# *STREPTOCOCCUS SUIS* INFECTION: OVERVIEW OF CASE REPORTS IN THAILAND

Polakit Teekakirikul[1] and Viroj Wiwanitkit[2]

[1]Faculty of Medicine, Chulalongkorn University; [2]Department of Laboratory Medicine, Faculty of Medicine, Chulalongkorn University, Bangkok, Thailand

**Abstract.** This paper presents an overview of reports of *Streptococcus suis* infection in Thailand from 1987-2000. Nine reports (N=27 samples) have been collected and analyzed descriptively. The demographic data and clinical data showed 15 samples (55.6%) of all samples had a history of contact with pig, raw pork product or a history of raw pork, or uncooked pig's blood, consumption. The ages of the patients ranged from 23 to 72 years (mean 47 ± 8.91). Most presented with fever (N=27,100%), headache (N=11,40.74%) and neck stiffness (N=13,48.15%). Twelve (44.44%) cases developed septic shock, and only one survived with loss of hearing ability. Two cases were the first report of human *S.suis* endocarditis from Thailand. One case was probably the first case report of *S.suis* peritonitis. Laboratory results and treatment have been also reviewed and may highlight the importance of microbiological laboratories that have limited facilities for identification of the organism.

## INTRODUCTION

*Streptococcus suis* was first described as an important microorganism in pigs and humans in the 1960's in Scandinavia (Perch *et al*, 1968). *S.suis* is a well-established porcine pathogen (Higgins *et al*, 1990). It causes epidemics of septicemia and meningoencephalitis in pigs and piglets (Windsor and Elliott, 1975). However, the infection also occurs in man, particularly those who handle raw pork or are in contact with live pigs. The infection in humans is usually caused by *S.suis* serotype II (Lancefield group R) and often presents as acute meningitis and septicemia. Severe hearing loss in the early course of meningitis is the typical complication of this infection (Phuapradit *et al*, 1987). Most subsequent cases of this infection have been reported in pig-breeding countries, Western European countries (Arends and Zanen, 1988), Canada (Sanford and Tilker, 1982), and also in Hong Kong (Chau *et al*, 1983; Kay *et al*, 1995).

The first two cases in Thailand were reported from Ramathibodi Hospital in 1987 (Perch *et al*, 1983) and there have been eight further reports since. In this study, we review reports of this infection, to summarize and find the definitive clinical data of cases with *S.suis* infection in Thailand, including initial diagnosis and treatment. This may aid recognition and raise awareness of this infection in Thailand.

Correspondence: Dr Viroj Wiwanitkit, Department of Laboratory Medicine, Faculty of Medicine, Chulalongkorn University, Bangkok 10330, Thailand.

## MATERIALS AND METHODS

We used the search engine, PubMed (www.pubmed.com), Medline (www.medline.com) and the Thai Index Medicus of Chulalongkorn University (md3.md.chula.ac.th) and Siriraj hospital (www.medlib.si.mahidol.ac.th), to find all available report papers relating to *Streptococcus suis* infection in Thailand and associated *S. suis* literature. The key words which were used to search for case reports and study were '*Streptococcus suis*, Case Report, Thailand'. Nine reports (N=27 samples), published between 1987-2001, have been retrospectively reviewed. Demographic data and clinical data, such as signs, symptoms, complications, laboratory results and treatment, were collected and summarized by percentage. The overall data were analyzed descriptively.

## RESULTS

This study reviewed each set of data for 27 patients infected with *S. suis*. Demographic data (Table 1) showed that 24 (88.89%) were male and 3 (11.11%) were female. The patients' ages ranged from 23 to 72 years (mean ± SD. = 47 ± 8.91). Seven (25.93%) had a history of close contact with pigs or pork products, and two (7.40%) were butchers. Eight cases (29.63%) had a past history of consuming raw pork or uncooked pig's blood. Most patients (25 cases, 92.65%) had no underlying disease. One had previously been diagnosed with rheumatic heart disease and one had suffered from gouty arthritis.

The clinical manifestations of almost all patients

are acute onset, and four patients (14.81%) had sub-acute onset. Clinical data are shown in Table 2. All patients presented with fever. Eleven patients (40.74%) presented severe headache. Ten patients (37.04%) had fever with myalgia, seven (25.93%) developed nausea and vomiting. Two (7.40%) had fever with chill and dyspnea. Only one presented with generalized abdominal pain and developed paraplegia in a car accident. Eight patients (29.63%) had acute watery diarrhea. Only two patients had a history of direct skin injury, one with an open wound accidentally made by minor cuts to the forearm while slicing pork meat, the other, blunt abdominal trauma that was the suspected route of infection.

Most cases showed normal consciousness and alertness on admission. Thirteen of 27 patients (48.15%) with neurological infection had stiffness of the neck. Eleven patients (40.74%) had dermatological manifestation, including generalized discrete ecchymosis, diffuse erythematous petechiae rash and hemorrhagic blebs were seen in only two patients (7.40%). Physical examination revealed hypothermia in eight patients (29.63%), and all of them had tachypnea which later progressed to respiratory failure. Four cases (14.81%) had jaundice and one case had hepatomegaly with stigmata of chronic liver disease. Two patients had third cranial nerve palsy, two had septic arthritis and one had bilateral rectus muscle palsies. Cardiac murmur from valvular regurgitation was detected in both cases of *S. suis* endocarditis.

*S.suis* meningitis was diagnosed in 14 cases. The most prominent complication of *S.suis* meningitis was sensorineural deafness. All of the meningitic patients developed deafness early in the course of infection, except one who could not be evaluated and died during hospitalization. The onset of bilateral deafness was acute, with progression of permanent hearing loss within 1-7 days (mean 3.9 ± 1.39) after treatment. The deafness was accompanied by tinnitus and vertigo. One was complicated with hydrocephalus. Twelve of 27 cases (44.44%) were diagnosed with septicemia and finally developed septic shock. One of these was diagnosed as streptococcal toxic shock syndrome, due to fulfilling the diagnostic criteria, but *S.suis* was isolated instead of *S.pyogenes*. Two cases presented with both meningitis and septic shock.

Laboratory investigation (Table 3) showed polymorphonuclear leukocytosis in almost all cases (14 cases, 77.78%), except for four cases (22.22%) having septic shock with leukopenia. Twenty-five of 27 (92.6%) cases were reported with positive blood cultures. The organism was initially reported as *S. viridans* (14 of 25 cases, 56%), *S.suis* (8 of 25 cases, 32%), alpha hemolytic streptococcus (2 of 25 cases, 8%) and gamma hemolytic streptococcus (1 case, 4%). In addition, in one case of *S.suis* peritonitis, neither a hemoculture nor a urine culture grew any organism, but peritoneal fluid was cultured and grew alpha hemolytic streptococcus. Lumbar punctures were performed in 14 patients, the organism was isolated from cerebrospinal fluid (CSF) in 13 cases (92.9%), Gram stain of the CSF sediment revealed gram-positive cocci in 9 of 14 patients (64.3%). The white cell counts in the CSF were variable and were reported to range from 95 to 10,000/$mm^3$ (1,816 ± 29.27) with neutrophils from 0 to 90% (57.3 ± 34.96). In three patients (27.3%),

Table 1
Demographic data of the patients.

| | | N | % |
|---|---|---|---|
| Total cases | | 27 | 100 |
| Male | | 24 | 88.9 |
| Female | | 3 | 11.1 |
| Age | - range | 23-72 | |
| | - mean ± SD | 47 ± 8.9 | |
| Occupation | - gardener | 8 | 29.63 |
| | - farmer | 4 | 14.81 |
| | - butcher | 2 | 7.4 |
| | - other | 13 | 48.15 |
| History of contact with pig or raw pork | | 7 | 25.93 |
| History of raw pork or uncooked pigs blood consumption | | 8 | 29.63 |
| No history of contact or consuming pig or pork | | 12 | 44.44 |
| History of chronic alcohol consumption | | 16 | 59.26 |

Table 2
Clinical manifestation of the patients.

| | | N | % |
|---|---|---|---|
| Total cases | | 27 | 100.0 |
| Symptoms and signs | | | |
| Fever at the onset of disease | | 27 | 100.0 |
| Stiffness of neck | | 13 | 48.15 |
| Skin manifestation | | 13 | 48.15 |
| Hypotension / Shock | | 12 | 44.44 |
| Central, peripheral cyanosis | | 11 | 40.74 |
| Headache | | 11 | 40.74 |
| Severe myalgia | | 10 | 37.04 |
| Acute diarrhea | | 8 | 29.63 |
| Hypothermia | | 8 | 29.63 |
| Nausea,vomiting | | 6 | 22.22 |
| Jaundice | | 4 | 14.81 |
| Calf tenderness | | 3 | 11.11 |
| History of skin injury | | 2 | 7.4 |
| Cardiac murmur | | 2 | 7.4 |
| Hepatomegaly | | 1 | 3.7 |
| Prior to admission (day) | - range | 0-14 | |
| | - mean ± SD | (5.39 ± 3.7) | |
| Deafness (permanent) | | 12 | 44.44 |
| Third cranial nerve palsy | | 2 | 7.4 |
| Peritonitis | | 1 | 3.7 |
| Endocarditis | | 2 | 7.4 |
| Septic arthritis | | 2 | 7.4 |
| Acute renal failure | | 11 | 40.74 |
| Disseminated intravascular coagulopathy | | 11 | 40.74 |
| Acute respiratory distress syndrome | | 11 | 40.74 |
| Improve after treatment within | - range (day) | 1-10 | |
| | - mean ± SD | 5.13 ± 2.64 | |
| Recovery | | 15 | 55.56 |

the CSF contained lymphocyte pleocytosis. The glucose concentration in the CSF was low (18.3 ± 40.1) and protein was raised in all cases (265.1 ± 150.04).

In 25 patients, the isolated organism was usually susceptible to penicillin. Twenty-four of these (96%) received large doses of intravenous penicillin (18-24 million units per day) for 10-14 days. One of them (4%) received intravenous ceftriaxone. In the remaining two cases of all reported cases, the organisms were resistant to penicillin. One patient with *S.suis* peritonitis was fully susceptible only to vancomycin, but was administered intravenous ceftriaxone, metronidazole and cloxacillin. Another case was sensitive to ampicillin and was treated with intravenous ampicillin (12 grams per day). Fifteen of all cases (55.56%) started to improve within 1-10 days and recovered from the infection at the completion of their antimicrobial courses. However, deafness in most patients remained permanent. Twelve cases (44.44%) were reported to have died after admission. Eleven cases developed septic shock and expired within 24-48 hours after admission, except for one who died within 7 days of admission. Only one case, who had developed peritonitis, died within 11 days of hospitalization.

## DISCUSSION

*Streptococcus suis* is a gram-positive coccus classified as Lancefield group D,R or S streptococci. It is capable of inducing alpha hemolysis of red blood cells. It also produces several types of capsule and up to 28 serotypes of capsular antigens. Serotypes I and II have been reported as human pathogens, especially

Table 3
Laboratory investigation on first day of patient admission.

| Laboratory investigation | Positive tests (case) | Total tests (case) | % | Mean±SD |
|---|---|---|---|---|
| CBC | | 18 | | |
| Leukocytosis | 14 | | 77.78 | |
| Leukopenia | 4 | | 22.22 | |
| Thrombocytopenia | 11 | 17 | 64.7 | |
| Blood sugar | | 16 | | |
| Hypoglycemia < 80 mg% | 10 | | 62.5 | |
| Positive blood culture | 25 | 27 | 92.6 | |
| Initial report as | | | | |
| *S. viridans* | 14 | | 56 | |
| *S.suis* | 8 | | 32 | |
| alpha hemolytic streptococcus | 2 | | 8 | |
| gamma hemolytic streptococcus | 1 | | 4 | |
| Cerebrospinal fluid culture | 13 | 14 | 92.86 | |
| CSF Gram stain (positive cocci) | 9 | 14 | 64.29 | |
| CSF protein | | 11 | | 265.09 ±150.04 |
| CSF sugar | | 11 | | 18.27 ± 40.07 |
| WBC | | 12 | | 1,816.5 ± 29.27 |
| Lymphocytes | | 9 | | 43.09 ± 35.43 |
| Neutrophils | | 9 | | 57.27 ± 34.96 |

type II (Smith *et al*, 1997; Fongcom *et al*, 2001).

*S. suis* was first diagnosed in the 1960s' as being an important pathogen in both pigs and man (Perch *et al*, 1968; Avihingsanon *et al*, 1999). Most subsequent cases of *S.suis* infection have been reported from western European countries (Arends and Zanen, 1988; Avihingsanon *et al*, 1999), such as Holland (Stokes and Ridgway, 1980; Phuapradit *et al*, 1987), the United Kingdom (Perch *et al*, 1968; Phuapradit *et al*, 1987), Germany (Chau, 1983; Phuapradit *et al*, 1987) and Belgium (Zanen and Engel, 1975; Phuapradit *et al*, 1987) and also in North America, Asia and Australia (Phuapradit *et al*,1987; Arends and Zanen, 1988; Robertson and Blackmore, 1989; Fongcom *et al*, 2001).

Clinical features were acute meningitis and septicemia (Pootong *et al*, 1993). Fourteen patients presented with meninigitis and 12 patients with septic shock. Both meningitis and septic shock were presented in two cases.

The other associated clinical features were toxic shock syndrome, arthritis, diarrhea, endophthalmitis, endocarditis, myocarditis, spondylodiscitis and purpura or hemorrhagic blebs (Kohler *et al*, 1989; Pootong *et al*, 1993; Arend *et al*,1995; Kay *et al*, 1995; Leelarasamee *et al*, 1997). There were two cases of human endocarditis. To our knowledge, these are the first reported cases of endocarditis caused by *S.suis* serotype II documented in Thailand. Our review found *S. suis* peritonitis in one case. This is probably the first case report of peritonitis caused by *S. suis*. There were 11 cases of disseminated intravascular coagulation (DIC), acute renal failure (ARF) and acute respiratory distress syndrome (ARDS). Almost all cases progressed rapidly, ended within 24-48 hours, and had no features of meningitis. This may be attributed to bacterial virulence factors and host resistance factors. All cases had a history of chronic alcohol use, which could predispose them to infection due to the immunocompression effect of alcohol.

The most prominent complications were early hearing loss, followed by permanent deafness and loss of balance (Zanen and Engel, 1975; Fongcom *et al*, 2001). Sensorineural hearing loss can complicate other pyogenic meningitides but it is much less common, rarely severe and is usually transient (Phuapradit *et al*, 1987; Anonymous, 1986), so it is the most significant clinical finding that strongly suggests a diagnosis of *S. suis* meningitis.

*Streptococcus suis* infection has been strongly associated with intensive contact with pigs and pork (Arends and Zanen, 1988; Avihingsanon *et al*, 1999). Fifteen (55.56%) of reviewed cases had a history of contact with or consumption of pig and raw pork. It has been suggested that people who are in daily contact with pork and pigs should minimize skin trauma and use protective hand wear since the skin is thought to be the main entry-route of this organism into humans (Tanphaichitra, 1987; Arends and Zanen, 1988; Avihingsanon *et al*, 1999). Approximately 20% of the patients had minor cuts or burns before illness (Perch *et al*, 1968). Two cases had histories of skin injury. One was a butcher. The other, who had an abdominal trauma and manifested peritonitis had a risk behavior of contact with *S. suis*, in that he ate raw pork. His trauma may have allowed the organism to penetrate the abdominal cavity, where it subsequently caused peritonitis. However, many patients had no history of injury, so that respiratory or oral routes of infection were possible. *S. suis* infection usually occurs in healthy adults. Alcoholism, diabetes and malignancy were noted in certain cases, and could be considered predisposing factors. Nine reported cases were adults and more than half had a history chronic alcohol use.

Most of the patients had polymorphonuclear pleocytosis in the CSF, which reduced glucose levels and elevated protein concentration. Occasionally, the CSF findings were similar to those of tuberculous or fungal meningitis. Initially, two cases were treated like tuberculous meningitis. Diagnosis of *S. suis* infection should therefore be considered in the differential diagnosis of lymphocytic meningitis. In the majority of cases the initial diagnosis, which was based on Gram stains of the CSF, was pneumococcal and listeral meningitis. In the laboratory, the organism can be mistakenly identified as other organisms, such as *S.pneumoniae, S.viridans* or group D enterococci, due to similar colony appearances (Lutticken *et al*, 1986; Vilaichone *et al*, 2000). Most authors suggests that several cases of *S. suis* infection in Thailand were misdiagnosed due to the feasibility of the laboratory to identify this organism. Identification methods for *S. suis* are not available in most microbiological laboratories (Leelarasamee *et al*, 1997; Vilaichone *et al*, 2000). Though treatment and outcome would not be changed if the proper identification and report of *S. suis* were emphasized, the opportunity to study the magnitude of the problem and the natural history of the illness will be missed. In addition, the cumulative case reports are fewer than the actual numbers. Thus, evidence of the infections is inadequate to remind workers who come into close contact with pigs or pork to take preventive measures (Leelarasamee *et al*, 1997). In this review, the initial reports showed 14 cases of viridans streptococci. The reports should remind us to differentiate diagnoses of patients with bacterial meningitis with early deafness as *Streptococcus suis*, particularly in chronic alcoholic patients. Most cases of *S. suis* infection survived despite a stormy clinical course if the diagnosis had been made early and appropriate treatment started without delay.

Most *Streptococcus suis* is very sensitive to penicillin. Penicillin-resistant *S. suis* was previously reported in two patients. The treatment of such cases should be based on the sensitivity test of the isolated organism. The response to treatment for *S. suis* meningitis is excellent. The prognosis of meningitis is good and relapse of the disease rarely occurs (Chotmongkol *et al*, 1999). On the other hand, cases of septic shock had poor prognoses. One of twelve cases survived despite the severe clinical course. After treatment, deafness, unilateral or most commonly bilateral, was likely to remain permanent in about 50% of cases (Kay, 1991; Chotmongkol *et al*, 1999). One hundred percent of meningitic cases result in permanent deafness.

*Streptococcus suis* may be more common than it was thought to be. The organism is under-recognized, because the identification of *S.suis* is not feasible in most microbiological laboratories. Laboratories need to be improved so that the organism may be correctly identified. In addition, strains of the organism are resistant to multiple antimicrobial agents. Detection of resistant agents, the use of alternative antimicrobial agents may be necessary for successful treatment. Understanding the clinical features and having awareness of the risk factors may prevent this fatal infection and help patients to recover without apparent morbidity.

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