Early-Onset Fulminant Sepsis in a Preterm Neonate due to *Streptococcus gallolyticus*: A Case Report and Literature Review

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**Abstract**

*Streptococcus gallolyticus* is an uncommon cause of neonatal infections. We describe the first case of fulminant lethal neonatal sepsis due to *S. gallolyticus* reported in literature. Our patient was an extremely low birth weight premature infant born to a mother with prolonged rupture of amniotic membranes and chorioamnionitis. We also review the cases of neonatal *S. gallolyticus* infections reported in literature. Fifty-eight percent neonatal *S. gallolyticus* infections presented in the first week of life. Importantly, *S. gallolyticus* meningitis is more commonly reported with early-onset infections compared with group B streptococcal meningitis, which is more common with late-onset infections. *Streptococcus gallolyticus* should be included in differential for neonatal sepsis, particularly in the presence of meningitis in the first week of life. Most cases are sensitive to penicillin; however, cases of reduced sensitivity to penicillin have also been reported.

**Keywords**

► neonatal sepsis  
► *Streptococcus bovis*  
► *Streptococcus gallolyticus*  
► *Streptococcus pasteurianus*  
► neonatal meningitis  
► chorioamnionitis  
► preterm

*Streptococcus gallolyticus* is a group of bacteria that belong to the nonenterococcal group D streptococci previously known as *S. bovis/S. equinus* complex (SBSEC).1 *Streptococcus gallolyticus* has been reported as a cause of adult gastrointestinal tract infections and infective endocarditis for decades but is an uncommon cause of neonatal infections.1,2 However, over the past decade, there have been increasing reports of neonatal sepsis, meningitis, and intrauterine infections due to *S. gallolyticus*. Here, we report an unusual case of a preterm, extremely low birth weight (ELBW) male neonate who developed fulminant early-onset sepsis due to *S. gallolyticus*. To the best of our knowledge, no prior cases of fulminant lethal sepsis due to *S. gallolyticus* have been reported to date. We also review the cases of neonatal *S. gallolyticus* infections reported in literature.

**Case Presentation**

A male infant was born at 26 weeks of gestation to a 25-year-old G5 P5 mother with good prenatal care. Pregnancy was complicated by chronic hypertension and premature prolonged rupture of membranes 12 days before delivery for which the mother received 7 days of latency antibiotics (48 hours of intravenous ampicillin followed by 5 days of oral amoxicillin and a single dose of azithromycin) that was completed 5 days prior to delivery. She developed chorioamnionitis prior to delivery for which she received one dose of ampicillin.

Mother had a history of trichomonas infection during pregnancy which was treated. Her other prenatal infectious laboratories including group B streptococcal (GBS) culture

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were negative. The infant was born via spontaneous vaginal delivery with a birth weight of 950 g. In the delivery room, the infant required positive pressure ventilation and intubation. APGAR scores were 6, 3, and 4 at 1, 5, and 10 minutes, respectively. The infant was then admitted to the neonatal intensive care unit (NICU).

The infant’s arterial cord blood gas pH was 6.96 with a pCO2 of 76 mm Hg and a base excess of -15.9 mmol/L. His venous cord blood gas pH was 7.17 with a pCO2 of 42 mm Hg and a base excess of -12.7 mmol/L.

The infant had mixed metabolic and respiratory acidosis on admission (pH 6.9) and required high ventilator support. The respiratory acidosis improved with ventilator adjustments and surfactant administration; however, he had persistent metabolic acidosis. He also had leukopenia (white blood cell count 1.5 × 10^3/mm^3), thrombocytopenia (platelet count was 89 × 10^3/mm^3), and an elevated C-reactive protein level of 21.1 mg/L. Blood culture was sent on admission and the infant was prescribed ampicillin and gentamicin.

Around 4.5 hours of life, the infant became hypotensive and rapidly deteriorated despite fluid resuscitation and receiving pressors (dopamine and dobutamine). A repeat blood culture and tracheal aspirate were obtained, but the infant died at 5.5 hours of life after he remained unresponsive to resuscitative efforts.

Parents declined an autopsy. Both blood cultures resulted positive for gram-positive coccii within 12 hours of incubation, which were further identified as S. galolyticus using MALDI-TOF (matrix-assisted laser desorption/ionization time-of-flight) biotyper. Unfortunately, genotyping was not possible in our laboratory, and hence, we were unable to further classify this pathogen. The tracheal aspirate culture was negative. Placental pathology confirmed acute chorioamnionitis of the fetal membranes.

**Discussion**

This is the first case of S. galolyticus in an ELBW infant leading to fulminant sepsis. Streptococcus galolyticus has been often used interchangeably with S. bovis in literature. Over the years, SBSEC has undergone numerous taxonomical changes. Based on their ability to ferment mannitol, S. bovis has been classified in the older literature into two biotypes, mannitol-fermenting biotype I and mannitol nonfermenting biotype II. Biotype II has been divided further into subtypes 1 and 2 based on starch and bile-esculin hydrolysis and trehalose acidification. The most recent taxonomic classification uses genetic methodology to classify SBSEC into four species S. galolyticus (further divided into subsp. galolyticus, pasteurianus, and macedonicus), S. alactolyticus, S. infantarius (divided into subsp. infantarius and colt), and S. equinus. 

Fig. 1 shows a simplified taxonomical classification of S. bovis.

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**Fig. 1** Taxonomical classification of S. bovis: This figure shows the correlation between the previously used biochemical/phenotypic classification and the new genetic classification of nonenterococcal group D Streptococcus. Reconstructed based on the description by Dekker and Lau, Schlegel et al, and Jans et al. Methods used for analysis include MALDI-TOF (proteomic-based), 16s rRNA, sodA, and groEL sequencing (single-gene-based) and/or whole genome sequencing. Streptococcus equinus and S. macedonicus likely belong to biotype II/1 based on phenotypic data. Phenotypic data for S. alactolyticus is variable, and hence, biotypic classification is not possible. BE, bile-esculin; MALDI-TOF, matrix-assisted laser desorption/ionization time-of-flight; SBSEC, Streptococcus bovis/Streptococcus equinus complex; SG, Streptococcus galolyticus; subsp., subspecies.
**Streptococcus gallolyticus** is prevalent in the bowel flora in humans. In adults, *S. gallolyticus* subsp. *gallolyticus* is commonly associated with infective endocarditis, bacteremia, gastrointestinal infections including hepatobiliary infections, and colon cancer. 1–3 *Streptococcus pasteurianus* has been commonly associated with meningitis.1 Although uncommon, *S. gallochyticus* subsp. *gallochyticus* and *S. pasteurianus* have emerged as important causes of neonatal sepsis in recent years. *Streptococcus gallochyticus* subsp. *macedonicus* has not been associated with infections in humans. *Streptococcus infantarius* has been associated with non-colon cancers and is an uncommon cause of adult sepsis. Only two cases of neonatal infections with *S. infantarius* subsp. *coli* (also known as *S. lutetiensis*) have been reported in literature.6

To review the cases of neonatal invasive *S. gallochyticus* infections reported in the English literature, we performed a MEDLINE search and found 66 cases of neonates (<28 days old) reported to be infected by *S. bovis*. Twenty-nine cases were classified only as *S. bovis* and four cases as *S. bovis* biotype II. Infections with *S. pasteurianus* (*S. bovis* biotype II/2) have been much more commonly reported compared with that with *S. infantarius* (*S. bovis* biotype II/1) in both neonates and adults, thus making it likely that the cases without further identification beyond *S. bovis*/*S. bovis* biotype II belong to the *S. gallochyticus* species. However, due to lack of certainty, these cases (n = 33) were not included in this review. Of the remaining 33 cases, two cases were reported as *S. lutetiensis* infection and one case as *S. alactolyticus* infection and hence were also not included. We analyzed the remaining 30 cases of neonatal *S. gallochyticus* infections reported in literature before November 30, 2021, and the present case (n = 31) (Table 1).2,7–21 Of the 30 cases reported in literature, only 10 cases were reported from the United States.10,13,14,21

Fifty-eight percent of the patients presented during the first week of life. There was a slightly higher incidence of early-onset (<6 days) (n = 17; 55%) and late-onset infections (>6 days) (n = 14; 45%) due *S. gallochyticus*. Gestational age was unknown for one infant and 12 of 30 (40%) infants were premature (gestational age 26–36 weeks). Presenting symptoms included respiratory distress, apnea, metabolic acidosis, fever, lethargy, abdominal distension, loose stools, congestion, poor feeding, and seizures. In five cases, further identification beyond *S. gallochyticus* was not performed. When classification was available, *S. pasteurianus* was more common than *S. gallochyticus* subsp. *gallochyticus* (25 vs. 1). Meningitis was reported in 19 patients (18 due to *S. pasteurianus* and 1 due to *S. gallochyticus* subsp. *gallochyticus*). Hede et al13 hypothesized that *S. gallochyticus* infection in neonates follows the pattern of early- and late-onset GBS diseases. However, unlike GBS infection, *S. gallochyticus* infection was associated with a higher rate of meningitis (63%), and early-onset *S. gallochyticus* infection was more likely to be associated with meningitis compared with late-onset infection (76 vs. 43%).22 Meningitis was more commonly reported in term neonates (16 of 18; 89%) compared with preterm neonates (2 of 12; 17%). In one patient, bacteremia was associated with infective endocarditis, and in another patient with liver abscess.2,18 Park et al15 reported a case of urinary tract infection due to *S. pasteurianus* in the absence of pyuria.

Most patients were treated with a penicillin and/or a third-generation cephalosporin and the duration of antimicrobial therapy ranged from 7 days to 8 weeks (median: 14 days; average: 15 days). Although all patients had a severe clinical course, most patients had a favorable outcome. All patients, except this case, survived the acute infection. One patient had to be rehospitalized 2 weeks postdischarge due to partially treated meningitis but had no long-term neurological sequelae.15 Only one patient with meningitis was reported to have long-term neurological deficits.13

This is the first reported case of fulminant lethal sepsis due to *S. gallochyticus*. Our patient was an ELBW preterm infant with history of prolonged rupture of amniotic membranes (12 days) and acute chorioamnionitis which may have resulted in the particularly severe course in this case. The exact route of *S. gallochyticus* infection in neonates remains uncertain. It is presumed that like GBS, *S. gallochyticus* infection occurs either vertically via transvaginal transmission or postnatal horizontal transmission.13 Fikar and Levy23 reported positive rectal and vaginal cultures from the patient’s mother 2 weeks following the onset of symptoms in a neonate with *S. bovis* meningitis. In another report, mother of the infant with *S. pasteurianus* meningitis grew *Escherichia coli* and Group D *Streptococcus* in the urine culture collected on fourth postpartum day.12 A case of intrapartum infection and postpartum bacteremia without neonatal infection has also been reported.24 Floret et al25 and Saegeman et al16 reported clusters of neonatal infections due to *S. pasteurianus* in their respective NICUs, likely due to horizontal transmission from health care workers. In one case series, one of the four patients had history of maternal contact with chicken who died 1 week prior to patient’s birth; however, postmortem testing of chickens was not performed.10

Similar to GBS, *S. gallochyticus* is often sensitive to penicillin; however, cases with reduced susceptibility to penicillin have been reported including two cases of neonatal meningitis due to *S. pasteurianus*.3,8,10 This organism is also susceptible to aminoglycosides, cephalosporin, and vancomycin, and high rates of resistance to quinolones, macrolides, and tetracyclines have been reported.3

**Conclusion**

*Streptococcus gallochyticus* must be considered an important differential for neonatal sepsis particularly, in the presence of meningitis in the first week of life when maternal GBS is negative. Appropriate identification and classification of the organism are important to further understand the epidemiology of neonatal infections due to *S. gallochyticus*. Culture sensitivity should be performed to determine appropriate antibiotic for treatment due to the increasing rates of reduced susceptibility to penicillin. Although no mortality was reported in previous cases of neonatal *S. gallochyticus* infections, this case shows that *S. gallochyticus* in ELBW infants may be lethal.
| Reference                        | Number of reported pts | GA (wk) | Delivery type | Birthweight (kg) | Reference Number of pts reported | Birthweight (kg) | GA (wk) | Delivery type | Age of presentation | Diagnosis | Site(s) organism isolated from | Clinical symptoms | Organism        | Final antibiotic therapy course | Final disposition |
|---------------------------------|------------------------|---------|---------------|------------------|-------------------|------------------|---------|---------------|---------------------|-----------|----------------------|------------------|---------------|-------------------------------|------------------|
| Gavin et al (2003)              | 21                     | Term    | Vaginal       | 3.925            | 1                  | Term            | 4                   | Vaginal             | 3 d              | SG subsp. pasteurianus     | Fever, seizures | Blood þ CSF | Bacteremia, meningitis | Survived         |
| Onoyama et al (2009)            | 7                      | Term    | Vaginal       | 3.19             | 1                  | Term            | 4                   | Vaginal             | 4 d              | SG subsp. pasteurianus     | Fever, decreased activity | Blood þ CSF | Bacteremia, meningitis | Survived         |
| Khan (2009)                     | 8                      | Not reported | Not reported | Not reported     | 3                  | Not reported    | 3                   | Not reported        | Blood þ CSF | CSF                  | Bacteremia, meningitis | Penicillin and gentamicin/C2 | Survived         |
| Floret et al (2010)             | 9                      | Not reported | Preterm      | Not reported     | 3                  | Not reported    | 3                   | Not reported        | Blood þ CSF | CSF                  | Bacteremia | Penicillin/C2            | Survived         |
| Klatte et al. (2012)            | 4                      | Not reported | Term         | Not reported     | 3                  | Not reported    | 2 – 13 d            | Vaginal             | Blood þ CSF | CSF                  | Bacteremia | Penicillin/C2            | Survived         |
| Nagamatsu et al (2012)          | 1                      | Term    | Vaginal       | 3.092            | 1                  | Term            | 4                   | Vaginal             | 3 d              | SG subsp. pasteurianus     | Fever, seizures | Blood þ CSF | Cefotaxime/C2              | Survived         |
| Thimmann et al. (2012)          | 1                      | Term    | Vaginal       | 3.188            | 1                  | Term            | 3                   | Vaginal             | 3 d              | SG subsp. pasteurianus     | Fever, lethargy, poor feeding, decreased oral intake, abdominal distension | Blood þ CSF | Cefotaxime/C2              | Survived         |
| Hede et al (2015)               | 2 (twins)              | 32      | C-section     | Not reported     | 2                  | Not reported    | 2 – 13 d            | Vaginal             | Blood þ CSF | CSF                  | Bacteremia | Penicillin/C2            | Survived         |
| Williams et al. (2016)          | 1                      | Term    | Vaginal       | 3.05             | 1                  | Term            | 3                   | Vaginal             | 4 d              | SG subsp. gallolyticus     | Fever, lethargy, irritability, cold extremities | Blood þ CSF | Cefotaxime/C2              | Survived         |
| Nagamatsu et al (2012)          | 1                      | Not reported | Term         | Not reported     | 3                  | Not reported    | 36                 | Vaginal             | 3 d              | SG subsp. pasteurianus     | Fever, lethargy, cold extremities | Blood þ CSF | Cefotaxime/C2              | Survived         |
| Park et al. (2015)              | 1                      | Not reported | Term         | 3.6              | 1                  | Term            | 3                   | Vaginal             | 27 d             | SG subsp. pasteurianus     | Fever, lethargy, cold extremities | Blood þ CSF | Cefotaxime/C2              | Survived         |
| Saegeman et al. (2016)          | 2                      | Not reported | Term         | 3.25 – 4.19     | 2                  | Not reported    | 2 – 24 h            | Vaginal             | Blood þ CSF | CSF                  | Bacteremia | Penicillin/C2            | Survived         |
### Table 1 (Continued)

| Reference | GA (wk) | Birthweight (g) | Age of presentation | Symptoms | Sepsis, meningitis | Organism | Sites of infection | Final antibiotic therapy | Number of neonates reported | Delivery type | Diagnosis | Final disposition |
|-----------|---------|----------------|---------------------|----------|------------------|-----------|------------------|-------------------------|---------------------------|----------------|----------|-----------------|
| Chen et al (2021) | 36 | 1300–1500 | 2–5 d | Respiratory distress, fever | Sepsis | *Streptococcus pasteurianus* | Ampicillin | Survived | 1 | Vaginal | Sepsis | Died at 5 h |
| Geetha et al (2021) | 26 | 1200–1500 | 3–5 d | Respiratory distress, fever | Sepsis | *Streptococcus pasteurianus* | Ampicillin | Survived | 4 | Vaginal | Sepsis | Died at 5 h |
| Williams et al. | 36 | 1300–1500 | 2–5 d | Respiratory distress, fever | Sepsis | *Streptococcus pasteurianus* | Ampicillin | Survived | 1 | Vaginal | Sepsis | Died at 5 h |
| Saegeman V, Cossey V, Loens K, Schuermans A, Glaser P. | 36 | 1300–1500 | 2–5 d | Respiratory distress, fever | Sepsis | *Streptococcus pasteurianus* | Ampicillin | Survived | 4 | Vaginal | Sepsis | Died at 5 h |

Conflict of Interest
None declared.

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*Abbreviations: CSF, cerebrospinal fluid; GA, gestational age; GBS, group B streptococcus; S., Staphylococcus; SG, Streptococcus gallolyticus; subsp., subspecies; UTI, urinary tract infection.*
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