Severe fetal brain damage subsequent to acute maternal hypoxemic deterioration in COVID-19

Coronavirus disease 2019 (COVID-19) following severe acute respiratory syndrome coronavirus 2 infection can cause severe complications in pregnancy, impacting neonatal outcome. There is evidence that, during pregnancy, women become more susceptible to cell-mediated viral infections due to their physiological adaptation. Subsequently, they become more prone to cardiopulmonary decompensation caused by reduced pulmonary and cardiac reserves[1]. As a consequence, the rate of admission to the intensive care unit (ICU) is slightly higher in pregnant compared with non-pregnant women with COVID-19 (7% *vs* 4%)[2]. Hypoxemia as a result of maternal respiratory failure leading to inadequate oxygen supply to the placenta and the fetus can cause fetal distress[3,4]. We report a case of rapidly progressing COVID-19 in pregnancy.

The patient was a 36-year-old woman, gravida 6, para 4, who developed COVID-19 symptoms at 25 + 5 weeks of gestation. One week after admission, her oxygen saturation (SpO_2) dropped suddenly to 87%, while receiving 3 L/min of supplemental oxygen. She was then transferred to ICU, where her lung function deteriorated rapidly, requiring intubation and venovenous extracorporeal membrane oxygenation (ECMO) within 6 h after admission. During intubation, she suffered cardiogenic shock accompanied by acute renal failure, requiring a high dose of catecholamines and dialysis. In this critical state, the lowest SpO_2 was 77% and cardiotocography (CTG) showed intermittent prolonged fetal bradycardia (heart rate of 86 bpm). Given the pathological CTG, a Cesarean section was considered. However, the maternal condition was critical and general anesthesia was not feasible. Antiviral therapy with remdesivir was initiated, and betamethasone was administered for fetal lung maturation. The catecholamine dosage was then reduced steadily, and the patient was weaned from ECMO at 27 + 2 weeks.

The first ultrasound scan was performed at 27 + 0 weeks during ECMO and showed a normal, appropriately developed male fetus with normal fetal Doppler values. Within the next few days, we observed localized cerebral hyperechogenicity, progressing to bleeding, followed by the formation of porencephalic cysts and disintegration of the cerebellar hemispheres (Figure 1a). We observed worsening ventriculomegaly, fading basal ganglia and a ruptured falx cerebri (Figure 1b, Videoclip S1). Middle cerebral artery peak systolic velocity increased to 85.3 cm/s (multiples of the median of 2.3), indicating bleeding and anemia. The mother was counseled regarding the unfavorable outcome of the child, with a high risk for severe disability. After consideration, she opted for termination of pregnancy. Feticide and labor induction were performed at 30 + 3 weeks (birth weight of 1591 g). Samples of amniotic fluid, fetal blood, chorionic villi and fetal cerebrospinal fluid were collected at the time of feticide for virological studies (Table 1) and genetic tests (no anomaly).

The autopsy showed an atrophic cerebral cortex with dilated ventricles and hydrocephalus in addition to intraventricular bleeding. Changes caused by acute hypoxia were discerned throughout the entire central nervous system. No evidence of microangiopathy, thromboembolism or systemic fetoplacental inflammation was found. In the placental tissue, there were minor regressive changes compatible with prolonged hypoxia without signs of villitis or intervillitis.

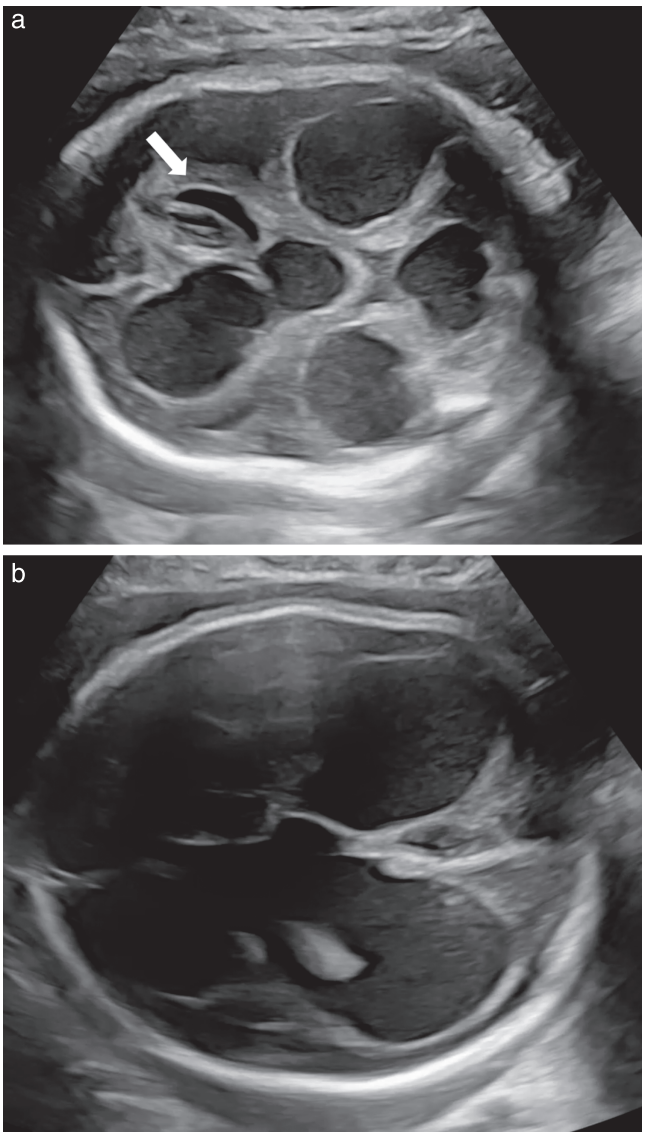

Figure 1 Grayscale ultrasound images of fetal head obtained at 29 + 4 weeks of gestation in a pregnancy with coronavirus disease 2019, showing progressive hydrocephalus with third and fourth ventricle dilatation, development of porencephalic cysts (arrow) and a disintegrating cerebellum with significant loss of the hemispheres (a) and progressive macrocephaly and hydrocephalus *e vacuo* (anterior ventricular diameter, 25.9 mm; posterior ventricular diameter 32.8 mm) (b).

Table 1 Findings of severe acute respiratory syndrome coronavirus 1/2 screening tests in the mother and fetus

Specimen	*RT-PCR*	*qPCR*	*IgG*
Amniotic fluid	Positive (37 Ct)	—	—
Chorionic villi (native)	Positive (38 Ct)	—	—
Fetal cerebrospinal fluid	Negative	—	—
Fetal blood	—	Negative	Positive
Fetal nasopharyngeal swabs	Negative	—	—
Fetal anal swabs	Negative	—	—
Maternal plasma	—	—	Positive

Ct, cycle threshold; IgG, immunoglobulin G; qPCR, quantitative polymerase chain reaction; RT-PCR, reverse transcription polymerase chain reaction.

The observation of massive fetal brain damage secondary to critical cardiopulmonary deterioration and acute maternal hypoxia highlights the importance of close monitoring and sufficient oxygenation ($SpO_2 > 95\%$)[5] of women with COVID-19 during pregnancy.

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SUPPORTING INFORMATION ON THE INTERNET

The following supporting information may be found in the online version of this article:

Videoclip S1 Neurosonography at 29 weeks of gestation showing macrocephaly and hydrocephalus with porencephalic cysts, dilated lateral, third and fourth ventricles, a ruptured falx cerebri and fading basal ganglia. The corpus callosum was not detectable and the cerebellum had undergone cystic transformation with disintegration of the hemispheres.

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