



Case report

Stillborn child with diffuse SARS-CoV-2 viral infection of multiple organs

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ABSTRACT

In May 2020, a pregnant woman in her 37th pregnancy week was diagnosed with COVID-19 in St. Petersburg in Russia. All treatments failed and the patient died after 11 days due to acute respiratory distress syndrome. A stillborn child was removed by caesarian section. Pathological investigations showed that the child died due to antenatal asphyxia with aspiration pneumonia. The child was positive for SARS-CoV-2 and immunohistochemical investigations showed viral infection and cellular changes in several organs such as pancreas, brain, spleen, and adrenals. These results emphasize the importance of vaccinating pregnant women against SARS-CoV-2.

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Introduction

For pregnant women infected with SARS-CoV-2, there may be an increased risk for hospitalization, preterm birth, and maternal mortality [1–3]. Therefore, attention to the importance of a global COVID-19 maternal immunization plan has been drawn [4], as it has been indicated that mRNA COVID-19 vaccines are safe and without significant side effects for pregnant women [5].

Most neonates born to infected women tested negative for SARS-CoV-2, and the majority of those testing positive for the virus presented with mild symptoms [6,7]. Infections of infants with SARS-CoV-2 have primarily been observed when the mother was infected within one week of delivery [7]. For most cases, it is unclear whether the mother-to-child transmission occurred in utero, in-trapartum, or early in the postnatal period. Rare cases of SARS-CoV-2 in utero vertical transmission has been reported [8,9], but so far, only placental involvement was reported, whereas fetal organ infection has not been documented.

Here, we report a pregnant woman that died due to COVID-19 in the 39th gestation week. Investigation of her stillborn child showed

in utero infection with SARS-CoV-2 and that the child also died due to the infection. Immunohistochemical investigations of the child showed viral infiltration and cellular changes in several organs.

Case presentation

In May 2020, a 34-year-old woman at gestational week 38 was admitted to hospital with respiratory symptoms and slightly increased temperature three days after the first symptoms appeared. Two days later, the respiratory symptoms aggravated and she was transferred to our hospital (S.P. Botkin Infectious Hospital), where she tested positive for SARS-CoV-2 by PCR. CRP, D-dimer, and IL-6 values were highly increased (Table 1) and she received amoxiclav, azithromycin and kaletra. Intravenous immunoglobulin prepared from convalescent plasma from recovered COVID-19 patients or other antibody-based therapies were not considered at this time of the pandemic. At this stage, the uterus had a normal tone and the fetus was alive and moving. Blood values, however, worsened and eleven days after disease onset, the patient died due to severe viral pneumonia with acute respiratory distress syndrome (ARDS). A stillborn boy of 4240 g and 55 cm was removed by caesarian section. Fetal heart rate monitoring was not performed continuously and therefore the exact time of death is unknown. Viral placentitis with chronic insufficiency and acute placental decompensation was observed.

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Table 1

Laboratory data of a pregnant woman infected with SARS-CoV-2. At day 6 after disease onset, she was admitted to hospital. At day 11, she died due to acute respiratory distress syndrome.

	Days after disease onset					Normal range
	Day 5	Day 7	Day 9	Day 10	Day 11	
Haemoglobin	97-103 g/L					115-165 g/L
LDH	488 U/L	444 U/L	1521 U/L	3040 U/L	2850 U/L	140-280 U/L
CRP	394 mg/L	255 mg/L	388 mg/L	420 mg/L	45 mg/L	0.8-3.0 mg/L
Total protein	56.4-48 g/L					60-83 g/L
ALT					325 U/L	7-35 U/L
AST					1152.4 U/L	10-36 U/L
Ferritin			71.8 µg/L	139.0 µg/L	238.4 µg/L	12-150 µg/L
D-Dimer			3.82 µg/mL	2.90 µg/mL	4.12 µg/mL	≤ 0.5 µg/mL
Fibrinogen			5.85 g/L	5.76 g/L	4.67 g/L	2-4 g/L
IL-6			90.6 pg/mL	101.0 pg/mL	13.8 pg/mL	< 5.0 pg/mL
PCT					0.89 ng/mL	< 0.15 ng/mL

During autopsy of the child, lung and trachea swabs were positive for SARS-CoV-2 and pathological investigations showed antenatal asphyxia with aspiration pneumonia. In all organs, endothelial cells with enlarged light nuclei appeared and proliferative overgrowth of bronchial epithelium and macrophages was observed. Proliferative changes in the lungs as observed in adults infected with SARS-CoV-2 were noticed, but without signs of ARDS (Fig. 1A). Nodular hyperplasia in the adrenal cortex was detected and mononuclear infiltration and cellular changes were documented in liver and kidney and more pronounced in the pancreas (Fig. 1B,C) as

found in adult COVID-19 patients. Virus antigen was detected in brain, kidney, heart, spleen, adrenal, and pancreas (Fig. 1D).

Discussion

We describe a case of a pregnant woman with COVID-19 leading to intrauterine infection with SARS-CoV-2 causing the death of both mother and child. Thus, we confirm the possibility of intrauterine transplacental viral challenge of the fetus. In several organs of the stillborn child, we observed viral infiltration and cellular changes.

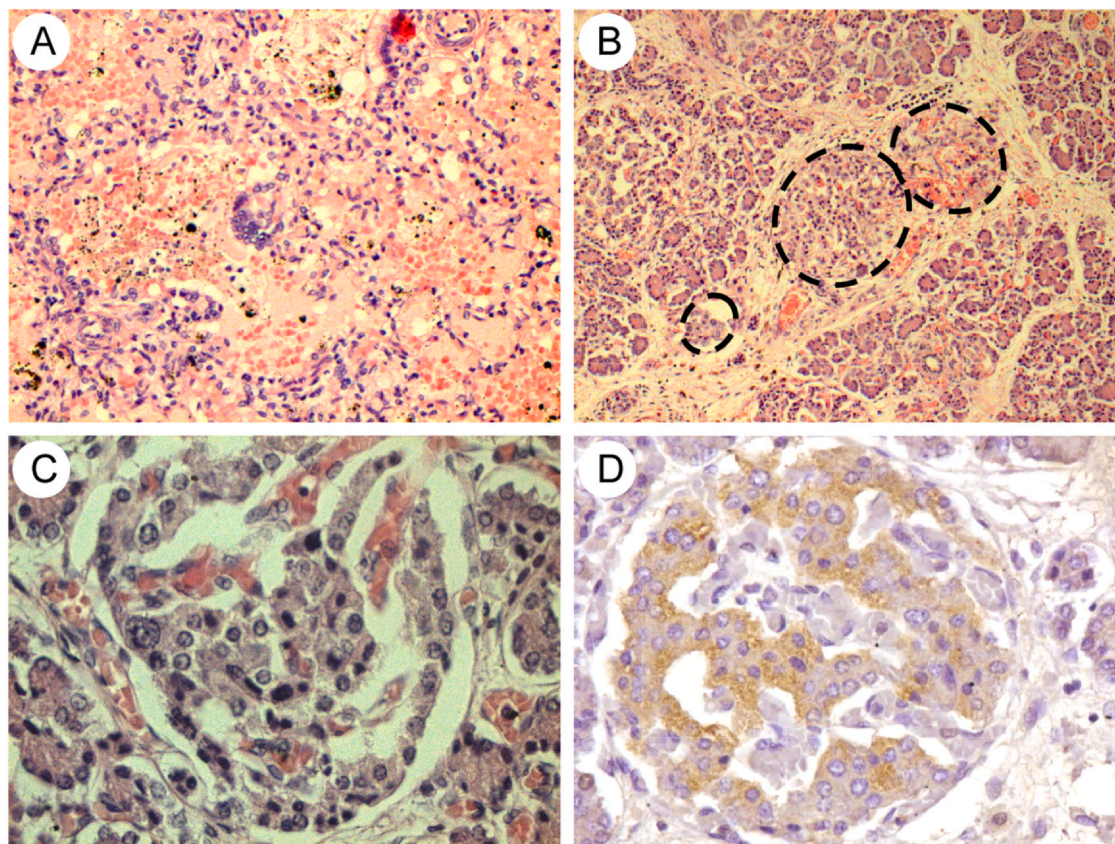


Fig. 1. Organs from stillborn child with COVID-19 show viral infiltration. (A) H&E stained lung section showing lymphocytic infiltration (red) and proliferation of epithelial cells. 100x magnification. (B) H&E stained pancreas section showing lymphocytic infiltration (red). Islets are indicated in black. 100x magnification. (C) H&E stained sections demonstrating cellular changes in an endocrine pancreatic islet. 400x magnification. (D) Coronavirus spike proteins in the islets detected by immunohistochemistry (brown). 400x magnification.

In adult COVID-19 patients, SARS-CoV-2 were shown to infect and replicate in cells of the endocrine and exocrine pancreas [10,11]. Moreover, in both the exocrine and endocrine pancreata from COVID-19 patients, infiltration with immune cells and signs of necroptosis have been observed [11]. This implies that beta-cell infection with SARS-CoV-2 might lead to either direct or indirect impairment of the beta-cells functions causing variable degrees of metabolic dysregulation [12]. Several studies report hyperglycemia and ketoacidosis after an infection with SARS-CoV-2 [13,14], and new-onset diabetes after COVID-19 has been reported in a number of studies [15,16]. However, it remains a subject of discussion if COVID-19 can indeed directly or indirectly lead to new-onset diabetes or accelerate pre-existing unrecognised diabetes or prediabetes.

Previously, a direct infection of the adrenal gland with SARS-CoV-2 has been detected of COVID-19 patients [17], and as the stillborn child was positive for SARS-CoV-2 in the adrenal, a direct cytopathic effect may possibly be confirmed.

Whether an intrauterine infection with SARS-CoV-2 might lead to lasting consequences for surviving children, as observed in adults, still needs to be investigated. At present, pregnancy and neonatal outcomes are being investigated in different registries of pregnant women with suspected or confirmed SARS-CoV-2 infection in order to guide treatment and prevention [18–20].

Currently, a fierce discussion if pregnant women should be vaccinated against coronavirus is taking place. Therefore, this case is of particular interest as we show that a stillborn boy had viral infiltration in brain, kidney, pancreas, heart, adrenals and probably other organs. These data indicate the importance of vaccination during pregnancy in order to protect both the mother and the child.

Consent

Unfortunately, the patient and her child died before written and signed consent to publish was obtained. According to the rules of the ethics committee in Russia, written consent from relatives to deceased patients is not necessary. Therefore, only verbal consent was obtained from the husband after the death of the patient and her child.

Ethical approval

Consent from relatives to the patient was obtained according to the rules of the local ethics committee.

CRediT authorship contribution statement

MAV were involved in clinical care of the patient and clinical documentation. TN and YS made autopsies, VZ, TN, YS, and NS performed the histopathological study. CS reviewed the literature and wrote the first draft. SRB edited the initial draft. All authors read and approved the final submitted version.

Declaration of Competing Interest

The authors declare that they have no competing interests.

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