CASE REPORT

Spontaneous Meningitis Due to Streptococcus salivarius Subsp. salivarius: Cross-reaction in an Assay with a Rapid Diagnostic Kit that Detected Streptococcus pneumoniae Antigens

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Abstract

Streptococcus salivarius subsp. salivarius occasionally causes meningitis associated with iatrogenic or traumatic events. We herein describe a case of meningitis caused by this organism in a patient without any apparent risk factors. In an assay of the patient’s cerebrospinal fluid, cross-reaction occurred with Streptococcus pneumoniae antigen-coated latex particles in the Pastorex™ Meningitis Kit. In the in vitro assays, three of the five clinically isolated S. salivarius strains showed cross-reactions with the kit, indicating that these strains expressed pneumococcal antigen-like antigens. This case shows that meningitis caused by S. salivarius can occur spontaneously and it may sometimes be misdiagnosed as S. pneumoniae infection.

Key words: Streptococcus salivarius, pastorex meningitis kit, meningitis

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Introduction

Streptococcus salivarius, a member of the viridans streptococci family, is normally found in the human oral cavity and intestinal tract (1). This organism is considered to be less pathogenic than other viridans streptococci; however, invasive infections, including endocarditis, bloodstream infections in cancer patients and meningitis, have been repeatedly described (2-5). According to a recent classification, S. salivarius consists of two subspecies: S. salivarius subsp. salivarius and S. salivarius subsp. thermophilus; the latter has been identified only in dairy products (6).

Identifying S. salivarius using conventional assays is complicated due to its biochemical heterogeneity and phenotypic characteristics that are close to those of the Streptococcus bovis group (7, 8). In addition, some S. salivarius strains have antigens that are cross-reactive to the antisera used to differentiate Streptococcus species (9-11). Consequently, molecular approaches are used as an alternative to conventional phenotypic identification (12). We herein describe a case of spontaneous meningitis caused by S. salivarius subsp. salivarius. The recovered organism was indeterminable using conventional phenotypic methods and showed a positive reaction on a commercial rapid diagnostic kit for detecting Streptococcus pneumoniae antigens before ultimately being identified using molecular methods.

Case Report

A 78-year-old previously self-supported Japanese man was referred to an emergency department with rapid onset of impaired consciousness. He had been healthy until the morning of the day of admission, without any preceding symptoms. His daughter found him lying on his back unconscious in the evening. He had a significant medical history of dilated cardiomyopathy and atrial fibrillation and had taken aspirin, diuretics, enalapril, carvedilol and lansopra-

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zole for these conditions. He had no relevant medical family history.

On the initial evaluation, the patient was disoriented (Glasgow coma scale: E4V4M5) without paralysis, anisocoria or neck stiffness. His vital signs were as follows: body temperature: 36.1°C, blood pressure: 134/100 mmHg, pulse rate: 119 beats/min, respiratory rate: 28 breaths/min and percutaneous oxygen saturation on room air: 96%. Physical examinations of the head and trunk showed no remarkable findings, including erosion or bleeding in the oral cavity, cardiac murmurs, pulmonary rales or purpura on the patient’s skin. Blood tests revealed an elevated leukocyte count (13,400/μL) and mild elevation of the C-reactive protein level (1.2 mg/dL) (Fig. 1). Radiological studies, including chest X-ray and computed tomography and magnetic resonance imaging (MRI) of the head, did not detect any abnormalities, except for an old cerebellar infarction.

On day 2 of hospitalization, nuchal rigidity became apparent. A cerebrospinal fluid (CSF) examination revealed pleocytosis (737/μL, polymorphonuclear cells: 664/μL), an elevated protein concentration (398 mg/dL) and hypoglycorrhachia (<10 mg/dL). Gram stains of the CSF identified Gram-positive cocci in one field (Fig. 2), which were not observed in other fields. An assay of the CSF using the Pastorex™ Meningitis Kit (Bio-Rad Laboratories, Hercules, USA), a latex agglutination test used to identify organisms that commonly cause meningitis, demonstrated agglutination of S. pneumoniae antigen-coated particles. The morphological features were not typical of S. pneumoniae; however, we initially diagnosed the patient with S. pneumoniae meningitis based on the positive findings of the Pastorex™ Meningitis Kit. As a result of the patient’s impaired renal function (estimated creatinine clearance: 16 mL/min), the administration of ceftriaxone (4 g/day), ampicillin (8 g/day), vancomycin (1 g/day) and dexamethasone (10 mg/day) was initiated. A culture of the CSF showed pure growth of Gram-positive, catalase-negative cocci that formed α-hemolytic colonies on sheep blood agar. The organism was indeterminable using the api² 20 Strep (Sysmex-BioMérieux Japan, Tokyo, Japan) and WalkAway® 96SI (Siemens Healthcare Diagnostics, Tokyo, Japan) kits and was finally identified as S. salivarius subsp. salivarius via a homology search of partial sequences of the 16S rRNA gene (13) and sodA gene (14) using the Basic Local Alignment Search Tool. The same organism was also recovered from two sets of blood cultures obtained immediately before the antibiotics were given.

The minimum inhibitory concentration against the organism, measured according to the guidelines of the Japanese Society of Chemotherapy (15) using a Dry Plate (Eiken Chemical, Tokyo, Japan), was 0.06 μg/mL for penicillin G.
<0.25 μg/mL for ampicillin, <2 μg/mL for cefaclor, <0.12 μg/mL for cefotaxime, <0.12 μg/mL for cefepime, <0.12 μg/mL for meropenem, 0.06 μg/mL for erythromycin, 0.06 μg/mL for clindamycin, 2 μg/mL for levofloxacin, 0.5 μg/mL for tetracycline, 0.5/9.5 μg/mL for trimethoprim-sulfamethoxazole and 0.5 μg/mL for vancomycin. Therefore, the ampicillin and vancomycin were discontinued on day 8.

Other infectious sites were investigated using chest and abdominal computed tomography on day 2, transthoracic echocardiography on day 9 and spinal MRI on day 16; however, no other infectious sites were identified. The administration of ceftriaxone was continued until day 44, with dose reduction to 2 g/day after day 30. The patient’s mental status improved during the treatment; however, he continued to require assistance with dressing and bathing at discharge due to muscle weakness. The patient was transferred to another facility for rehabilitation on day 77, then readmitted on day 220 due to pneumonia. He died on day 252. At autopsy, no malignancies were macroscopically detected in the gastrointestinal and respiratory tracts.

To confirm the results of the assay with the Pastorex® Meningitis Kit, five S. salivarius subsp. salivarius strains were examined, including one strain recovered in the present case and four strains collected from the blood of other patients and identified using partial sequencing of the sodA gene (14). The organisms were inoculated into Bacto Brain Heart Infusion (Becton Dickinson, Sparks, USA) broth and cultured at 37°C overnight. Following centrifugation, portions of the supernatants were boiled for five minutes and assayed with the Pastorex® Meningitis Kit and BinaxNOW® Streptococcus pneumoniae Antigen Card (Alere Medical, Matsudo, Japan), a commercial rapid diagnostic kit for detecting S. pneumoniae C-polysaccharide antigens using immunochromatography. Three of the supernatants, including the one prepared with the strain recovered in the present case, were found to contain S. pneumonia antigen-like antigens using the Pastorex® Meningitis Kit. In contrast, these three supernatants gave negative results in the assays performed using the BinaxNOW® Streptococcus pneumoniae Antigen Card.

Discussion

A literature review showed that the majority of S. salivarius meningitis cases developed following iatrogenic or traumatic contamination of the CSF, while others were associated with possible translocation from the gastrointestinal tract (5). As far as we know, only two cases of S. salivarius meningitis occurring in Japan have been published. In these cases, the authors speculated that the causative organisms entered the CSF via bacteremic translocation due to trauma in the oral cavity (16) and the presence of a lesion of early gastric adenocarcinoma (17). In the present case, the patient exhibited neither findings suggesting direct contamination of the CSF with intraoral organisms nor the presence of malignancy in the gastrointestinal tract. We suspected the concurrent presence of infective endocarditis based on the findings of S. salivarius bacteremia (18); however, there were no apparent clinical manifestations, such as cardiac murmurs, cardiac valve vegetation or metastatic abscesses, that indicated infective endocarditis. Therefore, spontaneous S. salivarius meningitis was thought to have arisen without any preceding factors in this case.

Several rapid diagnostic kits for detecting S. pneumoniae antigens in clinical materials and cultured organisms are commercially available. These kits are generally thought to be highly sensitive and specific; however, cross-reactivity to other organisms, especially viridans streptococci, has also been described (11, 19-23). Regarding S. salivarius, to our knowledge, only one report has mentioned cross-reactivity in the assays of blood cultures using the SlideX Pneumo-Kit, which is based on latex agglutination (11). The present study shows that some, but not all, clinically isolated S. salivarius strains express S. pneumonia antigen-like antigens that are detectable in assays using the Pastorex® Meningitis Kit. The characteristics of the cross-reactive antigens remain unclear; however, the antigens may not be reactive with anti-C polysaccharide antisera due to negative reactions in the assays using the BinaxNOW® Streptococcus pneumoniae Antigen Card. Further studies of cross-reactive antigens may improve the specificity of rapid diagnostic kits for detecting S. pneumoniae antigens.

Bacterial meningitis is a serious disease that frequently results in undesirable outcomes. Therefore, precisely identifying the causative agent is important for treating patients and accumulating epidemiological knowledge. S. salivarius meningitis is usually associated with trauma and medical interventions; however, physicians should be aware that this organism can occasionally cause spontaneous meningitis and may be misdiagnosed as S. pneumoniae.

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

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References