



Case report

Human case of bacteremia due to *Streptococcus suis* serotype 5 in Japan: The first report and literature review



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ABSTRACT

Streptococcus suis is a zoonotic pathogen that can be transferred from pigs to humans. The serotypes 2 and 14 are prevalent among patients with *S. suis* infections, while other serotypes (i.e., 1, 4, 5, 16, and 24) have been detected in rare human cases. To the best of our knowledge, the present patient handling with raw pork is the first human case of uncomplicated bacteremia due to *S. suis* serotype 5 in Japan. We confirmed the new sequence type 752 of this isolate. Virulence-associated gene profiling was performed; both *sly* (encoding the hemolysin *sulysin*) and *mmp* (encoding a muramidase-released protein) were detected without amplification of *epf* (encoding the extracellular factor). Our polymerase chain reaction-based results indicated that this isolate possessed both *tet*(O), the tetracycline-resistance determinant, and *erm* (B), the macrolide/lincosamide-resistance determinant. In addition, we provide the review of literature concerning clinical and microbiological features of four human cases of infection due to *S. suis* serotype 5. Clinicians should be aware of this microorganism when examining and treating patients with fever, who are handling raw pork or having close contact with infected pigs even if they are immunocompetent.

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Introduction

Streptococcus suis is a zoonotic pathogen that can be transferred from pigs to humans, including humans (with or without wounds) who handle raw pork or have close contact with infected pigs (e.g., pig farmers). Serotypes 2 and 14 are prevalent among patients with *S. suis* infections, although other serotypes (1, 4, 5, 16, and 24) have been detected in rare human cases. Kerdsin et al. [1] screened among 179 human *S. suis* strains isolated from clinical specimens in Thailand (2006–2008) and reported that 165 (92.2%) and 12 (6.7%) strains were of serotype 2 and 14, respectively, whereas only one (0.6%) each was of serotype 5 and 24 [2]. We herein report a human case of uncomplicated bacteremia due to *S. suis* serotype 5 in Japan. Furthermore, we provide the review of literature concerning

clinical and microbiological characteristics of 4 human cases of infection due to *S. suis* serotype 5.

Case report

A 48-year-old man was admitted to our hospital with fever, rigors, and swelling of the right forefinger. The patient was a heavy user of alcohol without the underlying liver disease who had been working for a kushiyaki (meat skewer restaurant), a job that included handling raw pork with his bare hands and occasional accidental stabbing of a finger with a skewer. Two days before visiting our hospital, this individual had deeply stabbed his right forefinger with a skewer. On arrival in the emergency room, the patient had a body temperature of 39.4 °C, and exhibited no neck stiffness or meningism, nor peripheral stigmata of infective endocarditis; precordial examination revealed no audible cardiac murmur. Leukocyte cell count and C-reactive protein were 8200/μL and 0.40 mg/dL, respectively.

After admission, blood culture by duplicate bottles revealed the presence of gram-positive cocci. Given the patient's routine handling of raw pork, infection by *S. suis* was suspected; this species identification was confirmed based on percent probability

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(98.9%) match to biochemical parameters obtained using Rapid ID 32 Strep API (SYSMEX bioMérieux Co., Ltd., Tokyo, Japan). The isolate was stored at -80°C pending further characterization. A transeophageal echocardiography, a computed tomography of the chest-abdomen-pelvis, and a magnetic resonance imaging of the brain failed to reveal evidence of infective foci. Therefore, the patient was diagnosed with uncomplicated bacteremia due to *S. suis*, and was treated with a 2-week course of penicillin G (8 million units, three times per day, daily dose 24 million units). Treatment was successful; the patient remained well, with no recurrence of bacteremia, during 12 months of follow up.

This speciation was further confirmed based on 99.86% (1415/1417 bp) sequence identity to *S. suis* S735 (T), in addition to amplification of species-specific glutamate dehydrogenase gene from the patient isolate [3]. Polymerase chain reaction (PCR)-based capsular typing demonstrated that the isolate was of serotype 5 [3]. Multilocus sequence typing (MLST) was performed by sequencing 7 housekeeping genes (*aroA-cpn60-dpr-gki-mutS-recA-thrA*) according to the website for *S. suis* (<http://pubmlst.org/ssuis/>); our results revealed the presence of a novel sequence type (ST) 752 [allelic profile, 8-21-5-264(new allele)-44-22-23] for this strain. Virulence-associated gene (VAG) profiling was performed as previously described [4]; both *sly* (encoding the hemolysin sulysin) and *mrp* (encoding a muramidase-released protein) were detected without amplification of *epf* (encoding the extracellular factor). Furthermore, antimicrobial testing suggested that the isolate would be classified as resistance to tetracycline (TC) and macrolide/lincosamide (ML) (clarithromycin and clindamycin). Note, however, that these classifications employed the breakpoints for viridans group streptococci, since the Clinical and Laboratory Standards Institute guidelines do not provide

breakpoints for *S. suis*. Our PCR-based results indicated that this isolate possessed both *tet(O)*, the TC-resistance determinant, and *erm(B)*, the ML-resistance determinant [5,6].

Discussion

Strains of serotype 5 are routinely isolated from diseased pigs [7]. According to the MLST database, the porcine-linked serotype 5 isolates have been reported from UK, Denmark, China, Vietnam, and Poland. Clinical and microbiological features of four human cases of *S. suis* serotype 5 infections are shown in Tables 1 and 2. Three previous patients infected with the serotype 5 strains have been documented: a patient eating raw pork who developed spontaneous bacterial peritonitis in Thailand [2], a pig farmer with the wound who developed septic arthritis in Sweden [8], and a pig farmer without the wound who developed arthroplasty infection and streptococcal toxic shock-like syndrome in the US [9]. Spontaneous bacterial peritonitis due to the other serotypes [10,11] as well as the arthritis and the streptococcal toxic shock syndrome are already documented. On the other hand, to our knowledge, this is the first report on the arthroplasty infection associated with the serotype 5. We should further clarify the relationship between the arthroplasty infection and this serotype, based on the collection of human cases and the literature review. To the best of our knowledge, the present patient handling with raw pork is the first human case of uncomplicated bacteremia due to serotype 5 in Japan.

Because most of human *S. suis* infections are associated with clonal complex (CC) 1 strains including ST1 strains [12], CC1 strains are considered to be the most hazardous ones for humans. CC1 strains have been frequently isolated from diseased pigs in

Table 1
Clinical features of four human cases of *Streptococcus suis* serotype 5 infection.

Year of case report (ref. No.)	Country	Age (yr) & gender	Comorbid illness or condition	Contact with pig or pork	Presence of wound	Clinical diagnosis
2011 [2]	Thailand	66, male	Alcohol misuser with the liver cirrhosis	Eating raw pork	None	Spontaneous bacterial peritonitis
2014 [8]	Sweden	65, male	Right coxarthrosis	Pig farmer	Cutting the hand	Septic arthritis
2014 [9]	US	74, male	Bilateral total hip arthroplasty & the splenectomy	Pig farmer	None	Arthroplasty infection & streptococcal toxic shock-like syndrome
This case	Japan	47, male	Healthy except for a heavy user of alcohol	Handling with raw pork	Puncture wound on the right 2nd finger	Bacteremia

Table 2
Microbiological characteristics of four human cases of *Streptococcus suis* serotype 5 infection.

Year of case report (ref. No.)	Country	Source of isolate	Identification method	Serotyping method	Sequence type (ST) by MLST	Virulence-associated gene	Antimicrobial resistance class ^a [resistance gene]
2011 [2]	Thailand	Ascites	Sequencing of 16S rRNA gene	Co-agglutination test	ST181	ND	ND
2014 [8]	Sweden	Synovial fluid & blood	MALDI-TOF MS	Co-agglutination test & microscopic examination of capsule swelling with type-specific serum	ND	ND	None
2014 [9]	US	Joint aspiration & blood	Sequencing of 16S rRNA gene	PCR-based capsular typing	ND	<i>mrp+ epf- sly+</i>	Macrolide [ND]
This case	Japan	Blood	Rapid ID32 Strep API, sequencing of 16S rRNA gene, & <i>gdh</i> amplification	PCR-based capsular typing	Novel ST752 (allelic profile, 8-21-5-264-44-22-23) ^b	<i>mrp+ epf- sly+</i>	Tetracycline & macrolide/lincosamide [<i>tet(O)</i> & <i>erm(B)</i>]

MALDI-TOF MS, matrix-assisted laser desorption/ionization-time of flight mass spectrometry; MLST, Multilocus sequence typing; ND, not determined; *gdh*, glutamate dehydrogenase; PCR, polymerase chain reaction.

^a Breakpoints for viridans group streptococci were used since there are no breakpoints for *S. suis* by the Clinical and Laboratory Standards Institute guidelines.

^b The single locus variant (allele profile, 8-21-5-45-44-22-23) was ST108 of the isolates from the heart and lung of pigs in Japan.

Japan. Interestingly, we confirmed the new sequence type, ST752, of this isolate. The single locus variant (allelic profile, 8-21-5-45-44-22-23) was found to match that of an ST108 strain isolated from the heart and lung of pigs in Japan, suggesting domestic distribution of the pigs harboring strains of ST108 as well as CC1 with potential pathogenicity in humans. Consistently with the previous document [8], the VAG profile of our isolate was *mrp*+/epf-/sly+. However, future work will need to evaluate serotype 5 strains for the presence of other virulence-associated factors. Resistance of *S. suis* to antimicrobials (macrolide/lincosamide, sulphonamides, and tetracycline) commonly used in pigs is documented worldwide, with resistance in up to 85% of strains [13]. Bojarska and the colleagues [12] have reported that five isolates (24%) of 21 invasive human infections were non-susceptible to ML and TC, and harbored the *tet*(O) and *erm*(B) genes. Therefore, resistance should be considered when any of these classes are not effective in human clinical settings.

In conclusion, clinicians should be aware of this microorganism when examining and treating patients with fever, who are handling raw pork or having close contact with infected pigs even if they are immunocompetent.

Informed consent

The patient gave his informed consent for the writing of this article.

Conflict of interest

The authors have disclosed no relevant financial relationships.

Ethical approval

In this study, ethical approval was not required.

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