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The Cost of Swine Dining: *S. Suis* as a Cause of Meningitis, Permanent Hearing Loss, Idiopathic Thrombocytopenia and Multi-level Spinal Facet Septic Arthritis

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Abstract

S. suis is a zoonotic pathogen found primarily in swine that has been described to cause human infection with various presentations and a high incidence of long-term neurologic sequelae. Most published literature cases have been reported in Southeast Asia, with only a paucity of reports in North America, particularly in the United States. It is unclear if the disease is absent in this area or has been misdiagnosed. Here, we report the case of a 48-year-old female swine worker who suffered immune-mediated thrombocytopenia, facet joint arthritis, and bilateral sensorineural hearing loss precipitated by occupationally acquired meningitis caused by *S. suis*. Following therapy with antibiotics and corticosteroids, the patient fully recovered except for hearing loss, which was permanent necessitating cochlear implant placement. We hope to raise clinicians' awareness of this rare, potentially devastating, but treatable disease by describing this case. *S. suis* should be suspected in patients with unexplained symptoms, particularly headache and meningeal signs, who have a history of pig exposure or pork consumption.

Keywords: *S. Suis* • Meningitis • Zoonosis • Hearing loss • Idiopathic thrombocytopenia

Introduction

S. suis is an emerging zoonotic pathogen with various presentations in pigs and humans, ranging from asymptomatic to life-threatening conditions, such as meningitis and sepsis [1]. From 1968 when the first case of *S. suis* infection was described in Denmark [2], until 2016, 1776 cases have been reported in the literature worldwide [3]. Most published cases are from Southeast Asia [4]. From 2006, when the first case of *S. suis* was reported in the United States (US), until 2017 only 9 cases have been reported in the US and Canada [5]. The results of cross-sectional studies investigating serologic data from swine-exposed humans indicate that *S. suis* exposure is more common than previously thought [6]. Considering that the US and Canada combined are the second largest swine producers in the world, it remains unclear whether the low prevalence of *S. suis* infection is related to underdiagnosis rather than the actual absence of the disease [7]. By describing this case, we aim to increase awareness of *S. suis* infection and its variable presentation, elaborate on diagnostic tools, and emphasize the importance of timely initiation of treatment.

Case Presentation

A 48-year-old female with a history of alcohol use presented to the hospital at the end of April with nausea, vomiting, headache, and diarrhea for 72 hours. On the physical exam, she appeared lethargic and ill, with a fever and tachycardia. A vesicular lesion on her upper lip and a petechial rash on her chest were present. Initial blood work showed leukocytosis, mild transaminitis, and profoundly low platelet count with no schistocytes on peripheral smear (Table 1).

Dexamethasone (DXM) was administered for Idiopathic Thrombocytopenia (ITP), while acyclovir was initiated for possible Herpes Simplex Infection (HSV). Ceftriaxone and metronidazole were added to the treatment regimen for a potential intrabdominal process. Both Computed Tomography (CT) of the head and abdomen/pelvis, with and without contrast, had no acute findings. Ceftriaxone and metronidazole were subsequently discontinued. Blood cultures were obtained after antibiotic initiation and remained with no growth. Over the next 24 hours (hospital day 2), her fever resolved; However, she

Table 1. Lab values on admission. *Bone marrow aspirate with immature platelet fraction.

Lab Parameter	Lab Value (Reference Range)
White blood cells	15,040 cells/mL (4,000–10,800 cells/mL)
Absolute neutrophil count	13,540 cells/mL (1,800–7,800 cells/microL)
Hemoglobin	15.8g/dL (12.0-16.0 g/dL)
Hematocrit	43.30% (37.0-47.0%)
Platelet count	22 × 103 cells/mL (140,000–400,000 cells/mL)
BMA with IPF*	17.3% (0.9–8.5%)
Sodium	124 mmol/L (134–146 mmol/L)
Potassium	3.6 mmol/L (3.4-5.0 mmol/L)
Chloride	90 mmol/L (98-112 mmol/L)
HCO_3	20 mmol/L (21-29 mmol/L)
Blood urea nitrogen	19 mg/dL (8-20 mg/dL)
Creatinine	0.44 mg/dL (0.50-1.10 mg/dL)
Bilirubin total	0.8 mg/dL (0.2-1.0 mg/dL)
Alkaline phosphatase	59 IU/L (35-104 IU/L)
Alanine aminotransferase	44 IU/L (10-40 IU/L)
Aspartate aminotransferase	99 IU/L (10–40 IU/L)

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developed expressive aphasia and bilateral hearing loss (hospital days 2 and 3). On hospital day 4, the patient was transferred to the academic hospital for further management of meningoencephalitis associated with acute hearing loss and ITP.

At this point, the differential diagnosis included viral diseases: HSV, varicella zoster, mumps, rubella, and rickettsial disease. Doxycycline was added to acyclovir. MRI of the brain was performed with no acute findings; however, MRI of the spine revealed an abnormal T2 signal between the levels of C3 and T1 with multilevel C-T facet joint arthrosis, presumed to be related to degenerative changes. With the administration of DXM and platelet transfusion, platelet count gradually improved, allowing lumbar puncture to be performed 24 hours after transfer (hospital day 5) (Figure 1).

Cerebrospinal Fluid (CSF) analysis revealed 520 WBC with 60% of neutrophils, protein 85 (15-60 mg/dL), and glucose 46 (45-80 mg/dL). The CSF HSV PCR was negative; therefore, acyclovir was discontinued. CSF culture did not grow any organisms.

Given initial lethargy, followed by the development of transient aphasia and hearing loss, detailed social history was obtained 48 hours after the transfer (hospital day 6), revealing that the patient had been working on a local swine farm for the last three years, assisting in the delivery of piglets. According to the patient, five mother pigs and twenty piglets per week died from an unknown cause. This occupational exposure, along with the clinical course, led to a broadened differential diagnosis, including brucellosis and *S. suis* infection. Doxycycline was continued, and ceftriaxone and rifampin were added to the regimen. On day 9 of hospitalization, Metagenomic Next-Generation Sequencing (mNGS) and Universal PCR (uPCR) revealed *S. suis* in blood and CSF, respectively. The patient's condition gradually improved, except for persistent hearing loss, and she was discharged on ceftriaxone 2gm intravenous every 12 hours.

A follow-up visit 21 days later showed persistent hearing loss and intermittent bilateral arm weakness. A repeated MRI showed a new C7-T1 facet joint effusion. Upon consultation with neurosurgery, the presumptive diagnosis of *S. suis* facet joint septic arthritis was made. The patient completed six weeks of ceftriaxone. All symptoms resolved except for permanent sensorineural hearing loss, requiring cochlear implant placement.

Results and Discussion

S. suis is a porcine pathogen that can be transmitted to humans through direct contact with pigs or *via* the consumption of infected raw meat [1]. In addition to pork exposure, the major behavioral risk factor for severe *S. suis* disease is alcohol use [8]. Our patient had a history of occupational exposure to pigs and a history of alcohol use. Despite all medical advances, it is evident that thorough patient history is still a primary tool for diagnosing infectious diseases. When the patient's condition limits history, such as in our case, all efforts should be made to obtain a history from family members or healthcare providers familiar with the patient.

Another reason for delayed diagnosis in our case, and underdiagnosing of *S. suis* in general, was negative culture results. When patients are evaluated in the acute care setting for sepsis and particularly for meningitis, ceftriaxone is frequently used as part of the empirical regimen. Ceftriaxone is active against *S. suis*, and if a blood draw or lumbar puncture is delayed until after antibiotic administration, as in our patient, it can inhibit bacterial growth. Emerging molecular technics, such as uPCR and mNGS, can detect genetic material from clinical specimens and do not require the presence of viable organisms, allowing microbial identification for days after antibiotic initiation. uPCR uses broad-range PCR primers followed by sequencing to hypothetically identify bacterial or fungal pathogens present [9]. mNGS requires a small amount of genetic material from a patient's samples for a whole genome sequencing. The read sequences are linked to a catalog of clinical pathogens, identifying the potential causative agent: virus, bacteria, fungus, or parasite [10]. While both are highly sensitive, uPCR can detect only known sequences, while mNGS have a greater discovery power [11]. Our patient's blood mNGS and CSF uPCR were positive, despite antibiotic administration prior to culture attainment and subsequently negative blood and CSF cultures. Health systems may consider incorporating molecular technics in the algorithms for the diagnosis of meningitis and encephalitis to improve patients' outcomes and minimize empirical unnecessary broad-spectrum antibiotic use.

Human infections with *S. Suis* most frequently present as meningitis, septicemia, and endocarditis [8]. While meningitis has a low mortality rate compared with other meningitis [8,12], it carries a high risk of neurological sequela, with sensorineural hearing loss being the most common (31.6%) [8]. Septicemia, particularly toxic shock syndrome, and endocarditis carry a higher mortality rate [13]. In addition, sporadic cases of enteritis, peritonitis, endophthalmitis, uveitis, spondylodiscitis, and septic arthritis have been described [14]. Our patient presented with nonspecific symptoms associated with profound thrombocytopenia. She never had typical meningeal signs, and hearing loss developed several days after admission after her fever had resolved.

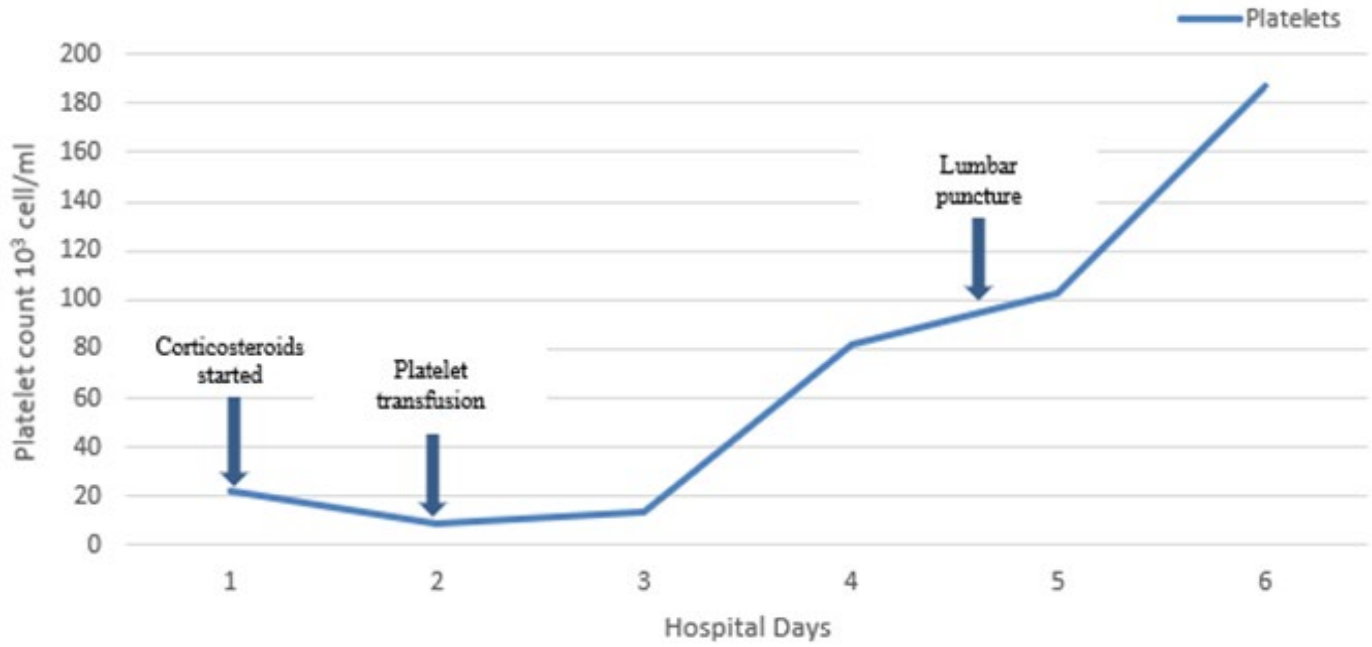

Figure 1. Idiopathic thrombocytopenia- response to treatment and timing of lumbar puncture. Platelet count was 22 × 10^3 on admission and corticosteroids were initiated immediately. Platelet count continued to decrease 9 × 10^3, so platelet transfusion was given on day 2. Corticosteroids were continued. Platelets gradually improved over the next 48 hours allowing lumbar puncture to be performed on hospital day 5.

Bacterial products, such as lipopolysaccharide, a major virulence factor of *S. suis* [15], may attach to platelet surfaces and increase platelet phagocytosis leading to thrombocytopenia [16]. Considering various presentations of *S. suis* infection, thrombocytopenia in patients with occupational hazards should raise suspicion for *S. suis* infection.

Data suggest DXM decreases mortality in pneumococcal meningitis and neurological sequela in all bacterial meningitis [17,18]. The effect of DXM on *S. suis*-related mortality is unknown [19]. A randomized control trial showed DXM protective effect against hearing loss in *S. suis* patients [19,20]. On the other hand, case series indicate that some *S. suis* patients treated with DXM may still develop hearing loss [21,22]. Our patient was started on DXM for ITP early upon admission, with platelet improvement. Despite the delay in antimicrobial treatment, her clinical course was favorable, but permanent hearing loss still developed. Some data suggest that DXM reduces systemic rather than neurological complications in patients with other bacterial meningitis [23,24], which our experience may support. More studies are needed to evaluate the role of DXM in treating *S. suis* infection.

Conclusion

S. Suis infection is an emerging zoonosis with substantial implications for both humans and pigs, yet it appears to be underdiagnosed in the US and Canada. Raising clinicians' awareness and employing a comprehensive range of diagnostic technics, including traditional patient history taking and innovative molecular methods are crucial in overcoming diagnostic obstacles, initiating prompt treatment, and mitigating the impact of *S. suis* infection.

Author Contributions

Conceptualization, G.S., A.K., B.O.; methodology, G.S..; investigation, G.S., A.K., S.S.; resources, G.S., A.K., S.S; writing—original draft preparation, G.S., A.K., S.S, B.O.; writing—review and editing, G.S.., A.K., S.S, B.O.; visualization, G.S.; supervision, G.S.; project administration, G.S.. All authors have read and agreed to the published version of the manuscript.

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Conflicts of Interest

The authors declare no conflict of interest.

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