

Patient Report

Congenital cystic periventricular leukomalacia in a small-for-gestational age full-term infant

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The mother was 36 years old with a birth history of gravida two para 2. Fetal ultrasonography indicated mild ventriculomegaly from 22 weeks of gestation and intrauterine growth retardation from 28 weeks of gestation (Fig. 1), with unexplained causes. The mother had gestational diabetes, which was being monitored without medication, and pre-natal infections including toxoplasma, rubella, herpes and cytomegalovirus infection during pregnancy, but these were ruled out as causes.

Case report

A small-for-gestational age (SGA) infant was born at 40 weeks of gestation, with birthweight 1806 g; height 44 cm, and head circumference 30.7 cm. Apgar scores were 9 and 10 at 1 and 5 min, respectively, and no abnormal pathological findings were found in the placenta and umbilical cord. The infant appeared alert and looked healthy without spasms. Primitive reflexes including palmar grasp, rooting, and a Moro reflex were present, and no hypotonia and spasticity were noted on physical examination. Laboratory data at birth were pH 7.402, PCO₂ 33.7 mmHg, HCO₃ 20.9 mmHg, white blood cells 11 600/µL, hemoglobin 18.5 g/dL, platelet count 163 000/µL, aspartate aminotransferase 32 IU/L, alanine aminotransferase 3 IU/L, total/direct bilirubin 2.7/0.5 mg/dL, lactate dehydrogenase 970 IU/L, blood urea nitrogen 10 mg/dL, creatinine 0.8 mg/dL, glucose 62 mg/dL, Na 141 mEq/L, K 5.0 mEq/L, Cl 105 mEq/L, Ca 9.6 mg/dL, C-reactive protein <0.01 mg/dL, IgM 8 mg/dL and karyotypic analysis 46, XY.

Brain computed tomography (CT) at birth showed irregular ventricular dilatation and cystic periventricular leukomalacia (PVL) near the left ventricular anterior horn (Fig. 2a), and brain ultrasonography (US) showed the same findings. Brain magnetic resonance imaging (MRI) at 7 days of age showed cystic PVL and irregular ventricular dilatation (Fig. 2b,c). Auditory brainstem response audiometry at 13 days of age showed no abnormal findings, and an electroencephalogram (EEG) at 14 days of age showed slightly low activity but no epileptic waves.

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After discharge from the neonatal intensive care unit the patient had a generalized spasm at 2 months of age. EEG showed a spike and wave complex in the left hemisphere. At 4 months of age the patient had a tonic spasm and an EEG showed hypersynchrony. Brain MRI at 6 months of age showed irregular ventricular dilatation and loss of white matter (Fig. 3). Thus, we diagnosed West syndrome and subsequently the patient developed spastic quadriplegia.

Discussion

In this report we describe an SGA full-term infant with cystic PVL at birth. Although cystic PVL in premature infants is the major neuropathology for spastic motor deficits in cerebral palsy or epilepsy,¹ cystic PVL in full-term infants is a rare neurological disorder of which the characteristics remain unknown.

Most cases of PVL in full-term infants are diagnosed after 4 months of age based on clinical manifestations, including developmental delay, motor abnormalities, and a history of seizures. Miller *et al.* described 12 full-term children with PVL, including seven with PVL of unexplained cause at 24.4 months.² These cases, however, did not include cystic PVL. Sie *et al.* also reported PVL in 19 full-term infants, and found that the most commonly encountered risk factors were dysmaturity or maternal pre-eclampsia during pregnancy;³ but once again there were no cases of cystic PVL.

The characteristics of occurrence of cystic PVL in an SGA infant are poorly understood. Ancel *et al.* suggested that the risk of cystic PVL may be lower among preterm SGA infants born to mothers with hypertension, antenatal hemorrhage, or preterm premature rupture of the membrane, compared to infants born after preterm premature rupture of the membrane with short latency and idiopathic preterm labor.⁴

Murata *et al.* described early changes associated with cystic PVL that may be apparent histologically within hours of insult, but at least 2–6 weeks are required before lesions can be visualized on US.¹ Therefore, if cystic PVL is observed within 7 days after birth, the origins must be intrauterine,¹ and we suggest that the cause of cystic PVL in fetal onset is different from that in postnatal onset, based on the reports of Yamamoto *et al.*⁵ and Nakamura *et al.*⁶

Yamamoto *et al.* investigated the fetal brain on transvaginal US and examined the relationship between fetal periventricular echodensity (PVE) and neonatal PVL. In PVE the quantified echogenicity



Fig. 1 Fetal ultrasonography at 30 weeks of gestation, showing mild ventriculomegaly.

is higher than in a normal brain, and PVE usually precedes the occurrence of PVL. No cystic PVL was found in US of the fetal brain in 63 high-risk fetuses at 17–32 weeks of pregnancy; instead, fetal PVE was detected in 42 fetuses, and the authors concluded that neonatal PVL was preceded by antenatal persistent fetal PVE.⁵

Nakamura *et al.* reported two autopsy cases of cystic brain lesions *in utero*. The first infant was born at 27 weeks of gestation with a birthweight of 460 g as a donor in twin-to-twin transfusion syndrome, and died immediately after birth. An autopsy showed multicystic encephalomalacia in the distribution of the anterior cerebral artery. The second infant was stillborn at 30 weeks of

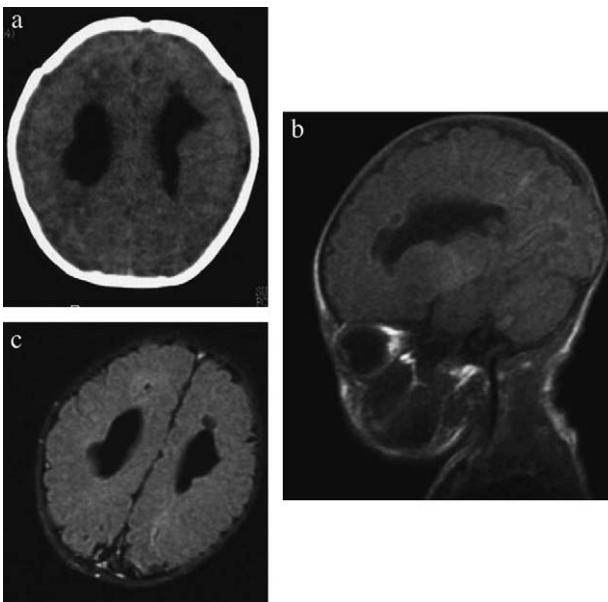


Fig. 2 (a) Computed tomography scan at birth, showing cystic periventricular leukomalacia (PVL) and ventricular dilatation. (b) Diffusion magnetic resonance image at 7 days of age, showing cystic PVL and irregular ventricular dilatation. (c) T1-weighted MR image at 7 days of age, showing cystic PVL and irregular ventricular dilatation.

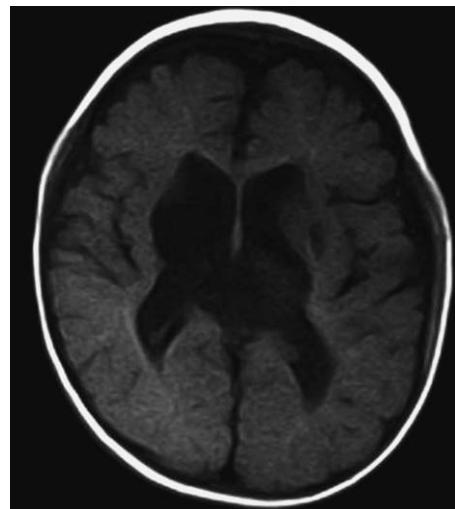


Fig. 3 Brain magnetic resonance image at 6 months of age showing irregular ventricular dilatation and loss of white matter.

gestation at a birthweight of 1030 g. An autopsy showed thanatophoric dysplasia with associated chronic PVL. The authors concluded that multicystic encephalomalacia and chronic PVL were caused by persistent circulatory disturbance *in utero*.⁶

In the present patient, although mild fetal ventriculomegaly was noted from 22 weeks of gestation, PVE and cystic PVL were not observed during pregnancy. We speculate that some persistent circulatory disturbance, perhaps induced by a traumatic event, may have occurred before 22 weeks of gestation and fetal PVE may have developed at that time, but we were unable to obtain information about traumatic events that may have affected the mother. We were also unable to perform fetal MRI, which would have been helpful for diagnosis of antenatal cystic PVL. Consequently, we propose that a diagnosis of congenital cystic PVL is appropriate for the patient, and our experience suggests that congenital cystic PVL in full-term SGA infants should be considered as a possible diagnosis in cases where fetal ventriculomegaly is noted on antenatal examination.

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