Korean Journal of Pediatrics Vol. 50, No. 7, 2007

□ Case Report □

Two cases of *Chryseobacterium meningosepticum* infection in a neonatal intensive care unit

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We report on two premature infants who developed nosocomial infection caused by *Chryseobacterium meningosepticum* in a neonatal intensive care unit (NICU). One premature infant developed sepsis, meningitis, and hydrocephalus, and was treated successfully with ciprofloxacin plus trimethoprim-sulfamethoxazole combination therapy for 4 weeks and with a ventriculoperitoneal shunt. The other premature infant, who was in a chronically debilitated state, had infection that had colonized only in the respiratory tract but had no clinical signs for 66 days. Extensive environmental surveillance demonstrated that the suction bottle apparatus was the source of infection. We prevented the spread of infection by closing the NICU temporarily, isolating the patients early in their infection, and eradicating the source of infection source. **(Korean J Pediatr 2007;50:698-701)**

Key Words : *Chryseobacterium meningosepticum*, Ciprofloxacin, Neonatal intensive care unit

Introduction

Chryseobacterium meningosepticum (formerly known as *Flavobacterium meningosepticum*) is a nonglucose-fermenting, nonmotile, catalase and oxidase-positive, aerobic, Gram-negative bacillus found typically in plants, soil, and water sources, including the hospital environment[1]. Premature infants and immune-compromised adults are susceptible to *C. meningosepticum*, and this microorganism is sometimes responsible for epidemic sepsis and meningitis in newborn infants in hospital nurseries[2].

In this report, we describe two patients who developed *C. meningosepticum* infection: one premature infant with *C. meningosepticum*-induced sepsis, meningitis, and hydrocephalus who was treated with combination therapy of ciprofloxacin and trimethoprim-sulfamethoxazole and a ventriculoperitoneal shunt, and one colonized patient with no symptoms. We also discuss the epidemiological features of this infection and the methods to prevent its spreading.

접수 : 2007년 5월 31일, 승인 : 2007년 6월 22일
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Case Report

Patient 1

The patient was born by vaginal delivery weighing 1,860 g after 32 weeks of gestation because of prolonged rupture of membrane (PROM) for 63 hours and preterm labor. He exhibited frequent apnea on day 2, and was treated with aminophylline and nasal continuous positive airway pressure for 3 days and oxygen therapy for the next 4 days. Initially, he was treated with prophylactic ampicillin and gentamicin for 3 days because of PROM. His initial infection parameters were within normal limits and the blood culture was negative. On day 11, frequent apnea and hypoactivity developed suddenly, we suspected for a possible nosocomial infection, thus samples were obtained for routine cultures, and empirical antibiotics were started, including vancomycin and amikacin. Laboratory investigation revealed thrombocytopenia (114,000/mm^3), and C-reactive protein (CRP) concentration of 13.0 mg/dL. On day 13, his respiratory status worsened, and he was intubated. Amikacin was changed to meropenem because of his rapidly worsening disease course and identification of Gram-negative bacilli in the Gram staining of blood. A lumbar puncture revealed bacterial meningitis findings including WBC 11,200/μL, RBC 310/μL, polymorphonuclear

cells 97%, glucose 4 mg/dL, and protein concentration 1,812.5 mg/dL. On day 14, he developed frequent subtle type seizures and was started on an phenobartital. Despite the altered antibiotics, the CRP concentration increased to 18.6 mg/dL and multidrug-resistant, ciprofloxacin-susceptible *C. meningosepticum* was isolated in a blood culture on day 16. We changed meropenem to ciprofloxacin and trimethoprim-sulfamethoxazole based on the antimicrobial sensitivity results and supplemented this with intravenous immunoglobulin (400 mg/kg/day) for 5 days. Cerebrospinal fluid (CSF) culture also grew *C. meningosepticum*. On day 18, his ventricle dilated rapidly after the initial meningitis and developed hydrocephalus (Fig 1). The patients clinical and laboratory findings improved after the change to ciprofloxacin and trimethoprim-sulfamethoxazole. He was treated with this therapy for a total of 4 weeks and performed external ventricle drainage to relieve the CSF pressure 3 times and was discharged on day 82. He required an operation to insert a ventriculoperitoneal shunt on day 93. Follow-up examinations to the age of 15 months by corrected age show normal growth parameters for his age and appropriate neuromotor development.

Patient 2

The patient was born weighing 2,050 g by emergency cesarean section in the 34th week of gestation because her mother had eclampsia and suddenly developed cardiac arrest. Immediately after birth, the infant received neonatal resuscitation and she was treated for severe hypoxic ischemic encephalopathy. On day 65, she was still receiving mechanical ventilation and was diagnosed with stage 3 hypoxic ischemic encephalopathy and recurrent aspiration pneumonia. At this time, the first appearance of *C. meningosepticum* infection (patient 1) was confirmed in the neonatal intensive care unit (NICU). The patient was tested for *C. meningosepticum* infection. Laboratory investigation revealed no signs of infection and no growth in the blood or CSF, but *C. meningosepticum* was isolated in tracheal aspirate samples and the nose and throat swabs. We performed periodical cultures of the tracheal aspirate samples and nose, and throat swabs, and we confirmed that she was colonized for up to 66 days after recognition of the first colonization. During the period of colonization, she showed no clinical signs of infection and her CRP concentration remained low. She was until now admitted to hospital and was tested periodically for colonization about *C. meningosepticum*. However, after applying infection-control measures, culture studies of her tracheal secretions and throat and nasal swabs have found no trace of organisms.

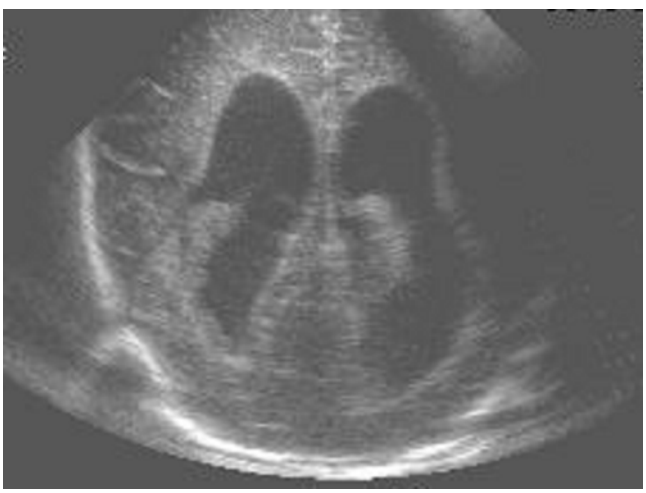

Fig. 1. Brain ultrasonography on 18th hospital day shows dilation of ventricle (patient 1).

Discussion

C. meningosepticum is a ubiquitous, water-borne saprophytic bacteria. Intermittent epidemics in NICUs have been reported[3], the exact source of the infection in the NICU was not elucidated in most epidemics, environmental studies show that this organism can survive in chlorine-treated water, often colonizing sink basins and taps, and creating potential reservoirs for infections inside hospital environments[4]. Most sources are derived from water-containing materials and water[5]. In our patients, the first sepsis and meningitis case of *C. meningosepticum* was identified in our NICU. At this time, we started examining blood cultures, CSF cultures, tracheal secretions, and nasal and throat cultures for all 14 neonates in the NICU and 9 neonates in the newborn nursery. We also performed environmental surveillance evaluations of the NICU and newborn nursery including several samples and swabs. Nasal, throat, and hand swabs were taken from all neonatal staff and nurses. *C. meningosepticum* was isolated from water inside suction bottles and suction bottle caps. We identified that the origin of infection was a suspicious biofilm on the suction bottle caps were made of steel. These suction bottles were reused without disinfection and had been washed with sterile water only. We believe that the humid conditions inside the suction bottle provided an environment that allowed the organism to

propagate. Thus, we changed all suction bottles to plastic. And the NICU was closed to further admissions and was disinfected using hypochlorous acid with special emphasis on objects containing or in contact with water. Patient and carrier were isolated, and the remaining uninfected newborns were moved to other wards. After initiating these control measures, no other cases have been identified.

C. meningosepticum infects mainly newborns and immune-compromised hosts. Prematurity is a primary risk factor in neonates, and half of infections involving neonates are in babies weighing less than 2,500 g at birth[6]. In neonates, meningitis is the most common form of infection, has a mortality rate of up to 57%, and may produce severe postinfection sequelae including hydrocephalus, deafness, and developmental delay[4]. Our patient also developed meningitis, which progressed rapidly to hydrocephalus. In neonatal patients with *C. meningosepticum* infection, the clinician should first consider the risk of meningitis and neurological sequelae.

Historically, *C. meningosepticum* has unusual antibiotic sensitivity patterns. *C. meningosepticum* may exhibit resistance to aminoglycosides, tetracyclines, chloramphenicol, erythromycin, clindamycin, teicoplanin, and cabapenem, but may exhibit variable sensitivity to trimethoprimsulfamethoxazole and doxycycline. *C. meningosepticum* is usually sensitive to rifampin in vitro and this drug is used for combination therapy. In the past, vancomycin alone or in combination with rifampin has been successful in treating meningitis in infants[7]. However, many studies have shown that vancomycin has marginal in vitro activity, so the effectiveness of vancomycin against *C. meningosepticum* infections has been questioned recently[6, 8]. Evaluation of a worldwide collection of unique Chryseobacterium strains indicates that vancomycin and other anti-Gram-positive antimicrobial agents may not represent satisfactory therapeutic options and that the newer quinolones (garenoxacin, gatifloxacin, and levofloxacin) may represent the most appropriate antimicrobial agents to treat infections caused by this pathogen[4]. Chryseobacterium shows intermediate or high susceptibility to ciprofloxacin[2]. In our patient, the most effective antibiotics were ciprofloxacin and trimethoprim-sulfamethoxazole. Although quinolone antibiotics are not yet accepted as safe for children because of the risk of joint cartilage damage, no documented arthropathy in humans has been published so far[9] and some have treated newborns successfully with ciprofloxacin without complications[10, 11]. Thus, we treated our patient with ciprofloxacin and trimethoprim-sulfamethoxazole combination therapy and have observed no side effects.

In conclusion, physicians should consider the possibility of *C. meningosepticum* infection in newborns with meningitis when Gram-negative rods are detected on Gram stain. It is important to take early precautions in colonized uninfected patients to prevent transmission, to initiate early epidemiological control measures, and to begin early treatment with appropriate antibiotics, which should be chosen based on the antibiotic susceptibility results.

한 글 요 약

신생아 중환자실에서 발생한 *Chryseobacterium meningosepticum* 감염 2례

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윤 혜 선

*Cryseobacterium meningosepticum*은 흙, 병원, 수돗물을 포함한 물이 있는 환경에서 발견되는 그람 음성 막대균으로, 미숙아, 노인과 같이 면역성이 결여된 인체에 기회감염을 일으키고, 미숙아에서는 패혈증, 뇌수막염과 같은 중증 질환을 유발하여 사망률과 합병증 발생이 높다. 특히, 균주가 병원내 배수관, 기계장비등을 통해 오염되어 신생아실에서 폭발적 유행이 가능하다. 저자들은 미숙아에서 발생한 다항생제 내성 *C. meningosepticum*에 의한 패혈증, 뇌수막염을 ciprofloxacin으로 치료한 1례와 동기간에 무증상 보균상태를 보였던 1례와 성공적인 환경검사와 조절에 대해서 보고하는 바이다.

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