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Possible intrauterine transmission of SARS-CoV-2: Ultrasound findings and viral molecular detection in amniotic fluid



Possible transmisión intrauterina del SARS-CoV-2: Hallazgos ecográficos y detección molecular viral en líquido amniótico

Dear Editor,

The coronavirus disease-19 (COVID-19) is an infectious disease associated to the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), a novel single-stranded RNA-enveloped virus primarily transmitted person-to-person by close contact through respiratory droplets. In addition, studies have shown the effects of SARS-CoV-2 infection during pregnancy including potential vertical transmission of the virus.^{1–3} Although the mechanisms of intrauterine transmission are not fully understood,⁴ it has been found that SARS-CoV-2 infection may lead to placental vascular lesions, breakdown of the placental barrier and fetal intrauterine viremia.⁵ In this rare report, we present fetal ultrasound (US) findings and RT-PCR results in a possible case of vertical transmission of SARS-CoV-2.

We describe the case of a 42-year-old pregnant woman with past medical history of hypertension and gestational diabetes. At 11 and 20 weeks of gestational age, she had flu-like symptoms (runny nose, sore throat, cough, sneezing and headache) and the results of RT-PCR for SARS-CoV-2 were positive at both time points. At 25 weeks of gestation, US findings showed symmetric hyperechogenic signals (“in mirror”) in the right and left fetal hypochondrium suggesting liver calcifications, and placenta exhibiting punctate hyperechogenic foci also compatible with calcifications (Fig. 1A and B). At 28 weeks of gestation, there was a significant progression in calcifications and changes in placental shape (Fig. 1C). In the 32nd week, the pregnant woman was vaccinated with AstraZeneca/Oxford COVID-19 vaccine.

STORCH (syphilis, toxoplasmosis, rubella, cytomegalovirus, and herpes simplex virus) screening test results were negative. At 36 weeks of pregnancy, there was a reduction in fetal movements with amniochorial detachment (Fig. 1D), and the patient was referred for a cesarean delivery. On admission for delivery, the patient had no symptoms suggestive of COVID-19 and the RT-PCR result from nasopharyngeal swab was negative. A full-term female infant weighing 2238 kg was born uneventful with an Apgar score of 9 and 10 in 1 and 5 min, respectively. Intraoperative amniotic

fluid was collected for RT-PCR analysis, which showed a positive result for SARS-CoV-2 (cycle threshold value: 30). On the 2nd postpartum day, nasopharyngeal swabs were collected from the mother and newborn and the RT-PCR results were negative. SARS-CoV-2 IgG antibodies were detected in neonatal blood serum two days after birth, but IgA results were negative. Intrahepatic calcifications continued to be found on ultrasound examination after birth (Fig. 1E). No clinical or neurological complications were documented during the first six months of life.

Vertical transmission can be defined as the generational transmission of viruses from mothers to their offspring, whether intrauterine, intrapartum or in the early postnatal period. There is limited evidence on the vertical transmission of SARS-CoV-2. In a review of 51 studies with 336 infants, only one amniotic fluid sample was positive for SARS-CoV-2 by RT-PCR.⁶ It is known that SARS-CoV-2 uses the angiotensin-converting enzyme 2 (ACE2) receptor for the entry into the host cells especially in kidneys, heart, respiratory and gastrointestinal tract tissues. In addition, previous studies have also shown the expression of ACE2 in the placenta.⁷ Despite these findings, the potential mechanisms of maternal-fetal transmission of SARS-CoV-2 remain unclear. A recent study has found a high expression of ACE2 in the placenta during the first and second trimesters of pregnancy, which suggests a potential risk for intrauterine infection, placenta dysfunction, and pregnancy complications from SARS-CoV-2.⁸ Contrasting results have been observed during the third trimester of pregnancy. In a prospective cohort study performed by Edlow et al.,⁹ it was suggested a nonoverlapping placental ACE2 and TMPRSS2 (a vital serine protease for the SARS-CoV-2 infectivity) expression as a protective mechanism against vertical transmission of SARS-CoV-2 during the third trimester, despite the decreased transplacental transfer of anti-SARS-CoV-2 antibodies to the fetus.

In this report, our patient had two positive results for SARS-CoV-2 infection during the first 20 weeks of pregnancy and placental changes in the following weeks. In addition, hepatomegaly and persistent calcifications were found in the fetus. Although intrahepatic calcifications are common findings in chromosomal disorders and infections,¹⁰ there was no diagnosis of aneuploidy or congenital malformation and the results for STORCH were negative. Furthermore, there is evidence of increased expression of ACE2 in liver fibroblasts and hepatocytes from first to second trimester, which suggests that fetal liver is a vulnerable target organ of SARS-CoV-2.⁸

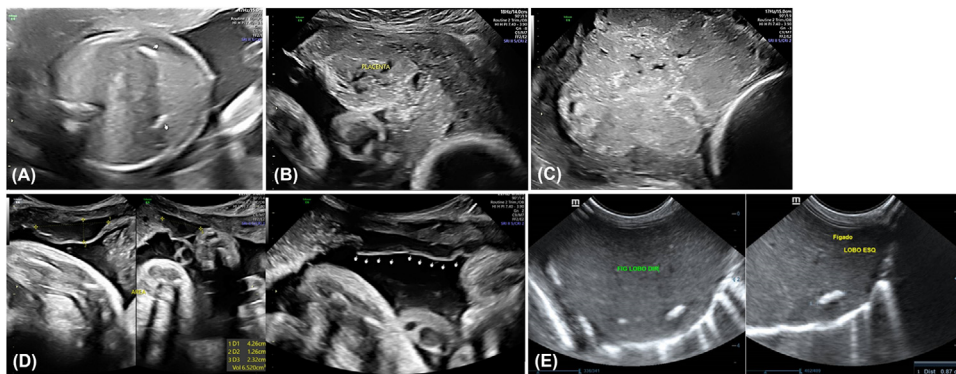


Fig. 1. Ultrasound images at 25 weeks of gestation showing liver (A) and placental (B) calcifications. At 28 weeks of gestation, there was progression of calcifications and changes in placental shape (C). At 36 weeks of pregnancy, the patient presented amniochorial detachment (D). Two days after birth, the child had persistent calcifications in the right and left liver lobes (E).

Our findings are suggestive of a possible *in utero* SARS-CoV-2 transmission, since there is evidence of maternal SARS-CoV-2 infection during the first weeks of pregnancy, placental and fetal changes suggestive of viral infection, and a positive RT-PCR result for the detection of SARS-CoV-2 RNA from a sterile sample (amniotic fluid) during childbirth. Although the child had no clinical or neurological complications after delivery, this case reinforces the possibility of vertical transmission of SARS-CoV-2 and the need for vaccination of pregnant women against COVID-19.

Authors' contributions

All authors contributed equally to the manuscript.

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Conflict of interest

The authors have no competing interests to declare.

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Uso del panel «FilmArray® blood culture identification 2» en un caso de endoftalmítis causado por *Candida parapsilosis*



Use of the “FilmArray® blood culture identification 2” panel in a case of endophthalmitis due to *Candida parapsilosis*

El sistema FilmArray® (BioFire Diagnostics, Salt Lake City, UT, EE: UU.) es una PCR múltiple que integra la preparación de las muestras, amplificación, detección y análisis. Uno de los paneles disponibles es el «Blood Culture Identification 2 (BCID2)», que permite buscar hasta 43 dianas distintas asociadas a bacteriemia, incluidos 5 genes de resistencia antimicrobiana, directamente de hemocultivos positivos. El objetivo de esta carta es presentar nuestra experiencia acerca del uso de esta técnica de PCR para ayudar en la orientación etiológica y terapéutica en un caso de endoftalmítis causado por *Candida parapsilosis* (*C. parapsilosis*).

Un hombre de 79 años anticoagulado y antiagregado con diabetes mellitus e hipertensión arterial, es operado de cataratas mediante facoemulsificación e implante de lente intraocular sin incidencias. Seis meses después, el paciente comienza con dolor,

fotofobia y ligero descenso en la agudeza visual en ese mismo ojo. A la exploración se describe fenómeno de Tyndall positivo, leve fimosis capsular con fibrosis y depósitos blanquecinos. Se realiza ecografía oftálmica que muestra datos de desprendimiento completo de retina y líneas móviles igualmente fijas al disco óptico sugestivas de membranas residuales a la endoftalmítis (fig. 1). Se toma muestra de humor vítreo (no diluida) previa a infusión de suero salino y posteriormente se lleva a cabo la vitrectomía pars plana. Se mandan muestras al laboratorio de microbiología: humor vítreo y acuoso, así como cassette de vitrectomía y del complejo saco capsular-lente intraocular. Se administra ceftazidima y vancomicina intravítrea (1000 mg y 500 mg diluidos en 50 ml, respectivamente).

A su llegada al laboratorio de microbiología, las muestras de humor vítreo y acuoso diluidas se procesan por centrifugación (5 min a 3000 rpm) y se transfiere todo el sobrenadante a otro tubo excepto los últimos 0,5 ml. El sedimento se resuspende en estos 0,5 ml para realizar tinciones de Gram y siembras de cultivo. Las muestras son sembradas en agar chocolate (Becton Dickinson, Franklin Lakes, NJ, EE. UU.), agar tripticosa soja al 5% de sangre de carnero (Becton Dickinson, Franklin Lakes, NJ,