Streptococcus suis Infection in Northern Thailand

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Abstract

A ten-case report of *Streptococcus suis* infection was reported in Lamphun, northern Thailand from 1999 to 2000. Ten patients were admitted to Lampoon Provincial Hospital with a history of high fever, watery diarrhea, severe myalgia and ecchymosis rashes. The disease progressed rapidly and all patients died within 24–48 hours after admission from complications such as disseminated intravascular coagulation (DIC), acute renal failure (ARF) or acute respiratory distress syndrome (ARDS). Epidemiological data revealed that all cases were healthy men aged between 40–49, residing in the same geographical area and had a history of raw pork or uncooked pig's blood consumption prior to their illnesses. Blood culture and genetic investigation (16 s rRNA polymerase chain reaction with restriction enzyme *Pst*I) confirmed diagnoses of the same species of *Streptococcus suis* infections.

Key word : Severe *Streptococcus suis* Septicemia, Oral Route of Infection, in Alcoholic Patient

**FONGCOM A, PRUKSAKORN S,
MONGKOL R, THARAVICHITKUL P, YOONIM N
J Med Assoc Thai 2001; 84: 1502-1508**

Uncommon human infection and disease caused by *Streptococcus suis* type II has been reported in Europe, North America, Asia and Australia[1-3]. The majority of reported cases provided strong evidence for the percutaneous route of infection related to pigs or raw pork handling. Most patients presented with the following syndrome: meningitis and septicemia. Nevertheless, septicemia without meningitis has also been reported[4]. The most prominent complications were early hear-

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ing loss followed by permanent deafness and loss of balance[5]. Other complications included arthritis,[6] uveitis, and endophthalmitis[7]. Very few patients died as a direct result of infection *per se*.

There have been a few reports on *Streptococcus suis* type II infection in Thailand[3,8]. In all reports, except one, the presenting symptoms were sub-acute meningitis. The two exceptional cases presented with severe septicemia resembling toxic shock syndrome caused by *Staphylococcus aureus* infection[9]. Interestingly, most patients had a history of pig or raw pork contact prior to the infection.

Case Description

This study reviewed, the medical records, next-of-kin interviews and data of 10 patients admitted to Lamphun Provincial Hospital in Lamphun, Thailand from 1999 to 2000. Presenting with similar clinical syndromes, all cases were clustered during the same period of time and from the same geographic area. The clinical data suggested that they were infected by *Streptococcus suis*. Complications included severe septicemia, septic shock, disseminated intravascular coagulation (DIC), acute renal failure (ARF) and acute respiratory distress syndrome (ARDS) without evidence of meningitis. All patients also reported a history of chronic alcohol use and most of them had eaten raw pork and uncooked pig's blood 2–4 days before their illness. This latter evidence suggested the oral route of infection.

Epidemiological data showed that the patients were men aged between 40-49. They seem to have been healthy prior to their illnesses. The outbreak of infection peaked during 2 seasons: wet (July to October) and winter (January to March) of the two years. Other demographic data, including some clinical data, are shown in Table 1.

Clinical manifestation and laboratory investigation

All patients had a history of high fever for a few days prior to admission. In all cases, the most prominent symptom was severe myalgia. However, only 3 cases tested positive for calf tenderness (as

Table 1. The demographic data and clinical manifestation of the patients.

		n	%
Total cases		10	100
Male		10	100
Age	- range	40 – 49	
	- mean ± S.D.	44 ± 2.8	
Occupation	- gardener (working in longan garden)	8	80
	- farmer	2	20
Past history of contact with pig or raw pork		0	
Past history of raw pork or uncooked pig blood consume		7	70
Chronic alcohol consumption history		10	100
Predominate symptoms and signs			
	- fever at the onset of disease	10	100
	- severe myalgia	10	100
	- skin lesion / ecchymosis	10	100
	- hypotension / shock	10	100
	- central and peripheral cyanosis	10	100
	- onset of illness <72 hours•	9	90
	- acute diarrhea	7	70
	- hypothermia on admission	7	70
Other symptoms and signs			
	- calf tenderness	3	30
	- jaundice	3	30
	- URI symtoms	1	10
	- hepatomegaly	1	10
	- stiffness of neck	0	
	- cardiac murmur	0	

• onset of illness = the time interval between the first day of fever and shock

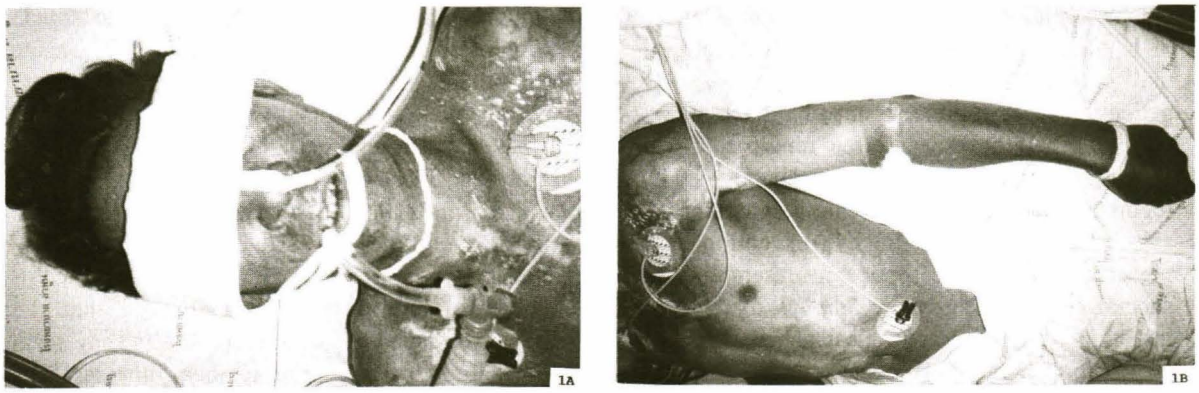

Fig. 1AB. Ecchymosis rash predominately on face and extremities.

seen in Leptospirosis). Seven of the ten patients had watery diarrhea on the second day of illness, some were followed by bloody diarrhea. After that, they became tachypnic and hypotensive with ecchymosis lesions. Appearing initially on the face and extremities, the bloody rashes progressed rapidly to the whole body surface.

Most cases showed normal consciousness on admission and none of the patients had stiffness of the neck. Physical examination revealed hypothermia in 7 patients. All of them had tachypnea which later progressed to respiratory failure. Three cases had jaundice and one case had hepatomegaly with stigmata of chronic liver disease. Dermatological manifestation included generalized discrete and congruent ecchymosis predominately on the face and extremities as shown in Fig. 1. No skin blebs and desquamations were seen. Laboratory results are shown in Table 2.

The characteristic investigation found among these patients, which differentiated them from other causes of septic shock, were profound hypoglycemia in all 10 cases and leukopenia in 5 cases. All of them had at least 2 (out of 3 specimens) positive blood cultures. The organism was initially reported as viridans streptococci, which was susceptible to most antibiotics such as penicillin, ampicillin, cephalosporin exept to aminoglycoside and cotrimoxazole. Blood samples from the last 3 cases were sent to Chiang Mai University Hospital's microbiological laboratory for species identification. The electropheresis of 16s rRNA analysis of 2 isolates, from the 2 patients residing in the same village, after addition of restriction endonuclease (*Pst* I) was done. PCR restriction fragments were sequenced and the nucleotides showed 100 per cent homology to *Streptococcus suis* published sequence in Gene bank.

Treatment

Upon admission, all patients were admitted to the medical intensive care unit with the diagnoses of severe septicemia, septic shock, ARF and DIC. The pattern of acute renal failure was compatible with acute tubular necrosis caused by other infections. Forty per cent of cases had clinical symptoms and chest radiography compatible with ARDS. All patients received respiratory support *via* a volume-controlled ventilator and circulatory support by central venous pressure and fluid-electrolyte monitoring.Vasopressive agents and susceptible antibiotics were used in all cases and peritoneal dialysis was initiated for treatment of ARF and severe metabolic acidosis. Platelet and fresh frozen plasma were transfused in some cases for treatment of coagulopathy. All cases died within 24-48 hours after admission from refractory septic shock and cardiac arrhythmia.

DISCUSSION

Pathogenic in pigs, *Streptococcus suis* is a gram-positive cocci bacteria 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 capsules, up to 28 serotypes of capsular antigens. Serotype I and II have been reported as human pathogens, especially type II[10].

Table 2. Laboratory investigation on first day admission of the patients.

Lab investigation	Positive test (case)	Total test (case)	%	Mean ± SD
CBC		10		
- Leucopenia	4		40	
- Leucocytosis	4		40	
- Thrombocytopenia	9		90	
U/A		8		
- Abnormal finding *	8		100	
Blood sugar		10		
- Hypoglycemia (BS < 80 mg%)	10		100	51.1 ± 19.1
LFT		6		
- Elevated AST	6		10	579.2 ± 352.6
- Elevated ALT	5		83	28.3 ± 304.3
- Elevated total bilirubin	6		100	5.8 ± 3.1
- Elevated alkaline phosphatase	5		83	146.83 ± 50.5
- Hypoalbumin, hypocholesterol	3		90	
Coagulopathy		5		
- prolong PT,PTT	5		100	
Chest X-ray			10	
- abnormal •	4		40	
Metabolic and renal		10		
- serum creatinine	10		100	3.4 ± 1.1
- metabolic acidosis	10		100	
- serum potassium ≥5.0	2		20	4.57 ± 1.0
Anti-HIV		5		
- negative	5		100	
Leptospirosis titer		2		
- negative	2		100	
Positive blood culture		10		
Initial report as viridans streptococci	10		100	

* Abnormal urine profile compatible with ATN
• Abnormal chest X-ray compatible with early ARDS

Common diagnoses were meningitis and septicemia with typical complications as follows: permanent deafness and loss of balance. Almost all patients experienced mild illness and rather rapid recovery. In addition, sub-clinical infection has also been reported among specific occupations such as pig farmers and pork butchers etc[1]. The major route of infection was believed to be percutaneous through a skin opening *via* exposure to living pigs or infected pork.

This case series showed that all 10 patients had been infected during the same period of time and within the same geographical areas suggesting an outbreak situation by *Streptococcus suis*. They also had a similar syndrome of septicemia, refractory septic shock, DIC, ARF and ARDS. However, the series revealed a number of deviations from the mild illnesses commonly seen in other reports; all cases progressed rapidly, ended within 24–48 hours after admission and had no clinical manifestation of meningitis. At least 3 possible factors could explain such differences: (1) bacterial virulence factor - several biomarkers studies were conducted with regard to virulence of *Streptococcus suis* such as Suilysin, Muramidase-released protein (MRP) and extracellular factor portein (EP)[11]. (2) host resistance factor - all cases had a history of chronic alcohol use which could be the most important predisposing factor due to the immunosuppression effect of alcohol. Alcohol could interfere with either mechanical defenses such as reduction of gastrointestinal tract mucosal barrier or humoral and cell-mediated immunity[12]. (3) environmental factor - due to the peak of outbreaks observed in this series, climate or seasonal change might be responsible for disease fatality. It was reported in Hong Kong that

Table 3. The phenotypic characteristic of *Streptococcus suis* (A) and *Streptococcus* from the patients (B).

Phenotypic characteristic	A	B
Alpha hemolysis on blood agar	+	+
Ability to grow in oxygen	+	+
Ability to grow in oxygen and 5% carbondioxide	+	+
Ability to grow in anaerobiosis	+	ND
Ability to grow in 40% bile	+	ND
Hydrolysis of :		
- Hippurate	-	-
- Esculin	+	+
Acid formation from :		
- Inulin	+	+
- Lactose	+	+
- Mannitol	-	-
- Raffinose	-	+
- Salicin	+	+
- Sorbitol	-	-
- Trehalose	+	+

ND = not done
(Adapted from Bergey's Manual of Determinative Becteriology.9th ed. 1994 pp. 553)

a hot and humid climate could possibly increase the infection rate by promoting bacterial overgrowth in the environment and subsequent epidemic in pigs(13).

This study also underscored the importance of behavioral modification. Like other northern provinces, local residents in Lamphun have long been famous for their raw meat and uncooked animal blood consumption, especially while drinking alcohol. As the rate of alcoholism rises, *Streptococcus suis* infection could potentially become more clinically severe.

One limitation of diagnosis of *Streptococcus suis* infection was the identification of the organism. It appeared that both *Streptococcus suis* and others viridans streptococci produced alpha-hemolysis on blood agar plate. Routinely,the bacteria recovered from blood samples was initially reported as viridans streptococci(8,9). The simple test that could differentiate them were growth in 40 per cent bile, fermentation of inulin and hydrolysis of esculin. However, these tests would be useful only when clinician suspected and requested them. Phenotypic comparison between *Streptococcus suis* and those recovered from the patients is shown in Table 3. The confirmation test could also create another diagnosis limitation because it is available only in The University's hospital. These laboratory limitations could greatly reduce the number of *Streptococcus suis* infections.

(Received for publication on December 4, 2000)

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รายงานผู้ป่วยที่เสียชีวิตจากการติดเชื้อ*เสตร็พโตค็อคคัส ซูอิส*ในจังหวัดทางภาคเหนือของประเทศไทย

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รายงานผู้ป่วย 10 ราย ที่เข้ารับการรักษาในโรงพยาบาลลำพูนในช่วงปี 2542–2543 ซึ่งทั้งหมดเป็นผู้ป่วยชาย มีอายุระหว่าง 40–49 ปี พบมีอาการป่วยในช่วงระยะเวลาเดียวกัน และมีภูมิลำเนาอยู่ในเขตพื้นที่เดียวกัน ผู้ป่วยทุกรายมีอาการไข้สูง, ปวดเมื่อยกล้ามเนื้อ, อุจจาระร่วงและมีจุดจ้ำเลือดออกตามตัว ไม่พบอาการแสดงของเยื่อหุ้มสมองอักเสบ ผลตรวจระดับน้ำตาลในเลือดต่ำและอาการของโรคดำเนินไปอย่างรวดเร็ว ผู้ป่วยทั้งหมดเสียชีวิต จากภาวะติดเชื้อในกระแสโลหิต และช็อค (septic shock), ภาวะไตวายฉับพลัน (acute renal failure), การเกิดลิ่มเลือดในหลอดเลือด (disseminated intravascular coagulation) และการหายใจล้มเหลว (acute respiratory distress syndrome) ภายใน 24–48 ชั่วโมงหลังรับไว้ในโรงพยาบาล ผลการเพาะเชื้อในเลือดที่ได้จากผู้ป่วยทั้ง 10 ราย รายงานเบื้องต้นเป็นเชื้อ viridans streptococci ตัวอย่างเลือดจากผู้ป่วยสามรายสุดท้าย ได้ส่งตรวจทางพันธุกรรม พบว่าผล 16 srRNA sequence เข้าได้กับเชื้อ*เสตร็พโตค็อคคัส ซูอิส*. ผู้ป่วยส่วนใหญ่มีประวัติรับประทานเนื้อสุกรหรือ เลือดสุกรดิบ ก่อนเกิดอาการป่วยและผู้ป่วยทุกรายมีประวัติการดื่มสุราเรื้อรัง

คำสำคัญ : การติดเชื้อในกระแสโลหิตจากเชื้อ*เสตร็พโตค็อคคัส ซูอิส*, ทางการกิน, ในผู้ป่วยที่ดื่มสุราเรื้อรัง

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จดหมายเหตุทางแพทย์ ฯ 2544; 84: 1502–1508

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