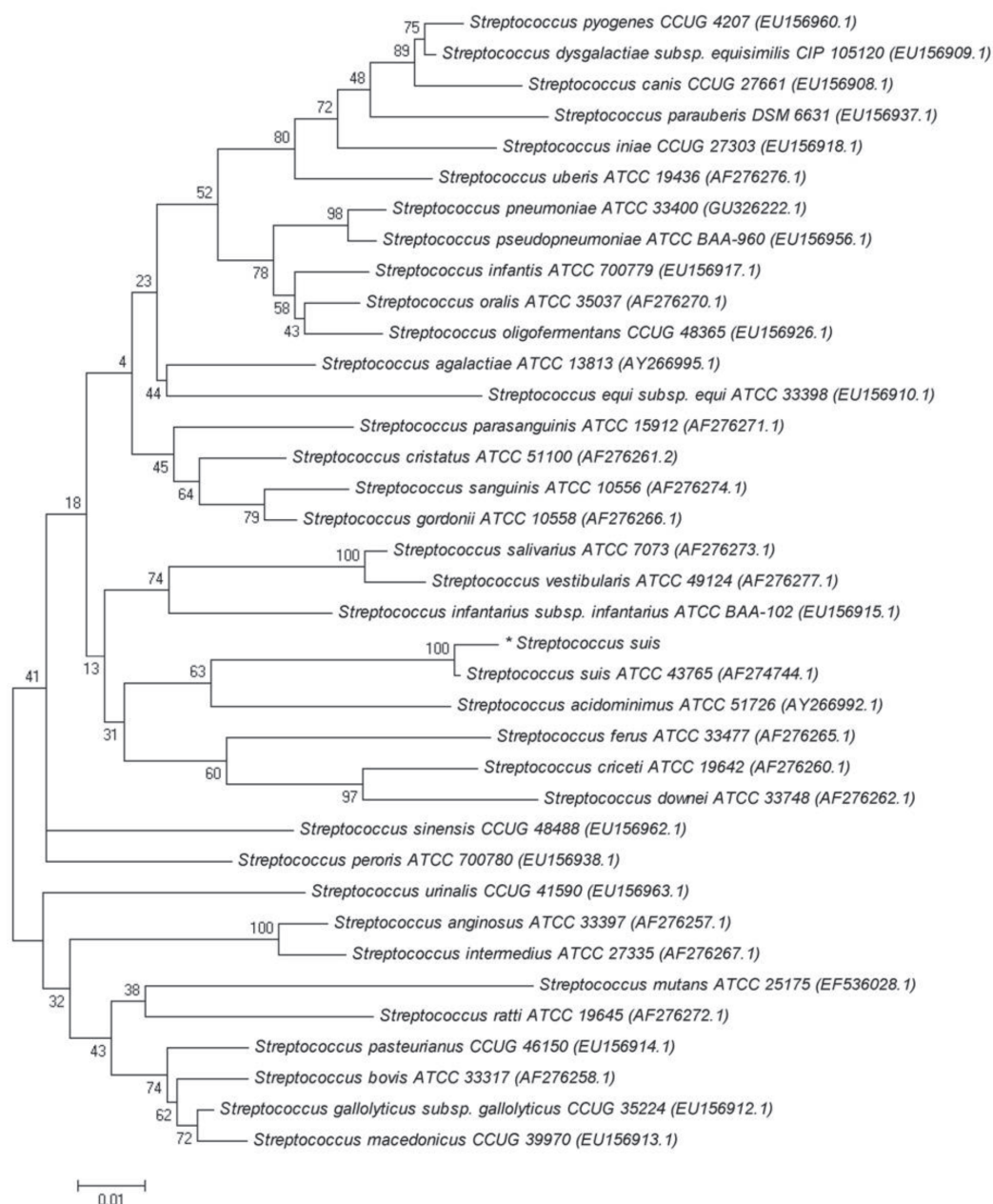


Fig. 4. (Continued from the previous page) Molecular phylogenetic tree constructed by neighbor-joining method using the 16s rRNA (A) and *tuf* gene (B) sequences of our *S. suis* isolate and various *Streptococcus* species. Reference sequences were from the type strains of the species and accession numbers are given in parentheses. All names and accession numbers are given as cited in the GenBank database.

0.73; bioMérieux).

We performed 16S rRNA gene sequencing for the CSF isolate. The 16S rRNA gene fragments were amplified by standard methods according to CLSI guidelines [6]. Two subregions of the 16S rRNA gene were amplified using the following primer pairs: forward, 4F: 5'-TTG GAG AGT TTG ATC CTG GCT C-3' and reverse, 534R: 5'-TAC CGC GGC TGC TGG CAC-3' and forward, 27F: 5'-AGA GTT

TGA TCM TGG CTC AG-3' and reverse, 801R: 5'-GGC GTG GAC TTC CAG GGT ATC T-3'. The *tuf* gene fragments were amplified with the forward (55C-F: 5'-GCC AGT TGA GGA CGT ATT CT-3') and reverse (55C-R: 5'-CCA TTT CAG TAC CTT CTG GTA A-3') primers. Purified PCR products were sequenced directly by using the BigDye Terminator Cycle Sequencing Kit 3.1 (Applied Biosystems; Foster City, CA, USA) on an ABI Prism 3100 ge-

netic analyzer (Applied Biosystems). A GenBank BLAST (The Basic Local Alignment Search Tool) search revealed that 16S rRNA gene and *tuf* gene sequences of the isolate show 100% (664/664 bp) and 99% (407/409 bp) homology with the corresponding sequences of a previously sequenced *S. suis* strain, respectively (GenBank accession number, CP000837.1). For further phylogenetic analysis, the CSF isolate 16S rRNA and *tuf* gene sequences were aligned using ClustalW [7]. Phylogenetic trees (Fig. 4) were constructed using the neighbor-joining method by using the MEGA 5 software package (<http://www.megasoftware.net>) and Kimura two parameters as the substitution model [8-10]. The statistical significance of the phylogenies was assessed by bootstrap analysis with 1,000 pseudoreplicate datasets. The tree is drawn to scale, with branch lengths in the same units as those of the evolutionary distances used to infer the phylogenetic tree.

Antibiotic susceptibility tests were performed using the MicroScan MICroSTREP plus panel (Dade Behring; West Sacramento, CA, USA). The CSF isolate was susceptible to all the antimicrobial agents tested (penicillin, ampicillin, cefotaxime, ceftriaxone, cefepime, meropenem, vancomycin, and chloramphenicol). On the basis of the results of susceptibility test, the patient's antibiotic therapy was changed to intravenous penicillin G (24 million units over 24 hr).

Although the patient's headache gradually improved, he experienced continued dizziness, bilateral hearing loss, and showed symptoms of vestibular dysfunction. On day 16 at the hospital, an MRI of the internal auditory canal revealed abnormal enhancement of the vestibular cochlea on both sides, which was suggestive of bilateral labyrinthitis. On day 22 at the hospital, the patient was discharged and referred to a local hospital close to his home. Because the patient requested outpatient treatment, the parenteral antibiotic therapy was modified to once-daily dose of ceftriaxone (2 g every 24 hr), as an alternative to 6 times-a-day administration of penicillin G.

After completing a 4-week course of parenteral antibiotic therapy, the patient continued to experience dizziness, hearing difficulty, and headache during the 5-week follow-up. It was subsequently determined that the patient had sustained a hand abrasion a week before disease presentation and continued to handle pig carcasses at work without any protection, such as wearing gloves.

DISCUSSION

S. suis is a gram-positive facultative anaerobe, which is coccoid or ovoid in shape and occurs as single cells, in pairs,

or in short chains. On the basis of the capsular polysaccharides, 35 serotypes of *S. suis* have been identified. Although the serotype was not identified in this case, serotype 2 is most commonly associated with diseases in pigs and human beings and is the most frequently reported serotype worldwide [1, 11, 12]. Most *S. suis* strains produce narrow zones of α -hemolysis on sheep blood agar plates. *S. suis* serotype 2 colonies show α - and β -hemolysis on sheep and horse blood agar plates, respectively [13]. Because the growth of *S. suis* on sheep blood agar plates is commonly used to identify the species in routine diagnostic laboratories, this species may be mistaken for viridans streptococci. Although bacteriological diagnosis was made using commercial identification systems in this case, *S. suis* infections are often misidentified, or may remain undiagnosed [2]. *S. suis* is commonly misidentified and reported as *Streptococcus* species, α -hemolytic or viridans streptococci, *Enterococcus faecalis*, *Aerococcus viridans*, or even *Streptococcus pneumoniae* [2, 14]. An *S. suis* infection should be considered in regions with pig-farming industries or in patients who are in contact with pigs or raw pork, if optochin-resistant *Streptococcus* are cultured from a CSF sample obtained from a patient with meningitis. Further microbiological investigations are required for the identification of α -hemolytic streptococci other than *S. pneumoniae*.

Molecular techniques with PCR have improved the rate of detection of *S. suis*. The 16S rRNA gene sequencing technique is a useful and definitive method for most *Streptococcus* spp. For certain genera or groups of microorganisms, the use of alternative gene targets such as the *tuf* gene is necessary, because some species may share 99% to 100% 16S rRNA sequence identity [6]. Thus, 16S rRNA and *tuf* gene sequencing were performed in this case. In phylogenetic analysis, the CSF isolate presented here was homologous with *S. suis* type strains based on 16S rRNA (GenBank accession number, AF009477.1) and *tuf* gene sequencing (AF274744.1), respectively (Fig. 4). Serotype-specific PCR assays and serological tests can be useful tools for the identification of *S. suis* serotypes [1, 15, 16]. Some commercial biochemical identification systems also report the biotype of *S. suis* (biotype I or II) [2]. Wertheim et al. suggested that the *S. suis* biotype should not be mistaken for serotype 1 or 2, as was done in some previous reports [2, 17, 18].

S. suis infections have been reported worldwide. However, the majority of human cases have occurred in Asia (China, Thailand, Vietnam, and Japan) [1, 2, 19]. *S. suis* infections in humans rarely occur in Korea. To date, only one *S. suis* infection in humans has been reported in Korea [20]. However, the possibility of undiagnosed *S. suis* infections

cannot be excluded. Although most reports of *S. suis* infections are sporadic cases, outbreaks of human *S. suis* infections are infrequently reported. Of note, the 2005 outbreak that occurred in Sichuan Province, China, involved 215 cases and caused 38 deaths, emphasizing the importance of *S. suis* as an emerging zoonosis [21].

S. suis infections in humans are most often reported from countries where pig rearing is common, and the people who are in daily contact with pigs are usually affected. The relatively high mean-patient age, the almost complete absence of children in the case series, and the high male-to-female patient ratio support the notion that *S. suis* infection is principally an occupational disease [2, 4, 21-23]. In our case, the patient was exposed to *S. suis* through infected tissues of pig carcasses, which were handled without proper protection, such as gloves. Besides occupational exposure, processing or consuming uncooked or partially cooked pork products is also a risk factor for infection [2, 22-24]. Patients are generally healthy prior to infection with *S. suis*, although predisposing factors, such as diabetes mellitus, alcoholism, and malignancy have been reported [25].

S. suis infection is typically manifested as meningitis. One remarkable symptom of *S. suis* meningitis is sensorineural hearing loss, which may be reported by up to half of the patients either at presentation or a few days later. This hearing loss is often bilateral, profound, and permanent [3, 22]. Deafness with or without vestibular dysfunction is thought to be attributed to direct infection of the cochlea. *S. suis* is believed to enter the perilymph via the cochlear aqueduct through the lytic action of exotoxins [3]. Patients with *S. suis* meningitis may also show permanent incapacitation by vertigo and gait instability because of vestibular dysfunction. Such patients should immediately receive vestibular rehabilitation to improve their independence in daily activities [3, 26].

Analogous to protocols for any case of with suspected bacterial meningitis, immediate antibiotic administration is the first step in the treatment of bacterial meningitis. For empirical treatment, ceftriaxone with vancomycin (the same treatment dose and duration that is used for pneumococcal meningitis) is a good choice until the diagnosis is confirmed. *S. suis* is sensitive to many antibiotics [1, 2]. Thus, once *S. suis* is verified as an infectious agent, antibiotic treatment accompanied with other associated treatments is very effective. After the confirmation of the presence of an *S. suis* infection, patients are generally treated with penicillin G, accompanied by one or more other antibiotics including ceftriaxone, gentamicin, chloramphenicol, and ampicillin. Penicillin G (24 million units over 24 hr for at least 10 days)

or ceftriaxone (2 g every 12 hr for at least 10 days) has been used successfully for the treatment of *S. suis* meningitis. Relapse of *S. suis* meningitis has been reported after 2 weeks of treatment with penicillin or ceftriaxone. However, the patients responded to a prolonged antibiotic treatment for 4-6 weeks [1, 2, 23, 27]. The use of dexamethasone as an adjunctive treatment to reduce mortality and improve the outcome of bacterial meningitis remains controversial [28]. Quick diagnosis and early antibiotic treatment are the most important factors in decreasing the damage caused by *S. suis* infection. Therefore, in patients presenting with meningitis, if characteristic features such as prominent and early hearing loss are observed, *S. suis* should be considered regardless of the patient's occupational background.

Currently, there is no human *S. suis* vaccine. Therefore, prevention of transmission to humans depends on the control of spread of *S. suis* from infected pigs. Improvement of pig-raising conditions and pig vaccination are both effective methods to reduce the risk of human infection. Furthermore, increasing awareness of the disease by educating high-risk populations is also expected to help avoid human infection. Individuals with open wounds should wear gloves when handling raw or uncooked pork, and anyone who prepares pork should wash his or her hands and clean all the utensils thoroughly after contact [1, 29].

To the best of our knowledge, this is the first report of *S. suis* meningitis in humans in Korea. This case should remind clinicians that *S. suis* meningitis affects people who are in daily contact with pigs. During diagnosis, *S. suis* infection should not be confused with infections caused by other *Streptococcus* species. Prevention through public health surveillance is needed, and people with occupational exposures to swine and/or pork products should be educated. Increased awareness among both clinicians and microbiologists is required to fully appreciate the importance of *S. suis* infection as an emerging zoonosis and to promote early diagnosis and prevention of sequelae.

Authors' Disclosures of Potential Conflicts of Interest

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

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