CASE REPORT

EARLY ONSET NEONATAL BACTERIAL MENINGITIS CAUSED BY *STREPTOCOCCUS GALLOLYTICUS* SUBSP. *PASTEURIANUS*

Anucha Thatrimontrichai, Prasin Chanvitan, Waricha Janjindamai, Supaporn Dissaneevate and Gunlawadee Maneenil

Division of Neonatology, Department of Pediatrics, Faculty of Medicine, Prince of Songkla University, Hat Yai, Songkhla, Thailand

Abstract. We report a case of neonatal meningitis due to *Streptococcus gallolyticus* subsp. *pasteurianus* born to a mother with an asymptomatic urinary tract infection due to *Streptococcus* group D and *Escherichia coli*. In the past, this organism may have been reported as *Streptococcus bovis* or *S. bovis* biotype II/2. Accurate identification of this organism is necessary to determine the etiology of infection and give correct treatment of neonatal meningitis, caused by this organism.

Keywords: meningitis, newborn, streptococcal infections, *Streptococcus*

INTRODUCTION

Neonatal meningitis is a serious infection of the central nervous system and it can cause long term morbidity and significant mortality. The common etiological organisms of neonatal meningitis are group B *Streptococcus* and *Escherichia coli*. *Streptococcus* group D or *Streptococcus bovis* rarely cause neonatal meningitis. We report a case of *Streptococcus gallolyticus* subsp. *pasteurianus* meningitis in a neonate. Early onset *S. bovis* meningitis presenting during the first day of life can have a poor prognosis, however this patient responded to antibiotics and survived.

Correspondence: Anucha Thatrimontrichai, Division of Neonatology, Department of Pediatrics, Faculty of Medicine, Prince of Songkla University, Songkhla 90110, Thailand.
Tel: +66 (0) 7428 1257; Fax: +66 (0) 7442 9618
E-mail: tanucha@medicine.psu.ac.th

CASE REPORT

A male baby was born by spontaneous vaginal delivery at 39 weeks gestation with a birth weight of 3,188 grams to a mother after an uneventful pregnancy and labor without premature rupture of membranes. He developed a fever (38.6ºC) during the second day of life. His complete blood count (CBC) performed then was within normal limits. On the third day of life, he became lethargic, had poor feeding and developed slightly bulging anterior fontanel. He had no seizures, respiratory distress, jaundice or gastrointestinal problems. A repeat CBC showed a hemoglobin of 13.5 g/dl, white blood cell (WBC) count of 2.5 x 10^9 cells/l with 42% segmented neutrophils, 14% bands, 29% lymphocytes, 11% monocytes, 3% atypical lymphocytes and 1% metamyelocytes. His platelet count was 203 x 10^9 cells/l, and his

C-reactive protein was 9.6 mg/dl. Electrolytes, serum glucose, blood urea nitrogen, creatinine and chest radiograph were all normal. A septic work-up (hemoculture and lumbar puncture) was carried out and he was treated empirically with cefotaxime 250 mg per kilogram body weight per day and gentamicin 4 mg per kilogram body weight per day. The cerebrospinal fluid (CSF) was hazy with a WBC of 190 x 10^6 cells/l (polymorphonuclear leukocytes of 90% and mononuclear cells of 10%), red blood cells of 540 x 10^6 cells/l, a glucose of 26 mg/dl (blood glucose of 116 mg/dl), a protein of 192.6 mg/dl and a few gram-positive cocci in chains were present on Gram stain. *Streptococcus* group D, with more than 10^5 colony forming units(cfu)/ml, was initially isolated from the CSF culture and it was susceptible to ampicillin, cefotaxime, fosfomicin, imipenem, penicillin and vancomycin; a blood culture (1 ml of blood in a Pedi-BacT bottle) showed no organisms.

His mother had no fever and no dysuria during peripartum. A maternal septic work-up was carried out on the 4th postpartum day in an effort to find the cause of the neonatal infection. Her CBC was within normal limits. Urinalysis showed WBC of 0-1/ high power field (HPF), with a few bacilli and cocci per HPF, nitrite and leukocytes were both negative. The midstream urine culture showed *Streptococcus* group D and *E. coli* > 10^5 cfu/ml. We did not identify the subspecies of *Streptococcus* group D in the maternal urine. The sensitivity pattern of *Streptococcus* group D identified from the midstream urine was the same as from the baby's CSF, the *E. coli* sensitive to gentamicin and third-generation cephalosporins. A cervical swab for bacterial culture showed a few gamma *Streptococci*, not in group D, and *E. coli*.

After receiving antibiotics for 2 days, the infant still had fever and a repeat lumbar puncture was performed. The CSF revealed white blood cells of 3,100 x 10^6 cells/l (polymorphonuclear leukocytes of 95% and mononuclear cells of 5%), red blood cells of 51,250 x 10^6 cells/l, a glucose of 51 mg/dl, a protein of 300 mg/dl and no organisms on Gram stain. The repeat lumbar puncture demonstrated a traumatic lumbar puncture. A repeat bacterial culture of the CSF had no growth. The infant had fever for 5 days.

On the 9th day of life, additional testing was performed to determine whether the infant had immunoglobulin or complement deficiency, asplenia or polysplenia. He had normal serum complement [β1C (C3C) of 156 mg/dl (90-180 mg/dl)], normal immunoglobulin G (875 mg/dl) and a normal splenic size on abdominal ultrasound. An ultrasound of the brain revealed no hydrocephalus, cerebral hemorrhage, ventriculitis, cerebral abscess, cerebral infarction or subdural empyema except for a right intraventricular hemorrhage grade I. The patient received cefotaxime for 14 days and intravenous gentamicin for 5 days. After 5 days of treatment, the baby appeared well. On discharge, an otoacoustic emission test was normal. The mother received no antibiotics and the results of a repeat urine culture on 41 days postpartum were negative for significant bacterial colonies.

DISCUSSION

The common signs of neonatal sepsis and/or meningitis are fever and lethargy. Group D streptococcus, a gram-positive bacterium, is an important cause of neonatal sepsis (Bavikatte *et al*, 1979) and meningitis (Buchino *et al*, 1979). The group D streptococci consist of enterococcal and

Table 1
Review of cases of neonatal *Streptococcus bovis* meningitis.

Author, Year	Symptom onset	Sex	Gestational age (weeks)	Birth weight (grams)	Total WBC in CSF (% Neutrophils)	Blood culture	Outcome
Alexander and Giacoia, 1978	<24 h	NR	Near Term	NR	32,000 (96)	Positive	Survived
Alexander and Giacoia, 1978	<24 h	NR	Near Term	NR	2 (0)	Positive	Died
Buchino *et al*, 1979	9 d	NR	NR	2,528	0	Negative	Survived
Buchino *et al*, 1979	19 d	NR	NR	3,664	7	Negative	Survived
Fikar and Levy, 1979	2 d	Male	NR	4,734	3,580 (89)	Positive	Survived
Figura and Mattei, 1982	24 h	Male	Term	3,400	NR	Positive	Survived
Cheung *et al*, 2000	4 wk	Male	32	2,340	1,825 (63)	Positive	Survived
Koh and Ho, 2002	19 d	Female	34	1,675	0	Positive	Survived
Gavin *et al*, 2003	3 d	Male	Term	3,925	2,100 (90)	Positive	Survived
Gerber *et al*, 2006	1 d	Female	38	NR	NR	Positive	Survived
Gerber *et al*, 2006	8 d	Female	39	NR	8,825 (80)	Negative	Survived
Onoyama *et al*, 2009	4 d	Female	Term	3,192	12,970 (98.7)	Positive	Survived
Khan, 2009	3 d	NR	NR	NR	4,500 (98)	Positive	Survived
This Study	3 d	Male	39	3,188	190 (90)	Negative	Survived

CSF, cerebrospinal fluid; NR, not recorded; WBC, white blood cell

Table 2
Clinical presentation of cases of neonatal *Streptococcus gallolyticus* subsp *pasteurianus* meningitis.

	Gavin *et al*, 2003	Onoyama *et al*, 2009	Khan, 2009	This study
Year	2003	2009	2009	2012
Onset of symptoms	3 days	4 days	3 days	3 days
Sex	Male	Female	NR	Male
Gestational age	Term	Term	NR	39 weeks
Birth weight (grams)	3,925	3,192	NR	3,188
Premature rupture of membrane	No	No	NR	No
Clinical signs	Fever, irritable, seizure	Fever	Apnea, lethargy	Fever, lethargy, poor feeding
Complete blood count				
Leukocytes (x 10^6 cells/l)	3,400	3,600	2,800	2,500
Hemoglobin (g/dl)	13.2	12.8	NR	13.5
Platelets (x 10^6 cells/l)	201,000	279,000	NR	203,000
C-reactive protein (mg/dl)	NR	6.5	2.2	9.6
Hemoculture	Positive	Positive	Positive	Negative
Cerebrospinal fluid				
Leukocytes (x 10^6 cells/l)	2,100	12,970	4,500	190
Neutrophils (%)	90	98.7	98	90
Glucose (mg/dl)	4	21	NR	26
Protein (mg/dl)	600	3,320	NR	192.6
Gram-stained smears	Gram-positive cocci in pairs and short chains	Gram-positive cocci	Gram-positive cocci in chains	Gram-positive cocci in pairs and short chains
Susceptibility	Penicillin and ceftriaxone	Penicillin and cefotaxime	Penicillin and cefotaxime	Penicillin and cefotaxime
Repeated CSF culture	NR	Negative	Negative	Negative
Treatment	Penicillin G (50,000 U/kg every 8 h for 14 days)	Cefotaxime (200 MKD for 14 days), panipenem-betamipron (120 MKD for 3 days) and IVIg (300MKD for 2 days)	Cefotaxime and vancomycin (for 2 days) then penicillin (120 MKD) and gentamicin (4 MKD) for 12 days	Cefotaxime (250 MKD for 14 days) and gentamicin (4 MKD for 5 days)
Complications				
Intracranial hemorrhage	NR	No	NR	Right IVH grade I
Subdural abscess	NR	No	NR	No
Outcome	Survived	Survived	Survived	Survived

IVIg, intravenous gamma-globulin; IVH, intraventricular hemorrhage; MKD, milligrams per kilograms per day; NR, not recorded

non-enterococcal subtypes. Many former group D streptococci have been reclassified and placed in the genus *Enterococcus* (including *Streptococcus faecalis*, *S. faecium*, *S. durans*, and *S. avium*). Currently, *Streptococcus faecalis* is *Enterococcus faecalis* and is the most common human pathogen. The other non-enterococcal group D strains include *Streptococcus bovis* and *Streptococcus equinus*, which are normal inhabitants in the gastrointestinal and genitourinary tracts of humans.

Although non-enterococcal group D (Buchino *et al*, 1979) and *Streptococcus bovis* (Gavin *et al*, 2003) are uncommon causes of neonatal infection, they can cause neonatal meningitis. The pathogenesis of invasive *S. bovis* infection in infants is unclear. Some have reported most infants with *S. bovis* meningitis develop late-onset disease or healthcare-associated infections (Cheung *et al*, 2000; Grant *et al*, 2000; Gerber *et al*, 2006). Reports of neonatal meningitis caused by *S. bovis* group strains are summarized in Table 1. Sporadic cases of *S. bovis* infected neonates may present with either bacteremia or meningitis; 10 of 14 cases (71.4%) had meningitis with concurrent bacteremia (Alexander and Giacoia, 1978; Buchino *et al*, 1979; Fikar and Levy, 1979; Figura and Mattei, 1982; Cheung *et al*, 2000; Koh and Ho, 2002; Gavin *et al*, 2003; Gerber *et al*, 2006; Khan, 2009; Onoyama *et al*, 2009). Four reported preterm infants had *S. bovis* bacteremia and meningitis (Alexander and Giacoia, 1978; Cheung *et al*, 2000; Koh and Ho, 2002). Male and female neonates were equally represented among cases (Alexander and Giacoia, 1978; Buchino *et al*, 1979; Fikar and Levy, 1979; Figura and Mattei, 1982; Cheung *et al*, 2000; Koh and Ho, 2002; Gavin *et al*, 2003; Gerber *et al*, 2006; Khan, 2009; Onoyama *et al*, 2009). Neonatal *S. bovis* meningitis has a clinical presentation similar to that of neonatal group B Streptococcal infection. Early-onset (≤3 days of life) neonatal cases of *S. bovis* meningitis are more common (8 of 14 cases, 57%) than late onset (4-30 days) (Alexander and Giacoia, 1978; Buchino *et al*, 1979; Fikar and Levy, 1979; Figura and Mattei, 1982; Cheung *et al*, 2000; Koh and Ho, 2002; Gavin *et al*, 2003; Gerber *et al*, 2006; Khan, 2009; Onoyama *et al*, 2009). Term newborns are more likely to have *S. bovis* meningitis than preterm neonates (Alexander and Giacoia, 1978; Buchino *et al*, 1979; Fikar and Levy, 1979; Figura and Mattei, 1982; Cheung *et al*, 2000; Koh and Ho, 2002; Gavin *et al*, 2003; Gerber *et al*, 2006; Khan, 2009; Onoyama *et al*, 2009). The survival rate of infants with *S. bovis* meningitis treated by penicillin or ampicillin with or without gentamicin is 13 of 14 (92.9%) cases (Alexander and Giacoia, 1978; Buchino *et al*, 1979; Fikar and Levy, 1979; Figura and Mattei, 1982; Cheung *et al*, 2000; Koh and Ho, 2002; Gavin *et al*, 2003; Gerber *et al*, 2006; Khan, 2009; Onoyama *et al*, 2009). Only one patient died from *S. bovis* meningitis within 24 hours after birth, therefore early-onset symptoms may represent a risk factor for mortality (Alexander and Giacoia, 1978).

S. bovis variant (biotype II) is further divided into type II/1 and type II/2 based on differential biochemical characteristics and phylogenetic analysis (Schlegel *et al*, 2003; Chen *et al*, 2008). An outbreak of *Streptococcus gallolyticus* subsp. *pasteurianus* healthcare-associated bloodstream infections was reported among premature neonates (Floret *et al*, 2010). *S. bovis* biotype II/2 and *S. gallolyticus* subsp. *pasteurianus* are rare organisms causing neonatal meningitis (Gavin *et al*, 2003). *S. gallolyticus* subsp. *pasteurianus* meningitis were reported to be the cause of meningitis in

5 adults (Sturt *et al*, 2010), all of whom survived. *S. gallolyticus* subsp. *pasteurianus* neonatal meningitis appears to be associated with an excellent prognosis; all four patients in whom a prognosis was recorded, survived (Gavin *et al*, 2003; Khan, 2009; Onoyama *et al*, 2009; this study) (Table 2). The clinical signs of *Streptococcus gallolyticus* subsp. *pasteurianus* meningitis in neonates are not different from *S. bovis* meningitis. All reported cases had leukopenia, a high C-reactive protein level, hypoglycorrhachia and neutrophilia (90-98%) in the CSF (Gavin *et al*, 2003; Khan, 2009; Onoyama *et al*, 2009; this study). The reported cases of *Streptococcus gallolyticus* subsp. *pasteurianus* meningitis in neonates had no serious neurologic involvement initially (Gavin *et al*, 2003; Khan, 2009; Onoyama *et al*, 2009; this study), but close follow-up of cognitive and developmental milestones over the next several years will be necessary to determine the presence of any sequelae.

Penicillin-resistant *S. bovis* has been found in adult endocarditis (Savitch *et al*, 1978) and neonatal meningitis (Khan, 2009). For this reason, an aminoglycoside should be added initially for synergy until susceptibility test results are available (Fikar and Levy, 1979) in spite of high levels of gentamicin-resistant *S. gallolyticus* subsp. *pasteurianus* (Chow *et al*, 2007). Penicillin G is considered an effective medication for neonatal bacteremia or meningitis caused by *S. gallolyticus* subsp. *pasteurianus*. Therefore, an accurate identification of the organism is critical to proper selection of antibiotics.

ACKNOWLEDGEMENTS

We thank the International Affairs Unit for helping with English.

REFERENCES

Alexander JB, Giacoia GP. Early onset nonenterococcal group D streptococcal infection in the newborn infant. *J Pediatr* 1978; 93: 489-90.

Bavikatte K, Schreiner RL, Lemons JA, Gresham EL. Group D streptococcal septicemia in the neonate. *Am J Dis Child* 1979; 133: 493-6.

Buchino JJ, Ciambarella E, Light I. Systemic group D streptococcal infection in newborn infants. *Am J Dis Child* 1979; 133: 270-3.

Cheung M, Pelot M, Nadarajah R, Kohl S. Neonate with late onset *Streptococcus bovis* meningitis: case report and review of the literature. *Pediatr Infect Dis J* 2000; 19: 891-3.

Chow VC, Hawkey PM, Chan EW, *et al*. High-level gentamicin resistance mediated by a Tn4001-like transposon in seven nonclonal hospital isolates of *Streptococcus pasteurianus*. *Antimicrob Agents Chemother* 2007; 51: 2508-13.

Figura N, Mattei C. Neonatal *Streptococcus bovis* (non-enterococcal group D streptococcus) septicemia and meningitis. Report of a case. *Ann Sclavo* 1982; 24: 440-2.

Fikar CR, Levy J. *Streptococcus bovis* meningitis in a neonate. *Am J Dis Child* 1979; 133: 1149-50.

Floret N, Bailly P, Thouverez M, *et al*. A cluster of bloodstream infections caused by *Streptococcus gallolyticus* subspecies *pasteurianus* that involved 5 preterm neonates in a university hospital during a 2-month period. *Infect Control Hosp Epidemiol* 2010; 31: 194-6.

Gavin PJ, Thomson RB, Jr, Horng SJ, Yogev R. Neonatal sepsis caused by *Streptococcus bovis* variant (biotype II/2): report of a case and review. *J Clin Microbiol* 2003; 41: 3433-5.

Gerber JS, Glas M, Frank G, Shah SS. *Streptococcus bovis* infection in young Infants. *Pediatr Infect Dis J* 2006; 25: 1069-73.

Grant RJ, Whitehead TR, Orr JE. *Streptococcus*

bovis meningitis in an infant. *J Clin Microbiol* 2000; 38: 462-3.

Khan A. Relative penicillin resistance in *Streptococcus bovis*. A case of neonatal meningitis. *J Paediatr Child Health* 2009; 45: 474-5.

Koh TH, Ho S. *Streptococcus bovis* meningitis in a neonate with Ivemark syndrome. *Scand J Infect Dis* 2002; 34: 63-4.

Onoyama S, Ogata R, Wada A, Saito M, Okada K, Harada T. Neonatal bacterial meningitis caused by *Streptococcus gallolyticus* subsp. *pasteurianus*. *J Med Microbiol* 2009; 58: 1252-4.

Savitch CB, Barry AL, Hoeprich PD. Infective endocarditis caused by *Streptococcus bovis* resistant to the lethal effect of penicillin G. *Arch Intern Med* 1978; 138: 931-4.

Schlegel L, Grimont F, Ageron E, Grimont PA, Bouvet A. Reappraisal of the taxonomy of the *Streptococcus bovis*/*Streptococcus equinus* complex and related species: description of *Streptococcus gallolyticus* subsp. *gallolyticus* subsp. nov., *S. gallolyticus* subsp. *macedonicus* subsp. nov. and *S. gallolyticus* subsp *pasteurianus* subsp. nov. *Int J Syst Evol Microbiol* 2003; 53: 631-45.

Sturt AS, Yang L, Sandhu K, Pei Z, Cassai N, Blaser MJ. *Streptococcus gallolyticus* subspecies *pasteurianus* (biotype II/2), a newly reported cause of adult meningitis. *J Clin Microbiol* 2010; 48: 2247-9.