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Streptococcus suis infection and risk factors for mortality[☆]

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KEYWORDS

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Summary *Objective:* *Streptococcus suis* infection is a re-emerging zoonotic disease reported worldwide. This study is aimed to describe the clinical features and determine the risk factors for mortality of this life-threatening disease.

Methods: A retrospective cohort study was conducted among patients diagnosed with culture-confirmed *S. suis* infection in a tertiary-care hospital in Northern Thailand during 2005–2007. Risk factors for mortality were determined by Cox's regression analysis.

Results: There were 66 patients with a mean age of 52.9 years; 68% were males. The most common risk of *S. suis* infection was eating under-cooked pork (59%). Clinical presentations included acute meningitis (52%), sepsis (27%), septic shock (12%), endocarditis (8%), and septic arthritis (1%). Hearing loss was observed in 35% and was associated with meningitis. The overall mortality rate was 17%; 11% occurred in 24 h. Cox's regression revealed that septic shock ($p = 0.014$) and elevated alanine transaminase (ALT, $p = 0.013$) were risk factors for mortality. *Conclusions:* *S. suis* infection is common in Northern Thailand, where people often eat raw pork, and commonly presents with acute meningitis or sepsis. The mortality rate is high. The risk factors for mortality are septic shock and elevated ALT. Awareness of this disease and public education are essentially needed.

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Introduction

Streptococcus suis is a gram positive facultative anaerobe, coccoid or ovoid, and appears as single cell, in pairs, or in chains.¹ Association of *S. suis* infection and contact with pigs or pork products is well established.² Previous studies from Thailand have demonstrated that a history of raw pork or uncooked pig's blood consumption is associated with

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S. suis infection.^{3,4} *S. suis* infection is a re-emerging zoonotic disease and has been increasingly reported worldwide.^{5–14} There was a large outbreak of human *S. suis* infection in Sichuan Province, China in July 2005 and killed 38 patients.¹⁵ In Thailand, *S. suis* infection has recently become an important re-emerging infectious disease.^{14,16–18} Currently, *S. suis* is the most common cause of acute bacterial meningitis in some area of Southeast Asia.^{19,20} Permanent hearing loss, a sequela from *S. suis* infection, has been recognized.^{6,8,20} Although the mortality rate of *S. suis* infection is high, there has been limited data regarding the risk factors for mortality in this life-threatening disease. In this retrospective cohort study we sought to describe clinical characteristics of *S. suis* infection in Northern Thailand and determine the risk factors for hearing loss and mortality of this disease.

Materials and methods

Study design

This retrospective cohort study was conducted at Sawanpracharak Hospital, Nakornsawan province, Northern Thailand. It is a tertiary-care center, 700-bed hospital. This study was carried out between January 2005 and October 2007. All patients with culture-confirmed *S. suis* infection were included. Medical records were retrieved and reviewed by authors. The data including demographic information, risk exposure, clinical manifestations, medical history, physical examination, laboratory data, treatment and outcomes were collected.

Microbiological method

All strains of *S. suis* were identified by isolation of an alpha hemolytic *Streptococcus* on sheep blood agar plates at 37 °C in the presence of 5% CO₂ from blood or cerebrospinal fluid or joint fluid culture. The organism was subsequently identified by the API 20 Streptococcus commercial kit (API 20 STREP Bio-Merieux SA, Marcy l'Etoile, France). Antimicrobial susceptibility test was performed by agar disk diffusion (Kirby–Bauer) in all strains. The minimal inhibitory concentration (MIC) of penicillin and ceftriaxone using *E*-test was carried out in 48 strains.

Definitions

S. suis infection was defined as positive culture of clinical specimen from a sterile site for *S. suis* in a patient with compatible clinical signs and symptoms of infection. Acute meningitis was defined as a patient having meningeal inflammation and positive CSF culture for *S. suis*. Sepsis without localized infection was defined as a patient having sepsis syndrome and blood culture grew *S. suis* but no localized infection to any organs was found. Endocarditis was defined as a patient having signs and symptoms of endocarditis and blood culture grew *S. suis*. Septic arthritis was defined as a patient having acute arthritis and blood or joint fluid culture grew *S. suis*.

Statistical methods

Means ± standard deviation (SD), median (range), and frequencies (%) were used to describe patients' characteristics.

Chi-square test and Fisher exact test were used comparing categorical variables where appropriate. Student's *t*-test was performed to access the differences between the two means. Mann–Whitney *U* test was used, when the continuous variables were not normally distributed. Kaplan–Meier survival analysis was used for evaluating the probability of death at different time points.²¹ Cox's proportional hazard model was used for determining significant risk factor for mortality. All analyses were performed using the SPSS 13.0 program. A *p*-value of less than 0.05 was considered statistically significant.

Results

There were 66 adult patients with a mean (SD) age of 52.9 (11.5) years and 68% were male. Of 66 patients, 39 (59%) had a history of eating under-cooked pork or internal organs; 7 (11%) had alcoholic liver disease; 4 (6%) patients had occupational contact with raw pork, i.e., butcher or abattoir worker; the others had no identified risk factors. Occupational contact with raw pork in the study province was handled without protection, i.e., not wearing gloves or gown. Diabetes mellitus was observed in 4 (6%) patients. No post-splenectomy or cancer was found in the study patients. Clinical presentations of *S. suis* infection included acute meningitis, sepsis without localized infection, septic shock, endocarditis, and septic arthritis. Signs and symptoms were fever, headache, stiffness of neck, seizure, and gastroenteritis. Table 1 shows the clinical characteristics of study patients. Median (range) duration of illness was 17 (1–75) days. Complications of *S. suis* infection were hearing loss (19 patients, 29%), disseminated intravascular coagulation (DIC, 4 patients, 6%), congestive heart failure (3 patients, 5%), intracerebral hemorrhage (2 patients, 3%), and endophthalmitis, subdural empyema, peritonitis and intervertebral discitis in one patient each.

Blood cultures grew *S. suis* in 57 patients (86%). Of 34 patients with meningitis, CSF cultures grew *S. suis* in all patients. CSF profiles (median values) were as follows: white blood cell 450 cells/mm³, PMN 62%, L 30%, protein 309 mg/dL, and glucose 3 mg/dL. Of 34 patients with meningitis, 12 (35%) patients had positive gram stain from CSF. Table 2 shows the laboratory results of all patients. All strains of *S. suis* were susceptible to penicillin and ceftriaxone. MIC₅₀ and MIC₉₀ of penicillin were 0.032 and 0.094 µg/ml, respectively. The corresponding MICs of ceftriaxone were 0.047 and 0.380 µg/ml, respectively. All patients received penicillin or ceftriaxone for medical treatment.

The overall mortality rate was 17% and two-thirds of death occurred in the first 24 h of admission. By Kaplan–Meier analysis, the 75% survival period was 30 days (Fig. 1). In univariate analysis, patients who died were more likely to have occupational contact with raw pork without protection (*p* = 0.016), headache (*p* = 0.021), gastroenteritis (*p* = 0.008), septic shock (*p* < 0.001), DIC (*p* < 0.001), low platelet (*p* = 0.025), low serum bicarbonate (*p* < 0.001), low albumin (*p* < 0.001), high alanine transaminase (ALT, *p* = 0.040), and high total bilirubin (*p* = 0.001), as shown in Tables 1 and 2. Cox's regression analysis revealed that only septic shock [hazard ratio (HR) 22.03; 95% confidence interval (CI), 1.88–158.28; *p* = 0.014] and ALT > 400 U/L (HR 44.97; 95% CI, 2.27–191.72; *p* = 0.013) were significant risk factors for mortality.

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