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Research Article

Novel Insights into Fetal Death Concomitant with COVID-19 Infection

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Abstract

Objective: Identify Sars-Co V-2 in maternal floor placentae and relate to fetal death.

Sample: Two placentas of fetal death were studied with COVID infection and Massive perivillous fibrin deposition (MPFD).

Methods: We took pregnancies with fetal deaths and study the presence of Sars-Co V-2 associated to MPFD. It was used PCR and anatomopathological studies.

Results: We found the virus with PCR in placenta with MPFD.

Conclusion: Covid 19 and its complications show us a new area of study. Think that the MPFD associated with infection could be the cause of bad perinatal outcome. More studies will have to be performed, urgently, for avoid fetal death.

Keywords: COVID 19; Plancenta Fibrin Deposition; Fetal Death

Introduction

In December 2019, a series of viral pneumonia cases emerged in Wuhan, Hubei, China. The analysis from respiratory tract samples indicated a novel coronavirus, which was named 2019 novel coronavirus (2019-nCoV). Coronaviruses are RNA viruses belonging to the family Coronaviridae and distributed in humans and other mammals [1].

The epidemics of the two beta coronaviruses, severe acute respiratory syndrome coronavirus (SARS-CoV) and Middle East respiratory syndrome coronavirus (MERS-CoV) have mortality rates of 10% for SARS-CoV and 37% for MERS-CoV. The mortality rate of SARS-CoV 2 is 2.5 per 1000 detected cases and the new variant of SARS-CoV-2 detected 2020 is 4.5 per 1000 [2].

Recently two publications of placenta histology in SARS-CoV-2 infection were published [3]. They reported massive fibrin deposition at placental villi with fetal death, and [4] showed the presence of intramural fibrin deposition, kariorrhexis and other lesions. Other authors reported the difference between placenta histology in SARS-Co V-2 infection and non-infection [5]. We include two patients, a 39-year-old woman, her first pregnancy, Caucasian, pregnant 38/40 weeks of gestation with SARS-CoV-2 and fetal death, and a 33-year-old, her third pregnancy, two previous caesarean sections, Caucasian, pregnant 38/40 weeks old gestation with SARS-CoV-2 and fetal death.

The placental histology showed massive deposition of fibrin. Our objective was to identify Sars-CoV-2 in maternal floor placentae and relate to fetal death.

Methods

The 39-year-old Caucasian patient presented at scan with diagnosis of fetal death. The pregnancy course without pathology, normal scan, and normal grow. Two risk factors were detected, smoke (non after 20 weeks) and the age. She did not have other co morbidities. Four weeks after fetal death she was infected. She was found to be positive for SARS-CoV-2 with RT-PCR. Presented high fever, cough, and body pain, treated with paracetamol. At third week she was diagnostic with pneumonia and treated with amoxicillin and clavulanic acid for 10 days.

Six days before the diagnosis of fetal death, the patient consult with reduce fetal movement. The non-stress test (NST) was normal, and she had normal vital signs. Her computed axial tomography and oxygen saturation were normal. After four days she was reevaluated with reduce fetal movement with the same NST. One day later that she was reevaluated with a scan and diagnosed with fetal death at 38 weeks of gestation. We did an elective caesarean section.

The second case was a patient of 33-year-old, Caucasian patient presented at medical practice with reduce fetal movement and we detected fetal bradycardia at 38 weeks. The pregnancy course without pathology, normal scan, and normal grow. No risk factors were detected. She did not have other co morbidities. Two weeks before fetal death she was infected. She was found to be positive for SARS-CoV-2 with RT-PCR. Presented fever and body pain, treated with paracetamol. She was taken to the operating room for an emergency cesarean section. We performed cardiopulmonary resuscitation. However, the fetus died. Postmortem consent was limited to external examination and examination of the placentas, with permission to research. Nasal swabs for SARSCoV-2 investigation were not taken from the babies. The first case: Fetal weigh 3600 g and mild maceration. The placenta weight was 375g, 3-vessel umbilical cord. The second case: fetal weigh 2800g and no maceration. The placenta weight was 304 g, 3-vessel umbilical cord.

The placentas were examined after fixation with formaldehyde because of the SARS-CoV-2 infection (Figure 1a).

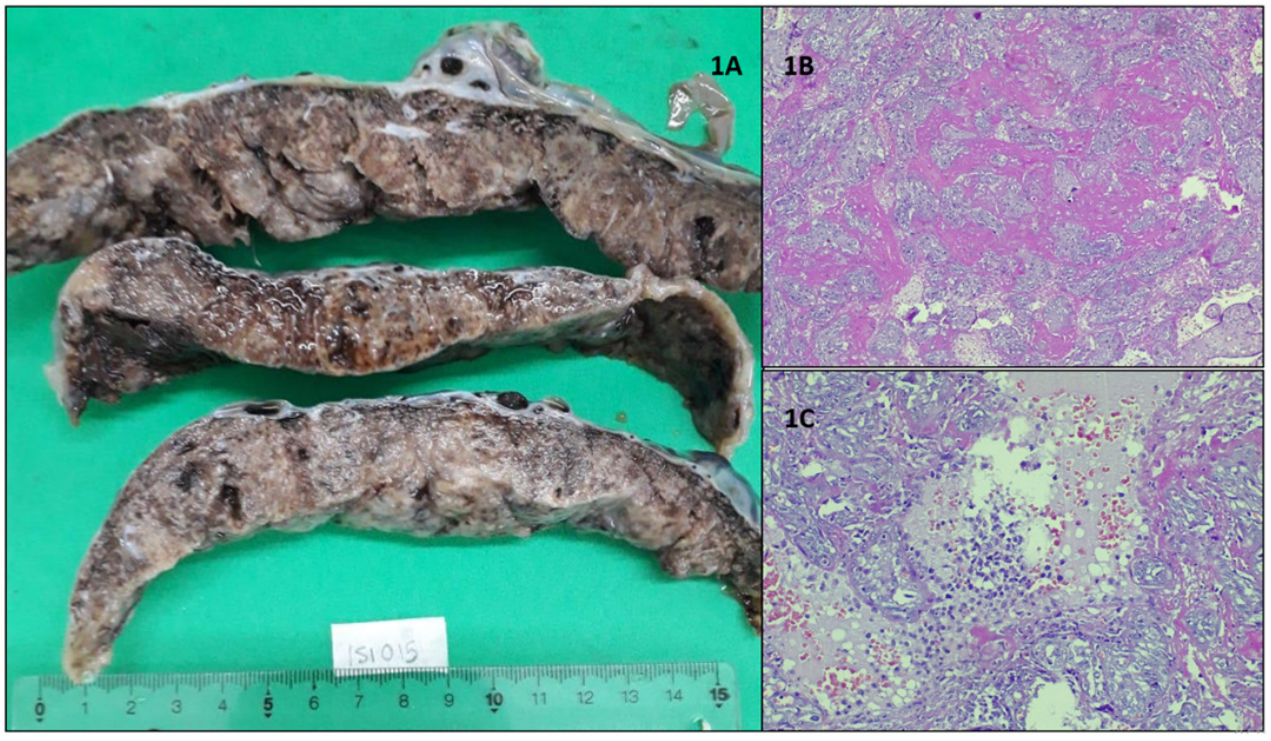

Figure 1: A) Gross examination of placenta, B) Massive perivillious fibrin deposition, C) Histiocytic intervellocitis.

Discussion

Main Findings

The anatomy pathological description showed on the cut surface that there was the typical characteristic MPFD. Routine histological examination with H&E staining of the placenta showed the villi encrusted in loose eosinophilic fibrinoid material (Figure 1b). There were only small clusters of preserved villi. Chronic inflammatory infiltrate. trophoblasts. Magnification fields showed cytopathic effects of the trophoblasts. The nuclear stain of the trophoblasts was preserved. Changes were also visible in the villous parenchyma (Figure 1c).

We digested the samples with buffer AVL (600ul) for lysis the tissues. Then we added K proteinase (60ul) following Quiagen protocols. After we used RT-PCR real time with DisCoVery reactives (genes and or like genes diana). The internal control was made with RNasa in a themocyclator CFX.

We detected SARS-Co-V2 in maternal floor of both placental with RT-PCR. We evaluated the cases with Relevant condition at death (ReCoDe) system [6]. Result: group F (maternal factors) we selected number 7. Other (Infection of SARS-Co V-2) 6.

Strengths and Limitations

The CDC (Centre for control of disease, USA) stablish the still birth or fetal death rate after 22 weeks or a 500g of fetal weight is equal to 4.8/1000 [7]. In our study we detect two fetal deaths in one month associated with COVID infection.

Interpretation

Since 2006, MARTIN [8], described massive perivellous fibrin deposition and cronic intervellositis associated with IUGR and intrauterine fetal death. In 2008, Dae-Woon Eom, described MPFD with increased risk of intrauterine growth retardation, intrauterine death, and pre-term delivery [9].

Next year, *Weber, et al.* related MPFD and chronic intervellositis (CHI). (Massive perivillous fibrin deposition and chronic intervillositis: frequently missed diagnoses with a high recurrence risk [8]. The CHI was described by P. Jindal et al, in 2006 there were recurrent spontaneous abortion [10,11]. In 2010 *R Uxa, et al.* [12] proposed an association with a genetic polimorphisms, the outcomes in the study group included perinatal death, preterm intrauterine grow restrictions (IUGR), preeclampsia and only 3 normal term deliveries. *Soddu, et al.* [13] reported two cases with MPFD and IUGR. Petersen et al published in 2013 [14] MPFD associated with perinatal adverse outcome. They proposed an association between MPFD and maternal floor infarction with maternal alloimmune or autoimmune mechanisms. In the same year, Romero et al. [15] describe MPFD like a manifestation of maternal antifetal rejection. Another hypothesis was the imbalance of angiogenic and antiangiogenic factor [16].

Different virus was detected in placentas with MPFD. Coxsackie virus A16. Weiming et al. [17]. Enterovirus, Henning et al. [18]. Covid 19, Mongula et al. [19]. SARS-Co-V2, Marton et al. [3]. We detected SARS-Co-V2 in placental tissue. It could be viral infection; a cause of MPFD. Think that it could be the cause of bad perinatal outcome a real possibility and we must alert to the medical community about it.

Conclusions

Fetal death is an adverse event that we must work to prevent it. In this case the association with the infection of SARS-CoV-2 is unclear and it must be continuing with the studies of placenta. Other pathologies are associated with massive perivillous fibrin deposition, and this open a new area of study. COVID infection affects pregnancy in acute way resulting in the fetal death. The evaluation of placenta and pregnancy it could be the first step to prevent fetal death.

Author Contribution

Writing-original draft preparation: M.Z., F.A.M.; Collected data concerning databases: M.Z., F.A.M. and J.I.P.; Sample analysis: A.A., G.O., P.D.; Writing-review & editing: M.Z. and F.A.M.

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Declaration of Conflicting Interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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