

CASE REPORT

Meningitis caused by *Streptococcus suis*

Sopheap Oeng¹, Lath Sokun², Veasna Tan², Nikki Townell¹, Ellen Baron^{*3}, Joanne Letchford¹

¹Diagnostic Microbiology Development Program, Cambodia

²Siem Reap Provincial Referral Hospital, Siem Reap, Cambodia

³Diagnostic Microbiology Development Program, Stanford University, USA

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ABSTRACT

Background: In most countries with full-service microbiology services, streptococcus-like organisms visualized in a gram-stained smear of cerebrospinal fluid (CSF) from patients presenting with meningitis syndrome would be assumed to be *Streptococcus pneumoniae*. However, in many areas of the world, predominantly in Southeast Asia, the organism may be *Streptococcus suis*. Although initial antimicrobial treatment is similar, additional treatment for specific co-morbidities, such as hearing loss, may be needed. This case, involving an adult male who presented with signs and symptoms of meningitis, describes the appropriate laboratory test procedures used to make the diagnosis and the subsequent patient management strategy.

Case presentation: A previously healthy 69-year-old rice farmer was admitted to the hospital with a one day history of fever, headache, neck stiffness, and altered consciousness. Initial laboratory studies were consistent with meningitis, but the CSF Gram stain did not reveal any organisms. Blood cultures obtained at admission grew alpha-hemolytic, optochin-resistant colonies consistent with *Streptococcus suis*, and the identification was confirmed by MALDI-TOF performed at another laboratory. Unusually, the isolate was penicillin non-susceptible. The patient received 4 g/day ceftriaxone and dexamethasone (to mitigate deafness) for 10 days and was discharged to home with moderate deafness but no residual infection.

Conclusion: Diagnosis of meningitis should include both blood cultures and CSF cultures obtained before any antibiotics are administered. In some patient populations such as those in Southeast Asia or if there is history of contact with pigs or raw pork, *S. suis* should be considered.

Key Words: Case report, Meningitis, *Streptococcus suis*, Cerebrospinal fluid laboratory analysis

1. INTRODUCTION

Streptococcus suis colonizes the upper respiratory tract of pigs and can cause systemic disease, particularly in piglets, resulting in significant economic loss in the swine industry.^[1] Although predominantly an animal pathogen, it can cause severe systemic infections in humans. In recent years, reports of human infections by this organism have increased significantly, with most cases occurring in Southeast Asia.^[1-3] Serotype 2 of *S. suis* is considered to be the most pathogenic for both humans and pigs.^[1,4-6]

Meningitis is the most common clinical manifestation.^[2,3,7,8] In the four Cambodian provincial laboratories supported by Diagnostic Microbiology Development Program (www.DMDP.org), *S. suis* is the most commonly isolated bacterial pathogen from adult patients presenting with meningitis. Humans can acquire *S. suis* infection through direct contact with pigs or pork, through an open wound, or by consuming undercooked pork.^[2,3,7-9]

In this report, we describe a case of *S. suis* meningitis in an

*Correspondence: Ellen Baron; Email: ellenjobaron@gmail.com; Address: Diagnostic Microbiology Development Program, Stanford University, USA

elderly rice farmer with no direct exposure to live pigs whose diagnosis depended on isolating the organism from blood cultures, not the cerebrospinal fluid (CSF). Because this is a rare cause of meningitis in regions other than Southeast Asia, the possibility of such a syndrome in a tourist or visitor should be considered. In the context of this case, the following factors are illustrated: the importance of collecting a blood culture when meningitis is suspected, the rare incidence of penicillin non-susceptibility in human non-*S. pneumoniae* streptococcal disease and thus the importance of in vitro susceptibility testing, the possibility of incorrect results for antimicrobial testing or inability of certain in vitro methods to correctly predict clinical response,^[10,11] and the ongoing need for One Health considerations in endemic settings of any unusual microbial disease that can pass from animals to humans. In addition, this case is described to highlight the challenges of properly identifying an organism that so closely resembles non-pathogenic other viridans streptococci in the low resource settings where the infection is most likely to occur.

2. CASE PRESENTATION

A 69-year-old previously healthy male was admitted with a 1-day history of fever, headache, neck stiffness and altered level of consciousness (Glasgow Coma Score=8/15) to a provincial hospital in Cambodia. He was a rice farmer with no occupational or domestic exposure to animals. He had no history of handling pigs or contact with pork, though he regularly consumed home cooked pork meals. No illness was reported amongst family members living within the same household. Somnolence and neck stiffness were detected on neurological examination. No other abnormality was noted on full examination, including the cardiovascular system.

On admission, he had a high white blood cell (WBC) count of $35.31 \times 10^9/L$ (reference range $4 - 10 \times 10^9/L$) with a neutrophilia of $33.23 \times 10^9/L$, low hemoglobin of 8.6 g/dL (13 - 17 g/dL) and platelet count of $10^9 \times 10^9/L$ ($150 - 410 \times 10^9/L$). Further laboratory results revealed an elevated C-Reactive Protein of 134 mg/L (<3 mg/L), alanine aminotransferase 56 U/L (<42 U/L), low albumin of 22 g/L (38 - 51 g/L) and normal creatinine 0.8 mg/dL (0.6-1.3 mg/dL).

A cerebrospinal fluid collected before administration of antibiotics was consistent with bacterial meningitis: significantly elevated WBC $10,240/mm^3$ ($<5/mm^3$), polymorphs 90%, low glucose 10 mg/dL (40 - 75 mg/dL), and high protein 166 mg/dL (8 - 43 mg/dL). The India ink wet mount was negative for Cryptococcus-like structures. Gram stain of sediment of centrifuged CSF revealed numerous WBCs but no organisms. The sediment was cultured on chocolate agar

(CHOC) and sheep blood agar (SBA) but showed no growth after three days incubation in a candle jar.

Blood cultures were collected at time of admission and before antibiotic administration. Two of two manual blood culture bottles (produced and quality-controlled by Central Media Making Laboratory, University Health Sciences, Cambodia) were visually turbid and appeared hemolyzed after 48 hours incubation. A Gram stain revealed gram-positive cocci in pairs and short chains (see Figure 1). After subculture and overnight incubation in a candle jar, growth of small, round, alpha-hemolytic, catalase-negative, optochin-resistant colonies were observed with noticeably stronger alpha hemolysis on the CHOC agar (see Figure 2).

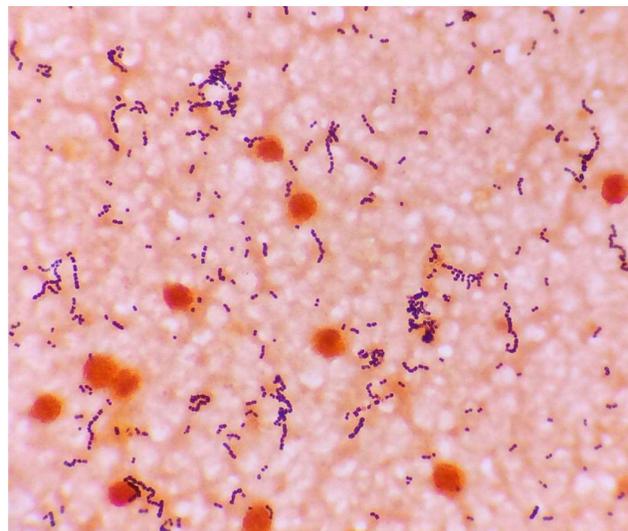


Figure 1. Gram stain of blood culture broth showing Gram positive cocci in pairs and short chains

Based on patient presentation and the blood culture results, the isolate was presumptively identified and reported as *Streptococcus suis*. The isolate identification was confirmed as *S. suis* by Matrix Assisted Laser Desorption Ionization - Time of Flight Mass Spectrometry (MALDI-TOF MS) at a reference laboratory at Angkor Hospital for Children, Siem Reap, Cambodia.

Antibiotic susceptibility testing revealed the isolate to be of intermediate susceptibility to penicillin with an MIC = $1.5 \mu\text{g/ml}$ (Etest gradient diffusion strip, bioMérieux, Marcy l'Etoile, France). There were discordant results for ceftriaxone, with a disk diffusion zone diameter of 22 mm, interpreted as resistant, while the ceftriaxone gradient diffusion strip MIC of $1 \mu\text{g/ml}$ was interpreted as susceptible.^[11] The isolate was determined to be susceptible by disc diffusion to vancomycin and resistant to erythromycin, clindamycin and chloramphenicol using *Streptococcus* spp. Viridans Group

breakpoints.^[11] All testing of antibiotics showed comparable results when repeated by the reference laboratory.

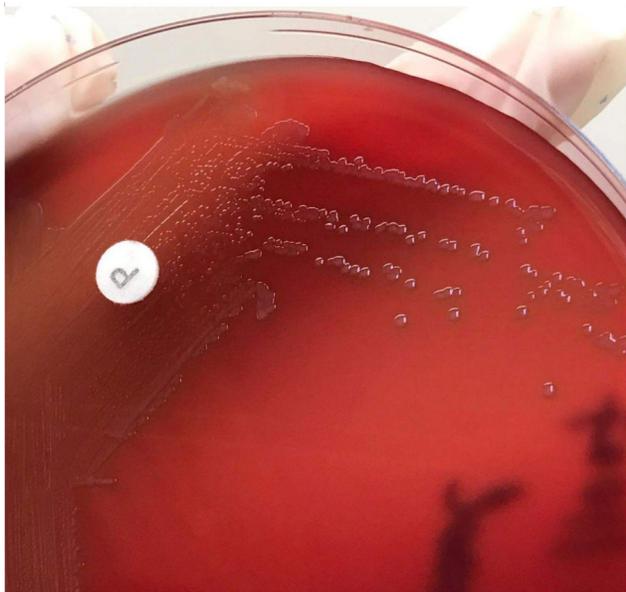


Figure 2. Small, alpha hemolytic colonies on SBA showing resistance to optochin

Following collection of cultures, the patient was empirically commenced on bacterial meningitis treatment: ceftriaxone 2 g twice daily and dexamethasone (10mg four times daily for 4 days) to mitigate hearing loss, a common sequel of bacterial meningitis. Despite concerns regarding the initial ceftriaxone disk susceptibility test result, it was agreed to continue that agent in view of patient's clinical improvement on ceftriaxone and pending ceftriaxone MIC test results. Although vancomycin was considered, it was not added in view of the patient's observed initial improvement. He improved significantly on treatment, making a full recovery except for the presence of moderate deafness (based on clinical assessment since hearing assessment instruments were not available in this part of Cambodia). On request of the patient, he was discharged after completing 10 days of ceftriaxone therapy. The patient remains well off antibiotic treatment with no evidence of relapsed infection.

3. DISCUSSION

S. suis is an important pathogen of pigs and piglets, causing economic loss in the swine industry.^[4-6] In recent years, reports of human infections, primarily meningitis, with this organism have increased significantly, possibly due to better medical laboratory practices and access to clinics, especially in Southeast Asia.^[3,12] Although in most parts of the world a streptococcal meningitis would be assumed to be due to *S. pneumoniae* until confirmed otherwise, in Southeast Asia it

is more likely to be *S. suis*.^[9] Particularly in China and Southeast Asia, many more humans are in close contact with pigs as they raise small numbers of pigs near their homes, than in other parts of the world where industrial swine management is more common. Humans can acquire *S. suis* infection through direct contact with pigs or pork, through an open wound, or by consuming undercooked pork. Our patient apparently had no contact with pigs except for the consumption of pork.

S. suis may be isolated from blood and CSF using standard culture media and microbiological techniques. It is a gram-positive coccus occurring in pairs or short chains and has similar colony morphology to viridans streptococci on routine culture media: small, round, alpha-hemolytic, optochin-resistant, and they will type as Lancefield group D.^[1] If the organism had been optochin-sensitive, *S. pneumoniae* would have been a more likely identification.

S. suis has been commonly misidentified and reported as viridans streptococci, *Enterococcus faecalis*, *Aerococcus viridans*, or even *Streptococcus pneumoniae*.^[1,3] In low resource settings, identification to species level may be challenging due to lack of access to commercial identification kits and automated identification systems. In Cambodia, laboratories use conventional tests for identification of streptococci: Gram stain, colony morphology, growth requirements, catalase, and optochin disk. Laboratories are encouraged to report presumptive identification of *S. suis* when they observe gram-positive cocci in pairs with alpha-hemolytic colonies, resistance to optochin, and CSF parameters consistent with bacterial meningitis, as in this case where CSF examination revealed a turbid CSF with very high WBC. However, viridans streptococci isolated from a blood culture without a positive CSF culture is problematic and laboratories are recommended to refer these isolates to a reference laboratory. Depending on availability, identification of *S. suis* can be performed using biochemical tests, optochin, API 20 Strep (bioMérieux, Marcy l'Etoile, France), PCR, and MALDI-TOF MS. The case described yielded positive blood cultures and a negative CSF culture, despite both specimens being collected at the same time, prior to antibiotic treatment. Others have made the same observation, without explanation.^[14] One possibility is prior antibiotic use, but this is not the case with our patient. This highlights the need to obtain blood cultures in patients with signs and symptoms of bacterial meningitis to optimize culture yield and pathogen detection rates.

S. suis meningitis typically presents with fever, headache, and neck stiffness in healthy middle-aged men due to their exposure to pigs. Altered level of consciousness is observed

in around one-third of patients.^[3,6,8] Mortality for *S. suis* meningitis is low (<3%) and most patients respond well to treatment making a full recovery, with the exception of hearing loss as was seen in this patient.^[2,7] Dexamethasone therapy is often associated with reduction in hearing loss.^[2,12] Other clinical presentations may include sepsis, arthritis, endocarditis, and endophthalmitis.^[1,3,4]

There are no standardized breakpoints for *S. suis* and our laboratory inferred susceptibility based on *Streptococcus* spp. Viridans Group CLSI M100 breakpoints.^[11] Testing of our isolate resulted in non-susceptibility to penicillin and different categorical interpretations for the ceftriaxone disk diffusion (22 mm, resistant) compared to gradient diffusion testing (MIC 1ug/ml, susceptible). Antibiotic recommendations for *S. suis* infection include penicillin, ceftriaxone and vancomycin, and penicillin non-susceptibility is rare.^[1,2,15] Penicillin has unfavorable CSF pharmacodynamic properties and thus it is not recommended for treatment of meningitis caused by non-susceptible *Streptococcus* spp.^[16] Ceftriax-

one (4 g/day) is the most commonly recommended empirical treatment regimen for bacterial meningitis. The ceftriaxone MIC of 1 ug/ml is significantly lower than the expected mean trough CSF levels in patients with meningitis on conventional doses of ceftriaxone. Achievement of ceftriaxone PK-PD targets is associated with good clinical outcomes.^[16]

Development of antimicrobial resistance in *S. suis* is thought to be associated with antibiotic usage in pig husbandry.^[15] Penicillin non-susceptible *S. suis* are common in pigs in Southeast Asia, however, it has rarely been reported in human infection.^[1,3,17] Increasing rates of antimicrobial resistance in *S. suis* in pigs and humans is concerning and heightens the need for antimicrobial stewardship programs in animal husbandry. Cambodia and other Southeast Asian countries should consider a One Health surveillance program to closely monitor both the incidence and resistance rates of this under-reported pathogen.

CONFLICTS OF INTEREST DISCLOSURE

The authors declare that they have no conflicts of interest.

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