CASE REPORT

An infantile late-onset case Group of B *Streptococcus* meningitis diagnosed with a rapid latex kit

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SUMMARY

Globally, vaccination has reduced the prevalence of meningitis caused by *Streptococcus pneumoniae Neisseria meningitidis*, and *Haemophilus influenzae*. However, neonatal Group B *Streptococcus* (GBS) meningitis continues to remain a problematic infection of the central nervous system. Here, we report a case of bacterial meningitis in a 34-day old male baby who presented with fever. A cerebrospinal fluid (CSF) test on the day of admission showed an increase in cell count with decreased glucose level. A rapid latex test of the CSF using a commercial kit diagnosed the causative pathogen as GBS. We administered the antibiotics ampicillin, cefotaxime, gentamicin and panipenem/betamipron to the patient for over 14 days. Partial seizures were frequently observed during the course and were well-controlled with midazolam and phenobarbital. Brain magnetic resonance imaging on day 17 showed subdural hygroma in the frontal region, and 99mTc ethyl-cysteinate dimer-single photon emission computed tomography confirmed a decreased cerebral blood flow predominantly in the left frontal region. After three years of follow-up, the condition of the patient improved without any neurological sequelae. Our report highlights that rapid identification of the causative organism is essential in infantile late-onset meningitis. In addition, we consider that the latex kit-based rapid testing of CSF is beneficial for identifying the causative agent of bacterial meningitis.

INTRODUCTION

Bacterial meningitis in children is one of the most serious central nervous system infections. With respect to neonatal meningitis particularly, prognosis remains poor and mortality rate is high.[1] Therefore, early diagnosis and timely and appropriate antibiotic treatment are important for neonatal meningitis. Cerebrospinal fluid (CSF) examination of newborns is troublesome for two major reasons: (1) small size of their body, and (2) difficulty collecting the fluid. Thus, alternatively a lumbar puncture is used to collect CSF and identify the causative bacterial agent.[2] Culture examination is time-consuming and requires a few days for analysis. In some cases, the causative bacteria cannot be identified by culture testing of fluids from the newborns.[2] Therefore, other methods need to be developed for identifying the causative agent of neonatal meningitis and start antibiotic treatment as early as possible. In this report, we present a late-onset case of neonatal *Streptococcus agalactiae* from Group B *Streptococcus*, (GBS) meningitis wherein the causative agent was identified using a commercial rapid latex kit.

CASE REPORT

A 34-day-old male infant was referred to the Dokkyo Medical University, Tochigi, Japan because of fever and poor feeding. The infant was born by vaginal delivery at 3,500 g at 41 weeks of gestation. He was the first child of his parents. His mother had a negative GBS test during the second trimester of pregnancy. A few days earlier, a one-month medical check-up revealed that the baby had no physical problems. However, the mother had been suffering from mastitis for 6 days.

At the time of admission, the level of consciousness of the baby was sluggish in response to pain stimuli, and he did not cry. Vital sign measurement showed tachypnoea of 70 times/minute; tachycardia of 200 beats/minute; and body temperature of 39.5℃. The anterior fontanelle appeared bulged, but the Kernig sign was negative. Finally, we suspected bacterial meningitis, and the infant was hospitalised after performing routine urine and blood biochemical tests with culture tests.

The blood test findings were as follows: WBC: 2,500/μL, haemoglobin: 11.1 g/dL, platelet: 280,000/mm3, aspartate aminotransferase: 39 U/L, alanine aminotransferase: 20 U/L, lactate dehydrogenase: 339 U/L, Na^+: 135 mEq/L, K^+: 4.2 mEq/L, Cl-: 104 mEq/L, glucose: 115 mg/dL, C-reactive protein: 0.90 mg/dL, IgG: 672 mg/dL, procalcitonin: 37.53 ng/mL, interleukin-2 receptor (IL-2R): 2139 U/mL. Notably, procalcitonin and IL-2R levels were prominently elevated. Brain computed tomography (CT) revealed no abnormalities. CSF from his lumbar puncture showed increased hydropressure and pleocytosis (70 polymorphonuclear cells/mm^3); reduced CSF glucose level (< 5 mg/dL); and increased CSF protein level (343 mg/dL). Due to the increased cell count, we performed a CSF latex kit test (Pastorex™ Meningitis, Bio-Rad Laboratories Co. Ltd., Japan) prior to CSF culture test, and the causative agent of bacterial meningitis was detected as GBS (Figure 1). We also performed a culture test of the vaginal sample of the mother and breast milk and breastfeeding stopped thereafter. Since the baby subsequently had frequent partial seizures, he was intravenously administrated midazolam and phenobarbital as an anti-convulsant. Due to his worsening respiratory status, oxygen administration and nasal directional positive airway pressure

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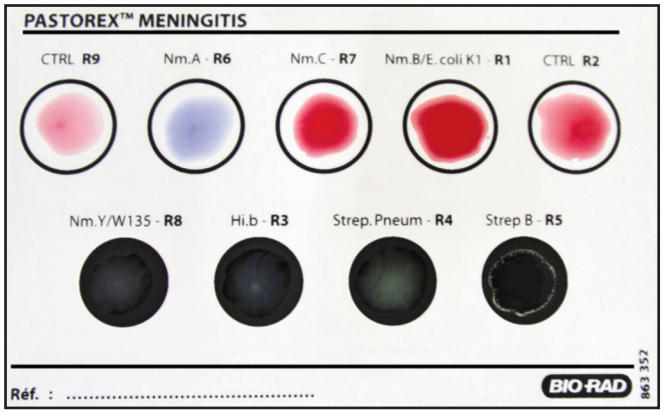

Fig. 1: Diagnosis of neonatal bacterial meningitis using cerebrospinal fluid (CSF) latex kit on admission. A circular latex agglutination reaction is observed on the black circle in the lower right. The causative bacterium is diagnosed as Group B Streptococcus (GBS).

were required. We started antibiotic treatment with 190 mg/kg/day ceftriaxone and 190 mg/kg/day ampicillin (ABPC) immediately. In addition, intravenous immunoglobulin (150 mg/kg/day) was administered for five days. Administration of vitamin K and treatment with disseminated intravascular coagulation were also initiated. On the third day, a second CSF puncture was performed wherein the cell count was found to have increased to 2,121 /mm^3. In addition, both blood and CSF culture tests at admission revealed GBS serotype III. Following this, antibiotic treatment was de-escalated to ABPC, and 5 mg/kg/day gentamicin was added in anticipation of a synergistic effect. On the fourth day, tracheal intubation was started because apnoeic attacks were frequent and the level of consciousness was unstable. Brain CT showed bilateral enlargement of the subdural space and we considered progress of subdural hygroma or subdural abscess. On the fifth day, administration of 100 mg/kg/day panipenem/betamipron (PAPM/BP) was commenced because the CRP levels continued to rise. The second CSF culture was negative on the sixth day of hospitalisation. In addition, the consciousness level of the baby improved. We performed a third CSF puncture; the cell count then decreased to 668/mm^3. Notably, the same serotype (GBS III) was detected in the vaginal culture of the mother. Additionally, another GBS serotype 7271 (GBS VII) was detected in her breast milk culture. Consequently, PAPM/BP treatment was continued for the next 14 days, and the baby's general condition improved.

Brain magnetic resonance imaging (MRI) performed on day 17 demonstrated progressed subdural abscess (Figure 2A), and ^{99m}Tc ethyl-cysteinate dimer-single photon emission CT (ECD-SPECT) showed a considerable decrease in the cerebral blood flow from the left frontal region to the temporal region (Figure 2B). The baby underwent a hearing examination on day 30, and the results were normal. The baby was discharged on the day 32 after admission. Subsequently, the clinical course of the baby was observed in an out-patient department.

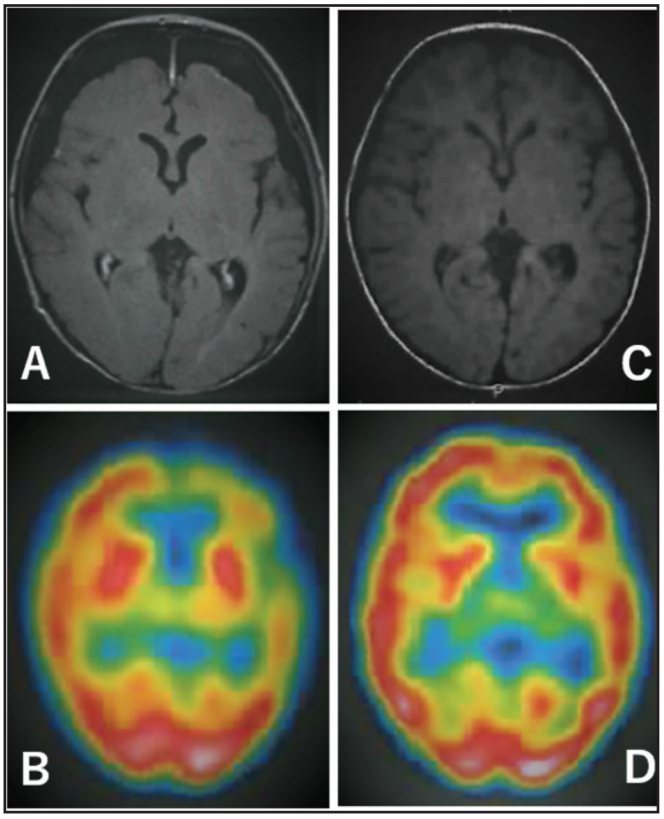

Fig. 2: Magnetic resonance imaging (MRI) and 99mTc ethyl-cysteinate dimer-single photon emission computed tomography (ECD-SPECT) A: Fluid-attenuated inversion recovery brain axial MRI showing subdural abscess of the patient at day 17 of hospitalisation. B: ECD-SPECT showing an area of hypoperfusion that is observed predominantly in the left frontal to temporal region of the patient at day 17 of hospitalisation. C: Brain axial T1-weighted MRI showing improvement of frontal subdural abscess at 3 years of age. D: ECD-SPECT showing improvement in cerebral blood flow at 3 years of age.

At three years of age, the brain MRI of the child showed improvement in the frontal subdural space enlarged with abscess (Figure 2C). ^{99m}Tc ECD-SPECT also showed an improvement in the decreased cerebral blood flow from the left frontal to the temporal region (Figure 2D). No obvious neurological sequelae, such as epilepsy or developmental delay, were observed, and after informed consent with parents, we ended his out-patient follow-up.

DISCUSSION

Bacterial meningitis is one of the most serious bacterial infections. It is characterised by several neurological sequelae and high mortality.[1,3] Worldwide, vaccines have remarkably reduced the incidence of bacterial meningitis caused by S. pneumoniae, H. influenzae, and N. meningitidis. GBS-mediated neonatal bacterial meningitis remains a major health concern not only in developing but also developed countries. GBS disease is classified as early-onset and late-onset if the onset age is 0-6 and 7-89 days after birth, respectively. In Japan, more than 20% of normal pregnant women are GBS-carriers.[4] Therefore, pregnant women

undergo GBS culture tests once or twice during pregnancy and those found GBS-positive are administered ABPC as the delivery progresses. However, the prevalence of late-onset GBS meningitis that develops in week-old newborns is increasing in Japan, and remains an important problem for effective infectious disease control.[5]

It is essential to identify the causative organism when diagnosing bacterial meningitis in newborns via CSF test and eventually start early antibiotic administration. Owing to a few major reasons, CSF testing in newborns is difficult, and in some cases, the causative bacteria cannot be identified by CSF culture testing.[2,3] Therefore, we strongly consider that the blood culture and baby and vaginal smear of the mother, and breast milk culture tests should be conducted along with the CSF culture test of the baby.

CSF and blood culture tests are time-consuming; therefore, alternative methods for identifying the causative bacteria are important. Our case also diagnosed GBS early timing with a latex meningitis kit and we started treatment with ABPC and CTX. However, the patient later developed a subdural abscess. Therefore, we treated patient with PAPM/BP, which has CSF transferability. Taking advantage of the early diagnosis, it may have been possible to prevent the aggravation if higher dose antibiotic treatment was performed from the time of admission. In recent years, polymerase chain reaction (PCR) has been reported to rapidly identify the causative agent of bacterial meningitis, wherein this method overcomes the time-consuming limitation of CSF culture test.[6] However, PCR testing of CSF is not economical, requires technical expertise, and is still not performed extensively across diagnostic laboratories. In this regard, the latex kit used in this report requires less than only a half hour and the diagnosis can be performed the absence of high-end facilities. In a Latex test using specimens of bacteria confirmed by conventional culture identification methods and this product is 100% accurate. However, there is a limitation depending on the condition of the clinically collected specimens. Therefore, bacterial culture remains the gold standard for confirmation of diagnosis. In any event, this kit is a simple, cost-effective, and useful tool for diagnosing bacterial meningitis in suspected/affected individuals of all ages.[7]

CONCLUSIONS

For neonatal bacterial meningitis, it is important to identify the causative organism at an early stage and thereby initiate suitable antibiotic treatment. The rapid latex kit is a useful method for the early identification and selection of antibiotics for subsequent treatment in case of suspected cases of bacterial meningitis.

COMPLIANCE WITH ETHICAL STANDERD AND INSTITUTIONAL APPROVAL

This report was performed with the approval of the Ethical Committee of the Department of Pediatrics, Dokkyo Medical University, Japan.

CONFLICT OF INTEREST

The authors have no conflict of interests concerning in the present study or findings presented in this study.

INFORMED AND CONSENT

Informed consent for publishing this case report was obtained from the patient's parents.

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