

***Streptococcus suis*: what has been found in the past decades?**

豬鏈球菌：在過去的數十年發現了什麼？

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Streptococcus suis (SS) infection has aroused tremendous attention recently. We report a restaurant worker who suffered acute confusion due to SS meningitis. Sporadic cases have been reported in Hong Kong since 1981. Little was known in the past about its characteristic fulminant clinical deterioration. We explored the literature and discuss the epidemiology, pathogenesis, clinical manifestations and management of this disease. (*Hong Kong j.emerg.med.* 2006;13:46-49)

豬鏈球菌感染最近引起了極大的注意。我們報告一名酒樓工人因豬鏈球菌腦膜炎而引致急性精神錯亂的個案。自 1981 年以來，香港已有零散的個案報告。以往，對於它暴發地惡化的臨床特性知道得很少。我們探查文獻並討論這疾病的流行病學、發病機理、臨床現象及處理法。

Keywords: Bacterial meningitis, bacterial polysaccharides, deafness, sensorineural hearing loss, streptococcus infections

關鍵詞：細菌性腦膜炎、細菌多糖、失聰、感覺神經性失聰症、鏈球菌感染

Case summary

A 49-year-old 'dim-sum' restaurant worker presented in September 2004 to our accident and emergency department with acute confusion. His speech became confused while on duty in the early morning and was brought in by his colleagues. No further information was available. On arrival, his blood pressure was 152/82 mmHg and pulse rate was 107 beats per minute. The tympanic temperature was 37.7°C. The pulse oximeter reading was 98% on room air. The examination showed that the patient was confused and drowsy with a Glasgow Coma Scale score 7 out of 15 (eye 2/4, verbal 2/5, motor 3/6). The pupils were

equal and reactive. No neck rigidity was noted. Cardiovascular, respiratory and abdominal examinations were unremarkable. The Babinski sign was negative on both sides. Bedside blood sugar was 8.9 mmol/L. The electrocardiogram revealed sinus tachycardia without ischaemia. The presumptive diagnosis was acute confusion suggestive of intracranial infection. He was admitted to our neuro-medical unit for management. Full blood count showed leukocytosis with neutrophil predominance. Renal and liver function tests were unremarkable. Urgent computed tomography (CT) of the brain showed mild brain swelling (Figure 1). Lumbar puncture revealed turbid cerebrospinal fluid (CSF) with high opening pressure of about 50 cm H₂O. Gram-positive diplococci were seen on Gram stain and smear. Meningitis was diagnosed and the patient was treated in the intensive care unit. The physicians started intravenous antibiotics (cefotaxime and ampicillin) and dexamethasone 0.4 mg/kg twice daily was also given for two days. Subsequent blood and CSF cultures confirmed *Streptococcus suis* (SS) meningitis. The ENT

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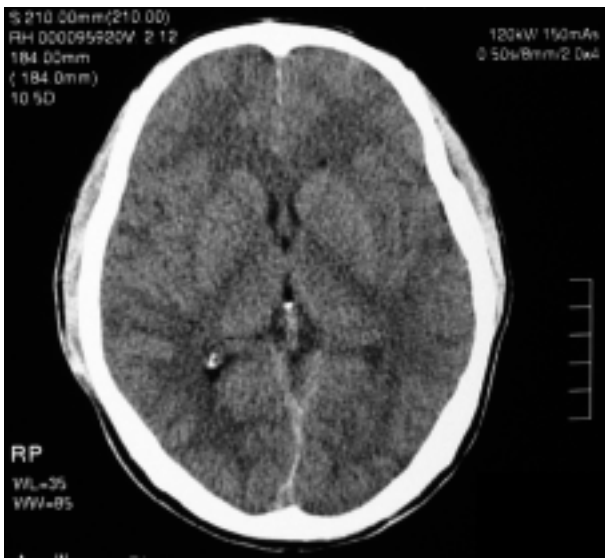


Figure 1. CT brain scan showing cerebral swelling with loss of cortical differentiation.

surgeon was consulted during hospitalisation for the possibility of sensori-neural deficit. He was discharged at the end of October with bilateral hearing deficit. Follow-up CT brain did not reveal any hydrocephalus or collection of fluid. Retrospectively, he recalled there was a small wound over his left middle finger, which might be the portal of entry for his meningitis.

Discussion

SS infection attracted enormous attention in Hong Kong because of the outbreak in the cities of Neijiang (内江) and Ziyang (资阳) in the province of Sichuan (四川) in July and August 2005. About 206 victims were affected with 38 mortalities.¹ The first reported case in Hong Kong was in 1981 while the first identified patient internationally was in Denmark in 1968.^{2,3} In Hong Kong, 36 and 25 patients were identified during 1981–1984 and 1984–1993 respectively. SS is one of the major bacterial meningitides in Hong Kong.⁴ A total of 10 patients were reported in the past decade.⁵ About 70% of the cases occurred during the summer season.⁴ Sporadic SS infection occurs worldwide, for example, in Belgium, China, Croatia, France, Hong Kong, Greece, Germany, the Netherlands, Sweden, Thailand, Taiwan and the United Kingdom.^{4,6-13} The occupations of the

victims included butchers, cooks, farmers, housewives, meat transporters, poachers and even waiters.^{4,6} Most of the victims had been exposed to pork at work, either while handling unprocessed pork without gloves or after sustaining minor injuries like superficial abrasions during handling.⁸ The majority of them were healthy adults while some had concomitant medical illnesses such as alcoholism, diabetic mellitus, splenectomy, malignancy and compromised immunity.^{4,6,12} The mean age of the victims in Hong Kong was 55 years old (range 20-75) while 49 years old was reported in the Netherlands. The male:female ratio was 1.7:1 and 6.5:1 in Hong Kong and the Netherlands, respectively.^{6,14}

SS is a Gram-positive, facultative, anaerobic coccus. It colonizes as natural habitats in the nasopharynx, tonsils, genital organs and gastro-intestinal tract of some piglets.^{4,15} Type 2 is the most virulent among the 35 serotypes identified. Its pathogenesis and fulminant clinical progress have remained mysteries for decades. Evidence recently revealed that SS invades the body via several mechanisms. First, it possesses many virulent factors, including muramidase-released protein, extracellular factor, sulysin (a haemolysin), superoxide dismutase, hyaluronidase, bacteriocins and various proteases. The most crucial one is called capsular polysaccharide (CPS). CPS down-regulates the phagocytes in the body, giving SS an anti-phagocytic property. It has been proven in animal models that the anti-phagocytic ability persists for hours, even when the CPS is removed. It also releases many pro-inflammatory cytokines and chemokines, including tumour necrosis factor alpha, interleukin-1, interleukin-6, interleukin-8 and monocyte chemotactic protein. Second, SS interacts with, and is taken up by, monocytes. The whole complex disseminates easily through the blood stream, causing intracranial infection. Third, in order to cross the blood-brain barrier, SS interacts directly and indirectly with leukocytes which trans-migrate the barrier effortlessly. All this explains the rapid clinical deterioration despite the wound, the main portal of entry, often being negligible.¹⁵

SS affects nearly all systems because of its ease of dissemination. The incubation period ranges from

hours to days.^{4,6} Chill is the most frequently reported symptom.⁶ Other features related to meningitis such as confusion, headache, high fever and neck stiffness are also common.^{1,4,6-13} Arthritis, bronchopneumonia, cellulitis, endocarditis, endophthalmitis, septicaemia and disseminated intravascular coagulation have been documented.^{4,5}

Permanent sensorineural hearing loss is the most common morbidity reported and it ranges from 50–60%.^{1,4,6} SS spreads its infection in the subarachnoid space to the perilymphatic system via the cochlear aqueduct. The corollary is exudative otitis interna and perineuritis of the vestibulo-cochlear nerve.¹⁵ The presence of SS antigen in the meningeal, perineural and labyrinthine tissues confirmed this route of spread. Hearing loss may occur irrespective of prompt initiation of antibiotics.^{15,16}

Necrosis of fingers and toes was another complication reported. Tambyah et al reported a 53-year-old butcher suffering from SS meningitis as a result of dissemination from his wounded toes. Gangrene, rhabdomyolysis with creatine kinase 7531 U/L and purpura fulminans were detected. Purpura fulminans is also known as dopamine gangrene. It is a rare complication due to septicaemia, but is usually associated with meningococcaemia in which the mortality rate may be as high as 80%.¹⁷ Fortunately the butcher survived after intensive care but with bilateral hearing loss and amputated toes.⁷

Lumbar spondylo-discitis has been reported in Greece. A 61-year-old housewife contacted unprocessed pork without gloves six days before her meningitis. Lumbar

spondylo-discitis was noted on X-ray spine when she complained of low back pain during intensive care. The condition subsided after ceftriaxone but she was left with permanent deafness.¹¹

SS type 2 is the most virulent strain within its family. However, type 1 may also be fatal. Kopic et al reported two severe cases in Croatia. The first one presented to the hospital for general malaise, fever, cyanosis and hypotension. He died 16 hours after admission despite active resuscitation. SS type 1 was cultured from his blood. Another patient presented to the hospital for purulent meningitis. SS type 1 was detected in the CSF. He survived with permanent deafness and ataxia. Retrospectively both cases sustained small injuries over their hands several days before the attack.¹⁰ We summarise the clinical manifestations in Table 1.

The diagnostic accuracy of lumbar puncture was reported to be from 70–92%.^{4,6,14} Elevated protein concentration, decrease in glucose and increased white cell count are typical findings in CSF analysis. Direct Gram stain revealed Gram-positive cocci in pairs or short chains. *Streptococcus bovis* could cause diagnostic error since its morphology is similar to SS.⁶

SS is usually sensitive to penicillin, ampicillin, cephalothin, co-trimoxazole and vancomycin. Resistance to tetracycline, erythromycin, clindamycin and gentamicin has been reported. Prompt treatment improves survival. The unusually large number of deaths in Sichuan requires further investigation. Poor prognosis is associated with predisposing factors such as alcoholism, diabetes mellitus, splenectomy and immuno-compromised states.⁶ Relapse has been

Table 1. Summary of clinical manifestations of *Streptococcus suis* infection.

General	Chill as preceding symptom, fever, malaise, myalgia
Central nervous system	Confusion, meningitis
Eye	Endophthalmitis
Cardiovascular system	Septicaemic shock, endocarditis
Respiratory	Bronchopneumonia
Gastrointestinal	Diarrhoea
Others	Arthritis, cellulitis, gangrene, skin necrosis, purpura fulminans, rhabdomyolysis, disseminated intravascular coagulation

reported after antibiotic treatment and in immunocompromised patients.^{4,6} However, there is no evidence that earlier initiation of antibiotics would lower the incidence of hearing loss. Based on clinical trials over the past 10 years, concomitant dexamethasone reduces the incidence and severity of sensorineural hearing loss in paediatric patients suffering from bacterial meningitis.¹⁸⁻²⁰ Dexamethasone inhibits the cytokine-mediated neurotoxic effect of bacteriolysis, especially *Haemophilus influenzae*, *Streptococcus pneumoniae* and pneumococcus. It is believed to be effective as well in SS meningitis if one assumes the pathogenic processes in bacterial meningitis are similar in Gram-positive coccal infections. Nevertheless, no clinical trial or meta-analysis has been conducted in adults. The dosage should be, if given, 0.15 mg/kg intravenous every 6 hours for 4 days, 0.4 mg/kg intravenously every 12 hours for 2 days or a maximum of 16 doses. The first dose should be given 15–20 minutes before the antibiotics.^{20,21}

SS infection could be easily avoided by proper education, careful handling of unprocessed pork with gloves, and meticulous hand-washing after handling. We should manage the confused patient with a systematic approach and with careful examination of the extremities where subtle signs may be detected. We believe this case report will widen our knowledge of SS infection.

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