

Two cases of human endocarditis in Thailand due to *Streptococcus suis*

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Streptococcus suis infection, an important zoonotic occupational disease in humans, is associated with meningitis, arthritis, and perceptive deafness but rarely endocarditis. We report two patients with endocarditis caused by *Streptococcus suis*. The first case was a 47-year-old otherwise healthy man. The second case was a 31-year-old woman who had rheumatic heart disease. Both cases had *S. suis* bacteremia and endocarditis without meningitis.

Key words : Human endocarditis, *Streptococcus suis*.

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Streptococcus suis เป็นเชื้อที่สำคัญที่ทำให้เกิดการติดเชื้อที่ลิ้นหัวใจในสุกร สำหรับในคน เชื้อนี้ทำให้เกิดเยื่อหุ้มสมองอักเสบ ซึ่งมีลักษณะสำคัญคือ มีภาวะแทรกซ้อนทางประสาทหู ทำให้เกิดอาการหูหนวก แต่การติดเชื้อที่ลิ้นหัวใจมีรายงานน้อยมาก ได้รายงานผู้ป่วย 2 รายที่มีการติดเชื้อที่ลิ้นหัวใจจากเชื้อ *S. suis* ผู้ป่วยชายรายแรกอายุ 47 ปี มีอาชีพฆ่าหมูและสุกร ไม่มีโรคประจำตัว ผู้ป่วยรายที่ 2 เป็นแม่บ้านอายุ 31 ปี มีโรคประจำตัวคือ ลิ้นหัวใจรั่ว (RHD, MR) ผู้ป่วยทั้ง 2 รายมาด้วยอาการไข้ หนาวสั่น และหอบเหนื่อย โดยไม่มีอาการทางระบบประสาทมา 2 สัปดาห์ ตรวจพบหลักฐานว่ามีการติดเชื้อที่ลิ้นหัวใจ ผู้ป่วยทั้ง 2 รายมีการตอบสนองต่อการรักษาดี

Streptococcus suis (*S. suis*) is a well-established porcine pathogen.⁽¹⁾ It is categorized as a Lancefield group R hemolytic streptococcus which causes epidemics of septicemia and meningoenzephalitis in adult pigs and piglets.⁽²⁾ However, human infection from this organism has been reported to be increasing in European countries,^(3,6) and recently in Hong Kong.⁽⁷⁾ Thus, now it is recognized as an occupational disease, particularly in persons who handle raw pork or are in contact with live pigs.⁽⁸⁾ Although its clinical features and epidemiology are characteristic, the disease is still unfamiliar and is not thoroughly described in most current textbooks of Medicine and Infectious Disease.⁽⁹⁻¹⁰⁾ The endocarditis caused by *S. suis* is frequently observed,⁽¹²⁾ however, it has rarely been reported in human cases^(14,15) We herein report two cases of *S. suis* endocarditis, and we believe that this is the first such report in Thailand.

Case Reports

Case 1

A 47-year-old man was admitted to King Chulalongkorn Memorial Hospital due to a 2 - week course of fever with chills and mild dyspnea. He was otherwise in good health and had no known underlying disease. Physical examination revealed stable vital signs, diffuse erythematous and petechial rashes at all extremities as well as subconjunctival hemorrhage at the right eye. No dental caries were observed. Furthermore, a grade IV diastolic murmur of aortic regurgitation was detected. He did not have either meningism or any abnormalities on a neurological examination.

Laboratory investigation upon admission revealed a hematocrit level of 34.4 %, a white blood cell (wbc) count of 14,090/ml with a differential count of 77.9 % neutrophil and 11.7 % lymphocytes and a platelet count of 8×10^9 /ml. The screening test for disseminated intravascular coagulation was negative. The urine examination showed a specific gravity of 1,007, a trace amount of protein, 5-7 red blood cells/low power field (LPF) and 2-3 wbc /LPF. A mild cardiomegaly without pulmonary infiltration was shown by chest x-ray. Echocardiography detected a vegetation of 1.1 x 0.6 cm in size at the left ventricular outflow tract as well as a moderate aortic regurgitation and a mild mitral regurgitation. Immediate blood samples were taken for bacterial culture by the radiometric BACTEC system. After three days of incubation, all sets of blood culture specimens were positive for the presence of bacteria, which was later identified as an α - hemolytic streptococci when isolated on sheep blood agar.

Case II

A 31-year-old woman was admitted to King Chulalongkorn Memorial Hospital due to a 2-week course of fever with chills and progressive dyspnea. She had previously been diagnosed with a rheumatic heart disease which resulted in a moderate mitral regurgitation and a mild tricuspid regurgitation for ten years. The long term prophylaxis of recurrent acute rheumatic fever with daily oral penicillin V was given to her until three years prior when she lost to follow up. Physical examination revealed a high grade fever and tachycardia. Chest examination revealed fine crackle at both basal lung fields. There was a subconjunctival hemorrhage at the right eye.

No dental caries were observed. A grade III diastolic murmur of aortic regurgitation and a grade III pansystolic murmur of mitral regurgitation were detected. She had no meningism and any other abnormalities after a neurological examination.

Laboratory investigations upon admission revealed a hematocrit level of 31.1 %, a white blood cell count of 16,200 /ml with a differential count of 80.1 % neutrophils, 11.4 % lymphocytes and 6.54 % monocytes and a platelet count of 248×10^9 /ml. The urine examination showed a specific gravity of 1,007, a trace amount of protein, 20-40 rbc/LPF and 4-8 wbc/LPF. A moderate cardiomegaly with mild pulmonary congestion was shown by chest x-ray. A vegetation of 0.7 x 0.7 cm in size at the left ventricular outflow tract as well as a moderate aortic regurgitation and a moderate mitral regurgitation were detected by echocardiography. Immediate blood samples were taken for bacterial culture by the radiometric BACTEC system. In the next three days all sets of blood cultures specimens yielded the positive results for bacteria which was later identified as α -hemolytic streptococci upon isolation on sheep blood agar.

The following characteristic features of *S. suis* were observed in both cases: (1) an ability to grow on Tryptic soy agar but an inability to grow in either 6.5 % sodium chloride or hydrolyse bile aesculin agar; (2) an ability to assimilate a unique set of proteins and sugars including arginine, glucose, lactose, maltose, salicin, sucrose and trehalose; and (3) an inability to assimilate another set of sugars, including arabinose, mannitol, raffinose and sorbitol. The final identification as *Streptococcus suis* II was determined by the API 20 Streptococcus System (API BioMerieux Sa, France) . The antimicrobial susceptibility test

was performed by the agar diffusion method. It was relatively sensitive to penicillin, ampicillin, cephalexin, erythromycin cotrimoxazole and vancomycin. The minimal inhibitory concentration (MIC) of penicillin for this organism was 0.023 mg/L and 0.012 mg/L in the case I and case II patients, respectively.

Case I was treated with 18 million units of intravenous penicillin G sodium. His general condition improved and his fever resolved within seven days. The blood culture specimens were negative after one week of therapy. He developed however, a diffuse pruritic maculopapular rash all over the body as well as leukopenia and eosinophilia on the 20th day of his admission. The therapy was changed to intravenous vancomycin. He was relatively well when he was discharged from the hospital after a 5-week course of the antibiotic therapy.

Case II was also treated with 18 million units of intravenous penicillin G sodium for four weeks with intravenous gentamicin of 1 mg/kg body weight every eight hours added in the first two weeks of therapy. Her general condition improved and her fever resolved within five days. The blood culture specimens were negative after one week of therapy.

Discussion

Streptococcus suis is a zoonotic pathogen which causes meningitis, septicemia and endocarditis in pigs. Human infection is rare and often manifests as a meningitis syndrome, which in most cases results in permanent deafness.⁽¹⁷⁾ *S. suis* was first described in the 1960s in the Scandinavian journal as being an important pathogen of both pigs and man.⁽¹⁸⁾ Most of the subsequent cases of *S. suis* infection have been reported from western European countries⁽¹³⁾ and also

as a major cause of meningitis in Hong Kong.⁽⁷⁾

S. suis is classified by utilization of Lancefield's antigenic grouping into three serogroups: serogroup R and S, the two major serogroups, and serogroup T, a minor one. There is a cross-reaction between *S. suis* antigen and a Lancefield's group D antiserum. Thus, before performing this agglutination reaction the antiserum used must be absorbed with *S. faecalis* a member of group D *Streptococcus*, to eliminate the false positive result. For the reason mentioned above, it was once proposed that the name of the species of these *Streptococcus* be *Streptococcus subacidus* and that it belonged to a subgroup of *Streptococcus* Lancefield group D. *S. suis* was then further subdivided into two types, type 1 (now corresponding to group S Lancefield) and type 2 (now corresponding to group R Lancefield). *S. suis* group R was isolated predominantly in older pigs, whereas an outbreak of piglet septicemia was associated with *S. suis* group S. This may explain why *S. suis* type 2 (group R) had been reported as a cause of disease in man.^(8,19)

S. suis infection has been strongly associated with intensive contact with pigs and pork.⁽¹³⁾ It has been suggested that people who are in daily contact with pork and pigs should minimize skin trauma and use protective handwear since the skin is thought to be the main avenue of entry of this organism into humans.^(13,19) *S. suis* infection in man mainly manifests as a meningitis syndrome which was reported in over 90 % of series of patients, but extraneurological manifestations including bacteremia (80 %), arthritis (21 %), diarrhea (18 %) and pneumonia (7 %) were also occasionally observed. In most cases, bacteremia usually occurs concomitantly with meningitis.

Bacteremia without meningitis is rarely observed.⁽¹⁴⁾

The majority of meningitic patients present with a hearing loss (48 %) during the early weeks of illness. Recovery is associated with a residual deafness and a vestibular disturbance (31 %) as well as an ocular involvement including uveitis and endophthalmitis (7 %).^(17,21-23) There is no explanation for a relatively high incidence of the eighth cranial nerve in *S. suis* meningitis. It is postulated that the surface antigens of *S. suis* have some affinity for meninges and the eighth cranial nerve.^(24,25)

There have been at least seventeen reports of *S. suis* infection in the English-language literature,⁽²⁶⁾ and at least nine cases of meningitis due to *S. suis* were previously reported in Thailand.^(27,28) Twenty three capsular serotypes have been described.⁽¹¹⁾ The capsular serotype 2 is the most prevalent in diseased animals. This particular capsular serotype is known to cause human infections, mostly meningitis.⁽¹³⁾ To date, capsular serotypes 2,4 and 14 have been reportedly associated with human infection.⁽¹⁵⁾ To our knowledge, this is the first reported case of human endocarditis caused by *S. suis* serotype 2 documented in Thailand. One patient had no known predisposing risk factors for endocarditis. Both patients were occupationally exposed to pigs, and although no skin lesions were found, the avenue of entry was suspected to be the skin.

To date, *S. suis* infection has been susceptible to penicillin which remains the drug of choice for treating this illness (at least twelve million units/day).⁽²⁶⁾ When the treatment is started early in the course of disease, the outcome is relatively favorable. No other antibiotics have proven to be effectively used in spite of good results from an in vitro susceptibility test.

Our two patients were fortunate that their condition promptly given to make them recover without deficit was diagnosed early and appropriate treatment was from a potentially fatal infection.

Table 1. Summary of data from 81 cases of *S. suis* infection.

References	No. of cases	No. contact with pig	No. with hearing loss	Skin manifestation	Other manifestation	No. of survivor
13	30	27	15	Petichiae gangrene	Arthritis, Uveitis endophthalmitis maculableeding neuritis, Pneumonia respiratory distress shock, Relapse	28
29	25	15	16	-	Arthritis, Diarrhea endocarditis sinusitis, Pneumonia shock	24
30	2	2	1	-	None	2
31	1	1	0	Arteritic lesion	Endocarditis	1
32	1	1	0	-	Pneumonia	0
33	1	1	0	Ecchymosis	None	0
34	1	1	0	-	Diarrhea, Jaundice	1
35	1	0	1	-	None	1
36	1	1	0	-	Endocarditis	1
14	1	1	0	-	Endocarditis	1
37	1	1	0	-	Endocarditis arthritis	1
2	1	1	1	-	None	1
20	1	1	1	-	Pneumonia, DVT	0
38	1	1	1	-	Central ophthamoplegia	1
39	1	1	1	-	Endophthalmitis uveitis	1
40	1	NS	1	-	None	1
6	1	1	1	-	Pneumonia, Arthritis	1
26	1	1	0	Purpura	Rhabdomyolysis	1
28	9	2	7	fulminans Hemorrhagic bleb, Purpura	Septic arthritis, Septic shock	8

Table 2. Summary of data from 6 cases of *Streptococcus suis* endocarditis.

References	Age	Heart disease	Occupation	Contact pig	Survival
36	48/M	No	Pig breeder	Yes	Yes
14	48/M	No	Slaughter	Yes	Yes
29	64/F	No	Housewife	Yes	Yes
37	55/M	No	Farmer	Yes	Yes
15	NA	MVP	Farmer	Yes	Yes
31	NA	No	Farmer	Yes	Yes

From these data , it is apparent that *S. suis* type 2 can be remarkably invasive, even in a healthy individual. Only a few cases of bacteremia or endocarditis without meningitis have been described. It seems that after entering the blood stream, the blood brain barrier is easily invaded by this organism. This invasive ability may be due to the polysaccharide capsule, which contains sialic acid, an anti-phagocytic substance.⁽¹³⁾

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