CASE REPORT

Flavobacterium menigosepticum Colonization in Pediatric Intensive Care Unit

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ABSTRACT During a period of one month 2 infants was infected by Flavobacterium meningosepticum. The ages of the patients were 3 days and 5 months. The organisms were resistant to many antibiotics. The pathogens were isolated from the bronchial secretion and considered a nosocomial infection. The primary source of infection could not be identified. We suspect that the humidifiers or ventilators are the source of infections. **[Paediatr Indones 1999; 39:287-292]**

Introduction

Members of genus Flavobacterium are uncommonly associated with human infection. Beyond the newborn period Flavobacteria are extremely rare pathogens. In 1944 Schulmann et al.[1] reported a case of meningitis due to a previously unidentified gram-negative bacillus isolated from a 9 day-old premature infant. The term Flavobacterium menigosepticum was proposed by King[2] in 1959 for this organism, based on her studies of bacterial isolates primarily associated with neonatal meningitis and septicemia.

Flavobacteria are distributed widely as saprophytes in fresh and salt water. In hospitals, flavobacteria have been found to be ubiquitous colonizers of the patient's environment and have been isolated from flower vases,[3] ice machines,[4] vials of intravenous drugs,[5] tap waters,[6] eye washes,[7] tube feedings,[6] sinktraps[8] and hand-cultures of hospital personnel.[6] By 1976, 82 cases of neonatal infection due to Flavobacterium

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meningosepticum were reported in the literature,[9] and many of these were associated with nursery epidemics. Infants who are premature and small for gestational age seem to be at particular risk. Greeter than 50 per cent of infected infants weigh less than 2500 g. almost all cases occur within 3 weeks of life, with 50 per cent manifesting illness prior to 7 days of age.[10] Our case was a 3 days and a 5 months old baby who was infected during pediatric intensive care admission on December 1998.

Report of the Cases

Case 1

A 2 day-old neonate, 32 weeks gestation, weight 2200 grams, born by Caesarian section with Apgar Score of 7/9, was admitted to Pediatric Intensive Care Unit Mitra Keluarga Hospital, Jatinegara, Jakarta, in 16 December 1998, with diagnosis of Grade III Hyaline Membrane Disease. The baby was ventilated since he was admitted. No sign of meningitis or other intracranial process was present. Normal perfusion was achieved after fluid resuscitation and ventilator support was adequate. Complete blood count revealed hemoglobin 15.6 g/dL, hematocrit 45 vol%, platelet count 173 /m_L, white blood cells count was 14,500 /m_L with differentiation as follow granulocyte 63 % , lymphocyte 29 %, monocyte 6 % and basophyl 2 %. Blood glucose was 91 mg/dL at admission. Enteral nutrition was started early with breast milk, after perfusion was adequate. Nutritional requirement was already fulfil by enteral nutrition 2 days after the baby was admitted. The baby had been treated with cefotaxime since he was in the neonatal ward. Since a nosocomial pneumonia was suspected, bronchial secretion was cultured 5 days after admission and reveal Flavobacterium meningosepticum and staphylococcus epidermidis with sensitivity pattern as follow: Flavobacterium meningosepticum was only highly sensitive to ciprofloxacin; intermediate sensitive to amoxicillin in combination with calvulanic acid, cefotaxime, ceftriaxone and cotrimoxazole resistent to amikacin, amoxicillin, ceftazidime, cefepime, cephalexin, gentamicin, meropenem and ticarcillin. Staphylococcus epidermidis was sensitive to cefepime, ciprofloxacin, cloxacillin, meropenem and vancomycin; intermediate sensitive to cefotaxime and cotrimoxazole; resistent to ampicillin and penicillin G. Weaning of ventilator were successfully done at the day 8 and the baby was transferred back to the perinatology ward at the day 10. No sign of meningitis were ever found.

Case 2

A five months old boy, weight 5200 g, was referred to Pediatric Intensive Care Unit Mitra keluarga Hospital, Jatinegara, Jakarta, on December 18, 1998, with the diagnosis of bronchopneumonia, multiple organ system failure, delayed development with brain

atrophy and myoclonic epilepsy. The patient had a history of severe asphyxia and had been hospitalized for almost all his live in the hospital that referred this case. On admission his Glasgow Comma Scale was 8. Nuchal rigidity was not present, nor Kernig and Brudzinsky sign. The anterior fontanel was flat. White blood cells count on cerebrospinal fluid was normal. The baby was in a severe respiratory distress. Rales were found in both lungs. Blood saturation was less than 80 % on pulse oxymeter. His chest x-ray revealed infiltrates in both lungs with atelectasis at the right upper lobe. The baby look cyanosis but the pulse was still palpable with the rate of 170 /minutes. Complete blood count revealed hemoglobin content 12.3 g/dL, white blood cells 13.000/μL and platelets counts 179.000/μL. He was then supported with ventilator for 19 days, until January 5, 1999. The patient had been given Cefotaxime for several days in the previous hospital. Microbial study on blood sample, drawn on admission reveal no organism was found.

Bronchial secretion culture revealed *Pseudomonas aeruginosa*, which was sensitive to amikacin, ceftazidime, cefepime, ciprofloxacin, gentamicin, meropenem and ticarcillin, intermediate sensitive to cefotaxime and ceftriaxone and resistant to amoxicillin, amoxicillin and clavulanic acid, cephalexin and cotrimoxazole; and *Acinetobater anitratus* which was sensitive to amikacin, amoxicillin, ceftazidime, cefepime, ciprofloxacin, cotrimoxazole, gentamycin, meropenem and ticarcillin, intermediate sensitive to amoxicillin and clavulanic acid cefotaxime and ceftriaxone, and resistant to cephalexin.

The second microbial study of the bronchial secretion was done on January 2, 1999 revealed Flavobacterium meningosepticum which resistant to amoxicillin, ceftazidime, cefepime, cephalexin, gentamycin, meropenem, and ticarcillin, intermediate sensitive to amikacin, amoxicillin and clavulanic acid, cefotaxime, ceftroiaxone, and cotrimoxazole, and sensitive to ciprofloxacin, erythromycin and vancomycin. Trimetoprim-Sulfametoxazole in combination with vancomycin was given for 14 days. Throat swab on January 21, 1999 reveal no Flavobacteria. This patient was discharge from the hospital on January 27, 1999. A few weeks later he was readmitted because of gastroenteritis and shock. No sign of sepsis or meningitis was found. Environmental sampling on December 1998 reveals bacterial profile as can be seen in Table 1.

From the hospital microbiology data, there was one adult patient who suffers from Flavobacterium menigosepticum infection one-year prior these cases. The case was an accident victim who was admitted to the Adult Intensive Care Unit, which is located in another floor of the hospital. These were the only cases that ever recorded in this hospital for the last 10 years.

Discussion

Flavobacteria are catalase positive gram negative rods organism with slightly swollen ends. They are nonmotile, oxidase positive, weakly fermentative, proteolytic and grow

on solid agar as 1-mm yellow-pigmented convex, glistening colonies of buttery consistency.[2] Flavobacteria are generally of low virulence. Rabbits administered 1-ml intravenous injections of 24 hour old broth cultures demonstrated no mortality or morbidity. Less than 30 percent mortality was found in mice inoculated with this organism intracerebrally.[2] The propensity for this organism to produce meningitis in the newborn is not understood, but infection may occur in association with heavy nasopharyngeal colonization leading to subsequent bacteremia and seeding of meninges. In older individuals, flavobacteria primarily play the role of opportunists.[11] Heavy nosocomial colonization combined with a blunted immune response probably accounts for the immunocompromised patient's poor capacity to handle these bacteria.

Heeg, Heizmann and Mentzel reported 7 neonates who were infected by Flavobacterium meningosepticum in a neonatal intensive care unit within three and a half months.[12] The patogens were isolated from the tracheal secretions, throat swabs, gastric juice and nose swabs.[12] Environmental sampling led to the isolation of Flavobacterium menigosepticum from the humidification fluid of the respirator, from vaporizers as well as from the artificial ventilation tubing.[12] In both of our cases here, Flavobacterium meningosepticum was isolated from bronchial secretion. Both patients had been intubated and supported by ventilators for several days. Even the environmental sampling did not found Flavobacteria in the patient's environment; we are still suspicious that the humidifiers or ventilators are the reservoirs.

Flavobacteria in our cases were only isolated from the bronchial secretion. Flavobacteria bacteremia had never been proven. However the development of meningitis should be monitored closely since the onset might be insidious due to the low virulence of the organism. Prognosis of *Flavobacterium meningosepticum* meningitis is extremely poor and the mortality rates are in excess of 60%.[13] Fifty per cent of survivors develop significant neurologic complications, often associated with hydrocephalus.[14]

Rapid identification of Flavobacterium infection is urgent, not only to ensure proper treatment but also to hasten appropriate infection control to prevent epidemic outbreaks. Identification of *Flavobacterium meningosepticum* is hindered by characteristically long periods required for oxidation of carbohydrates and weak or delayed indole production. Cultures may be misidentified as species of Alcaligenes or Pseudomonas.[10] Clinical isolation of an unidentified gram-negative rod that is catalase and oxidase positive and that shows multiple antibiotic resistance should raise suspicion of Flavobacterium meningosepticum infection. Cultures should be kept for several days for observation for typical carbohydrate reactions, which confirm the diagnosis.[10,15]

Recommended empiric anti-microbial treatment of gram negative infection usually resistant for Flavobacterium meningosepticum. Moreover, anti-microbial sensitivities determined by disc diffusion must be interpreted with caution. Aber found clinical isolates in which specific stains were sensitive by disc diffusion to gentamicin and rifampin but were resistant by agar gel dilution sensitivities.[16] Therefore, more direct

Table 1. Environmental sampling data, December 1998

Hospital kitchen		Pediatric intensive care ward	
Pan	*Acinetobacter anitratus*	Suction catheter	*Pseudomonas aeruginosa*
Spoon	*Staphylococcus epidermidis*	Drinking water tank	*Microphillic organism*
Wok	*Bacillus sp., Klebsiella pneumoniae*	Water humidifier	*Psudomonas sp Bacillus sp*
Rice steamer	*Bacillus sp.*	Suction rinse solution	*Acinetobacter anitratus*
Knife	*Bacillus sp, Enterobacter cloacae Acinetobacter anitratus*	Sterilized reuse suction catheter	Sterile
Cutting board	*Bacillus sp, Klebsiella pneumoniae*	Suction catheter used by the patient	*Pseudomonas sp Flavobact. meningospticum*
Wash basin	*Pseudomonas aeruginosa*	Water tap	Sterile
Bowl	*Sterile*	Drinking water dispenser	*Acinteobacter anitratus*
Strainer	*Acinetobacter anitratus, Bacillus sp.*	Used rubber milk pacifier	*Microphillic organism*
Plate	*Acinetobacter anitratus, Bacillus sp.*	Sterilized rubber milk pacifier	Sterile
		Bottle sterilizing container	Sterile

methods of measuring the minimal inhibitory concentration (MIC) than disc diffusion sensitivity should be used in determining the optimal microbial agents for therapy. Drugs that have been used alone or in combination with some success included erythromycin, vancomycin, co-methoxazole, and rifampin. In case of Flavobacterium meningosepticum meningitis, penetration of drug to the inflamed meninges should be considered. Intraventricular erythromycin,[9,17] or rifampin[9,13,14,18] has been used in conduction with systemic administration of these drugs. Significant mortality and morbidity often occur in immunocompromised individuals with bacteremia or meningitis. Cloramphenicol, vancomycin, ciprofloxacin or erythromycin have shown some success in these individuals. Chang et al. reported 106 isolates of flavobacteria, including 41 isolates of *Flavobacterium meningosepticum* and found that more than 90% of flavobacteria isolates were resistant to cephalothin, cefotaxime, ceftriaxone, moxalactam, aztreonam, imipenem, aminoglycosides, erythro- mycin and glycopeptides.[19] The majority of flavobacterium meningosepticum isolates were susceptible to piperacillin and to minocycline, but resistant to ceftazidime.[19] It is very rational to use antibiotic based on detailed examination of organism sensitivity, but the delay in specific identification due to the technical difficulties could lead to prolonged periods of suboptimal therapy.

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