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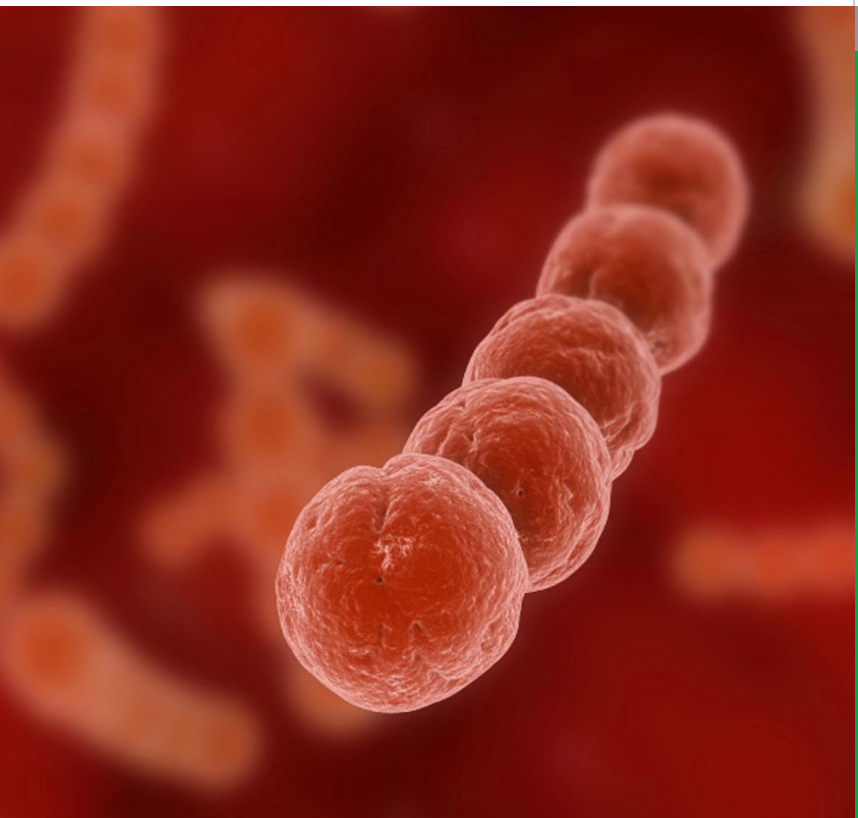
Extensive cystic periventricular leukomalacia following early-onset group B streptococcal sepsis in a very low birth weight infant



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Berger TM, Caduff JC, Neonatal and Pediatric Intensive Care Unit (BTM), Pediatric Radiology (CJH), Children's Hospital of Lucerne, Switzerland

This male infant was born to a healthy 41-year-old G4/P3 by spontaneous vaginal delivery at 30 6/7 weeks of gestation following premature rupture of membranes 20 hours earlier. The mother was HBsAg positive and group B streptococcal (GBS) carrier status was unknown. On the day of delivery, maternal CRP was 45 mg/l. No intrapartum antibiotic prophylaxis was given. The infant adapted well with an arterial umbilical cord-pH of 7.45 and Apgar scores of 5, 7, and 9 at 1, 5, and 10 minutes, respectively. He was easily stabilized on nasal CPAP, and, following insertion of an umbilical venous catheter, he was transferred to the NICU.

On admission, his vital signs were within normal limits (heart rate 165 beats per minute, blood pressure 54/30 (mean 36) mmHg, respiratory rate 46 breaths per minute, tcSaO2 95% with an FiO2 of 30%). His birth weight was 1450 g (P10), birth length 38 cm (P10) and his head circumference 32.5 cm (P25). His sepsis work-up was remarkable for a WBC of 9.8 G/l with I:T ratio of 0.71 and toxic granulations. C-reactive protein concentration was < 5 mg/l. After obtaining blood cultures, the infant was started on amoxicillin and gentamicin. Active and passive hepatitis B immunizations were administered. The C-reactive protein increased to a maximum value of only 26 mg/l on day of life (DOL) 2 and returned to 9 mg/l the next day.

On DOL 2, the infant's blood cultures were reported to be positive for GBS. In addition, placental cultures were also positive for GBS (both maternal and fetal side). At this point, a lumbar puncture was performed and revealed a cell count of 29/µl (granulocytes 16/µl, lymphocytes 13/µl) and 18'200 red blood cells. CSF gram stain and cultures were both negative.

On DOL 3, a routine cerebral ultrasound (US) examination revealed increased echogenicity of the periventricular white matter (left > right) with a more patchy appearance on the left (Fig. 2). These abnormalities were felt to be suspicious but inconclusive. A follow-up scan on DOL 6 was interpreted as showing slight regression of the previously observed periventricular white matter abnormalities (Fig. 3). Unfortunately, these hopes were destroyed when cerebral US examinations on DOL 16 and 38 revealed extensive bilateral cystic periventricular leukomalacia (PVL) (Fig. 4, 5). Clinically, no neurological abnormalites were noted and the infant was discharged home fully breastfed.

As expected, the patient developed severe disabling cerebral palsy. At the age of 5 years, he is microcephalic and severely growth restricted (body weight of 10 kg). He is non-ambulatory and communicates with only a few words. He has undergone bilateral hip surgery and his oral feedings are supplemented by tube feedings.

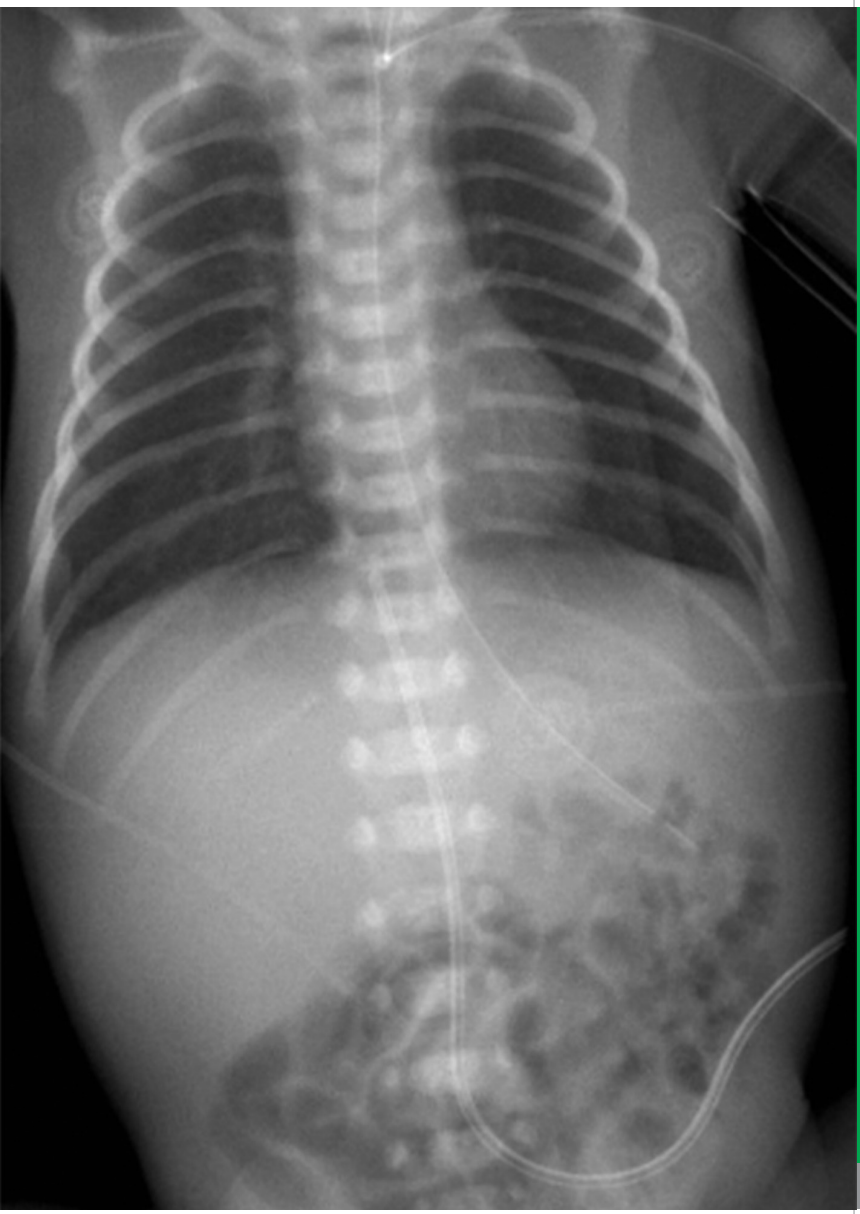

Fig. 1

Babygram on admission to the NICU: normal appearance of lungs (i.e., no evidence of HMD or pneumonia), appropriately placed umbilical venous catheter and nasogastric tube.

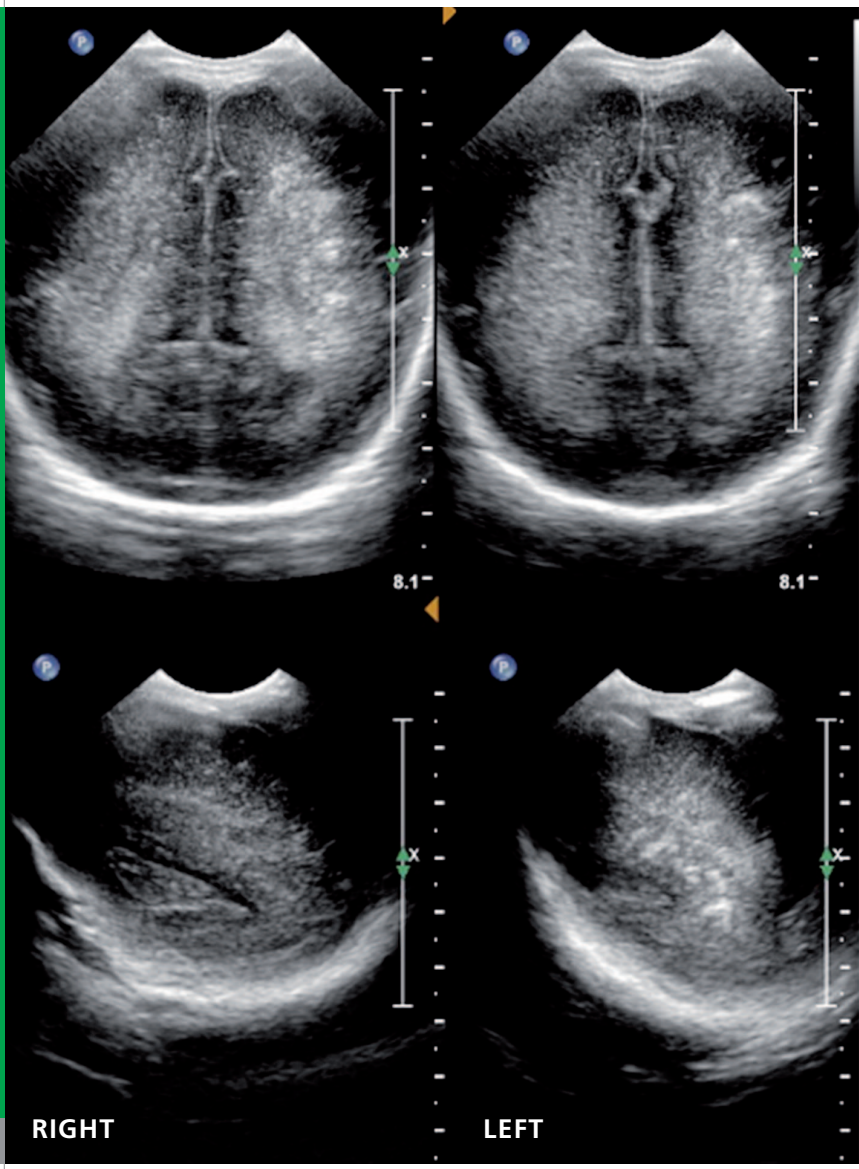

Fig. 2

Cerebral ultrasound examination (DOL 3): increased echogenicity of the periventricular white matter (left > right) (top: coronal views, bottom: parasagittal views).

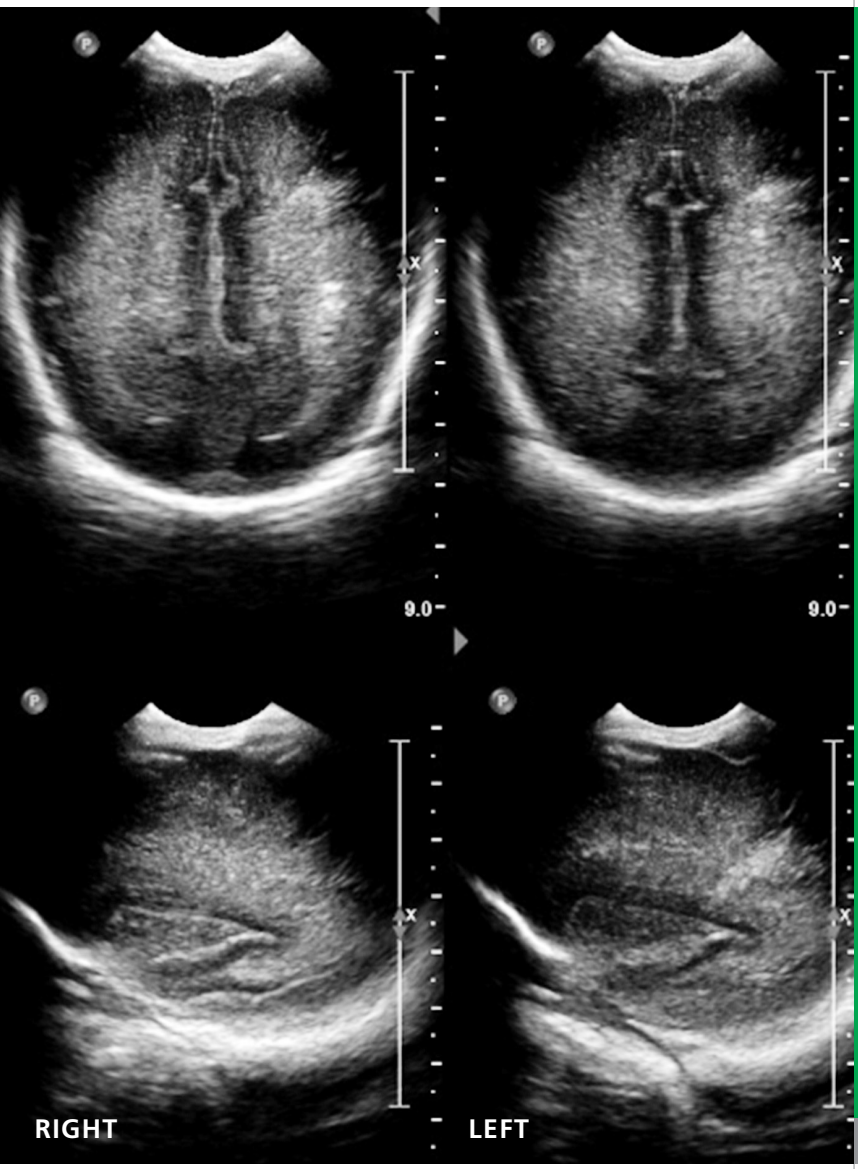

Fig. 3

Cerebral ultrasound examination (DOL 7): apparent slight regression of the previously observed periventricular white matter abnormalities (left > right) (top: coronal views, bottom: parasagittal views).

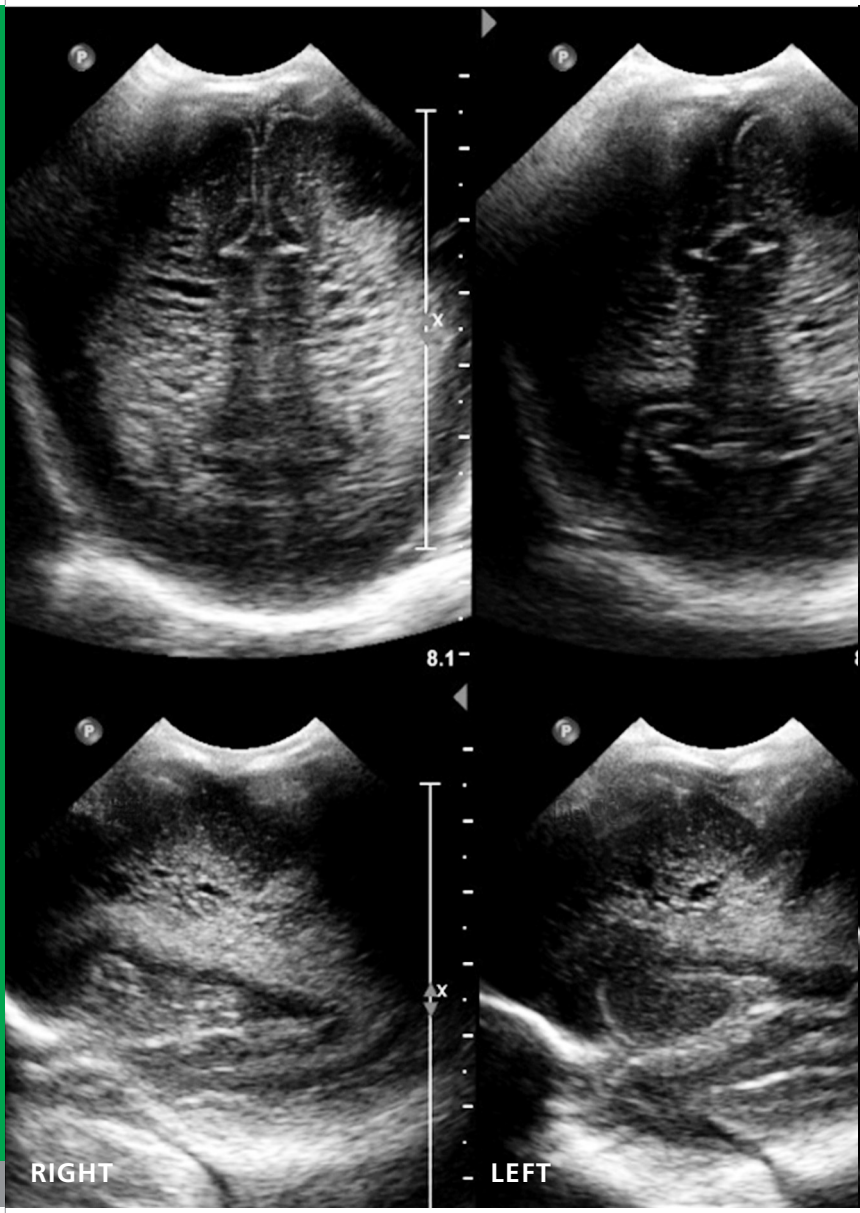

Fig. 4

Cerebral ultrasound examination (DOL 16): progression of the previously described white matter abnormalities to cystic PVL (top: coronal views, bottom: parasagittal views).

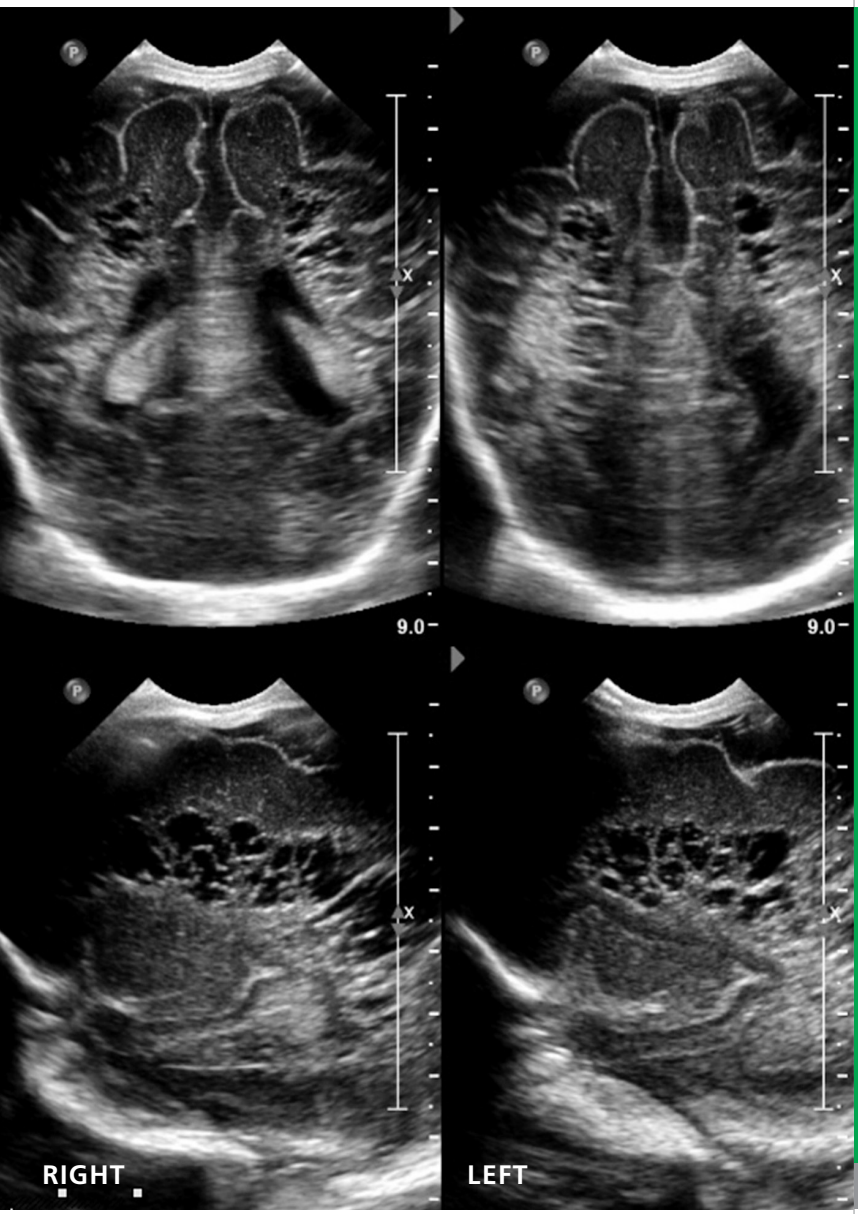

Fig. 5

Cerebral ultrasound examination (DOL 38): extensive bilateral PVL and enlarged subarachnoid spaces (top: coronal views, bottom: parasagittal views).

DISCUSSION

The risk of GBS sepsis is approximately 6/1000 for term infants born to GBS colonized mothers without antibiotic prophylaxis (1). This risk can be reduced by more than 90% by intrapartum administration of appropriate antibiotics (penicillin G, amoxicillin, or clindamycin) (1). In the presence of additional risk factors, the incidence of neonatal infection increases considerably (e.g., preterm birth at < 37 weeks of gestation, prolonged rupture of membranes, maternal fever (2): 75/1000; birth weight < 2000 g (3): 150/1000).

In our patient, maternal GBS status was not known at the time of delivery, and no antibiotics were given. Several risk factors were present, however: premature and prolonged rupture of membranes (19 hours), elevated maternal temperature (37.4° C), prematurity (30 6/7 weeks), and very low birth weight (1450 g). Although the infant did not appear ill, broad spectrum antibiotics were promptly administered. He remained hemodynamically stable without any cardiovascular support, and laboratory parameters of bacterial infection rapidly improved.

Periventricular leukomalacia (PVL) typically occurs in preterm infants. According to Volpe (4), the pathogenesis of PVL is linked to several maturation-dependent pathogenic factors that interact to render the cerebral white matter of premature infants vulnerable to injury. Two upstream mechanisms appear to play a major role

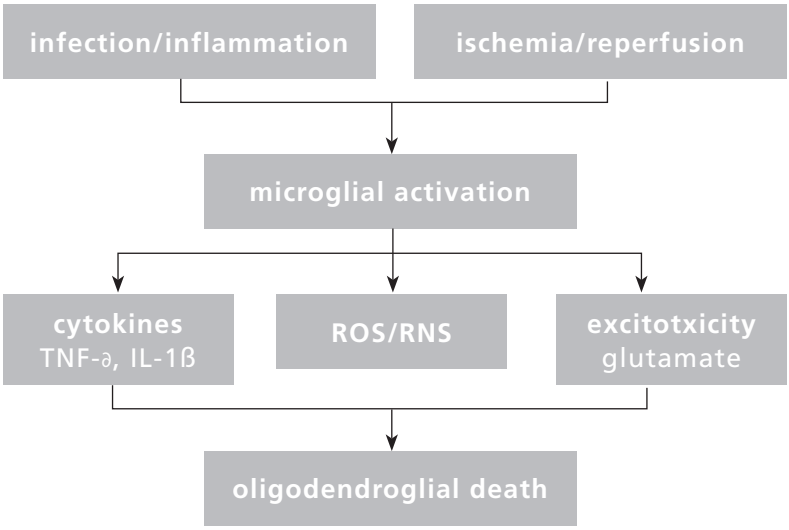

Fig.6

Schematic description of the major pathogenetic mechanisms involved in the development of periventricular leukomalacia in the susceptible preterm brain (ROS: reactive oxygen species; RNS: reactive nitrogen species).

infection/inflammation and ischemia/reperfusion (4). The two may operate in concert to potentiate each other. The critical downstream mechanisms are excitotoxicity and free radical attack (Fig. 6).

Following delivery, our patient's cardiorespiratory status was never critical and there were no episodes of hypocarbia (another well known risk factor for PVL). Therefore, presumably, global cerebral perfusion was maintained. In addition, systemic signs of inflammation, although present, were also remarkably mild. Nevertheless, he developed extensive bilateral cystic PVL.

In 1985, Faix and colleagues described the consequences of early-onset GBS sepsis in preterm infants (5). Over a two-year-period, there were 12 preterm infants with culture-proven early-onset GBS sepsis among 628 preterm infants admitted to their NICU (incidence 1.8%). Of these, 7 developed shock and 3 died at less than 12 hours of age. All 4 infants who survived GBS induced septic shock developed sonographic evidence of PVL. Interestingly, during the same time period, another 7 infants developed septic shock caused by other organisms (Klebsiella, E. coli), but none of the 4 survivors developed PVL. Three years later, Ogino et al. from Japan described the evolution of PVL in two patients with early-onset GBS sepsis (6). More recent reports of such an association, however, are lacking.

In summary, this case report illustrates the development of cystic PVL in a preterm infant with GBS infection without hemodynamic instability and thus highlights the importance of local inflammation in the pathogenesis of this catastrophic CNS lesion.

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Swiss Society of Neonatology
www.neonet.ch
webmaster@neonet.ch