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SEVERE ACUTE RESPIRATORY SYNDROME CORONAVIRUS 2 VERTICAL TRANSMISSION FROM AN ASYMPTOMATIC MOTHER

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Abstract: In utero transmission of severe acute respiratory syndrome coronavirus 2 infection is a point of debate. We report a case of severe acute respiratory syndrome coronavirus 2 vertical transmission from asymptomatic mother, with molecular detection in mother's blood at delivery and neonatal nasopharyngeal swabs at 5 and 28 hours of life and later IgG seroconversion. The newborn was asymptomatic.

Key Words: coronavirus disease 2019, severe acute respiratory syndrome coronavirus 2, vertical transmission, newborn, pregnancy

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Since coronavirus disease 2019 (COVID-19) pandemic began, caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), possibility of viral transmission from an infected mother to the fetus has been a point of debate and interest. Even if SARS-CoV-2 is mainly transmitted through droplets, congenital or intrapartum transmission are possible, as virus nucleic acid has been detected in blood samples.[1] This consideration has important implications in the management of pregnant women with SARS-CoV-2 infection.

Although most studies showed no evidence of mother-to-fetus transmission, isolated cases of possible vertical transmission have subsequently been reported. These cases are heterogeneous and include different types of samples and diagnostic tools: presence of the virus in early nasopharyngeal swabs, umbilical cord blood, amniotic fluid or placenta or presence of SARS-CoV-2 antibodies in blood.[2–4] A recent systematic review determined that transmission to the fetus can occur in 3.2% of infected women in the third trimester.[5] In the reported cases, pregnant women presented COVID-19 symptoms of diverse severity. We report a case of SARS-CoV-2 vertical transmission from an asymptomatic mother with viral molecular detection in blood and nasopharyngeal swab at delivery and in neonatal nasopharyngeal swabs in 2 samples (at 5 hours and at 28 hours of life), with SARS-CoV-2 IgG antibodies conversion at 23 days of life.

METHODS

Written informed consent was obtained for both patients. SARS-CoV-2 in clinical specimens was detected with the Hologic Aptima SARS-CoV-2 Assay (Panther System; Hologic Inc., San Diego, CA), which uses transcription-mediated amplification as a target amplification mechanism.[6]

The serologic determination of anti-SARS-CoV-2 IgG antibodies against the nucleoprotein (N) was carried out by a commercial chemiluminescent microparticle immunoassay method fully automated on the Alinity i system (Abbott Laboratories, Sligo, Ireland) and, for the simultaneous detection of IgM and IgA against the spike glycoprotein (S) and nucleocapsid protein (N), an automated indirect chemiluminescent immunoassay (VIRCLIA IgM + IgA Monotest; Vircell S.L., Granada, Spain) was used. Both assays generate a qualitative positive/negative result based on assay-dependent signal thresholds.

CASE PRESENTATION

The mother was a 28-year-old woman with no relevant medical history. Pregnancy controls were normal, including prenatal ultrasound examinations. At 37+0 weeks of gestation (12 days before delivery), her partner reported mild symptoms consistent with COVID-19, with SARS-CoV-2 molecular detection positive in nasopharyngeal swab. Being asymptomatic, as close contact study, a nasopharyngeal swab was performed to the mother at 37+4 weeks (8 days before delivery), and molecular detection of SARS-CoV-2 resulted positive. Upon admission for delivery at 38+5 weeks of gestation, as a standard hospital screening protocol (to confirm a preliminary positive result and establish isolation measures), another nasopharyngeal SARS-CoV-2 molecular test was performed on the mother, and it was still positive. At that day, SARS-CoV-2 was amplified in a blood sample, SARS-CoV-2 IgM + IgA antibodies (chemiluminescent immunoassay) were

indeterminate and IgG antibodies (chemiluminescent microparticle immunoassay) were negative. No COVID-19 symptoms were reported by the mother at any moment.

Rupture of membranes happened 3 hours before delivery. A girl was born following a normal vaginal delivery. Apgar tests were 9 and 10 at minutes 1 and 5, respectively. No resuscitation maneuvers were required. Neonatal weight, length and head circumference were normal (between percentile 23 and 50 for gestational age). Wearing the mother a mask and after hand hygiene, skin-to-skin contact was allowed, and both mother and newborn were later transferred to maternity ward in joint accommodation. Contact and droplet isolation measures between the mother and her daughter were warranted: hand hygiene, mask for the mother, even while breast-feeding and 2 m separation between crib and the mother's bed. Neonatal physical examination at 2 hours of life was normal. At 5 hours of life, a newborn's nasopharyngeal swab was obtained and SARS-CoV-2 molecular detection resulted positive. In case of possible swab contamination with maternal fluids, it was repeated at 28 hours of life, with another positive result. Histologic and microbiologic studies on the placenta and umbilical cord were not performed, as samples were not available due to hospital protocol for early disposal of biological samples from COVID-19 patients.

The newborn had a close monitoring and vital signs stayed in the normal range. Automated auditory brainstem response screening test and cranial ultrasonography were normal. She was discharged home at 3 days of age. A face-to-face and telephonic follow-up was scheduled, and neither the mother nor the neonate showed any symptom. At 23 days of life, SARS-CoV-2 molecular test was negative in neonatal nasopharyngeal swab. At that moment, SARS-CoV-2 serologic test was performed on the neonate, and IgM + IgA and IgG antibodies were positive. We retrieved a sample of the mother`s stored blood at 34 + 6 weeks of gestation (28 days before delivery) and, at that time, SARS-CoV-2 IgG antibodies were negative (same as the day of delivery). Six weeks after delivery, SARS-CoV-2 serologic test was performed on the mother again and, at that time, IgG antibodies were detected, although IgM + IgA remained in an indeterminate value.

Complete microbiologic results are summarized in Figure 1.

DISCUSSION

Following previous definitions,[7,8] this is a case of SARS-CoV-2 vertical transmission, due to early positive SARS-CoV-2 molecular detection at 5 hours of life and persistence of positive result on the second sample, collected after the first 24 hours of life. According to Shah et al,[7] it would meet diagnostic criteria for a neonatal infection acquired intrapartum; according to Blumberg et al,[8] for intrauterine transmission. In addition, the newborn's SARS-CoV-2 IgG seroconversion was assumed, as SARS-CoV-2 IgG antibodies were detected in neonate at 23 days of life and the mother was IgG seronegative at birth time. Therefore, the likelihood of transplacental transfer of maternal IgG to the fetus was limited. The mother's SARS-CoV-2 IgG seroconversion was also deduced, as SARS-CoV-2 IgG antibodies were detected 6 weeks after delivery, following 2 previous negative results. This indicates that the mother's infection happened close to delivery.

An important information of our case was SARS-CoV-2 molecular detection in the mother´s blood sample. Wang et al[1] reported that a small percentage of blood samples had positive polymerase chain reaction test results (<1%), suggesting that infection sometimes may be systemic. Hence, there is a theoretical risk of intrauterine transmission, since infection may result in viremia leading to fetal infection through a disruption in the placental interface. We cannot exclude the possibility of intrapartum transmission due to exposure to maternal blood, vaginal secretions or feces. Nevertheless, SARS-CoV-2 molecular detection was positive in neonatal nasopharyngeal swab as soon as 5 hours of life, making the option of intrapartum transmission less probable.

Assessing SARS-CoV-2 vertical transmission can be challenging, as neonatal samples' contamination with maternal fluids is possible. For vertical transmission confirmation, several samples from amniotic fluid before membranes rupture, placenta or umbilical blood cord are required. However, proper collection of these samples might be difficult during labor and delivery from a SARS-CoV-2 infected mother. We describe a case in which the diagnosis of vertical transmission was based on the detection of SARS-CoV-2 in maternal blood and a positive molecular detection in neonatal nasopharyngeal swabs taken at 5 and after 24 hours of life, with serological IgG conversion in the neonate. As we have seen in our case, neonatal IgG seroconversion would be useful in those situations in which mother infection happens very close to delivery. In our case, IgM antibodies were detected in the neonate at birth and at 23 days of life and were indeterminate in the mother at delivery and 6 weeks after. Their detection in the newborn can help diagnosing vertical transmission, but if not associated with SARS-CoV-2 molecular detection, their role remains unclear.[9]

In addition, in our case, the mother showed an asymptomatic SARS-CoV-2 infection with viremia at delivery. Although SARS-CoV-2 transmission from asymptomatic patients has been reported

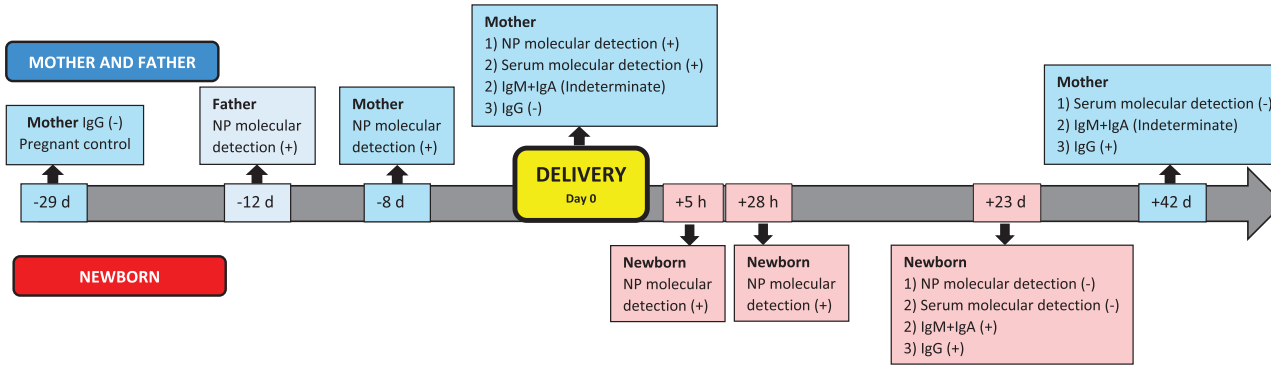

FIGURE 1. Timeline of microbiologic data. Molecular detection was performed with the Hologic Aptima SARS-CoV-2 Assay (Panther System; Hologic Inc., San Diego, CA), which uses TMA as a target amplification mechanism. (–) indicates negative result; (+), positive result; +d, post-delivery day; –d, pre-delivery day; +h, post-delivery hours; CMIA, chemiluminescent microparticle immunoassay; IgG, SARS-CoV-2 IgG antibody by CMIA (Abbott Laboratories, Sligo, Ireland); IgM + IgA, SARS-CoV-2 IgM and IgA antibodies by automated indirect chemiluminescent immunoassay (VIRCLIA IgM + IgA Monotest, Vircell S.L., Granada, Spain), NP, nasopharyngeal; TMA, transcription-mediated amplification.

from the beginning of COVID-19 alert,[10] most women transmitting SARS-CoV-2 to their fetuses or newborns usually have moderate or severe COVID-19 symptoms.[2–4] To the best of our knowledge, this is the first case of vertical transmission from an asymptomatic mother, in which, in addition, SARS-CoV-2 was detected in the mother's blood.

This case reinforces the need of SARS-CoV-2 screening of pregnant women admitted for delivery, as a positive result will have implications in the health and management of the mother and the newborn, with concerns for health workers.

Our case report has several limitations. The first sample was collected at 5 hours of life, but the baby was not thoroughly cleaned before testing. As this could result from the mother's contamination, a second sample was collected at 28 hours of life, after the baby meticulous cleaning and positive result was confirmed. Another limitation is the absence of testing for SARS-CoV-2 on placenta or umbilical cord samples. Other authors have studied those samples, and their results were useful for determining the moment of transmission.[2,3]

In conclusion, we report a case of SARS-CoV-2 vertical transmission from an asymptomatic mother to an asymptomatic newborn. This supports that asymptomatic pregnant women should be screened against SARS-CoV-2 infection during epidemic periods, and, in positive cases, vertical transmission to the newborn should be ruled out.

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SYSTEMIC CAT-SCRATCH DISEASE: A "TROUBLESOME" DIAGNOSIS

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Abstract: Diagnosis of systemic cat scratch disease may be challenging. Here, we describe a case of an immunocompetent girl exhibiting fever and multifocal hepatosplenic abscesses. Diagnostic tests for *Bartonella henselae* infection (enzyme immunoassay and polymerase chain reaction) were found steadily negative and the diagnosis, suspected on the basis of the Margilet's criteria, was finally confirmed by indirect immunofluorescent antibodies.

Key Words: *Bartonella henselae*, cat scratch disease, children, liver abscess, indirect immunofluorescent antibody assay (IFA)

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Cat-scratch disease (CSD) is commonly seen in children and young adults with a variety of clinical manifestations determined mainly by the status of the immune system of the infected person. Typically, patients present with a regional tender lymphadenopathy/lymphadenitis with or without a preceding visible primary inoculation papular lesion. Most immune-competent people with CSD are either afebrile or have a low-grade fever, with mild systemic nonspecific symptoms and spontaneous resolution in a few weeks. In 5%–20% of cases, however, the infection is disseminated with various complications such as prolonged fever, granulomas in the liver and spleen, and ocular or neurologic manifestations.[1]

According to criteria proposed by Margileth, the presence of at least 3 of 5 criteria confirms the diagnostic suspect of systemic CSD: history of contact with cat regardless of the evidence of scratch or inoculum site; negative Mantoux, IGRA tests, or serologies for other agents responsible for abscesses; polymerase chain reaction (PCR) assay positive for *B. henselae* and liver/spleen lesions observed by imaging; enzyme immunoassay (EIA) or immunofluorescence (IFA) positive with a single titer ≥1:64 or a 4-fold increase in titer between the acute phase and convalescence; histopathologic examination showing granulomatous inflammation suggestive of CSD.[2]

Owing to the lack of diagnostic gold standard criteria, searching for systemic CSD may be challenging.

We report a case of an immunocompetent girl with a systemic CSD presenting with an initially serologically negative, persistent high-grade fever associated with multifocal hepatosplenic abscesses.

CASE REPORT

A 13-year-old girl, "G," was admitted to our pediatric department due to 10-day persistent high-grade fever associated with nonspecific systemic symptoms such as malaise, anorexia, and generalized weakness. During the 3 days preceding hospitalization, she received treatment with amoxicillin-clavulanate without clinical improvement. Past medical history was unremarkable except for the most common diseases of childhood. Family history was unremarkable as well. Although she was in close contact with domestic and farm animals (including dogs, cats, rabbits, sheep, cows, and chickens), she did not remember to have had cat scratches.

At admission, general conditions were not compromised. Auxologic parameters were normal. Physical examination showed axillary temperature of 38.7°C. Blood pressure was 100/60 mm Hg; heart rate was 100 beats per minute, respiratory rate was 18