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【 CASE REPORT 】

A Rare Case of Meningitis Caused by *Streptococcus gallolyticus* subsp. *pasteurianus* in an Immunocompetent Young Adult

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Abstract:
Bacterial meningitis is a life-threatening condition that is mainly caused by *Streptococcus pneumoniae* and *Neisseria meningitis*. Although *Streptococcus gallolyticus* subsp. *pasteurianus* (*Sgp*) is also known to cause meningitis, its frequency is quite low, especially in adults. We herein report the first immunocompetent Japanese adult patient (20-year-old woman) with bacterial meningitis caused by *Sgp*. The patient showed dramatic improvement after antibiotic treatment. Although previous reports have described an association between *Sgp* infection and an immunosuppressive status, bowel and hepatobiliary diseases, or strongyloidiasis, our case did not demonstrate any of these conditions, suggesting that *Sgp* can cause meningitis even in young immunocompetent adults.

Key words: bacterial meningitis, *Streptococcus gallolyticus*, *Streptococcus gallolyticus* subsp. *pasteurianus*, *Streptococcus bovis*

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Introduction

Bacterial meningitis in adults is commonly caused by *Streptococcus pneumoniae* and *Neisseria meningitidis* (1). Other bacterial strains causing meningitis, such as *Listeria monocytogenes* and *Staphylococcus aureus*, are often associated with specific risk factors, including nosocomial, postoperative, or opportunistic infection (2). *Escherichia coli* and *Klebsiella pneumoniae* are both associated with meningitis in neonates and geriatric populations (1, 2). *Streptococcus gallolyticus* subsp. *pasteurianus* (*Sgp*), formerly known as a member of *Streptococcus bovis* Biotype II/2, is a bacterium that has been reported to seldom cause meningitis (3).

We herein report a rare case of bacterial meningitis caused by *Sgp* in an immunocompetent adult.

Case Report

A 20-year-old woman presented to the emergency department with complaints of headache and vomiting without diarrhea for the past 2 days prior to hospital admission. Early in the morning on the day of admission, the patient was transferred to our hospital for emergency care due to further worsening of headache and vomiting and poor speech. She was afebrile upon admission (36.7°C), with stable vital signs. On a physical examination, the patient appeared agitated, had an altered consciousness [Glasgow Coma Scale (GCS): E3V4M5, Japan Coma Scale (JCS): 20], and had nuchal rigidity but no anisocoria. Auscultation revealed no heart murmur. An arterial blood gas analysis showed respiratory alkalosis with secondary metabolic acidosis (pH 7.51, $PaCO_2$ 23.9 mmHg, PaO_2 103.1 mmHg, HCO_3 18.9 mmol/L).

Computed tomography (CT) of the head did not reveal

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Table. **Clinical Characteristics of *Sgp* and *Sgg* Infection.**

Characteristics	*Sgg*	*Sgp* (this case)
Complications (12, 13)		
Septic shock	13%	16%
Multiple organ failure	0%	2%
Thirty-day mortality	10%	17%
One-year motality	21%	58%
Coexisting condition (7-13)		
Meningitis	extremely rare	elderly<infant, neonate
Infective endocarditis	43-100%	8-33%
Gastrointestinal disorders		
Colorectal cancer	14-71%	0-22%
Pancreatic cancer	0%	17%
Chronic liver disease	14%	41-50%
Diabetes mellitus	0%	8-62.5%

any acute abnormalities. She had no significant medical history. Laboratory workup showed leukocytosis with neutrophilic predominance [10,000 white blood cells (WBCs)/μL, 88.5% neutrophils], elevated C-reactive protein levels (1.37 mg/dL, normal range <0.30 mg/dL) and normal blood glucose (74 mg/dL, range 70-109 mg/dL) and ammonia levels (33 mg/dL, range 12-66 mg/dL).

As bacterial meningitis was suspected, lumbar puncture was performed. Purulent fluid was grossly identified. A cerebrospinal fluid (CSF) analysis revealed pleocytosis (WBC count of 4,736 cells/μL, with 92.0% segmented cells, 4.5% mononuclear cells, 3.0% lymphocytes), elevated total protein concentration (330 mg/dL), and low glucose concentration (5 mg/dL). CSF Gram staining was negative for organisms. The patient was admitted to the intensive care unit and started receiving high-dose meropenem (6 g/day), vancomycin (1,500 mg/day), and dexamethasone (7.5 mg/day).

The clinical condition of the patient improved considerably after 24 h of treatment (GCS: E4V5M6, JCS: 0). Her CSF cultures and two of the four bottles of blood cultures grew *S. gallolyticus*. Confirmation of bacterial identification was conducted by a matrix-assisted laser desorption/ionization time-of-flight mass spectrometry technique and 16S rRNA sequencing, identifying *Sgp*. Magnetic resonance imaging of the brain showed no obvious abscess or aneurysm, and no cardiac lesions, including infective endocarditis, were found by a transthoracic echocardiogram. Based on the susceptibility of the bacteria, the antibacterial therapy was changed to ceftriaxone (4 g/day), and dexamethasone was discontinued. To search for a route of bacterial invasion, a dental evaluation was performed, but no active lesions considered to be a source of infection were observed. In addition, because *S. gallolyticus* infection is known to be associated with colorectal diseases, hepatobiliary disorders, and strongyloidiasis (4), we performed colonoscopy, abdominal ultrasound, a stool examination, and abdominal CT, all of which yielded negative results. None of these tests revealed any malformations, such as portosystemic shunt, that could be associated with bacteremia caused by enteric bacteria. There had been no recent changes in her bowel habit, no weight loss, no systemic symptoms - including skin rashes - prior to the onset of headache, and no unusual sexual activity. She was negative for human immunodeficiency virus, and her serum IgG level was near the lower limit of normal (791 mg/dL, range 800-1,700 mg/dL). The findings of a CSF analysis were normal after seven days of treatment.

The patient recovered quickly with complete resolution of symptoms after 14 days of antibiotic treatment. She was discharged on the 17th day of admission and followed up on an outpatient basis.

Discussion

S. gallolyticus is a Gram-positive coccus. Taxonomically, this strain is classified as *S. bovis/S. equinus* complex (SBSEC), a nonenterococcal group D *Streptococcus* spp. complex (5, 6). *S. gallolyticus* was previously referred to as *S. bovis* Biotype II/2. Current phenotypic, proteomic, and molecular genetic techniques allow us to more precisely subdivisions of SBSEC, and the designation described below is now recommended (5). At present, this strain contains the following seven subspecies: *S. gallolyticus* subsp. *gallolyticus* (*Sgg*), S. *gallolyticus* subsp. *macedonicus* (*Sgm*), *S. gallolyticus* subsp. *pasteurianus* (*Sgp*), *S. infantarius* subsp. *infantarius* (*Sii*), *S. lutetiensis*, *S. alactolyticus*, and *S. equinus* (6).

S. gallolyticus accounts for 5-10% of the intestinal flora in normal adults (4). Previous studies have shown that *S. gallolyticus* infection is associated with a range of clinical presentations, including meningitis, bacteremia, infective endocarditis, colorectal cancer, chronic liver disease, and diabetes mellitus (7-11). There have been many publications concerning this strain; however, reports on subspecies other than *Sgp* and *Sgg* are scarce. Therefore, we summarize the clinical characteristics of *Sgp* and *Sgg* in Table.

Despite the similar clinical courses in the acute phase of *Sgp* or *Sgg* infection, a previous study showed that the prognosis at one year was poorer in *Sgp* infection than in *Sgg*

infection (12, 13). However, there is a possibility that coexisting malignancies may influence the prognosis. Although there is known to be a difference in the background factors of the infection between *Sgp* and *Sgg*, *Sgp* infection seems to be more closely associated with pancreatic cancer, chronic liver damage, diabetes mellitus, and meningitis. In contrast, the association of *Sgp* with infectious endocarditis and colorectal cancer seems to be weaker than that of *Sgg* infection (7-13). Strongyloidiasis is another coexisting condition in *S. gallolyticus* infection. There have been a few publications describing the association of *S. gallolyticus* meningitis with strongyloidiasis (14, 15).

Previously, meningitis caused by *S. bovis*/SBSEC was reported as *S. bovis* meningitis, but recently, several papers described the subspecies of *S. bovis*/SBSEC (3, 8-12). In a retrospective analysis of the Dutch cohort of adults with community-acquired meningitis (3), *S. gallolyticus* was very infrequently identified, being found in only 5 of 1,561 cases (0.3%). Among them, subspecies identification was performed in only one case, which was reported as *Sgg*. That study also reviewed publications concerning *S. gallolyticus* meningitis from 1975 to 2015. Eight of the nine cases in which subspecies identification was performed were reported to be caused by *Sgp* (3).

Furthermore, we extensively searched for papers concerning retrospective analyses summarizing *S. gallolyticus* infection and found five reports of cases coming from Japan (11), China (9), India (10), Denmark (12), and Spain (8). While *S. gallolyticus* causes a variety of disease conditions, meningitis caused by this strain was described in only one case report from China, in which the subspecies was *Sgp* (9). The above studies led us to believe that the frequency of *S. gallolyticus* meningitis in adults was quite low and that the majority of cases of *S. gallolyticus* meningitis were caused by *Sgp*.

Next, we searched the literature for pediatric cases of *S. gallolyticus* meningitis. We found more cases in children than in adults, especially in neonates and infants, which suggested that the frequency of *S. gallolyticus* meningitis in children might be higher than that observed in adults (16-18). According to the subspecies analysis, most of the cases were reported to be caused by *Sgp*. We found only one case of meningitis with *S. lutetiensis* infection (19). Interestingly, meningitis caused by *Sgp* has been reported even in animals (20, 21). Although publication bias needs to be considered, *Sgp* seems to be the most meningitis-prone subspecies in SBSEC. In addition, neonates and infants may be more susceptible to *Sgp* than adults.

Based on information from the above literature search, we carefully collected the present patient's medical history and performed colonoscopy, abdominal ultrasound, a stool examination, and abdominal CT after remission was achieved. However, none of the conditions associated with *Sgp* infection, including strongyloidiasis, were identified. In addition, to identify bacterial migration and invasion routes from the intestinal tract to the CSF, we conducted dental examinations and searched for congenital malformations in the abovementioned imaging tests, but no abnormal findings were confirmed. In addition, based on the patient's medical history, we did not strongly suspect primary immunodeficiency; however, to search for latent immunodeficiency, an HIV test was performed and found to be negative. Serum IgG was around the lower limit of normal, but given the low albumin level, we considered it to be an effect of poor nutrition due to a decreased food intake for more than a few days and did not consider it to be due to an immunity problem. Since primary immunodeficiency was not strongly suspected based on our investigation, we decided to follow the patient on an outpatient basis instead of conducting a detailed evaluation of IgG subclass deficiency and leukocyte migration capacity in this hospitalization.

In conclusion, we herein report our experience with a rare adult case of bacterial meningitis caused by *Sgp*. Recently, the updated and revised taxonomy with available phenotypic, proteomic, and molecular genetic techniques has facilitated our understanding of the detailed associations between bacterial subspecies and meningitis. Being aware of the bacterial subspecies is important to clarify the accurate clinical picture of the infectious disease. There have been few reports on the association between *Sgp* and meningitis in immunocompetent adults, and further case studies are still anticipated in the future.

The authors state that they have no Conflict of Interest (COI).

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