



# Fatal Case of Early Onset Group B Streptococcal Infection in One of the Neonates of a Di-Chorionic/Di-Amniotic Gestation: is Microbiological Screening Enough for Prevention?

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## Abstract

Early onset Infection due to *Streptococcus agalactiae* or Group B streptococcus may be acquired during delivery or gestation and can present with severe sepsis, meningitis and pneumonia. Discordant twin gestations due to Group B streptococcus infection are rarely reported. We describe here a fatal gestational Group B streptococcus infection, in a neonate of a di-chorionic/di-amniotic gestation, delivered with cesarean section at week 32. Twin A was admitted immediately after delivery in the neonatal intensive care unit (NICU) and was treated with IV ampicillin after initial routine serum, blood, urine and cerebrospinal fluid tests. Antibiotic administration, respiratory and systems support, symptoms of systemic infection were rapidly offered. The infection was fatal developing rapidly within 24 hours. Blood cultures demonstrated infection by Group B streptococcus in only the presenting fetus. Maternal placental and high vaginal sample before antibiotic administration at the operation theater revealed identical molecular patterns of invasiveness markers (rib, alpha2/3 genes) and antibiotic resistance profiles of GBS suggestive of maternal transmission, most probably after silent chorioamnionitis. Maternal microbiological screening, with vaginal and rectal samples, at 29 weeks of gestation was negative for GBS. Culture microbiologic screening appears to have some limitations, especially, when an enrichment broth for GBS is not used. Molecular epidemiology seems useful to clarify the transmission route.

**Keywords:** Group B streptococcus; Prevention; Early onset; Discordant twins

## Introduction

Group B streptococcus (GBS, *Streptococcus agalactiae*) is a major cause of meningitis and sepsis, in newborns and infants. These infections are classified as early onset (from birth to Day 6) or late onset (from Days 7 to three months). The GBS that causes early-onset infection is usually transmitted from mother to newborn, and late-onset infection is usually transmitted via vertical or horizontal route. Rare cases of twins are reported both in mono-chorionic/di-amniotic and di-chorionic/di-amniotic twins showing unique disease course and outcomes [1,2]. It is supposed that genetic background, strain invasiveness and underlying maternal or embryo disease represent still non-elucidated factors of severe or fatal GBS infection in the newborn [3]. The CDC obstetric guidelines recommend culture-based microbiologic screening for all pregnant women during weeks 35–37 of gestation, but this might be earlier if a preterm delivery is suspected [3]. Because of low sensitivity of culture, negative screening results are associated with cases of invasive GBS [4]. We report here a rare case of GBS in one of two di-chorionic/di-amniotic discordant twins.

## The case

A 32-year old woman with a di-chorionic/di-amniotic gestation after IVF, was scheduled to have an elective caesarian section (CS) due to her request, on the basis of “only opportunity ever”. First trimester screening showed two healthy di-chorionic/di-amniotic embryos. Once per month the pregnant was examined by ultrasonography (US), and the necessary blood tests. At week 29 discordant embryos were found, with no pathological signs. Screening culture

for GBS performed at the same time was negative. At week 32 the gravid, with only 37.1 °C fever and no signs of infection underwent caesarian section due to a reverse flow in the ductus venosus of Fetus A, monitored during a doppler examination. Both of the twins were admitted immediately in neonatal intensive care unit (NICU). Twin A demonstrated Apgar score 2 at min1, 4 at min 5 and 5 at min 10 and 2060 gr weight. Twin B showed Apgar scores 7 min 1 and 8 min 5 and at day 7 of life, 1720 gr weight.

Upon admission, physical examination of twin A revealed initially fever (38.1°C) and later on low temperature, peripheral cyanosis, breathing difficulty, stressed appearance, irregular heart rate, lethargy and pale appearance, a clinical picture compatible with Infant respiratory distress syndrome (IRDS). Percutaneous saturation of oxygen air was unstable (less than 90%), and upon auscultation no inspiration crackles or expiration rhonchi were apparent. Total blood counts revealed white blood cells 18,800 / $\mu$ L, platelets 480,000 / $\mu$ L, and blood glucose 70 mg/dL, as well as elevated concentrations of serum C-reactive protein (12.0 mg/dL), total bilirubin 11.2 mg/dL, and  $\gamma$ -GT 181 IU/L in the first one hour after birth. Cerebrospinal fluid (CSF) revealed normal cell counts and glucose levels. GBS was cultured from blood, but not from urine or CSF. These findings suggested GBS systemic infection. The infant was treated with parenteral antibiotics (ceftriaxone 80 mg/kg/day), along with supportive management and oxygen. The infection however, was fatal developing rapidly with symptoms of pneumonia and progressive bradycardia within less than 12 hours.

Blood cultures demonstrated infection by Group B streptococcus in only the presenting fetus. High vaginal sample before antibiotic administration at placenta at the operation theater revealed GBS. In our hospital placenta samples for microbiology cultures and pathology investigation are taken immediately after birth, following a specific protocol used in IVF twin caesarians. Placenta culture from twin A revealed GBS whereas from twin B was sterile. The three isolated strains showed identical antibiotic resistance profiles and molecular patterns of invasiveness markers suggestive of maternal transmission. Chorioamnionitis was confirmed also by pathology characteristics of the placenta from twin A whereas twin B placenta was negative for GBS. This suggests transmission of GBS during the course of a silent chorioamnionitis from the mother. Antibiotic resistance profiles as detected by the Kirby-Bauer method were identical for all strains isolated either form the infant, placenta or from mother's vagina. The strains were sensitive to b-lactams and quinolones but resistant to erythromycin and clindamycin.

We had not the possibility to determine the capsular type and multilocus sequence, which is one of the most popular methods for molecular epidemiology of GBS. The specimens described above, along with the GBS isolate from the newborn, were analyzed by RT PCR to identify the species and their molecular epidemiology. RT PCR performed as previously described to detect indicated *rib 1*, *alp2/alp3* genes in the isolated strains; the isolates were identical in the presence of *rib1* gene, and erythromycin resistance [5]. As per our standard operation procedures, no GBS was identified during routine surveillance for newborns in the neonatal intensive care unit (NICU) using rectal swabs, or from standard cultures on samples from newborns in the same ward from day 1<sup>st</sup> and for up to one week after the newborn's admission. Twin B blood culture at day 6 showed growth of *Staphylococcus haemolyticus*. Bacteremia was transient without pathological symptoms. After 5 days of IV ampicillin administration twin B blood culture was negative and the twin B recovered.

## Discussion

The clinical syndrome presented in this patient was a typical infant respiratory distress syndrome (IRDS) with concurrent severe fulminant fatal septicemia. IRDS is one of the leading causes of admission of newborns in the NICU, especially for those born before 34 weeks of gestation (>30%). This may be caused by developmental insufficiency of the respiratory system due to immaturity but may also be caused by infection. A Maternal infection and colonization is highly associated with early-onset infectious disease of neonates [6,7]. Interestingly, twin B, was totally unaffected by GBS and survived despite its prematurity and lighter birth weight, suggesting that GBS infection caused the respiratory distress of twin A or enhanced an already occurring IRDS due to prematurity that eventually led to its death.

*Group B Streptococcus Rib1* gene encoded in pathogenicity islets detected in the isolated strain from the neonate has been reported to possess high degree of virulence in neonates, producing severe pathophysiology in experimental models and showing a good vaccine candidate [8]. To our knowledge, this is one of the rare reports to describe early-onset GBS infection in di-chorionic/di-amniotic with survival of one discordant newborn [2]. Because 95% of these patients presented symptoms within 2 days of birth, early-onset infection is believed to be transmitted by a vertical route.

The maternal screening test for GBS was negative three weeks before parturition in the current case. These observations suggest that culture-based microbiologic screening is limited in its capability to detect colonized GBS at delivery. At the same time, ultrasonography demonstrated discordant twins. This suggests that U/S is sensitive enough to demonstrate discordants, but not infection in some instances. If suspected infection, caesarian section must be performed after initial antibiotic prophylaxis, as in our case. Interestingly, twin B was the healthy infant despite the smaller weight. Silent GBS chorioamnionitis seems a threat for the embryo and must be suspected in high risk pregnancies. A novel approach is needed to improve sensitivity in order to identify GBS colonization. Vaginal colonization at delivery may differ from colonization during pregnancy. The PCR assay is a novel method to use instead or in addition to culture. A multiplex real-time PCR assay appears useful for the rapid detection of virulent GBS, and it is a novel antenatal screening method [9,10]. New point of care systems (POCs) such as antigen immunochromatography for GBS represents a new tool for the detection of GBS at the time of parturition [11]. Clinical trials need to be conducted to assess the efficacy and the costs versus benefits of near to the patient tests for future use.

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