

## Case Report

# Distinct perivillious fibrin deposition and evidence of persisting positive SARS-CoV-2 PCR in placental tissue after COVID-19 Infection in the second trimester

Beda Hartmann, Lisa Rindler\* and Selma Hoenigschnabl

OBGYN, Klinik Donaustadt, Austria

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**\*Corresponding author:** Lisa Rindler, Assistant Doctor, MD, OBGYN, Klinik Donaustadt, Austria, Tel: +436803335517; E-mail: [lisa.rindler@gmx.net](mailto:lisa.rindler@gmx.net)

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## Abstract

**Background:** The effects of Coronavirus disease 2019 in women during the second trimester of pregnancy and the health of the fetus, remain very poorly explored. This report describes a case in which the normal development of pregnancy was complicated immediately after the patient had experienced COVID-19 at the 21<sup>st</sup> week of gestation. Specific conditions included critical blood flow in the fetal umbilical artery, fetal growth restriction and hydramnios in the 25<sup>th</sup> week of gestation.

After informed consent, we decided just to wait and interrupted all examinations (CTG, Ultrasound) because of the high risk of severe adverse events at such an early premature birth. The patient finally delivered a healthy boy in the 39<sup>th</sup> week of gestation.

**Methods:** We performed a histological examination of the placenta and analyzed the placenta for the presence of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) through molecular and immunohistochemical assays and measured the fetal antibody response in the blood to this infection.

**Results:** In the immunohistochemical examination with antibodies against SARS-CoV-2 a partial positivity in the villous trophoblastic epithel cells could be demonstrated. The PCR swab of the placenta which was obtained was positive for SARS-CoV-2 with a crossing threshold value of 22,8. The histological examination of the placenta showed a Massive Perivillous Fibrinoid Deposition (MPFD) with multiple focal placental infarctions in the intervillous space, intervillous thrombus, and a localized chorangiomas.

**Conclusion:** According to many clinical and laboratory findings in this patient, the histopathological features and viral infection of the placenta suggest a prominent role for COVID-19 in this patient's presentation. This is highlighted by the presence of levels of SARS-CoV-2 RNA. In this patient, an infection with Sars-CoV-2 might have caused the development of the MPFD. These findings suggest that COVID-19 may have contributed to placental dysfunction and fetal growth retardation. Also with a SARS-CoV-2 PCR test with a crossing threshold value of 22,8, it must be assumed that the placenta has been potentially infectious.

## Introduction

The effects of SARS-CoV-2 on maternal and perinatal outcomes remain poorly understood due to the limited research on clinical manifestations and laboratory findings in pregnant women with Coronavirus disease 2019 (COVID-19) [1]. Published case reports and case series have individually reported wide variability in the rate of vertical transplacental transmission [2]. Very little remains known about maternal

and neonatal outcomes due to SARS-CoV-2 infection in the second trimester of pregnancy [3].

## Case report

The patient reported is a 27-year-old gravida I, para 0. She was initially sent to our department for antenatal diagnostics by a resident specialist at 24 weeks+4 days gestation in November 2020 because of a fetal growth restriction < 3. Percentile with an anhydramnion and a pathological blood flow

in the fetal umbilical artery. The patient was before diagnosed with a COVID-19 infection in the 21<sup>st</sup> week of pregnancy in October 2020. She had shown mild symptoms such as fever, shortness of breath, fatigue, and light coughing. In the 25<sup>th</sup> week, the pregnant woman was already COVID-19 negative and had no clinical signs of disease. Despite the previous COVID-19 disease, she was a healthy woman without any preexisting disorders. Because of a higher risk of preeclampsia, diagnosed in the combined test for the first time non she was taking 150 mg of Aspirin once a day. The ultrasound scan at our antenatal diagnostics confirmed the previously detected fetal growth restriction (< 3<sup>rd</sup> percentile) and the anhydramnion. The Doppler scan showed absent diastolic flow in the umbilical artery.

We performed a fetal lung maturation at 24 weeks+4 days gestation. The patient was seen again at 25 weeks+0 days gestation multiple blood tests including TORCH complex and another ultrasound with persisting results have been performed. The blood examinations didn't show any pathological results. Because of the high risks of neonatal morbidity and mortality at such an early premature birth different options for a further approach have been discussed. While the couple rejected every invasive diagnostic procedure, they agreed on a prospective approach to wait out. After four weeks in the following checkups, the amount of the amniotic fluid normalized. Sonographic growth controls were performed on a regular basis every 10 days, which showed a constant growth of the fetus. At 38 weeks 0 days of gestation labor was introduced because of decreasing child movements. As it's a standard procedure at our department in times of the COVID-19 pandemic, a nasal swab for a SARS-Cov-2 PCR was obtained, which proved to be negative. After induction of labor two times, 10 mg dinoprostion vaginal insert and 50 mcg Cyprostol p.o. the contractions started and the patient delivered a healthy boy via vaginal delivery with a birthweight of 2700 g (6. percentile) with an APGAR-score of 9/10/10 without any complications in 38 weeks and 2 days of gestation. Because of the COVID-19 infection in the second trimester, the placenta has been sent to the pathology department for a histological and immunohistochemical examination and a PCR swab for SARS-Cov 2 of the placenta has been obtained. A nasopharyngeal swab of the newborn for a SARS-Cov-2 PCR diagnostic has been obtained right after birth. An examination of a blood sample of the umbilical cord with an Elecsys Anti-SARS-CoV-2 S Assay' has been performed.

## Results

The histological examination of the placenta showed a Massive Perivillous Fibrinoid Deposition (MPFD) with multiple focal placental infarctions in the intervillous space, intervillous thrombus, and a localized chorangiomas. The umbilical cord was normal, without any signs of inflammation. In the immunohistochemical examination with antibodies against SARS-CoV-2, a partial positivity in the villous trophoblastic epithel cells could be demonstrated. The PCR swab of the placenta which was obtained was positive for SARS-CoV-2 with a crossing threshold value of 22,8. An examination of a

blood sample of the umbilical cord with an 'Elecsys Anti-SARS-CoV-2 S Assay' (Company Roche) [4], showed neutralizing SARS-CoV-2 antibodies in the newborn. The Elecsys Anti-SARS-CoV-2 s Assay is a quantitative serologic assay that measures antibodies against the receptor-binding domain of the S protein.

No examination of the maternal antibodies has been accomplished. The nasopharyngeal swab of the newborn for a SARS-Cov-2 PCR diagnostic that has been obtained right after birth was negative.

## Discussion

Reports of mother-to-child transmission of SARS-CoV-2 during the antepartum period remain limited. This report describes a case of second trimester COVID-19 associated with fetal growth retardation, MPFD and evidence of persisting positive SARS-CoV-2 PCR in the placental tissue. The morphological presentation of the placenta is a sign of chronic intervillous hypoxia.

MPFD is a recurring pathology with significant adverse outcomes in pregnancy including recurrent pregnancy loss, IUGR and IUFD. In patients with such clinical scenarios, the placental exam should definitely be performed and the identification of MPFD/MFI and other recurring pathologies should alert the pregnancy management team to the risk of recurrent complications in subsequent pregnancies. Closer monitoring should be provided and other treatment options considered [5].

Accounted to many of the clinical and laboratory findings in this patient, the histopathological features and viral infection of the placenta suggest a prominent role of Covid-19 in this patient's presentation. This is highlighted by the presence of SARS-CoV-2 RNA. These findings suggest that COVID-19 may have contributed to placental dysfunction and fetal growth retardation. Also with a SARS-CoV-2 PCR test with a crossing threshold value of 22,8, it must be assumed that the placenta has been potentially infectious. Fetal pathologists should therefore continue to ensure that standard precautions are followed when handling biological samples from patients suspected of SARS-CoV-2 infection [6].

The adverse neurodevelopmental outcome associated with MPFD/MFI suggests that, for children born with severe placental pathology, long-term follow-up should be provided, even if there are no significant problems during the perinatal and neonatal periods [5].

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