

***Streptococcus suis*: Bacteremia Presenting with Fever, Rashes, Arthritis and Neurologic Deficits**

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Abstract

Introduction: *Streptococcus suis* (*S. suis*) is a gram positive cocci acquired through exposure to infected swine. The most common clinical manifestation is meningitis often accompanied by bacteremia. *S. suis* is an emerging pathogen with significant complications, but remains to be underreported. Only 1,584 cases of *S. suis* infection have been reported worldwide with most of the cases concentrated in Southeast Asia where swine quantity is high.

Case Presentation: We report a case of a 52-year-old male who came in due to fever, generalized violaceous purpuric rash, headache, and nuchal rigidity. Patient was diagnosed with meningitis clinically. Patient consumed a diseased swine five days prior to admission. Blood culture was positive for *S. suis* II and clinical improvement was achieved with antibiotic treatment and administration of Dexamethasone. On follow-up check; however, patient had residual deafness on bilateral ears, which prompted referral to ENT service for further work-up and management. Our patient is the second

Filipino and the first documented case to be diagnosed in the Philippines.

Conclusion: Despite a booming hog industry in the Philippines and increasing prevalence in its neighboring countries, *S. suis* infection remains unreported in our country due to either lack of available diagnostics or misdiagnoses; therefore, a good clinical skills and high index of suspicion are warranted in the initial diagnosis of patients infected with *S. suis*. In order to prevent epidemic outbreak in the future, simple preventive measures like handwashing and wearing gloves after handling raw pork meat should always be practiced. With an increased awareness among clinicians and microbiologists and vigilance among high-risk individuals, we will promote early diagnosis of this pathogen and prevention of its sequelae

Keywords: streptococcus suis, meningitis, suis

Introduction

Streptococcus suis (*S. suis*) is often a neglected but emerging pathogen in pigs that can cause severe systemic infections in humans.^{1,2} This was first reported by veterinarians in 1954 among piglets.¹ Fourteen years later, the first human *S. suis* case was diagnosed in Denmark.² Over the past few years, the number of reported *S. suis* infections in humans has increased significantly.^{1,2} To date, there are more than 1000 cases of *S. suis* with most of them originating in Southeast Asia, where there is a high density of pigs.³ Outbreaks of the said pathogen were documented in neighboring countries particularly China, Vietnam and Thailand.^{1,2} Most at risk are those who handle or eat undercooked pork, or in some, transmission is through inhalation.³ Meningitis and sepsis are the most common clinical manifestations of *S. suis* infection while hearing loss is a frequent sequelae.^{1,2}

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In the Philippines, pork is the main meat staple, which comprises about 60 to 80% of meat and poultry production.^{4,5} It is interesting to note that despite the concentration of *S. suis* cases in neighboring countries and booming industry of pigs in our country, there are no available data on the epidemiology of *S. suis* infection.⁶

There is only one case report of a Filipino presenting with *S. suis* meningitis, but was diagnosed in the United States after his vacation in the Philippines.⁶ Here, we present a case of a 52 year-old male with *S. suis* bacteremia, presenting as meningitis, skin lesions, and arthritis. The implications of identifying this etiology will be discussed.

Case Presentation

This is a case of J.P., a 52 year-old Filipino male, married, a roman catholic from the Island Garden City of Samal (IGACOS) who works at a construction company and admitted for the first time in this institution. The patient came in due to fever and rashes. Five days prior to admission, patient allegedly cooked and consumed a diseased swine, which was already for disposal. The patient was the one who prepared and cooked it but ate the meat along with

four of his co-workers. Three days prior to admission, the patient reported undocumented fever relieved temporarily by paracetamol intake. This was associated with body malaise, myalgia and joint pain. No consultation was done nor medications were taken. One day prior to admission, there is persistence of fever now associated with chills and non-blanching petechial to purpuric, violet-black rashes at the sacral and trunk area which progressed to involve the lower extremities and eventually spread throughout the trunk and the face. Persistence of these symptoms prompted the admission. (Figure 1)

The patient has no known co-morbidities. Family medical history is unremarkable except for a hypertension in the paternal side. He occasionally smokes consuming two to three sticks in a month, drinks alcohol and denies any illicit drug use. He claims to have no sexual partner other than his wife. He often travels from Samal to Davao and vice versa because of the nature of his work. The patient was examined awake, weak-looking, afebrile but not in distress. Vital signs were as follows: blood pressure of 100/70 mmHg, heart rate of 78 bpm, respiratory rate of 18 bpm, and febrile at 38.1 degrees celsius. The skin was warm to touch with note of generalized non-tender, non-blanching, violaceous to black erythematous petechial and purpuric rashe, more prominent on both upper and lower extremities. (Figure 2) There were few abrasions and lacerations noted on his fingertips which he acquired from workplace. The sclerae were anicteric with note of bilateral conjunctival suffusion. No cervical lymphadenopathies were palpated. Cardiopulmonary and abdominal examination were unremarkable. Elbow and knee joints were warm to touch and tender with limited range of motion. The patient has a GCS score of 15 and was oriented to three spheres. Cranial nerves were all intact, except for cranial nerve VIII, which revealed sensorineural hearing loss on both ears. Motor strength was 4/5 on all extremities without any sensory deficit. Deep tendon reflexes were 2+ on all test points. Pathologic reflexes were absent however, patient had nuchal rigidity, Brudzinski and Kernig's sign. Fundoscopy was unremarkable. The consideration during the time of admission was Acute Bacterial Meningitis probably secondary to Meningococcal Infection.

Complete blood count revealed Leukocytosis with neutrophilic predominance and thrombocytopenia. Urinalysis revealed unremarkable result. Chest X-ray and cranial CT scan (Figure 3) with contrast were normal. Gram stain of the blood showed gram-positive cocci (Figure 4) and culture showed growth of *S. suis* II. CSF analysis revealed lymphocytic predominance without any growth of microorganisms after five days. 2d-echo is negative for any valvular abnormalities and vegetations (Figure 5). The patient tested negative for the following tests: Syphilis, HIV test, Typhidot and Dengue NS1.

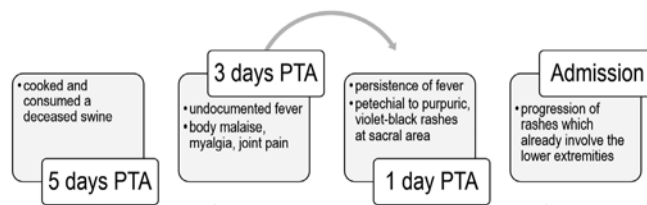


Figure 1. Summary of events that lead to the consult and subsequent admission of the patient



Figure 2. Actual lesions on admission comprising of violet-black non-blanching petechiae and purpura more prominent on the lower and upper extremities

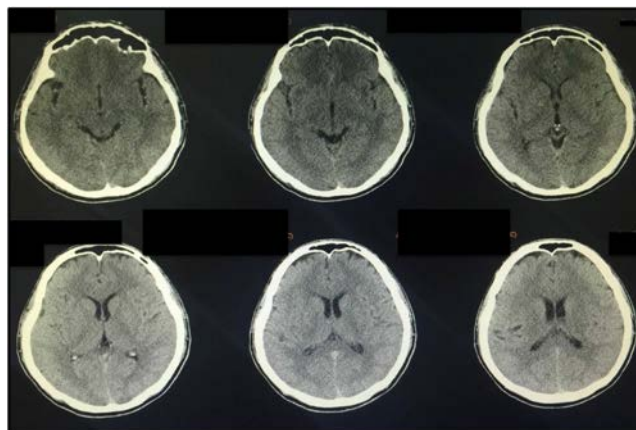


Figure 3. Cranial CT Scan

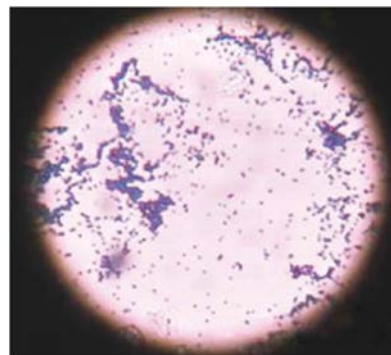


Figure 4. Gram stain of the specimen showing gram positive cocci

The patient was started with Ceftriaxone 2 gm IV every 12 hours for two weeks and Dexamethasone 4 mg/kg IV for four days. There was significant improvement of the skin lesions with improvement on the hearing loss on the seventh hospital day. (Figure 6) The rashes turned into dry and non-tender black scabs. Patient was then able to ambulate and was afebrile after 14 hospital days, hence patient was discharged improved.



Figure 5. Normal 2d echo of the patient without any valvular abnormalities



Figure 6. Healing lesions of the extremities after seven day-antibiotics

Discussion

Skin rash and depigmentation are common in patients with meningitis.⁸ In the setting of septicemia, meningitis and generalized skin lesions may occur together regardless of etiology. However, only few of them are documented. A number of microorganisms presents with rash similar to our patient. This includes *neisseria meningitis*, *Treponema pallidum*, *dengue virus* and *S. suis*.

Our closest differential is meningitis caused by *neisseria meningitis*, which presents with non-blanching rash similar to that of our patient's skin lesions.⁹ Rash develops in 50 to more than 80% of meningococcal disease.^{8,10} Because of the similarity in presentation, this cannot be ruled out without the validation of CSF and blood cultures.

Meningitis caused by *Treponema pallidum* is also one of our considerations. This presents with maculopapular rash in 80 % of the patients.⁸ The rash is seen mostly in palms and soles, which is not consistent with the presentation of the rash seen in our patient sparing the mentioned areas.^{9,11} Most cases with neurosyphilis had other skin lesion like prior chancre and usually occurs in patients with HIV.⁹ Their absence would make this a less likely diagnosis.

Another differential diagnosis is *dengue fever*. Meningitis is seen in around three to four percent of dengue fever.¹³ Araujo et. al (2012)¹⁴, Bhat et. al (2013)¹⁵, and Goswami,

et. al (2012)¹⁶ showed that meningitis could be a primary presentation of dengue fever. However, in contrast to our patient's rash, that of dengue fever occurs after the febrile phase on the day three to four of illness.¹⁰ Our patient's rash occurs during the peak of his febrile episodes; hence, making this a strong basis for ruling out dengue fever.

Despite its under-diagnosed status, *S. suis* infection is strongly considered because of the patient's exposure to a diseased pig.

Streptococcus suis (*S. suis*), a peanut-shaped facultative anaerobe, gram-positive coccus, is an important pathogen of swine and has been reported to cause severe systemic infections in humans usually in individuals with occupational exposure to pigs.^{6,7} However, it is also occasionally found in cattle, wild boars, horses, dogs, cats and birds.^{1,19}

Streptococcus suis (*S. suis*) is transmitted in humans through direct contact and often related to exposure through wounds on the skin while handling the infected pork or tending infected pigs.^{1,3} Other routes of transmission from pigs to humans, including droplet transmission through the respiratory tract and entry through the gastrointestinal tract after ingestion of infected pork have been suggested but not proven.¹⁹ The most probable transmission of the pathogen to our patient is through his lacerated wounds. It is interesting to note that four of his co-workers did not present with any symptoms after eating the cooked infected pork suggesting that the transmission of the micro-organism is most likely through uncooked or under cooked meat.¹⁹ The incubation period ranges from three hours to 14 days.^{1,20} Other studies reported that incubation period varies from 60 hours to one week.^{21,22} Our patient's first symptoms occur after 48 hours from his exposure to infection consistent with journals. Patients are healthy prior to infection with *S. suis*, although some predisposing factors such as splenectomy, diabetes mellitus, alcoholism, malignancy, and structural heart diseases were documented.^{2,23} Our patient is healthy with no known co-morbidities, which fits the usual profile of patients with *S. suis* bacteremia.

In a review article published in 2007 by Lun et. al²⁴, 409 human *S. suis* cases were documented. However, over the past few years, there has been an increasing number of recorded human cases in the literature with most of them originating from Southeast Asia.¹ Based on a journal by Huang et. al (2014)², a total of 1,584 cases were already reported by the end of 2012 including 189 probable cases identified in three outbreaks, mainly from Thailand (36%), Vietnam (30%), and China (22%) which are countries where pig-rearing is common.²⁴

Swine industry is the second leading contributor to Philippine agriculture coming in second to rice according to reports published by Zoila⁴ and Barroga⁵ Pork is the main

meat produced and consumed by Filipinos, which comprises about 60 to 80% of the Philippines meat and poultry production.^{4,5,25} Majority of Filipinos are therefore exposed to swine and its diseases.

What is peculiar; however, is that despite the booming industry of pigs in the country and the concentration of human *S. suis* cases in its neighboring countries, there are no available data on the epidemiology of *S. suis* infections in humans in the Philippines.⁶ This could be due to lack of resources in species identification in most of our institutions; therefore, under diagnosis is a likely scenario.

Interestingly, there is only one case report of a Filipino who had acquired *S. suis* meningitis. This was reported by Wongjittaporn²⁵ in 2014 describing an acquired *S. suis* meningitis from a 52-year-old male who returned to the USA from a trip to the Philippines presenting with fever and changes in behavior. It is important to note that the identification of the species was done at the United States and not in the Philippines. After an extensive literature search and inquiry of other big institutions, there was no reported data available for the Philippines. Likewise, in our institution, there was no reported case for the past decade as validated by the Department of Microbiology. Therefore, our patient is the second documented case of a Filipino with *S. suis* bacteremia and the first documented case to be diagnosed in the Philippines.

Streptococcus suis (*S. suis*) causes a systemic infection in humans that affects several organ systems. Meningitis is the most common clinical syndrome at 68%.²⁶ The presentation is generally similar to those of other bacterial pyogenic meningitis and include headache, fever, vomiting, and meningeal signs. The most striking feature, which was also observed in our patient, is hearing loss which may occur at 50 to 68% of those with *S. suis* meningitis.^{1,25} Hearing loss due to this infection is often bilateral, profound and permanent^{27,28,29} and is more common than in other causes of bacterial meningitis.^{27,30} It has been well documented that deafness results from spread of infection from meninges to the labyrinth, and the cochlear aqueduct is the primary conduit of the infection extension, causing more pronounced injury in the basal turn of scala tympani and more serious hearing loss in high frequencies.^{31,32}

Six percent to 31% of patients have skin findings, including petechiae, purpura, and ecchymoses.¹ Gangrene of the fingers and toes may also be seen in a minority of patients at later stage of the disease.^{1,34} Our patient presents with non-blanching petechiae and purpura which resolves after day seven of antibiotics and did not further progress to more severe form of skin lesions.

Arthritis may also occur at 12.9%.^{7,35} Warm elbow and knee joints on light palpation with limited range of motion

on both joints indicate presence of arthritis. Synovial fluid culture and radiographic procedures will be of great help in establishing presence of septic arthritis.³⁵

Endocarditis³⁶ and endophthalmitis³⁷ are less common manifestations. Of importance, infective endocarditis was reported to be more common than meningitis in Chiang Mai, Thailand.³⁸ Hence, 2d-echo was done in this patient revealing absence of any vegetations. Duke's criteria were not fulfilled; thus, infective endocarditis is ruled out.

Given all these clinical manifestations, we conclude that our patient is the first documented case of a Filipino with *S. suis* bacteremia presenting with meningitis, hearing loss, skin lesions and arthritis.

To determine the species involve, culture studies will be of great help. Since the infection always involves a bacteremic phase, blood culture is indicated.¹⁵ Our patient tested positive for *S. suis* biotype II after 48 hours of incubation. The majority of strains are alpha-hemolytic on bovine and sheep blood agar plates after 24 h of incubation at 37.6 C.^{6,13} Determination of *S. suis* to the species level can be performed with biochemical tests, such as optochin, Voges-Proskauer, salicin, trehalose, and 6.5% sodium chloride. Some commercial biochemical identification systems also report whether *S. suis* is biotype I or II.⁶ This should not be mistaken for serotype 1 or 2, as was done in some reports.^{6,39} The 35 *S. suis* serotypes can be identified by agglutination with a panel of antiserum samples.⁶

Since our patient presented with the classic triad of meningitis, CSF analysis should be performed. Typical results are increased protein and decreased glucose levels in the CSF together with appearance of neutrophils. CSF culture is positive in 80% of patients who have not received prior antimicrobial therapy.^{10,40} Our patient consented for lumbar tap after day seven of antibiotics; thus, altering the expected CSF result findings. The lymphocytic predominance and the negative culture result in the CSF analysis of our case are consistent with a profile of a patient with partially treated meningitis.^{40,41} A study conducted by Millwe et. al (2009)⁴² showed that none of the patients with meningitis with lumbar puncture performed more than eight hours of antibiotics use was culture positive supporting our result.

Although *S. suis* can be cultured from CSF or blood samples with use of standard microbiological techniques, it is often misidentified and reported as *Streptococcus species*, *α-hemolytic or viridans streptococci*, *Enterococcus faecalis*, *Aerococcus viridans*, or even *S. pneumonia*.² A study conducted by Fongcom, et. al (2009) revealed that up to 70% of all viridans streptococci cases in Thailand were confirmed as *S. suis* infections in the follow-up investigations.^{2,43} There was no similar report conducted in the Philippines but misidentification and absence of

resources in species identification could probably explain the underreported status in the country.

CT scan with contrast was done in this patient although it is not a routine procedure to pursue in patients with meningitis but it is helpful in patients prior to lumbar puncture to rule out any cause of intracranial pressure.^{40,44} Our patient's CT scan result revealed normal results consistent with early phase of meningitis. Contrast-enhanced CT may show beginning meningeal enhancement, which becomes more accentuated in later stages of disease.⁴⁴

Similar to the management of a patient with suspected bacterial meningitis, antibiotic treatment should be started without delay.¹ For empirical treatment, Ceftriaxone with or without Vancomycin for two weeks is recommended choice until the diagnosis is laboratory confirmed.^{1,15} Penicillin G is the preferred treatment for *S. suis* infection, although penicillin resistance has emerged in *S. suis* because of the farm practice of supplementing feeds with antimicrobial drugs. Our patient responded well with Ceftriaxone 2 gm IV every 12 hours for two weeks with significant lysis of fever as early as day three and note of healing lesions on day seven. However, a journal by Gottschalk et. al (2007)⁴⁵ showed that some patients with *S. suis* meningitis have experienced relapse after two weeks of treatment with penicillin or ceftriaxone but responded to prolonged treatment (four to six weeks).

The use of Dexamethasone as an adjunctive treatment may reduce mortality and improve the outcome of bacterial meningitis.¹ Administering dexamethasone may improve hearing loss in some cases.³⁰ In one randomized, double-blind, placebo-controlled clinical trial, Dexamethasone (0.4 mg/kg twice daily for four days) resulted in a significant reduction in the risk of death at one month and in the risk of death and disability at six months in patients with confirmed bacterial meningitis.⁴⁷

The reported case-fatality rates associated with *S. suis* meningitis vary and have generally been low in several meningitis series, compared with rates among patients in the same age group with meningitis due to *Streptococcus pneumoniae* and other bacterial agents.^{1,15} An outbreak in China in 2012 was associated with an overall case-fatality rate of 18%, but this reached 63% among patients with septicemia and septic shock.¹ Since our patient had septicemia, the mortality rate is very high but with early administration of antibiotics and dexamethasone, there was a significant improvement during the course in the wards and patient was then eventually cleared for discharge.

Patient came back to OPD after one month of discharge. On follow-up check-up, arthritis resolved with healed skin lesions. Patient is able to ambulate. However, there is still residual deafness on bilateral ears. While over-all prognosis

is good if administration of antibiotics is not delayed, the prognosis for hearing is guarded. Mai et. al (2008) reported that around 93 (66.4%) of 140 patients screened had mild-to-severe hearing loss at hospital discharge.³⁴

The patient was then referred to ENT service for Pure Tone Audiometry and Tympanometry for definitive screening of bilateral sensorineural hearing loss and amenable for any future work-up and management

Conclusion

The presence of a patient with *S. suis* bacteremia should increase our awareness and vigilance towards this pathogen because of high mortality rate and its ability to cause systemic infection. It is therefore essential to highlight the need of early administration of antibiotics and most importantly, simple preventive measures such as wearing gloves during processing pig meat, hand washing after handling raw pork meat and thorough cooking of pork. In addition, prevention through public health surveillance such as tapping the Bureau of Animal Industry is needed, and people with occupational exposures to swine products should be educated.

There is lack of data on the epidemiology of *S. suis* in the Philippines despite its high endemic status in the neighboring countries. This is attributed to the lack of resources in species identification in most of our institutions; therefore, under diagnosis is a likely scenario in a third world country like ours. Furthermore, misdiagnosis of *S. suis* to other species is also very common. It is; therefore, important to put premium to our clinical skills as physicians. For instance, in suspecting Meningococcemia, we should as well extract exposure to swine because of the similarity in their features. It is highly recommended to send highly suspected patients to higher institutions, with resources capable of identifying the species for early detection and management.

The outbreak of this species in our neighboring countries suggests that Philippines as a pig-rearing country might experience this epidemic in the near future. Therefore, with increased awareness among clinicians and microbiologists and vigilance among high-risk individuals, we will promote early diagnosis of this pathogen and prevention of its sequelae. Its presence should alarm us before this becomes an epidemiologic emergency.

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