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Pregnant woman infected by Coronavirus Disease (COVID-19) and calcifications of the fetal bowel and gallbladder: a case report

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Abstract

Introduction: COVID-19 was declared pandemic due to the rapid increase of cases around the world, including the number of pregnant women. Data about vertical transmission of Covid-19 are still limited and controversial: in most cases, although a positive mother, the virus could not be isolated in amniotic fluid, cord blood, breast milk or neonatal throat swab in these patients. No data have been published about possible intrauterine sonographic signs of infection.

Case presentation: A pregnant woman was diagnosed with SARS-CoV2 at 35+5 weeks of gestation and managed conservatively at home. At transabdominal ultrasound at 38+3 weeks, fetal bowel and gallbladder calcifications were noted. CMV and other infectious agents were ruled out; an iterative Caesarean Section was performed at 38+5 weeks without complications. Placenta resulted negative for SARS-CoV-2; the umbilical cord blood sample was IgG positive and IgM negative as per maternal infection. The baby developed respiratory distress syndrome requiring endotracheal surfactant administration and nasal-CPAP for one day but nasopharyngeal swabs at birth and after 48 hours were SARS-Cov2 negative. Neonatal abdominal ultrasound showed normal liver, acalculous gallbladder with mild parietal thickening. The baby was discharged in good conditions.

Conclusion: although gallbladder calcifications and echogenic bowel are highly suspicious of viral infection and were thought to be due to the vertical transmission of SARS-CoV-2, these findings were not corroborated by the results of our diagnostic tests; these sonographic findings might represent a false positive of fetal infection in mother affected by COVID-19 since vertical transmission appears to be rare.

Introduction

Coronavirus epidemics have occurred three times in the last twenty years: SARS, Severe Acute Respiratory Syndrome, in 2003, MERS, Middle-East Respiratory Syndrome in 2012, and nowadays coronavirus disease 2019 (COVID-19) [1]. On the 11th of March, the World Health Organization (WHO) declared that COVID-19 could be characterized as a pandemic [2]; the number of cases has spread rapidly across the world, including the number of pregnant women and their new-born [3]. Data about vertical transmission of Covid-19 are still limited and controversial: most of the studies showed that, although a positive mother, the virus could not be isolated in the vaginal swabs, amniotic fluid, cord blood and breast milk and neonatal throat swabs of these patients. In particular, Chen et al. reported data on 9 neonates with no cases of vertical transmission [4]. Ferrazzi et al. [5] reported data from 42 positive pregnant women from Northern Italy showing only 3 positive neonates; notably, 2 out of 3 babies were breastfed by their asymptomatic mother without surgical mask because COVID-19 was only diagnosed in the post partum period (horizontal transmission?) while one neonate was immediately separated from his mother because of post partum haemorrhage and afterwards he resulted positive (possibly vertical transmission). Zeng et al. reported data on 33 neonates and only 3 showed mild signs of infection [3]. Notably, Zhu et al. reported data on 10 neonates from 9 mothers and, although neonatal swabs were all negative, chest radiography showed abnormalities in 7 neonates at admission with signs of infections in 4/7 and shortness of breath as the most common symptom (N=6) [6], questioning the diagnostic value of testing.

To the best of our knowledge, no data have been published about possible intrauterine signs of infection at ultrasound. In this case report, we present the case of a pregnant woman diagnosed with SARS-CoV2 whose fetus showed possible signs of intrauterine infection.

Clinical Report

On 19th March, a 30 year-old woman from Sri-Lanka at 35+5 weeks' of gestation presented for the first time during this pregnancy at the emergency clinic of Policlinico di Modena, Italy, reporting fever not responsive to antipyretics drugs during the previous week. Otherwise, she was a not-smoking healthy woman, not taking any chronic therapy and whose pregnancy had a physiological course till the reported fever with all routine investigation resulted normal.

Physical examination at first presentation showed: temperature about 36.7°C (paracetamol taken the hour before), Oxygen saturation: 99%, good general condition but mild dyspnoea. Lung auscultation was normal. Serum blood tests showed leukocyte count of 5.56 migl/mm^3 cells, C-Reactive Protein 1.4 mg/dL, Hb 11,9 g/dl.

A single nasal and throat swab was taken and tested to be positive for SARS-CoV-2 with Quantitative Real-time PCR test (GeneFinder COVID-19 Plus RealAmp Kit); her obstetric check was normal for gestational age. Patient was then discharged from hospital, she was taught about the home management and self-isolation since symptoms were mild and not requiring hospitalization or any special care.

On 8th April, at 38+3 weeks of gestation, the patient executed a routine obstetrical check, in the COVID-19 dedicated area of our division.

Serum-blood tests and another nasopharyngeal swab were performed and a more detailed ultrasound obstetric examination was carried out showing a fetal biometry on 14th centile with normal Umbilical Artery Doppler and polyhydramnios. Notably, gallbladder appeared to be hyperechogenic likewise containing calcific bilious material (Fig 1). The bowel looked echogenic as well (Fig 2), as for multiple calcifications. The picture was similar to congenital CMV infection [7] but CMV, Toxoplasma, Parvovirus and Adenovirus resulted negative.

An elective iterative CS on maternal request was performed at 38+5 weeks of gestation without complications in a dedicated surgery room on 10th April. Post partum period had no complication, the lady was discharged on 14th of April.

We tested for SARS-CoV-2 with RT-PCR the placenta which resulted negative. Also the placental swabs were negative. In the blood from the umbilical cord sampled at birth resulted IgG positive and IgM negative, compatible with maternal infection.

Neonatal Outcome

The male neonate at birth presented spontaneous crying; APGAR was 8 at 1st minute and 8 at 5th minute. Weight: 2680 g - Length: 49 cm - CC: 34.0 cm

Soon after birth, the newborn developed respiratory distress syndrome requiring nasal-Continuous Positive Airway Pressure (CPAP) and endotracheal surfactant administration with InSurE (intubation surfactant extubation) tecnique. Nasal-CPAP was the continued for 1 day. Mild metabolic acidosis was corrected with sodium bicarbonate. Blood cell count, C reactive protein and liver enzyme were normal. CMV infection was excluded by negative urine CMV PCR. Abdominal ultrasound showed normal hepatic parenchyma, acalculous gallbladder with mild parietal thickening. Cerebral ultrasound scan was normal. The new-born initially received expressed fresh mother milk and after second day of life he was breastfed. The mother was wearing a surgical mask while breastfeeding according to CDC guidelines [8]. Nasopharyngeal swabs at birth and 48 hours after birth were SARS-Cov2 negative. Moreover, the newborn resulted IgG positive and IgM negative, compatible with maternal infection.

The new-born was discharged home with the mother after 5 days of life. The mother continued to breastfeed him, using recommended hygienic precaution (mask and hand hygiene during feeding and whenever she needs to look after the baby).

Discussion

Similar to non-pregnant patients, the predominant features of COVID-19 in pregnancy are fever, cough, dyspnoea and lymphopenia. Fetal complications of COVID-19 include miscarriage (2%), intrauterine growth restriction (IUGR; 10%) and pre-term birth (39%) [9].

There is a theoretical risk of vertical transmission, similar to that seen in SARS, as the ACE2 receptor is widely expressed in the placenta [10], with a similar receptor-binding domain structure between SARS-CoV-1 and SARS-CoV-2.

In our case report, we suspected a vertical transmission of SARS-CoV-2 because of sonographic features of fetal infections observed in the fetus.

Nevertheless, few neonates from COVID-19 infected mothers have tested positive for SARS-CoV-2 shortly following delivery, casting concerns about the possibility of vertical transmission. According to a recently published review of the literature [11], among 155 neonates that had nucleic-acid testing in throat swabs, only three tested positive with only one being suspected of vertical transmission of the virus [5] and the other two of horizontal transmission [5,11]. So far, there are no evidence of viral isolates in the amniotic fluid, vaginal fluid, cord blood, breast milk, neonatal throat swabs, neonatal feces, neonatal urine and neonatal gastric juice samples, in a subset of these patients. [4, 11]

At present, no sonographic features of SARS-CoV-2 have been reported in the fetus. This might be due to the very low reported rates of vertical transmission during third trimester. Data on first and second trimester are still lacking.

Our sonographic findings included echogenic bowel and anomalies of the gallbladder.

Anomalies of the gallbladder, including sludge and gallstones, are extremely uncommon in fetal life, with an incidence of 0.42%; its etiology remains unknown. Postulated causes include haemolytic disease and cholestasis but usually fetal cholelithiasis is a self-limiting disease without complications and with a spontaneous resolution after delivery and in the first year of life. [12]

Echogenic bowel has been associated with multiple factors such as aneuploidy, cystic fibrosis, growth restriction and fetal infections. First of all, we focused on common fetal infections, such as cytomegalovirus, toxoplasma, parvovirus, adenoviruses that were promptly ruled out. First trimester screening was at low risk for common aneuploidies, while cystic fibrosis was ruled out after birth, screening the baby that resulted negative.

Although echogenic bowel was found to have low predictive value for fetal infection at late gestation, being infection diagnosed only in 4.2% fetuses with this sonographic sign [13], the simultaneous presence of two gastrointestinal-tract sonographic findings raise the suspicion of typical gastrointestinal involvement that occurs in fetal infections. In this case, after excluding common infective agents, we suspected they could be due to the vertical transmission of SARS-CoV-2; however, they were not corroborated by the results of our diagnostic tests and therefore we can conclude that sonographic findings might represent a false positive of fetal infection in mother affected by COVID-19.

Conclusions

Gallbladder calcifications and echogenic bowel are highly suspicious of viral infection and were thought to be due to the vertical transmission of SARS-CoV-2. However, these findings were not corroborated by the results of our diagnostic tests: vertical transmission of COVID-19 appears to be rare and therefore these sonographic findings might represent a false positive of fetal infection in mother affected by COVID-19.

Ethical approval: The research related to human use has complied with all the relevant national regulations, institutional policies and has been conducted in accordance with the tenets of the Helsinki Declaration, and it has been approved by the authors' Institutional Review Board or equivalent committee.

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FIGURE CAPTIONS

Fig.1 - The gallbladder calcifications

Fig. 2 - Echogenic bowel with calcifications