Case Report

The first report of human primary pyogenic ventriculitis caused by *Streptococcus suis*: a case report

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Abstract: *Streptococcus suis* (*S. suis*), a gram-positive facultative anaerobe, has emerged as a zoonotic pathogen of suppurative infections in various human organs. Never reported is human primary ventriculitis caused by *S. suis*. A 70-year-old Chinese woman with a history of eating undercooked pork tongue was admitted to our hospital due to vomiting, headache and high fever. Brain magnetic resonance imaging (MRI) revealed intraventricular empyema and hydrocephalus, while cerebrospinal fluid (CSF) analysis showed purulent changes. *S. suis* was cultured in the CSF and blood samples of the patient, and confirmed as serotype 2 by real-time polymerase chain reaction (PCR). Therefore, the diagnosis of primary ventriculitis caused by *S. suis* was established. She was treated with intravenous (IV) meropenem for six weeks. To solve hydrocephalus, external ventricular drain (EVD) was performed, followed by ventriculoperitoneal shunt. Finally, the patient achieved a good outcome after a 6-month follow-up. *S. suis* is a rare pathogen in northern China but can cause severe infection and complications. *S. suis* infection should be considered when a patient with bacterial infection has a history of eating undercooked pork. MRI can help detect ventriculitis. It is worth noting that rapid and prolongated administration of IV antibiotics and timely neurosurgical intervention can achieve desirable outcomes.

Keywords: *Streptococcus suis* (*S. suis*); primary pyogenic ventriculitis; hydrocephalus; magnetic resonance imaging (MRI); case report

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Introduction

Streptococcus suis (*S. suis*) is a major zoonotic pathogen primarily found in the upper respiratory tract, alimentary and genital tracts of pigs (1). Transmission to humans often starts from close contact with contaminated pigs or consumption of raw or undercooked pork (2). Since the first in Denmark in 1968, more than 1,600 human *S. suis* infections have been reported in 30 countries worldwide, particularly in Southeast Asia (3). Wertheim *et al.* (4) have systematically summarized published cases of highly invasive diseases caused by *S. suis* in humans, including meningitis, brain abscess, endocarditis, and epidural abscess. In addition, septic shock may occur in critically ill patients infected with *S. suis*, leading to a mortality over 80.0% (5). However, ventriculitis in patients with *S. suis* infection has been rarely reported.

Pyogenic ventriculitis, characterized by ependymal inflammation and pus in ventricular system, is rare but serious and requires long-term antibiotics or surgical intervention (6). Lacking rapid diagnosis and treatment, pyogenic ventriculitis may result in hydrocephalus and even death. In adults, ventriculitis is generally recognized as complication of brain abscess, meningitis extension, or neurosurgery (7). In contrast, primary pyogenic ventriculitis is even rarer. We herein reported the first adult case of primary pyogenic ventriculitis caused by *S. suis*.

We present the following article in accordance with

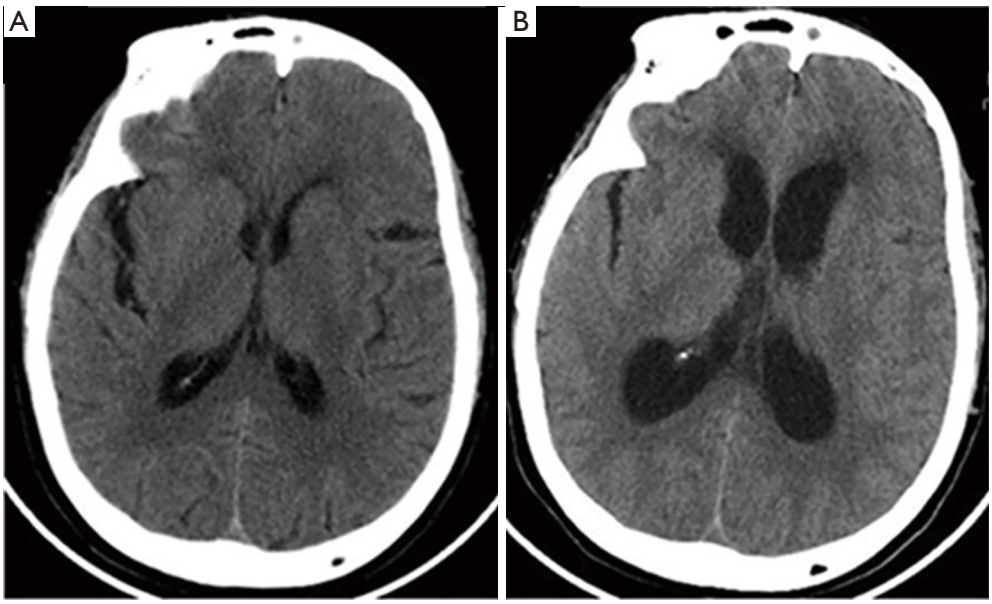

Figure 1 Time-dependent CT observations. (A) CT scan performed three days after the onset of illness revealed no obvious abnormalities; (B) CT scan obtained on admission showed bilateral hydrocephalus. CT, computed tomography.

the CARE reporting checklist (available at http://dx.doi.org/10.21037/apm-21-45).

Case presentation

A 70-year-old Chinese female, previously healthy, was admitted to our hospital for the chief complaint of headache, vomiting and fever. She was a farmer but had no close contact with farm animals.

A week before this admission, she developed headache of undetermined cause. Headache was severe (prominently in the frontal region) and concurrent with vomiting. Her symptoms persisted for three days before the visit to a local hospital. As the patient presented with a lack of meningeal irritation signs and her cerebral computed tomography (CT) did not reveal any feature of acute abnormalities (*Figure 1A*), no interventions were performed in the local hospital and she returned home at the same day. Four days later, she was transferred to our hospital due to worsening symptoms, especially sudden high fever. On arrival, the patient manifested fever of 38.6 ℃, blood pressure of 130/90 mmHg, heart rate of 118 beats/min, and respiratory rate of 25 breaths/min. During the physical examination, she was lethargic, but her orientation was not clouded. No focal neurological deficits or meningeal signs were identified. The other indicators in physical examination were normal.

Laboratory values showed C-reactive protein (CRP) of 38.98 mg/dL and the white cell count (WCC) of 10.56×10^9/L (86.4% neutrophils). Head CT scan revealed enlargement of the bilateral ventricles (*Figure 1B*). CSF was obtained through a lumbar puncture (*Table 1*). Gram stain of the CSF revealed rare gram-positive diplococci. Two sets of blood and CSF samples were prepared for bacterial culture. Meropenem (2 g IV q8h) was administered as empirical antimicrobials. In addition, mannitol (250 mL IV q6h) and methylprednisolone (80 mg IV qd) were given to reduce intracranial pressure (ICP) and inflammatory exudation.

At day 2 after admission, both blood and CSF cultures displayed significant abundance of one bacterial strain. *S. suis* was identified using the VITEK-2 compact system at day 3. Meanwhile, real-time PCR for *S. suis* serotype 2 was positive. Based on antibiotic susceptibility testing results (susceptible to penicillin, ceftriaxone, meropenem, levofloxacin, and vancomycin; resistant to erythromycin and clindamycin), IV meropenem was continued. Brain MRI at day 4 revealed hydrocephalus and hyperintense lesions involving the occipital horns of both lateral ventricles, reflecting the presence of intraventricular empyema (*Figure 2A*). Contrast-enhanced MRI demonstrated uniform enhancement of the ependyma in bilateral ventricles, suggestive of pyogenic ventriculitis (*Figure 2B*). All findings were used to establish a diagnosis of pyogenic ventriculitis caused by *S. suis*. However,

Table 1 Cerebrospinal fluid

Variable	Reference range	On admission	Day 6	Day 12	Day 20	Day 42
Opening pressure (mmH_2O)	80–180	300	230	165	145	130
Color	Clear	Yellowish	Yellowish	Yellowish	Clear	Clear
Cell count (10^6/L)	0–8	221	175	128	37	3
Differential count (%)						
Coenocytes		73	60	56	3	0
Monocytes		27	40	44	97	1
Protein (mg/dL)	15–45	534	453	284	139	24
Glucose (mg/dL)	40–75	8.46	10.8	24.1	38.7	53

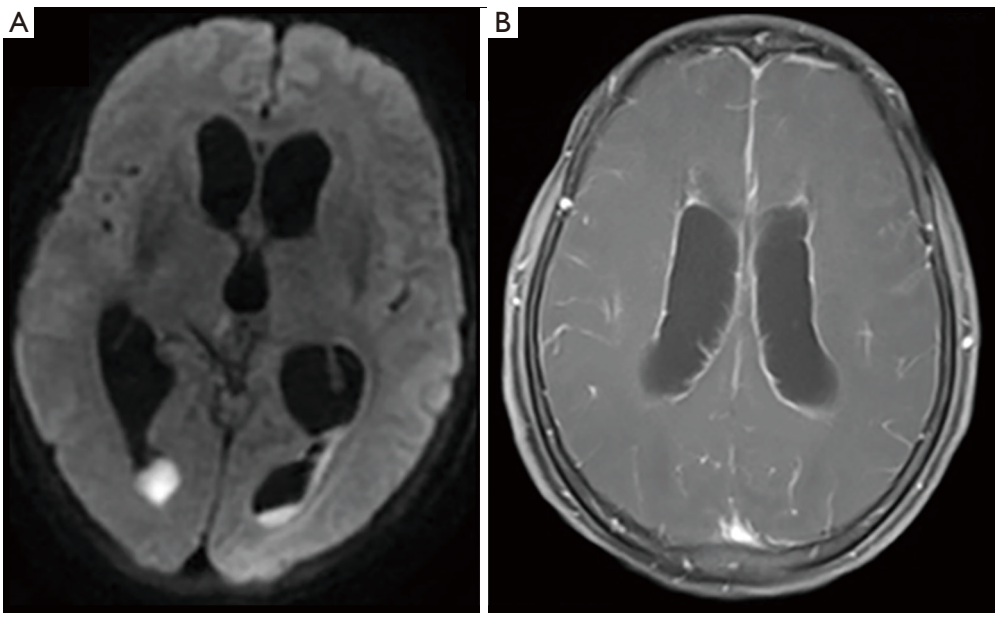

Figure 2 MRI findings. (A) The diffusion-weighted magnetic resonance imaging showed irregular intraventricular debris with restricted diffusion in occipital horns with a dilatation of all the ventricles. (B) Contrast-enhanced MRI showed abnormal enhancement of bilateral ependymal. MRI, magnetic resonance imaging.

contrast-enhanced CT scan of abdominal organs, including the liver, kidney and intestines, as well as other organs, such as lungs, did not show other infection foci. Transthoracic echocardiography did not reveal any abnormality. We interviewed the patient again, and she recalled eating undercooked pork tongue three days before falling ill. We examined her skin, but found no open wounds.

The patient became afebrile at day 6 after IV meropenem therapy, with negative blood culture. However, headache persisted. Repeated lumber puncture revealed that inflammation indexes slightly dropped in the CSF, with negative Gram staining and culture. CT showed that global ventriculomegaly was still present, without significant alleviation. Therefore, she was transferred to the neurosurgery department. An EVD was inserted into the right lateral ventricle to drain empyema and control ICP. Mannitol and methylprednisolone were finished after a total of 6 days of administration.

She regained consciousness after the operation, with a Glasgow Coma Score (GCS) of 15/15 and no defect. IV

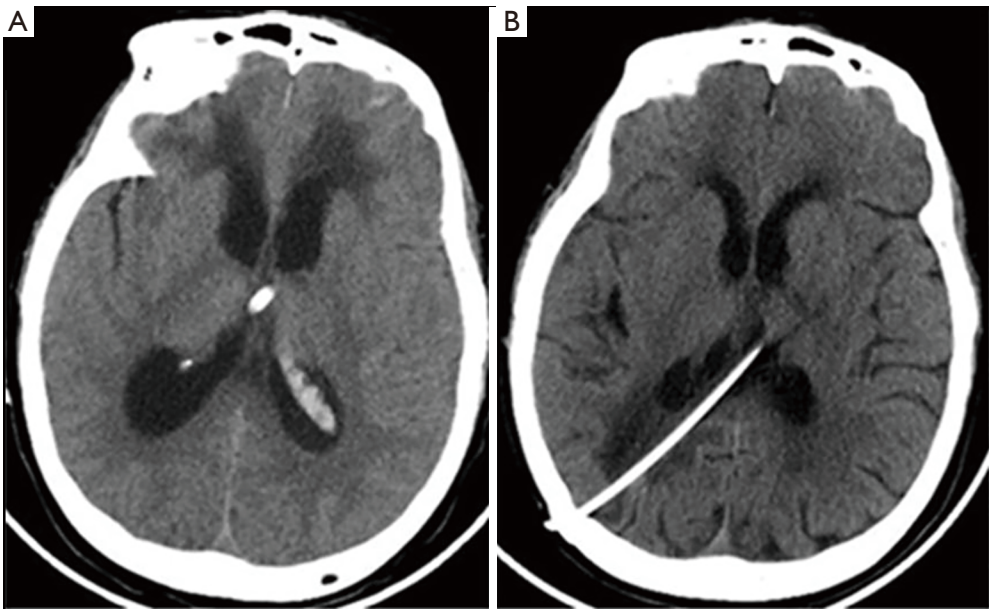

Figure 3 CT findings after treatment. (A) On day 12 of the hospitalization, CT scan before EVD removed showed the contractible bilateral ventricles; (B) follow-up CT performed 6 months after insertion of ventriculoperitoneal shunt revealed that the size of the ventricle has basically returned to normal with the catheter. EVD, external ventricular drain.

meropenem was continued postoperatively. Ventricular fluid culture was negative. Within a week, the patient's headache resolved, and the third lumber puncture revealed favorable changes in the CSF. Repeated CT showed obvious decrease in ventricular size (*Figure 3A*). Thus, the catheter was removed at day 12.

After 20 days of stay, the patient in a stable condition was transferred to another hospital for a 6-week treatment with antibiotics and the insertion of a ventriculoperitoneal shunt. At 6 months after discharge, infection and other neurological defects did not show up. Follow-up CT revealed collapse of all ventricles (*Figure 3B*).

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional committee and with the Helsinki Declaration (as revised in 2013). Written informed consent was obtained from the patient.

Discussion

We presented a case of primary pyogenic ventriculitis with *S. suis* cultured in both blood and CSF. Ventriculitis is a suppurative infection of ventricles, usually secondary to meningitis, ruptured abscess, and shunt/catheter-related infections. In contrast, only few cases of primary ventriculitis have been reported, mainly as group B streptococci neonatal infections (8,9). According to a review in 2017, only six adult cases had been described, respectively caused by *Neisseria meningitidis*, *Staphylococcus aureus*, and *Listeria monocytogenes*, etc. (10). None of these cases were resulted from *S. suis* infection. *S. suis* has been known as a zoonotic pathogen for more than 50 years, but severe infections in the central nervous system (CNS) in humans are rare.

Our patient developed persistent headache, with vomiting and subsequent fever. MRI showed periventricular hyperintense signals, ependymal enhancement and hydrocephalus, while the CSF showed purulent changes. Furthermore, *S. suis* was detected in the blood and CSF. The diagnosis was established as primary pyogenic ventriculitis caused by *S. suis*. Gastrointestinal tract is considered as a port of entry through which *S. suis* enters the human body after by consumption of contaminated raw porcine foods, as shown by previously reported cases in Asian countries (11).

S. suis is classified into 35 serotypes (1–34 and 1/2) based on the antigenicity of capsular polysaccharide (CPS). According to statistics, among the 1,642 cases of human infection with *S. suis* reported worldwide from 2002 to 2013, the most common serotype is serotype 2,

accounting for 74.7%, followed by serotype 14 (3). Basic studies have also confirmed that *S. suis* serotype 2 (SS2) can escape from natural immune surveillance and eradication through neutrophils (12). In recent years, cases caused by SS2 and SS9 have been reported in China, especially the predominant SS2 in southern China (13). In the typing of *S. suis*, real-time PCR shows high sensitivity, specificity and repeatability (14). In this study, this technique was used to detect *S. suis* nucleic acid and SS2 nucleic acid, respectively. The case was determined as an infection of SS2, which is in line with the epidemic situation in China.

The incidence of *S. suis* infection in the CNS keeps increasing. The most common manifestation of an *S. suis* infection is meningitis (50–60%), however, other manifestations of intracranial infection, such as ventriculitis, may occur (15). Yanase *et al.* (16) described the first case of human pyogenic ventriculitis secondary to meningitis caused by *S. suis*. In our case, however, we did not find the evidence supporting that the infection was secondary to meningitis, endocarditis, pneumonia, or brain abscess. To our knowledge, this is the first report of primary ventriculitis associated with an *S. suis* infection in humans. The mechanism of primary pyogenic ventriculitis is unknown. A recent review found that blood cultures were positive in most of the patients with primary purulent ventriculitis, suggesting that bacteremia may be the culprit (10). Based on blood and CSF cultures positive for *S. suis*, we hypothesize that this primary ventriculitis may arise from intracranial infection through hematogenous seeding.

Although extremely rare in humans, pyogenic ventriculitis caused by *S. suis* has been described in animal models. Lun *et al.* (1) reported that fibrin, edema and cellular infiltrates were typically observed in the CNS of pigs infected with *S. suis*, especially in the choroidal plexus. Furthermore, in a mouse model, bacteria were found to invade the CNS through the choroid plexus and brain endothelial cells, as a consequence of early transcription of TLR2, CD14 and inflammatory factors in these structures (17). These findings provide theoretical evidence that inflammation within the ventricles is associated with *S. suis*.

Our patient, together with five out of the six patients reviewed by Gronthoud *et al.*, did not present neck stiffness (10), suggesting that primary ventriculitis may lack the typical manifestations of meningeal irritation. Hence, if the patient shows intracranial infection (but no classical clinical manifestations) at presentation, or poor response to initial antibiotics as our patient did, purulent ventriculitis should be suspected. MRI is a main tool in diagnosing pyogenic ventriculitis. MRI features specific to ventriculitis include irregular ventricular debris, periventricular hyperintense signals, ependymal enhancement and hydrocephalus. Among these MRI findings, ventricular debris occurs in 94% of cases, and ependymal enhancement is less frequent (60%) (18).

The patient's symptoms were gradually alleviated after the initiation of IV antibiotic treatment. Antibiosis should be the first-line treatment for ventriculitis, because *S. suis* is susceptible to penicillin, ceftriaxone, and vancomycin and meropenem (2). Because patients with ventriculitis require 4–6 weeks of antibiotics, surgical interventions may be needed for obstructive hydrocephalus during such a long period (19). The present patient recovered completely after timely surgery despite that hydrocephalus appeared on admission. Therefore, antibiotic treatment and surgery, either alone or combined, are recommended as soon as the diagnosis is established.

In conclusion, this is the first reported case of primary ventriculitis caused by *S. suis*. *S. suis* infection should be suspected in patients closely contacting with contaminated animals (pigs) or eating undercooked pork. PCR and MRI are helpful in identifying infectious source and ventricular inflammation, respectively. Prolongated antibiotic treatment and ventricular drainage should be performed to improve prognosis.

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Footnote

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Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at http://dx.doi.org/10.21037/apm-21-45). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. All procedures performed in studies involving human participants were in

accordance with the ethical standards of the institutional and/or national research committee(s) and with the Helsinki Declaration (as revised in 2013). Written informed consent was obtained from the patient for publication of this study and any accompanying images.

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