



Case report

The first case of recurrent ultra late onset group B streptococcal sepsis in a 3-year-old child



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ABSTRACT

Group B streptococcus (GBS) is a commonly recognized cause of sepsis and meningitis in neonatal and young infants. Invasive GBS infection is classified into early onset GBS disease (EOD, day 0–6), late onset GBS disease (LOD, day 7–89) and ultra late onset GBS disease (ULOD, after 3 months of age). ULOD is uncommon and recurrence is especially rare. We present the first recurrent case of ULOD GBS sepsis in 3-year-old girl with a past medical history of hydrops fetalis and thoracic congenital lymphatic dysplasia. The first episode presented as sepsis at 2 years 8 months of age. The second episode occurred as sepsis with encephalopathy at 3 years 1 months of age. During each episode, the patient was treated using intravenous antimicrobials and her condition improved. Serotype examination was not performed in the first episode, but GBS type V was serotyped in the second episode. ULOD over 1 year of age is quite rare and may recur.

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Introduction

Group B streptococcus (GBS) is a commonly recognized cause of sepsis and meningitis in neonatal and young infants. Invasive GBS infection is classified into early onset GBS disease (EOD, day 0–6), late onset GBS disease (LOD, day 7–89) and ultra late onset GBS disease (ULOD, after 3 months of age) [1,2]. The characteristics of EOD and LOD have been well documented, but little is known about ULOD. Several cases of ULOD have been reported [2], but ULOD after 1 year of age is rare and recurrent case is especially rare. We report the first case of recurrent invasive ultra late onset GBS infection.

Case report

The patient was the first female child of healthy unrelated parents. She was diagnosed with hydrops fetalis and drainage of pleural effusions was performed before birth. At 30 weeks and 5 days gestation, the patient was born via caesarian section because of an increase in pleural effusion. Her birth weight was

2325 g, but the estimated body weight was considered to be about 1200 g because of edema. The patient was intubated and general care was provided in the NICU department. She was diagnosed with thoracic congenital lymphatic dysplasia using scintigraphy. She was treated using octeotides, diuretics and dexamethasone for two months and was eventually discharged at one year of age with home oxygen therapy. Maternal GBS colonization was negative. During NICU admission, GBS strains were never isolated from any cultures. There was no history of bacteremia nor seizures. She had no other significant past medical history except for a moderate delay of developmental milestones including walking at 2 years and 2 months of age, and still unable to speak meaningful words at 3 years of age.

At 2 years 8 months of age, the patient was admitted to a hospital with a history of high-grade fever (39.3 °C) and seizures. Laboratory studies revealed a total WBC count of 22600/mm³ with 76% neutrophils and 19% lymphocytes, and a C-reactive protein (CRP) result of 0.05 mg/dL. She was treated with intravenous sulbactam/ampicillin with the diagnosis of suspected bacteremia. Within 24 h her fever began to decrease and her mental status improved. Twelve hours after admission, blood culture was growing GBS. CRP increased to 7.33 mg/dL in 12 h. Nasal culture did not reveal GBS. She was discharged after 10 days of intravenous antimicrobial therapy.

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Five months after the first episode of GBS infection, at 3 years 1 month of age, she was admitted to a hospital for fever up to 40 °C. About two hours after admission, she had seizures. The convulsions were generalized tonic-clonic seizures, which were controlled with repeated doses of intravenous diazepam and midazolam along with supportive measures. Laboratory studies revealed a serum total WBC count of 9400/mm³ with 77% neutrophils and 17% lymphocytes, CRP 0.14 mg/dL and normal CSF parameters. The patient was empirically started on intravenous ampicillin and ceftriaxone. On the second day after admission, she was still febrile (40 °C) and toxic, with tachycardia including a heart rate of 180/min. Her neurological status did not improve. Laboratory studies revealed a serum total WBC count of 14200/mm³, AST 545 IU/L, ALT 241 IU/L, CRP 17.76 mg/dL and procalcitonin >100 µg/L. The electroencephalogram showed diffuse slow waves.

The patient was transferred to a tertiary hospital with a diagnosis of sepsis and encephalopathy. Antimicrobials were continued. Ultrasound revealed no signs of endocarditis. Neither intubation nor therapeutic hypothermia was performed. GBS was isolated in the blood culture, but CSF and urine cultures were sterile, and nasal and rectal cultures did not reveal GBS. MRI of the head revealed clinically mild encephalopathy with a reversible splenic lesion; MERS. After isolation of GBS from the blood, antimicrobials were deescalated to ampicillin alone for 14 days. The GBS isolate was serotyped as GBS type V. The patient was discharged on the 40th hospital day with mild neurologic sequelae, including brain atrophy. She also showed signs of temporal regression of motor function, which improved over time.

Quantitative immunoglobulin (Ig) and complement (C) values were normal (IgG 763 mg/dL, IgA 51 mg/dL, IgM 161 mg/dL, C3 71.0 mg/dL, C4 17.0 mg/dL, CH50 15.9 IU/mL). Neutrophil oxidative burst test results were normal (97%). IgG subclasses were also normal (IgG₁ 785.0 (65.9%), IgG₂ 324.0 (27.2%), IgG₃ 17.2 (1.44%), IgG₄ 65.0 (5.46%)). Neutrophil count was normal since birth, and no family members were compromised hosts. HIV testing was negative.

Discussion

We made two important clinical observations in this case. First, recurrent ULOD GBS infection is extremely rare among children over 1 year of age. To our knowledge, this is the first report of recurrent invasive GBS infection in ULOD. Second, ULOD GBS infection over 1 year of age, compared to infection before 1 year of age can be associated with underlying conditions.

A 2008 report from the USA identified 90 cases of invasive GBS disease in children aged 1 through 14 years from 1999 to 2005, but the details of clinical data for each case have not been reported [3]. The ULOD incidence rate in Japan was unknown, but the estimated incidence of invasive GBS disease in the United States is 0.22 per 100,000 population in individuals aged 1 through 14 years [3]. Ten other cases of ULOD among children aged 1 through 14 years have been reported [4–7]. Demographics and clinical data for each case are summarized in Table 1. Three patients were male, 6 were female (including our patient), and for 3, the gender was not reported. Only our case had recurrent ULOD infection. In our patient, both infections presented as sepsis: the first infection as sepsis and the second infection as sepsis with encephalopathy [8]. Although relapse or recurrence of neonatal and infantile GBS infection has been described, recurrent invasive GBS infection in ULOD has not been reported. Hypotheses regarding the cause of recurrence in EOD and LOD have been suggested by many authors. The combined effect of immature immune mechanisms and persistent mucosal colonization may permit reinvasion from the mucosal surface and the establishment of recurrent systemic GBS infection [9,10]. In our patient, GBS serotype V was found in the second infection but we did not examine the serotype in the initial infection. Recurrent GBS infection does not necessarily imply relapse with the same GBS serotype.

The definition of ULOD is somewhat ambiguous. ULOD is typically defined with a lower age threshold (>90 days), but its upper age limit is either variably defined or undefined. We chose to apply the term to children aged over 90 days to 14 years as Phares et al. defined [3]. The term “ULOD” is an extension of the terms of “EOD” and “LOD” neonatal GBS. Although the term “ULOD” may be reasonable to refer to sepsis that occurs in infants, it may be inappropriate to apply to sepsis in older children and ULOD above 1 year of age may have different pathophysiology. Therefore we believe that ULOD above 1 year of age should be conceptualized separately as “childhood” or “pediatric” ULOD.

ULOD GBS infection over 1 year of age, compared to infection before 1 year of age, appears to be associated with underlying conditions. In our review, 66% (8/12) had at least 1 underlying condition including neurologic disorders, hydrops fetalis with lymphatic dysplasia, congenital ectodermal dysplasia with hyper IgM globulinemia and congenital heart disease (Table 1). Three patients had undergone surgery for cerebrospinal fluid drainage, ventriculo-peritoneal shunt and ventriculostomy. A previous study showed that only 11% of children aged 90 days through 12 months had an underlying condition (excluding preterm birth), but 44% of children aged 1 through 14 years had at least 1 underlying

Table 1
Characteristics of invasive GBS disease among children aged 1 through 14 years.

Patient	Reference number	Age (y,m)	Gender	Gestational age	Clinical Manifestation	Underlying Condition	Outcome	Serotype
1	[4]	1y4m	Male	Term	Bacteremia	None	Alive	NT
2	[4]	1y6m	NR	Term	Bacteremia	None	Alive	II
3	[4]	1y9m	Female	Term	Endocarditis	Congenital heart disease	Alive	Ia
4	[4]	3y	Male	Term	Bacteremia	None	Alive	III
5	[4]	12y	Female	NR	Ventriculostomy-associated infection, meningitis	AV malformation, intraventricular hemorrhage	Death	Ib/c
6	[4]	14y	Female	NR	VP shunt infection, meningitis	Arnold-Chiari malformation	Alive	NT
7	[5]	1y5m	NR	34w3d	Bacteremia	Cerebellar tumor	Alive	NT
8	[5]	3y8m	NR	37w2d	Bacteremia	Congenital ectodermal dysplasia, hyper-IgM globulinemia	Alive	NT
9	[6]	5y	Male	NR	Meningitis	None	Alive	NT
10	[7]	9y	Female	NR	Meningitis	Lumbar spina bifida, hydrocephalus with VP shunt	Alive	NT
11	Our patient	2y8m	Female	30w5d	Sepsis	Hydrops fetalis, lymphatic dysplasia	Alive	NT
12	Our patient	3y1m	Female	30w5d	Sepsis, encephalopathy	Hydrops fetalis, lymphatic dysplasia	Alive	V

NT, not tested; NR, not reported; VP, ventriculoperitoneal.

condition, including neurologic disorders, immunosuppressive conditions, asthma, malignancy and renal disease [3]. Our review also suggests that ULOD above 1 year of age is more likely to be associated with underlying conditions. Our patient was born preterm and had hydrops fetalis and lymphatic dysplasia. Lymphatic dysplasia may be associated with insufficient immunity. In a previous report, the authors emphasized the importance of preterm birth for ULOD GBS meningitis, where ULOD referred to infants less than 1 year old [2]. Our findings including children aged 1 through 14 years did not suggest prematurity as a risk for ULOD.

Recurrent ULOD GBS infection is extremely rare among children over 1 year of age. ULOD over 1 year of age is more likely to be associated with underlying conditions compared to younger children. In patients with underlying conditions, ULOD may occur even over 1 year of age and can recur, therefore careful clinical evaluation is necessary.

Conflict of interest

None.

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