Streptococcus suis Toxic-shock Syndrome and Meningitis

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Abstract

Three cases with *S. suis* bacteremia and meningitis were reported. The first case was a 23-year-old butcher who was a regular drinker of alcohol for two years and developed streptococcal toxic-shock syndrome. The organism was transmitted to him through a minor cut in his right arm. The second cases was a 49-year-old female laborer who had been consuming locally produced alcohol for 20 years and developed fever and meningitis. Unfortunately, she succumbed in seven days despite intensive supportive and cefotaxime treatments. The third case was a 45-year-old regular alcoholic drinker and car painter who was seen at a private hospital due to contusion at his left lateral chest wall. However, fever and confusion due to meningitis was detected upon admission. Irreversible deafness developed within 48 hours of ceftriaxone therapy for meningitis. He finally recovered with deafness. *S. suis* was isolated from blood and cerebrospinal fluid cultures in all three cases though initially reported to be viridans group of streptococci.

Toxic-shock syndrome (TSS) is a well established clinical entity caused by *Staphylococcus aureus* and has been reported in Thailand[1]. The dramatic clinical features are created by elaboration of *S. aureus*, an exotoxin of the toxic-shock syndrome namely TSST-1 which behaves like a superantigen[2]. Recently, there has been a resurgence of highly virulent strains of *Streptococcus pyogenes* associated with an increased invasiveness in soft tissue infections[3] and clinically manifested like TSS[4]. Unlike TSS due to *S. aureus*, in which the site of infection may be elusive, streptococcal TSS is mostly associated with rapidly progressive soft tissue infection. Hence the name "flesh-eating bacteria" was used to describe the ultimate effect. At least three cases as such were presented at an academic meeting in Siriraj Hospital, Thailand in 1995 but none of them was published in a journal.

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Infection due to *Streptococcus suis* commonly manifests as meningitis[5], arthritis and endocarditis[6,7] in humans. A clinical case was first recognized in 1968, and up to 1989 a total of 108 cases were reported worldwide[8]. In Thailand so far, only six cases have been reported from Ramathibodi Hospital[9,10]. The disease is contracted in many cases by occupational exposure to pigs or raw pork. Prominent clinical features are fever, permanent deafness within the first seven days of meningitis and subsequent ataxia that developed in nearly 50 per cent of cases. Overwhelming septicemia is rare and we were unable to find a case report of TSS due to the organism in the world literature. Recently, three cases of *S. suis* meningitis were encountered by the authors and TSS was presented in one of these cases. Hence, we wish to report these cases and summarize the clinical features of all reported cases infected with *S. suis* in Thailand. Data of the first case with TSS was elaborated in more detail.

PATIENTS

A 23-year-old butcher was admitted to the hospital because of spiking fever and hypotension for one day. He had been healthy until five days earlier, when he accidentally made minor cuts in his right arm and hand while he was slicing pork for marketing. The wound was not treated since this occurred frequently during meat slicing and healed spontaneously. Three days later, he developed fever, malaise, watery diarrhea and hemorrhagic blebs developed on the cut wounds. One day before admission he was nauseated, vomited, was unable to walk and was taken to the emergency room. He had drunk approximately 50 mL of Thai whisky everyday for the last two years. On examination, temperature was 36.0°C, pulse was 110, and respirations were 42, blood pressure was 90/70 mmHg. He appeared lethargic and slightly icteric. The extremities were cold and moist. Hemorrhagic blebs were seen at right arm and thumb and petechiae on extremities. Septic shock due to *N. meningitidis, P. aeruginosa* or *Streptococcus pyogenes* was diagand 12 g of piperacillin and 600 mg of amikacin were initiated on the first day. Fluid loading was employed to resuscitate until central venous pressure was raised from 3 to 12 cm H_2O. However, he was still oliguric, dyspneic with peripheral cyanosis while on oxygen mask, had severe metabolic acidosis and hyperkalemia and developed into coma. He was transferred to the intensive care unit (ICU) for respiratory and circulatory supports on the following day. On entry to ICU, radiographs of the chest revealed diffuse bilateral haziness in lower lung fields compatible with adult respiratory distress syndrome. Bradycardia suddenly developed and electrocardiogram showed junctional rhythm at the rate of 50 per minute. He was intubated and connected to a ventilator with positive-end expiratory pressure. Swan-Ganz catheter was inserted to monitor fluid balance. Lumbar puncture was performed and revealed clear cerebrospinal fluid with a few leukocytes. Fresh frozen plasma and platelets were transfused to correct clotting defect due to disseminated intravascular clotting. Accordingly, he gradually recovered over the next five days. Examination of bloody fluid aspirated from the bleb showed only neutrophils and was negative upon bacterial culture. To our surprise, three specimens of blood and one cerebrospinal fluid (CSF) specimen cultures were positive for a viridans group of streptococcus. It was later identified to be *Streptococcus suis* type 2. He was finally given penicillin G sodium and recovered uneventfully. Determination of anti-streptolysin O in paired sera were negative for recent group A streptococcal infection. Details of hematologic and blood chemical values are shown in Table 1.

The second cases was a 49-year-old female laborer who developed spiking fever, nausea, vomiting for three days, confusion and semicoma for nine hours before admission. She had consumed locally produced alcohol for 20 years. No underlying disease was obtained from her relatives. Physical examination showed a hypersthenic build and tremor of the hand. No signs of chronic liver disease or abnormal signs of the nervous system could be found with the exception of agitation, stiffneck and semicoma. Meningitis was diagnosed and lumber puncture disclosed turbid fluid in which 10,000 leukocytes per mm^3 were found and 90 per cent of them were neutrophils. Gram-stain of CSF showed gram-positive cocci and pneumococcal meningitis was concluded clinically. However, cefotaxime was added to penicillin therapy in the light that alcoholism also predisposes to gram-negative bacterial infection and definite laboratory report was pending. Unfortunately, she developed convulsion, azotemia, ventricular tachycardia and finally septic shock which was not responsive to supportive treatment. She died seven days after hospitaliza-

Table 1. Hematologic and blood chemical values of the first case by days of hospitalization.

Variables	Day 1	Day 5	Day 14
Hematocrit (%)	54.4	35	33.9
White cell count (per mm^3)	47300	-	10000
Platelet count (per mm^3)	25000	45000	820000
Partial thromboplastin time (second)	80	30.2	29.4
Prothrombin time (second)	27	14.7	11.3
Creatinine (mg/dl)	6.3	1.3	0.9
Creatine phosphokinase (U/litre)	339	1314	-
Creatine phosphokinase MB (U/litre)	67	67	-
Lactate dehydrogenase (U/litre)	1316	1564	-
Aspartate aminotransferase (U/litre)	180	168	25
Total bilirubin (mg/dl)	2.8	-	-
ASO titer (Todd unit)	200	-	200

tion. Her hearing ability could not be evaluated during hospitalization. Blood and CSF cultures were positive for a viridans group of streptococcus which was later identified to be *S. suis*.

The third case was a 45-year-old regular alchohol drinker and car painter who was seen at a private hospital with contusion at his left lateral chest wall after he fell on slippery ground. However, fever and confusion had developed two and one day respectively prior to the accidental event. Stiffneck was detected on physical examination and lumbar puncture was immediately performed. It showed serosanguinous fluid with 1,000 leukocytes per mm^3. Gram-stain of CSF revealed gram-positive cocci and ceftriaxone was administered intravenously. Viridans streptococcus was initially isolated from blood and CSF cultures and was finally identified to be *S. suis*. Deafness developed on day one and was complete within two days. Fever subsided in day five of admission and he gradually recovered and was able to return home with irreversible deafness.

DISCUSSION

Clinical signs of severity of the first reported case fulfilled those criteria to be diagnosed as streptococcal TSS[11] but *S. suis* was isolated instead of *S. pyogenes*. His occupation rendered him accidentally acquired *S. suis* through a cut wound in his forearm during slicing pork meat. In fact, the suspected causative bacteria was initially *Streptococcus pyogenes* though history of cut wound and close contact with pork had been elicited at the beginning. TSS associated with *S. suis* infection in our case clinically differed from other cases of streptococcal TSS by lack of its relatedness-to prior deep tissue invasiveness. The virulence of the organism was not fully elucidated in our study but was reported to be associated with the presence of muramidase-released protein and an extracellular factor[12] which were detectable by double antibody sandwich enzyme-linked immunosorbent assays using specific monoclonal antibodies[13]. A hemolysin so called "suilysin" was shown to be another important factor to produce detrimental effects of an *S. suis* type 2 infection in mice[14]. In animal models, prior inoculation with porcine reproductive and respiratory syndrome virus definitely predisposed piglets to *S. suis* meningitis[15]. All these factors need further study to evaluate their contributions for manifestation of *S. suis* associated TSS. Recently, three cases of toxic shock-like syndrome due to a novel pyrogenic toxin-producing *Streptococcus agalactiae* (streptococcus group B) were reported[16]. It is probable that toxic substances produced by various groups of streptococci may vary in their physical properties and molecular structures but may react like superantigen[4] with host defense in a similar way to produce the TSS. Whether host factors such as HLA Class II antigen type[17,18] and specific Vß regions on lymphocyte[19] which predispose to severe group A streptococcal infection, may play a role in *S. suis* associated TSS, are yet to be proven. Nevertheless, chronic heavy alcohol drinking was uniformly obtained from all three cases. Thus, its contribution to rapid development and severity of infection can hardly be denied.

Though at least six cases of meningitis due to *S. suis* were previously reported in Thailand[9,10], we believe many isolates from blood and especially CSF culture, were incompletely identified and accordingly, reported to be viridans streptococci. At Siriraj Hospital during 1994-1995, viridans streptococci but none of *S. suis*, were isolated from eight cases of meningitis. When the patients' records were reviewed, two cases developed deafness in the early course of meningitis which is compatible with clinical manifestation of *S. suis* meningitis. Though treatment and outcome would not be changed if proper identification and report of *S. suis* are emphasized, we will miss the opportunity to study the magnitude of the problem and its natural history of illness. In addition, the cumulative case reports are less than actual numbers and thus evidence of the infection is inadequate to firmly remind those workers who come regularly in close contact with pigs or pork to take preventive measures. We must admit that the behavior risk of acquiring the disease, is prevalent among ordinary people and as in the first case, proper care of minor cut wounds is neglected or easily forgotten by ordinary people. This route of transmission could also happen to anyone who works in a kitchen or goes to buy and select meat from the supermarket. The report should remind general practitioners to educate their patients and warn them not to contract the disease through this route. The report will continuously remind people to take good care of superficial or cut wounds though most of them are fortunately healed without harm.

Most cases with *S. suis* infection survived despite the stormy clinical course as found in the Thai series (see Table 2). However, one case was also reported which succumbed to superimposed bacterial infection[20] rather than *S. suis* infection. Our first case with TSS survived without apparent morbidity including sensori-neural deafness. Hearing ability in another case could not be evaluated due to coma and critical condition. In the third case, deafness rapidly developed and was irreversible. Cochlear sepsis was proven in animal models to be primarily responsible for hearing loss rather than the eight the cranial nerve involvement by meningeal sepsis. The mechanism sheds light on possible prevention of deafness in *S. suis* meningitis if prompt treatment with penicillin is initiated as happened in our first case. Fortunately, most isolates were susceptible to penicillin with the exception of one isolate[9]. Rapid diagnosis of the etiology must heavily rely on gram-stain of CSF since this diagnostic method was 66 per cent effective in a Thai series. If gram-positive cocci in the chain was seen in CSF obtained from an alcoholic with meningitis, one must include *S. suis* as a likely pathogen and penicillin has to be administered immediately before cochlear sepsis takes place.

Table 2. Summary of clinical data of cases with *Streptococcus suis* infection in Thailand.

Total cases	9
Age (mean ± S.D.)	47.8 ± 14.3
- range	23-73
Male:female	6:3
Close contact with pig or pork product	4 (44%)
- butcher	2 (22%)
Habitual drinking of alcohol	2 (22%)
Mean duration of illness (day) prior to admission	4
- range	1-14
Stiffneck	9 (100%)
Deafness (permanent)	7 (77%)
Third cranial nerve palsy	2 (22%)
Septic arthritis	2 (22%)
Hemorrhagic blebs and purpura	2 (22%)
Septic shock	2 (22%)
Gram-positive cocci in CSF	6 (66%)
Isolation of *S. suis* from culture of	
- blood	8 (88%)
- cerebrospinal fluid	8 (88%)
Initial microbiological report as viridans group of streptococci	3 (33%)
Recovery	8 (88%)

In the era where direct contact with raw meat such as cow or monkey could lead to mad cow disease and Ebola hemorrhagic fever, this report adds another serious disease to the list and emphasizes proper care of a wound once contaminated with raw pork. This emerging infection can be serious or fatal and streptococcus group B and *S. suis* are added to the list of streptococci which can cause TSS. We confirm a previous report[9,10] that the infection is not uncommon and believed to be under-recognized since identification of *S. suis* is perhaps not feasible in most microbiological laboratories. We need to improve our laboratories by having a training program to further identify those viridans streptococcus isolated from blood and CSF in order to help us correctly estimate its frequency and morbidity in Thailand.

SUMMARY

Three cases with *S.suis* bacteremia and meningitis were reported. The first case was a 23-year-old butcher who was a regular drinker of alcohol for two years and developed streptococcal toxic-shock syndrome. The organism was transmitted to him through a minor cut in his right arm. The second case was a 49-year-old female laborer who had consumed locally produced alcohol for 20 years and developed fever and meningitis. Unfortunately, she succumbed in seven days despite intensive supportive and cefotaxime treatments. The third case was a 45-year-old regular alcoholic drinker and car painter who was seen at a private hospital due to contusion at his left lateral chest wall. However, fever and confusion due to meningitis was detected upon admission. Irreversible deafness developed within 48 hours of ceftriaxone therapy for meningitis. He finally recovered with deafness. *S. suis* was isolated from blood and cerebrospinal fluid cultures in all three cases though initially reported to be viridans group of streptococci. All isolates of *S. suis* were sensitive to penicillin. It was concluded that *S. suis* must be considered when a viridan streptococcus is isolated from cerebrospinal fluid in which pre-existing valvular heart disease can not be demonstrated. Meningitis with early onset of deafness is another feature that clinically leads to the diagnosis.

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กลุ่มอาการ ท็อกสิก-ช็อค และเยื่อหุ้มสมองและไขสันหลังอักเสบจากเชื้อสเตร็พโตค็อคคัส ซูอิส

อมร ลีลารัศมี, พ.บ., จุไรรัตน์ นิลกุล, วท.ม.**, สุรภี เทียนกริม, วท.ม.*, สมพร ศรียศชาติ, ปร.ด.***, วัฒนชัย สุแสงรัตน์, พ.บ.*****

ได้รายงานผู้ป่วย 3 ราย ที่ติดเชื้อสเตร็พโตค็อคคัส ซูอิส ผู้ป่วยชายรายแรก อายุ 23 ปี มีอาชีพชำแหละหมูและดื่มสุราเป็นประจำมา 21 ปี ผู้ป่วยได้รับเชื้อเข้าทางผิวหนังจากบาดแผลที่ข้อมือ บาดแผลดังกล่าวได้กลายเป็นถุงน้ำเลือด ผู้ป่วยมีไข้และช็อคตามมา มีอาการแสดงของความผิดปกติของการแข็งตัวในเลือด กล้ามเนื้อหัวใจอักเสบและเต้นผิดจังหวะเป็น junctional rhythm ภาวะการหายใจล้มเหลวจนต้องใช้เครื่องช่วยหายใจและมีภาวะไตวาย ผู้ป่วยได้ piperacillin และ amikacin เมื่อทราบผลการเพาะเชื้อ ได้เปลี่ยนเป็นเพนิศิลลิน ผู้ป่วยหายดีเป็นปกติโดยไม่มีหูหนวก ผู้ป่วยรายที่ 2 เป็นกรรมกรหญิง อายุ 49 ปี มีไข้ คลื่นไส้อาเจียนมา 3 วัน และเริ่มซึมและสับสน 1 วันก่อนมาโรงพยาบาล ผู้ป่วยดื่มเหล้าเป็นประจำมานาน 20 ปี การตรวจร่างกายพบว่ามีคอแข็ง หลังแข็ง ผลการเจาะหลังได้น้ำหล่อสมองและไขสันหลังขุ่น การย้อมสีแกรมของน้ำหล่อสมองและไขสันหลังพบเชื้อทรงกลมแกรมบวก ผู้ป่วยได้รับยาเพนิศิลลิน และ cefotaxime แต่ไม่ตอบสนองต่อการรักษาและถึงแก่กรรม ผู้ป่วยรายที่ 3 เป็นช่างทาและพ่นสีรถ และดื่มสุราเป็นประจำ ผู้ป่วยมาโรงพยาบาลเพราะผนังทรวงอกด้านซ้ายกระแทกกับพื้นหลังจากลื่นหกล้ม แต่มีไข้และเริ่มสับสน 1-2 วันก่อนมาโรงพยาบาล การตรวจร่างกายพบว่ามีคอแข็ง หลังแข็ง ผลการเจาะหลังได้น้ำหล่อสมองและไขสันหลังขุ่น การย้อมสีแกรมของน้ำหล่อสมองและไขสันหลังพบเชื้อทรงกลมแกรมบวก ผู้ป่วยมีอาการหูหนวกซึ่งเกิดขึ้นใน 2 วันแรกของการรักษา ผู้ป่วยรายนี้หายดีแต่หูหนวก การเพาะเชื้อจากเลือดและน้ำหล่อสมองและไขสันหลังจากผู้ป่วยทั้ง 3 ราย ได้เชื้อ *S. suis* แต่รายงานเบื้องต้นเป็น streptococcus กลุ่ม viridans ผู้รายงานได้รวบรวมลักษณะคลินิกของผู้ป่วยที่มีรายงานว่า ติดเชื้อชนิดนี้ไว้ด้วยกัน

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