Case Report

Journal of Future Medicine and Healthcare Innovation

Intrauterine Fetal Demise and Vertical Transmission of SARS CoV-2 Infection in Pregnancy - A Rare Case Report with Diagnostic Challenge

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Submitted: 2023, July 11; **Accepted:** 2023, Aug 03; **Published:** 2023, Aug 28

Citation: Annapoorna., Navakumar, N., Niyas, M., Viji., Vidyalekshmy, R., et al. (2023). Intrauterine Fetal Demise and Vertical Transmission of SARS CoV-2 Infection in Pregnancy - A Rare Case Report with Diagnostic Challenge. *J Future Med Healthcare Innovation, 1*(1), 04-06.

Abstract

SARS-CoV-2 infection during pregnancy is not usually associated with significant adverse effects. However, in this study, we report a fetal death associated with mild COVID-19 in a 32-week-pregnant woman. The virus was detected in the mother, stillborn fetal nasopharyngeal swab and placenta . Placental and fetal alveolar abnormalities (histopathology) were consistent with maternal vascular – placental insufficiency and fetal asphyxia, probably the cause of fetal death. Fetal surveillance along with maternal surveillance is warranted in pregnant women with COVID-19 to have favourable outcome.

Keywords: SARS CoV-2 Infection, Pregnancy, Intrauterine Fetal Demise, Vertical Transmission

1. Introduction

The first recognized outbreak in Wuhan, China, December 2019 is considered a global threat and its mortality rate according to WHO, ranges from 2-3% . CoV2 is the virus responsible for COVID-19,and is mainly transmitted through respiratory droplets. However, some cases of perinatal transmission have been described, although it is unclear if these occurred via the transplacental or other routes [1]. Most pregnant women with COVID-19 develop mild forms of the disease, with few cases of severe maternal morbidity and mortality, or perinatal deaths [2].

Only few previous publications reported placental histology and SARS-CoV-2 results in specimens from a stillborn fetus [3]. Here we report a case of vertical transmission SARS CoV-2 resulting in 3rd trimester intrauterine fetal demise in a mildly symptomatic pregnant woman.

2. Case Report

A 29-year-old,Indian nulliparous woman otherwise uncomplicated pregnancy who presented at the ED of local hospital at 32 weeks of gestation with rhinorrhoea, myalgia and fever for 3 days with stable hemodynamic status and thrombocytopenia (platelet count of 1 lakh/ mm3 of blood) was treated symptomatically. Her routine growth scan at 28 weeks of gestation showed a normally grown fetus. After 12 days she presented with ruptured membrane and decreased fetal movements and fetal heart sound could not be localised. The obstetric US confirmed intrauterine fetal demise. As part of routine screening of our inpatients her nasopharyngeal swabs for SARS-CoV-2 RT-PCR and was found to be positive. She was induced and delivered vaginally a macerated male fetus of weight 1.62 kg (3 rd centile) suggestive of fetal growth restriction and placenta of weight 290 gms. Fetal nasal swab was taken and sent for SARS CoV 2 antigen test which was positive. Placental membrane was positive for SARSCoV-2 which was reconfirmed by doing genexpert with CB NAAT and RTPCR of placental membrane simultaneously which detected e and n2 genes in genexpert also n gene and orf gene in RTPCR. Placental histopathological examination showed features of term chorionic villi with syncytial knots(Fig: 1a) and extensive perivillous fibrin deposition with areas of infarction (Fig: 1b) more than 75%. Basal plate showed fibrinoid deposition (Fig: 1 c) and neutrophilic infiltrate suggestive of maternal vascular insufficiency. In fetal autopsy microscopy of fetal lungs were in saccular phase, appropriate for gestation and also revealed alveolar spaces and bronchioles with nucleate and anucleate squamous cells(Fig2 a and 2 b), suggestive of amniotic fluid aspiration.

3. Discussion

This case of intrauterine fetal demise in a woman with confirmed COVID-19 without any other significant clinical or obstetric disorders can be attributed to SARS-CoV-2 infection in pregnancy, its vertical transmission combined with the placental insufficiency attributed to covid effects of placenta and fetal asphyxia. Covid infection can provoke inflammatory response in maternal systemic and placental level with can be extended to fetus. From previous studies it has been noted that vertical transmission as such is less likely to cause fetal demise unless it is associated with placental abnormalities, fetal asphyxia , fetal infection with inflammatory response or in a pre-Covid compromised fetus as in a growth restricted or abnormal fetus. Vertical transmission of SARS CoV-2 was confirmed by GENEXPERT and RTPCR of SARS-CoV-2 in placental sample which supports this hypothesis [4]. Placental histology showing villi with syncytial knots, perivillious fibrin deposition and infarction suggestive of maternal vascular insufficiency along with fetal asphyxia could have contributed to stillbirth. Amniotic fluid aspiration with squamous cells in fetal alveoli suggest acute fetal asphyxia , in our case also fetal lung showed features of amniotic fluid aspiration [5]. The RCOG guidelines on Covid infection in pregnancy advises for fetal surveillance to be started in form of fetal wellbeing scan from 2 weeks of acute Covid infection as the fetal effects are evident from 2 weeks of infection.

Prior studies have shown both “E” and “RdRp” gene of SARS-CoV-2 were found in the placental supernatants at viral loads equivalent of that of the maternal nasopharyngeal swab [6]. Along with viral RNA, the viral proteins could be readily detected in the cytotrophoblasts, syncytiotrophoblasts and some villus stromal cells. Indeed, we have shown that all these cell types in first trimester placenta not only expresses the canonical (ACE2) and the non-canonical (CD147) SARS-CoV-2 receptors, they readily express the proteins required for viral endocytosis, replication and release. Thus, the placenta is a permissive site for SARS-CoV-2 replication. The active viremia of the placental cells was further coupled with extensive placental inflammation as deduced by leucocyte infiltration in the intravillous spaces and decidua, fibrin deposition and lysis of syncytio-trophoblasts of the villus cells. Epidemiological evidence suggests a low possibility of mother to child transmission of SARS-CoV-2; however, this notion is based on reports of third trimester infection [7]. Also, most reports are classified only as probable case of congenital SARS-CoV-2 infection as the infection of the new born is reported hours or even days after birth [8]. Our case fully qualifies as vertically transmitted SARS-CoV-2 infection as we not only detected the virus in fetal nasal swab but also in the placental specimen. According to WHO classification system to determine in-utero of vertical transmission of SARSCoV-2 and fetal demise our case falls under possible in-utero infection as we have maternal covid RTPCR positive , stillborn fetus nasopharyngeal swab Covid antigen positive, placental membrane RTPCR along with GENEXPERT positive and histopathological evidence of placental covid infection [9].

A systemic review of seventeen published studies reported several adverse fetal and neonatal outcomes, including stillbirth (1.2%) and fetal distress(10.7%) [10]. Moreover, one pregnant woman with Covid-19 had a stillbirth, delivered by the cesarean section (CS) according to Liu et al. That occurred after she had a fever and a sore throat at the 34th week of gestation. Her condition worsened and needed to be transferred to the intensive care unit (ICU). The only available information about fetal and neonatal results is for women who were infected in their third trimester. It is still unknown whether the infection in the first or second trimester might increase the incidence of fetal and neonatal death [10].

Although the exact mechanisms of intrauterine SARS-CoV-2 transmission are unclear, there are two hypotheses. Angiotensin- converting enzyme 2 (ACE2), a possible surface receptor of sensitive cells for SARS-CoV-2, is expressed in human placentas. This could explain placental infection by the virus. Another possible explanation for intrauterine SARS-CoV-2 infection is through placental barrier damage caused by severe maternal hypoxemia in women with COVID-19 .Fetal demise in mother with Covid may be due to immunological causes like cytokine storm syndrome, sepsis, placental thrombosis or due to pathological causes like anemia, respiratory failure, fetal infections, thromboembolic complications causing placental insufficiency [10].

Hence, it’s found that even though the covid symptoms of mother are mild like a fever sore throat it can result in severe fetal problems like fetal growth restriction and even fetal death. So now it’s almost clear that not only maternal complications like medical multisystem and obstetric complications it can result in a series of perinatal complications like miscarriage, fetal growth restriction, prematurity, perinatal morbidity and mortality. Even its reported that intrauterine Covid infection causes multisystem inflammatory complications in infancy and childhood . Thus, the management protocols of pregnancy follow up after Covid infection should be modified in a stringent way as vertical transmission can result in fetal growth restriction and fetal death , hence surveillance for fetal growth pattern and amniotic fluid levels should be considered to prevent perinatal complications

More studies are needed to confirm the findings and to help guide the management of pregnancies in women with COVID-19.

4. Conclusion

In women with confirmed COVID-19 without any other significant clinical or obstetric disorders perinatal morbidity and mortality can occur irrespective of severity of covid infection hence warrants fetal surveillance also along with maternal surveillance. Here we have reported vertical transmission of covid with placental abnormalities and acute fetal asphyxia as the cause of IUFD, it may be due to other reasons also.

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