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(CASE REPORT)

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Case report: Relaps of *Streptococcus suis* infection in patient with Meningoencephalitis at Prof. Ngoerah Hospital, Bali

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Abstract

Background: *S. suis* is a facultative anaerobic Gram-positive bacterium that causes human infection. It is a primary health problem in the swine industry. Ceftriaxone is a therapeutic option for meningitis besides Ampicillin. Recently, the incidence of resistance to ceftriaxone was reported. The recurrence of *S. suis* in this patient is thought to be caused by ceftriaxone resistance due to inadequate initial therapy.

Case Presentation: A 43-year-old male patient came to the ER with headaches in the head and neck. The patient had a history of meningitis due to *S. suis* twice before. While in the ER, the patient was given ceftriaxone while awaiting culture results. Blood cultures showed *S. suis* infection using VITEK 2 COMPACT (Biomeriuex®) and ceftriaxone resistance. The patient was successfully managed with Ampicillin following these culture results, leading to good outcomes.

Discussion: *S. suis* is a gram-positive bacterial pathogen in pigs that can cause severe human infection, including meningitis, septicemia, endocarditis and deafness the most common complications. The patient experienced three relapses due to *S. suis*. On the third visit, blood culture results identified ceftriaxone-resistant *S. suis*. The patient's recurrent relapses could be attributed to several factors, including inadequate antibiotic administration, antibiotic resistance, weak immune system, contact with the source of infection and environmental variables, highlighting the complexity and challenges in treating S. suis infection.

Conclusion: The use of antibiotics in relapse cases has the potential to cause antibiotic resistance, so it's necessary to make guidelines for antibiotic therapy in *S. suis* infection to prevent recurrent infections.

Keywords: Ceftriaxone resistant; Meningoencephalitis; Relapse; *Streptococcus suis*

1. Introduction

A gram-positive facultative anaerobic bacterium known as *Streptococcus suis (S.suis)* is capable of causing a number of diseases in both people and pigs (1). Southeast Asia has a higher rate of *S. suis* infections because of the region's significant pig consumption and frequent small-scale pig farming (2-4).

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The most common clinical sign of *S. suis* infection in humans is meningitis, which can lead to irreversible hearing loss and vestibular dysfunction (5-7). This patient's recurrence is a rare occurrence, underscores the severity of this infection. Hence, we will explore the causes of relapse and additional management in this case study, highlighting the urgent need for further research and understanding.

This case describes relapsing *S.suis* bacterial meningoencephalitis in a 43-year-old male patient. During the blood culture examination, gram-positive cocci were found in both samples. This case is the third time the patient has been treated with bacterial meningoencephalitis caused by *S. suis* and the last culture was resistant to ceftriaxone antibiotics. So, proper management is essential for the patient's recovery.

2. Case report

A 43-year-old male patient with Javanese ancestry arrived at the emergency department complaining of a headache the day before admission. Headache that feels like the head is tied and spreads throughout the head and neck. The patient also reported that he had a fever four days previously accompanied by nausea, but this was not followed by vomiting. Additionally, the patient reported experiencing diarrhea three days ago. Additional problems are rejected, including double vision, slurred speech, sagging lips, seizures, and weakness in one half of the body.

The patient is a self-employed printer service provider. Although the patient has previously consumed pork, they have never consumed raw or undercooked meat. The patient had a mechanical valve replacement in the past in 2005. He was admitted with CHF ec RHD 7 months ago on May 26, 2022, three-sided blood culture was obtained positive culture of *S. suis* bacteria on one side and ceftriaxone antibiotics were recommended. But at that time the patient was only given ceftriaxone 1 g injection for one day and the next day the patient was discharged with the medicine taken home was heart medication. The patient was readmitted 3 months later on September 23, 2022 with suspected meningoencephalitis ec suspected bacterial dd TB and CHF et causa RHD, post mechanical valve replacement (in 2005). Due to high INR (3.29), the patient could not do lumbar puncture and 2-sided blood culture was performed with the results found *S. suis* bacteria on both sides and the patient received ceftriaxone therapy (2.0 g in 12-hour intervals) IV for 14 days.

When arrived on December 19, 2022, the patient spoke incoherently and was difficult to wake up with GCS E3V4M5. His vital signs were as follows: body temperature, 38.5°C; heart rate, 93/min; blood pressure, 125/70 mmHg; respiratory rate, 24/min; meningeal signs positif; and a murmur on cardiac examination. Other physical examination findings were within normal limits. Laboratory findings on admission were as follows (Tabel 1): WBC increased 19.33 x 103/µL; hemoglobin slightly decreased, 9.9 g/dL; and platelets, 275 × 103 /µL. Liver enzyme levels were slightly elevated: aspartate aminotransferase, 38.0 U/L and alanine aminotransferase, 22 U/L. Renal function was normal: blood urea nitrogen, 10.10 mg/dL and creatinine, 0.65 mg/dL. C-reactive protein level, 26.5 mg/L. INR was elevated, 2.18 which contraindicated lumbar puncture for LCS culture.

AP Thorax (Figure 1) Impression: No pulmonary anomalies; cardiomegaly with inadequate mitral heart arrangement. ECG reading Atrial fibrilation within the normal ventricle, 90–102 beats per minute. There were no indications of an intracranial hemorrhage, infarction, or SOL on the head CT scan with contrast. We found positive indicators of meningeal irritation; nevertheless, a 2-sided blood culture was the only test conducted because a lumbar puncture was impossible due to the patient's high INR. These results allowed us to diagnose meningoencephalitis caused by bacteria. As empirical therapy, the patient was given dexamethasone (10 mg in 6-hour intervals) and ceftriaxone (2.0 g in 12-hour intervals).

Gram stain and culture were performed on Blood agar and MacConkey agar medium after the two blood culture bottles yielded positive results after one day, with positive times of 23 hours 53 minutes and 23 hours 3 minutes. Gram stain from blood culture revealed gram-positive cocci bacteria (Figure 2). One day after incubation, tiny, spherical, and α-haemolytic colonies were discovered on blood agar medium (Figure 3), but no growth was observed on MacConkey agar medium. The biochemical test result of the catalase test was negative., gram-positive cocci were determined to be *S. suis* by VITEK-2 Antimicrobial Susceptibility Testing (VITEK 2 AST-GP67). The analysis yielded a probability of 99%.

According to the results of the susceptibility test, the bacteria was resistant to cefotaxime, ceftriaxone, and tetracycline but susceptible to benzylpenicillin, ampicillin, levofloxacin, erythromycin, linezolid, vancomycin, and tigecycline (Table 2). Antibiotic medication was switched from ceftriaxone to ampicillin 2g IV every 4 hours following the release of the blood culture results. Following an 10-day course of therapy, the patient was released. The patient's condition improved; the meningeal signs, headache, and fever disappeared. At the outpatient ward, benzylpenicillin G 1.2 million IU treatment is administered every 28 days as a prophylactic measure against rheumatic heart disease.

Table 1 Laboratory data of the patient

Variable	Reference range	Value on admission
Red blood cell (per µL)	4.500.000- 5.900.000	3.970.000
Hemoglobin (g/dL)	13.5-17.5	9.90
Hematocrit (%)	41.0 - 53.0	31.5
White blood cell (per µL)	4.100-11.000	19.330
Differential blood count (per µL)		
Neutrophils (%)	47-80	78.10
Lymphocytes (%)	13-40	14.80
Monocytes (%)	2.0-11.0	6.80
Eosinophil (%)	0.0-5.0	0.10
Basophil (%)	0.0-2.0	0.20
Platelets (per µL)	150.000-440.000	275.000
PPT (second)	10-12.7	23.9
INR	0.9-1.1	2.18
Aspartate aminotransferase (U/L)	5-34	38.0
Alkaline phosphatase (U/L)	11.00-50.00	22.20
Random Plasma Glucose (mg/dL)	70-140	111
C-Reactive Protein (mg/dL)	< 5	26.50
Urea nitrogen (mg/dL)	8.00-23.00	10.10
Creatinine (mg/dL)	0.72-1.25	0.65

Table 2 Antimicrobial susceptibility test results

	MIC Interpretation
Benzylpenicillin	S
Amoxicillin	I
Ampicilin	S
Cefotaxime	R
Ceftriaxone	R
Levofloxacin	S
Moxifloxacin	S
Erythromycin	S
Linezolid	S
Vancomycin	S
Tetracycline	R
Tigecycline	S

Note: The antimicrobial susceptibility of *S suis* strains was determined by Clinical and Laboratory Standards Institute (CLSI). Abbreviations: MIC, minimum inhibitory concentration; R, resistance; I, intermediate; S, sensitive.

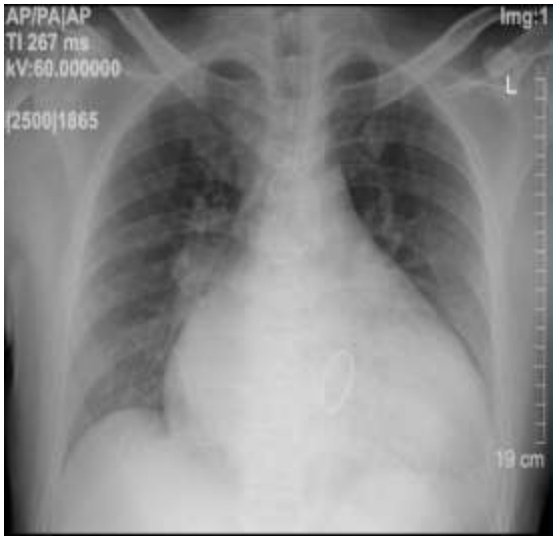

Figure 1 Thorax AP Imaging were shown cardiomegaly with insufficient mitral heart configuration

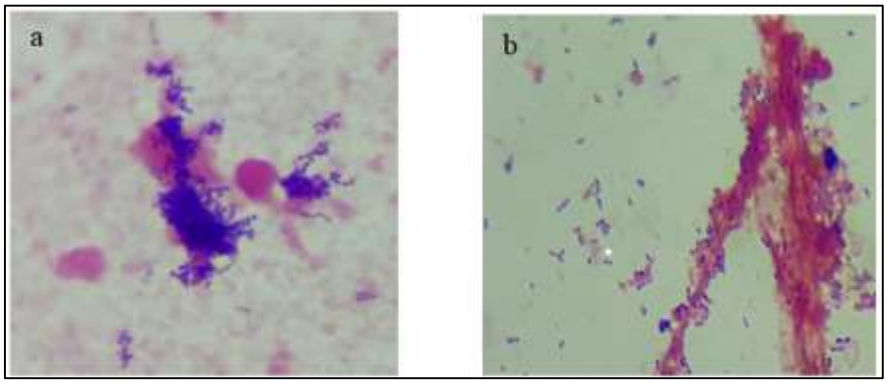

Figure 2 A large number of Gram-positive cocci were found in the blood smear, right side (a), left side (b) (Gram stain, × 100)

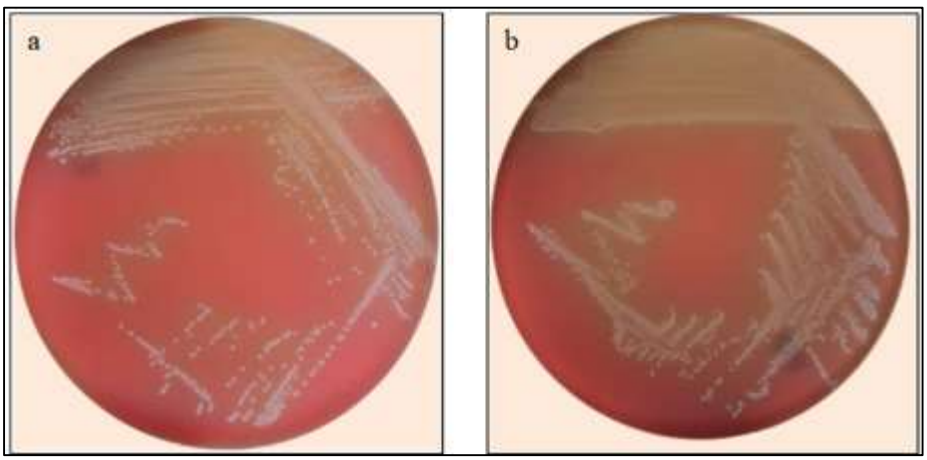

Figure 3 *Streptococcus suis* showed α-hemolysis medium-sized, off-white, smooth, moist colonies on blood agar after 24 h of incubation at 35 °C, right side (a), left side (b)

3. Discussion

We report a rare case of relapsing meningoencephalitis due to ceftriaxone-resistant *S. suis* infection in a patient with CHF e.c RHD with a history of mitral valve replacement. Although higher than in Europe, *S. suis* resistance to beta-lactam antibiotics is still meager in Asia (8). Tetracyclines, lincosamides, and macrolides have exceptionally high AMR rates (8). Antibiotic resistance in *S. suis* can result from a variety of factors, such as target mutation, which stops the antibiotic from binding to its target; enzymatic target modification; antibiotic modification, which includes the antibiotic being degraded or modified to prevent target binding; and eliminating the antibiotic from the cell by raising the efflux pump (8). Numerous hereditary components convey different qualities that present protection from anti-infection agents so *S. suis* can rapidly foster multiresistance (9).

In addition to the above, the development of biofilms may potentially be a factor in *S. suis*'s pathogenicity and incidence of antibiotic resistance (10). Drug resistance is caused by biofilms in a number of ways, including: Bacteria can be made to enter a quiescent state by biofilms, which lessens their sensitivity to antibiotics (11); Antibiotics may not be able to enter bacteria due to the physical barrier that biofilms can provide (12); A biofilm's inner layer has a high concentration of metabolites, which can enhance the action of efflux pumps that release antimicrobial drugs (13); Biofilm resistance to change can result via information exchange between cells, including quorum sensing, horizontal gene transfer, and multispecies communication (14). The bacteria in biofilms are under stress from drugs and nutritional scarcity, which encourages mutations (15).

We believe that these processes are not sufficient on their own. Rather, they collaborate and engage in mutual interactions to generate resistant bacteria within the biofilm. There are various reasons why this patient may experience recurrent relapses: Insufficient care. Recurrence of infection can be caused by *S. suis* bacteria if the initial therapy is inadequate or not done properly. As in this case, the patient was first infected with *S. suis* but ceftriaxone therapy was only given for one day at the hospital and discharged. Resistance to antibiotics. The development of antibiotic resistance in *S. suis* bacteria may lead to treatment failure and potential relapse; Weak immune system. A person who has a compromised immune system is more vulnerable to recurrent *S. suis* infection. This patient had CHF e.c RHD with a history of mitral valve replacement, which could affect immunity; Getting into contact with the infection source. A recurrence of illness may result from re-exposure to *S. suis* bacteria from the same source of infection, such as contact with contaminated pigs or animal products. This patient was not known to have a reinfection because there was no history of eating raw or undercooked pork preparations; Environmental variables. Exposure to *S. suis* bacteria or an unsanitary environment may raise the chance of recurrence, particularly in those with a history of illnesses (16).

Vegetation on the heart valves is also permitted by a history of mitral valve insertion (16). The way that *S. suis*, especially serotype 2, has an assortment of potential destructiveness factors, for example, multiple adhesions, extracellular protein factors, proteins delivered by muramidase, capsular polysaccharides, and suilysin, could be one clarification. These adhesions can make harm the heart valves (17-20). Therefore, precise diagnosis of this uncommon condition is made possible by high-resolution transthoracic echocardiography (16). However, transthoracic echocardiography was not performed on this patient due to equipment restrictions.

A variety of different kinds of antibiotics, including β-lactams, aminoglycosides (often in combination with β-lactams), amphenicols, and fluoroquinolones, are used to treat *S. suis* infections. Different nations, areas, and even farms use antibiotics in different ways, which has a significant impact on the AMR prevalence of *S. suis* (8). Multi-drug resistance is uncommon; however, resistance to tetracycline and macrolides is widespread (21). In this case report, empirical treatment with ceftriaxone was given before confirming pathogen identification. After identifying *S. suis* and obtaining drug sensitivity results, ceftriaxone was discontinued due to resistance and replaced with ampicillin for 10 days. The effectiveness of the treatment was evident as the leukocytes decreased from 18.03 x 10^3/μL at the start of ampicillin administration to 10.18 x 10^3/μL within 10 days. The patient's condition also improved with meningeal signs, headache, and fever disappearing.

Every 28 days, benzylpenicillin G 1.2 million IU is given to the patient in the outpatient ward as a preventative step against rheumatic heart disease. The patient receives benzathine penicillin G (BPG) as secondary antibiotic prophylaxis, administered intramuscularly every 3–4 weeks for an extended length of time (e.g., 10 years, till age 40, lifetime) (22).

4. Conclusion

S. suis infections rarely relapse in patients with meningoencephalitis. It has been demonstrated *that an interdisciplinary approach effectively achieves favorable outcomes and forecasts. As a result, proper handling is

required to prevent this, including administering sufficient and appropriate antibiotics, maintaining the immune system to prevent weakened immunity, avoiding contact with infection sources, and maintaining a healthy environment. Additional culturally relevant health interventions are required to prevent the spread of *S. suis.*

Compliance with ethical standards

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Disclosure of conflict of interest

According to the authors, there were no financial or commercial relationships that might have created a conflict of interest in this study.

Statement of ethical approval

Regarding this case report, the patient's informed consent has been obtained by the authors.

Statement of informed consent

Informed consent was obtained from all individual participants included in the study.

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Author contribution

I Nyoman Kurniawan did the majority of the data gathering; Ni Made Adi Tarini and Made Agus Hendrayana critically edited the article for significant intellectual content. I Nyoman Kurniawan also contributed to the study's idea and design..

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