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Case Report **Open Access**

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Streptococcus gallolyticus meningocephalitis in adults: the first case report in China

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ABSTRACT

We report on the first case of a *Streptococcus gallolyticus* meningocephalitis in China. The bacterium was first isolated from the patient's cerebrospinal fluid and has so far not been associated with human infections of the central nervous system. We hope our case report can give some references for the diagnosis and treatment of the *Streptococcus gallolyticus* meningocephalitis in China.

Keywords: *Streptococcus gallolyticus*, meningocephalitis, China, case report, adult

INTRODUCTION

Streptococcus gallolyticus is an uncommon cause of meningocephalitis so far apart from the bacteremia or the peritonitis. We report one case with meningocephalitis in which *Streptococcus gallolyticus* was isolated from the cerebrospinal fluid (CSF). The organisms were seen on a gram-stained preparation of CSF. The patient had a history of adenocarcinoma of colon and presented with hyperpyrexia, deliration and neck rigidity. After the antibiotic treatment for 2 weeks, finally he got fully recovery. A review of the literature revealed only about 42 cases of meningitis due to *Streptococcus gallolyticus* were reported and the present case report was the first one from china. The case indicates the importance of laboratory identification of specific organisms and provides experience in meningocephalitis caused by *Streptococcus gallolyticus*.

Table 1. Clinical characteristics for the patient with *Streptococcus gallolyticus* meningocephalitis

Characteristics	Patient data
Age (years)	80
Gender	Male
Predisposing factor (s)	Adenocarcinoma of colon Bibulosity
Clinical presentation	
Temperature (°C)	39.3
Neck rigidity	Yes
Headache	No
Score on Glasgow Coma Scale	13
Neurological deficits	Delirium
CSF findings	
Leukocyte count	74×10^6/L
Protein level (mg/L)	6058
CSF/blood glucose ratio	< 0.13
Cranial CT (MRI)	Normal
Cultures	
Blood culture	Negative
CSF culture	Positive
S. gallolyticus-associated disease	
Endocarditis	No
Colon adenocarcinoma	Yes
Strongyloidiasis	Unknown
Empirical treatment	
Antibiotics	Meropenem, linezolid
Dexamethasone	No
Outcome	Recovery

CSF: cerebrospinal fluid; CT: computed tomography; MRI: magnetic resonance imaging

CASE REPORT

An 80-year-old man was admitted to the emergency room of Guangdong Provincial Hospital of Chinese Medicine. He presented symptoms with deliration and neck rigidity. According to his wife's statement, the patient complained the abdominal pain 5 days ago. Meanwhile, he had a history of radical operation for adenocarcinoma of stomach and colon, as well as the percutaneous coronary intervention. Further questioning for his wife and daughter revealed that the patient has the habit of drink Chinese liquor for about 50 mL every day for decades before the partial resection of stomach. Even in the latest years, he still drank about 20 mL every day. The features of the patient are summarized in Table 1.

On examination, he was delirious with neck rigidity, but no febrile. There was no other neurological abnormalities. Meanwhile, there is no abdominal pain. Peripheral blood samples, including cultures, were taken and treatment with ceftriaxone (2 g intravenous drip, ivd q12h) as well as acyclovir (75 mg peros, po bid) were started immediately. Urgent brain computed tomography (CT) scanning was normal. Then the lumbar puncture was performed. Laboratory studies of CSF disclosed the following values: the CSF pressure, 130 cmH_2O; WBCs, 15×10^6/L; glucose < 1.11 mmol/L (serum glucose: 8.96 mmol/L); and protein, 4946 mg/L. He was diagnosed with central nervous system (CNS) infection and was transferred to the neurological department.

Day 1 physical examination showed a poor-nourished man in a mild altered consciousness. His vitals were: temperature 36.4 °C, blood pressure 145/59 mmHg, pulse rate 66 and respiration rate 20. Neurological examination revealed a delirious man who had decreased range of motion of his neck. No other abnormalities of neurologic system as well as the respiratory and digestive system were detected. Then, blood routine, high-sensitivity C-reactive protein (hs-CRP), procalcitonin including cultures were taken again. Magnetic resonance imaging (MRI), electroencephalogram (EEG) monitoring was performed. Combining

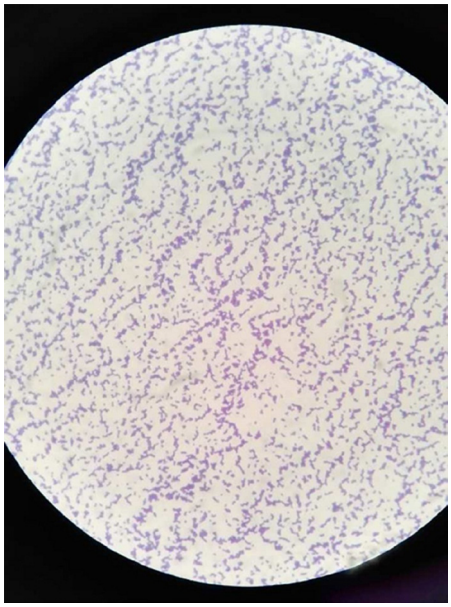

Figure 1. The microscopic view of cerebrospinal fluid culture (1:1000)

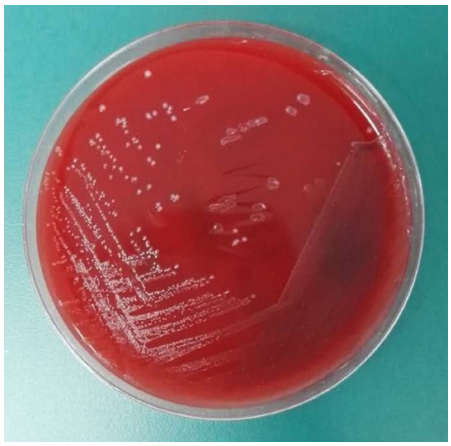

Figure 2. The macroscopic view of *Streptococcus gallolyticus* (1:1)

the patient's symptoms, positive signs, results of the blood test and CSF test, we considered the patient suffered from meningocephalitis and the treatment with meropenem (2 g ivd q8h) was started. Meantime, a lumbar puncture was performed for the second time.

Blood routine showed the following values: WBCs, 12.1 × 10^9/L (87.9% neutrophils, 7.7% lymphocytes, 4% monocytes). And CSF test found the following values: CSF pressure, 110 cmH_2O; WBCs, 74 × 10^6/L (15% neutrophils, 80% lymphocytes, 5% monocytes); glucose < 1.11 mmol/L (serum glucose: 8.33 mmol/L); and protein, 6058 mg/L. At this time, *Streptococcus gallolyticus* was isolated from CSF cultures [Figures 1 and 2]. Considering the permeability of linezolid through the blood brain barrier (BBB) and the sensitivity of linezolid (minimum inhibitory concentration, MIC /kindy-bauer, KB 29 mm) to the *Streptococcus gallolyticus*, the therapy with linezolid (0.6 g ivd q12h) was started.

Brain contrast enhancement MRI showed no signs of infection and the long-term EEG monitoring found no epileptic signs. The detailed report showed the background activity was no alpha wave and diffused slow

Table 2. Comparison of the clinical characteristic and test results with the patient

Characteristics	Day1	Day 3	Day 8	Day 14	Day 28
Clinical presentation					
Consciousness	Deliration	Consciousness	Consciousness	Consciousness	Consciousness
Neck rigidity	Yes	Yes	No	No	No
Headache	No	No	No	No	No
Fever	No	Yes	Yes	Yes	Unknown
Score on Glasgow Coma Scale	13	13	15	15	15
Temperature (°C)	36.4	37.8	38.3	38.2	Unknown
CSF findings					
Leukocyte ($\times 10^6$/L)	74	640	384	Unknown	32
Protein level (mg/L)	6058	5160	2342	Unknown	359
CSF glucose (mmol/L)	< 1.11	1.47	1.81	Unknown	Unknown
Blood findings					
Leukocyte ($\times 10^9$/L)	12.1	19.16	21.89	11.25	11.16
Neutrophils (%)	87.9	81.2	87.2	75	79
Monocytes (%)	4	6.7	4.8	10.8	7.1
Lymphomonocyte (%)	7.7	12	6.7	11.9	11.9
Serum glucose (mmol/L)	8.33	10.95	6.83	6.61	Unknown
Cultures					
Blood culture	Negative	Negative	Negative	Negative	Unknown
CSF culture	Positive	Negative	Negative	Negative	Negative
hs-CRP (mg/L)	Unknown	Unknown	57.04	34.03	25.3 (CRP)
Procalcitonin (ng/mL)	Unknown	0.58	0.17	0.17	0.04

CSF: cerebrospinal fluid; hs-CRP: high-sensitivity C-reactive protein

waves as well as low amplitude of beta were observed in all leads. No sleep cycle wave was observed as well.

Day 3, he developed a mild fever with the temperature of 37.8 °C. He became conscious but still cannot communicate with the others. A lumbar puncture was performed to evaluate the effect of the therapy. The WBCs in blood and CSF increased while the glucose and protein levels were improved [Table 2]. The cultures of CSF and blood were negative.

Day 8, the physical examination showed the neck rigidity was better than before and there were few rales in both lower lungs. Deep sputum cultures yielded multidrug-resistant baumanii and the amikacin (0.2 g ivd q12h) was added.

As the neurological function was improved, we performed another lumbar puncture and the results showed the WBCs decreased to 384×10^6/L and protein as well as the glucose increased to 2342 mg/L and 1.81 mmol/L separately indicating the antibiotic therapy was effective. Controversially, the WBCs and hs-CRP in the blood increased. Considering the symptoms and the results of CSF tests were both improved, the therapy with meropenem and linezolid was continued.

While the treatment was effective based on the CSF results. We did the other tests to rule out the infection of the other systems and the cacotrophy conditions. An echocardioram revealed no evidence of endocarditis and colonoscopy revealed the ascending colon polyps and haemorrhoids. The chest X-ray found no tumor. The abdominal CT scan was also negative.

The results of the marker for the systemic inflammation, CSF, clinical presentation are summarized in Table 2. All together, meropenem (2 g ivd q8h) was given for 16 days, linezolid (0.6 g ivd q12h) was given for 15 days and amikacin (0.2 g ivd q12h) was given for 5 days. Other treatments including nutritional supporting, early rehabilitation, bronchofiberscope, bed sore prevention were also given to the patients. Finally, the patient was completely awake and transferred to the rehabilitation facility.

Two weeks after discharge, we followed up the patient by telephone. His wife told us the lumbar puncture was performed once more in the rehabilitation facility and he could take care of himself independently. The laboratory studies of CSF and blood was almost normal [Table 2].

DISCUSSION

There are only about 42 adult cases about *Streptococcus gallolyticus* meningitis reported according to the literature. For now, the present case report was the first from the Chinese population. The detail of the diagnosis and treatment was documented which could provide experience for the subsequent patients of the CNS infection with *Streptococcus gallolyticus*.

We think that the gastrointestinal tract was probably the source of *Streptococcus gallolyticus* in our patient who had prior gastroenteritis and had the history of moderately differentiated adenocarcinoma of stomach treated with partial resection together with colonic adenocarcinoma. Many studies have confirmed the fact that patients with both benign and malignant of gastrointestinal lesions were susceptible to *Streptococcus bovis* (*S. bovis*) bacteremia[1-3]. A review of 119 cases of *S. bovis* endocarditis or bacteremia suggested that there were 48 patients accompanied with gastrointestinal neoplasms, 22 of which were adenocarcinoma[4]. Colonic carcinoma has been reported in up to 50% of patients with *S. bovis* bacteremia or endocarditis[5]. So, there is a strong link between *Streptococcus gallolyticus* infection and bowel disease. Nevertheless, the extent, nature, and basis of this association are still not completely understood.

According to the literature, the susceptible risk factor for the *Streptococcus gallolyticus* meningitis was cacotrophy, immunosuppression, endocarditis, colon carcinoma, strongyloidiasis and bibulosity[6-10]. Among the 42 adult patients reported[11], 43% (18/42) of the patients had the conditions such as immunosuppression, cancer and alcoholism. Meantime, 33% (14/42) of the patients had the infection with the strongyloidiasis, 63% (15/24) had the colon abnormalities, 8% (5/28) had the endocarditis. Furthermore, endocarditis has been reported to be caused by *S. gallolyticus ssp. gallolyticus* more frequently than by *S. gallolyticus ssp. Pasteurianus*[12,13]. So, it is necessary to test for strongyloidiasis and do the echocardiography and colonoscopy for the patients with *Streptococcus gallolyticus* meningitis. For our patient, it is definitely that he has the cacotrophy, colon carcinoma, but not the endocarditis. Unfortunately, in our patient, the stool examination was not performed repeatedly to detect strongyloidiasis.

Even though, the CNS infection has clinical characteristics, such as ardent fever, headache and neck rigidity. In many patients with CNS infection due to *Streptococcus gallolyticus*, the presenting differentiated from each other, as occurred in our patient. It was not until days after admission that our patient developed the febrile signs. The delayed fever may be the reason of his advanced age , the condition of cacotrophy or the nosocomial infection.

As we all know, bacterial infection of the CNS has the following characteristics of laboratory examination: the CSF pressure, WBCs, NEUT% and the protein were high, while the glucose in CSF was reduced. In our patient, we performed lumbar puncture repeatedly, but the CSF pressure was never higher than normal. This may be due to differences in individual immune responses. IgG and IgA but no IgM are seen in normal CSF because IgM has a larger molecular weight. Humoral immune responses often form antigen-antibody complexes; this reaction is often carried out in blood vessels, leading to severe vasculitis reactions in or near nerve tissue. It may be the characteristic for *Streptococcus gallolyticus* meningocephalitis which needs more clinical data. Meanwhile, we cannot ignore the fact that the cultures plays an important role for the differentiation of CNS infections. For the 42 patients, the positive incidence was 88% for CSF cultures and 87% for blood cultures[11]. We performed the blood culture repeatedly, the results were all negative. So we think that our patient might not be infected through blood but through the gastrointestinal tract.

Now, *Streptococcus gallolyticus* performed as a member of *S. bovis*, which has three hypotypes. Before then, *S. bovis* strains were divided into biotypes based on their ability to decompose the mannitol (biotype I) or not (biotype II)[14]. Biotype II was further subdivided into biotypes II.1 and II.2. Depending on the ability to produce acid from trehalose, to exhibit frequently b-glucuronidase, to degrade starch and b-galactosidase activity, Biotype II. 2 strains are distinguished from biotype II.1 strains. In 1990, Osawa[15] suggested a new species, *S. gallolyticus*, isolated from fecal excretion of a koala, for those organisms able to decarboxylate gallic acid. Subsequently, the further studies suggested that the *S. gallolyticus* species comprised *S. bovis* biotypes I and II/2[16]. Later studies about the sequencing of soda and DNA-DNA hybridization confirmed the need for the taxonomic change[17,18]. Therefore, Abdulamir *et al.*[6] suggested that the *S. gallolyticus* species includes three subspecies: *S. gallolyticus subsp. gallolyticus*, *S. gallolyticus subsp. pasteurianus*, and *S. gallolyticus subsp. macedonicu*. Among the three biotypes of *Streptococcus gallolyticus*, we know that *S. gallolyticus subsp. pasteurianus* causes meningitis, bacteremia, peritonitis, and chorioamnionitis in adults[19-21]. Since this was the first case of *Streptococcus gallolyticus* among Chinese population, we didn't detect the subtype because the technical reasons. We hope that our case report can provide some information for the detection of the *Streptococcus gallolyticus* related diseases and to make more precision diagnosis by the subtype detection.

From the review of the *Streptococcus bovis* infection of the CNS, we know that most cases of *S. bovis* infection can be treated with penicillin alone[22]. But as is known to all, the cultures plays an important role in the course of treatment. Savitch *et al.*[23] found that patients with *S. bovis* endocarditis were resistant to penicillin G. Several researches proposed that the empirical antibiotics should be chosen based on patient history, results of CSF gram stain and local community antibiotic resistance patterns[24]. For our patient, considering the history of the patient as well as the permeability of BBB to antibiotics, we chosen the meropenem (2 g ivd q8h) firstly[25]. We added linezolid as soon as the *Streptococcus gallolyticus* reported. Considering the results of sputum Gram stain we continued the treatment with meropenem. Eventually, our patient recovered very well as we follow up by telephone two weeks after the discharge.

The studies suggested that the mortality rate of the *Streptococcus gallolyticus* meningitis patients is about 24%[11], but we cannot ignore the fact that the total number of reported patients with *Streptococcus gallolyticus* meningitis was small. So, it is of great significance to form a standardized and effective diagnosis and treatment program for *Streptococcus gallolyticus* meningitis.

For now, all of the reports are from European and American countries. There are no reports from China. We hope our case report can give some references for the diagnosis and treatment of the *Streptococcus gallolyticus* meningocephalitis in China.

DECLARATIONS

Authors' contributions

Drafting the manuscript, and literature review: Dai YM, Zhao M, Lu HJ
Revising the manuscript: Wang LX

Availability of data and materials

The data and material used in the study could be open upon request.

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Conflicts of interest

All authors declared that there are no conflicts of interest relevant to this article.

Ethical approval and consent to participate

The study is approved and the patient consent is obtained.

Consent for publication

Not applicable.

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