KAWASAKI MED. J. VOL. 16 : NO. 1, 71-74 (1990)

Brief note

Bacteremia of Clostridium Difficile and Clostridium Perfrigens with Transient Eosinophilia in a Premature Infant

Accepted for publication on May 28, 1990

Key words : bacteremia — Clostridium difficile — Clostridium perfrigens — eosinophilia — premature baby

We report on a very low birth-weight infant in the course of resolution of pneumonia, with fever, rash and abdominal distention. She showed polymicrobial bacteremia of C. difficile and C. perfrigens, and simultaneously presented with transient eosinophilia. Simultaneous occurrence of these bacteremia and such eosinophilia have not been reported previously.

CASE REPORT

The patient was a 56-day-old female with rash, fever and abdominal distention but no diarrhea, from whom a blood culture presenting bacteremia of C. difficile and C. perfrigens was obtained.

She was born by vaginal delivery in a local hospital at 27 weeks of gestational age, weighing 1050 g, at Apgar score 8 in a minute, and was immediately transferred to our intensive care unit. On admission only a small amount of meconium was excreted. On the next day, because of abdominal distention, a gastrographin enema examination was performed under fluoroscopy to exclude atresia and malrotation. There were no abnormal findings other than worm-like meconium excreted after the enema. Nasal continuous positive airway pressure was applied for apnea during the first two weeks. Phototherapy for hyperbilirubinemia was also started. On the 10th day, fever developed, and pneumonia was confirmed by a radiograph of her chest. Cutaneous PO_2, however, did not reveal hypoxia. The infiltration subsided after intravenous administration of cefazolin sodium and tobracin, but the pathogen was not identified. In the course of resolution of the pneumonia, pneumatoceles were recognized at the same location. These disappeared gradually after the infant's recovery.

Suddenly on the 56th day, irritability, a fever of 38.0°C and the development of an erythematous maculopapular rash, mainly on her face and trunk, were noted. Because abdominal distention was still present, less than 100 ml/kg of weight/day of banked breast milk could be infused through a nasogastric tube. There was neither diarrhea, bloody stools, bilious vomiting, nor increased abdominal perstalsis. A radiograph of her chest and abdomen disclosed no abnormalities such as pneumatosis intestinalis or intrahepatic venous gas. A blood culture was obtained and the following day anaerobic gram positive baccilli grew. This was later confirmed to be toxigenic C. difficile (This identification was done at the Anaerobe Institute, University of Gifu), and C.

寺田喜平，河野祥二，片岡直樹，守田哲朗

TABLE 1. Laboratory data on admission

WBC	4300	GOT	13 IU/l
N. band	3%	GPT	8 IU/l
N. seg	6%	IgG	145 mg/dl
Eosino	21%	IgA	24 mg/dl
Mono	2%	IgM	36 mg/dl
Lymph	68%		
RBC	301×10^4		
Hb	9.4 g/dl		
Ht	27.6%	A culture of the nasogastric tube	
CRP	2+	Klebsiella sp.	
CSF		Str. faecalis	
Cell	15/3	A culture of venous blood	
glucose	40 mg/dl	C. perfrigens	
protein	60 mg/dl	C. difficile	
culture	(−)		

perfrigens. A culture from the nasogastric tube revealed only the Klebsiella species and Streptococcus faecalis. Her white blood count (WBC) was 4300, with 6% polymorphonuclear cells, 3% band forms, 21% eosinophils, 2% monocytes, and 68% lymphocytes. A lumbar puncture yielded normal cerebrospinal fluid.

She was soon started on cefotaxime and amikacin intravenously, and her fever and rash resolved over the ensuing 24 hours without exacerbating abdominal distention and diarrhea. The sensitivity of C. perfrigens and C. difficile against cefotaxime was 3+ and 0, respectively, and that of both against amikacin was 0 and 2+. After the fourth day of her illness, a C-reactive protein aggregation test came up negative. On the seventh day, her WBC was 5200, with 10% polymorphonuclear cells, 2% band forms, 3% eosinophils, 3% basophils, 8% monocytes, and 74% lymphocytes as normal differential counts of the WBC. Eosinophilia was not observed before or after this date. After her recovery from the bacteremia, her abdominal distension decreased to the extent that the quantity of infused milk could be increased. She was discharged when she was 118 days-old and has been growing normally since then.

COMMENT

Chow[1] disclosed that the incidence of anaerobic bacteremia in neonates was 1.8 cases per 1000 live births, and 26% of these had bacteremia. A death rate of 4% was recognized in Chow's series but an overall mortality of 26% among newborn infants with anaerobic bacteremia has been reported in the literature. Klein[2] showed that the anaerobia identified from the blood of neonates were Bacteroides 46%, Peptococcus or Peptostreptococcus 46%, Clostridium 6% and Veillonella 1.5%. The number of bacteremias or septicemias due to anaerobia is small, but one of these is Clostridium. In addition, anaerobia have a tendency to bring about polymicrobial bacteremia. Two anaerobia were recognized in this case.

C. difficile is one of the normal intestinal flora in neonates and is isolated from the stools of 50 to 60 percent of newborns.[3] However, its toxins are rarely detected in the stools of healthy infants.[4] The role of C. difficile in antimicrobial associated pseudomembranous colitis has been well established in adults,[5] and has been implicated as a cause of NEC in neonates, but its mechanism is not clearly understood. Necrotizing enterocolitis (NEC) in neonates is associated with two distinct events[6]: i.e. hypoxic injury to the intestine and bacterial invasion of the necrotic bowel wall, which explains the epidemic nature[7] and sepsis-like early symptoms of this condition. Her symptoms may be considered to be a sepsis-like early non-specific signs of NEC. Fortunately, the early administration of effective antibiotics may prevent the progression of subclinical NEC into clinical NEC. The long term abdominal distension could be associated with the possibility that C. difficile and C. perfrigens became predominant in her intestinal flora after usage of antibiotics for the pneumonia. This was suggested by improvement of the abdominal distension soon after treatment for the bacteremia.

Bacteremia or septicemia of C. difficile is very rare, there having been only one report[8] of this bacteremia in pediatric patients with NEC. There have, however, been some reports of other anaerobic bacteremia, such as C. perfrigens[9] and C. butyricum,[10] being isolated from the blood and/or the peritoneal fluid of patients with NEC.

This patient showed transient eosinophilia of 21% and neutropenia of 9% at the time of the bacteremia. During the newborn period, peripheral eosinophil counts are low.[11] The normal upper limit during childhood is regarded as 5%. Although the most common causes of eosinophilia are allergy, parasitic infection and collagen disease, there has been no report of eosinophilia associated with NEC or bacteremia of the clostridium species. Further observations are therefore needed.

Kihei TERADA, Shoji KAWANO*, Naoki KATAOKA and Tetsuro MORITA

Department of Pediatrics, Kawasaki Medical School, Kurashiki 701-01, Japan
**Department of Pediatrics, Ibara Municipal Hospital, Ibara 715, Japan*

REFERENCES

1) Chow, A.W., Leake, R.D., Yamauchi, T., Anthony, B.F. and Guze, L.B.: The significance of anaerobes in neonatal bacteremia: Analysis of 23 cases and review of the literature. Pediatrics **54** : 736-740, 1974
2) Klein J.O.: Infectious diseases of the fetus and newborn infant. W.B. Saunders. 1976, p.754
3) Welch, D.F. and Marks, M.I.: Is clostridium difficile pathogenic in infants? J. Pediatr. **100** : 393-395, 1982
4) Donta, S.T. and Myers, M.G.: Clostridium difficile toxin in asymptomatic neonates. J. Pediatr. **100** : 431-434, 1982
5) Spencer, R.C., Courtrey, S.P. and Nicol, C.D.: Polymicrobial septicemia due to Clostridium difficile and bacteroides fragilis. Br. Med. J. **289** : 531-532, 1984

6) Kliegman, R.M. and Fanaroff, A.A.: Necrotizing enterocolitis. N. Engl. J. Med. **310** : 1093–1103, 1984
7) Bell, M.J., Shackelford, P., Feigin, R.D., Ternberg, J.L. and Brotherton, T.: Epidemiologic and bacteriologic evaluation of neonatal necrotizing enterocolitis. J. Pediatr. Surg. **14** : 1–8, 1979
8) Brook, I., Avery, G. and Glasgow, A.: Clostridium difficile in pediatric infections. J. Infection **4** : 253–257, 1982
9) Pederson, P.V., Hansen, F.H. and Halveg, A.B.: Necrotizing enterocolitis of the newborn. Lancet **2** : 715–716, 1976
10) Howard, F.M., Flynn, D.M. and Bradley, J.M.: Outbreak of nectotizing enterocolitis caused by Clostridium butyricum. Lancet **2** : 1099–1102, 1977
11) Rudolph, A.M. (ed.): Pediatrics 17th ed. Norwalk, Appelton-Century-Crofts, 1982, p.1096