Case study
Importance of testing for maternal-fetal transmitted infectious diseases in the case of a Sars Cov-2 infected pregnant women

ABSTRACT

Maternal-fetal transmission of infectious diseases during the pregnancy poses a risk for the pregnant woman and for the future baby as well. The present case highlights the importance of testing during the pregnancy for all the infectious diseases included in the TORCH panel. We will consider the case of a 26-year-old woman, obese , at the third pregnancy, without co-morbidities or complications. She presented at the Emergency Room at 25 weeks of gestation with vaginal bleeding and abdominal pain. RT-PCR nasopharyngeal swabs collected at the moment of admission were positive for SARS CoV-2. The fetus was not alive. The first intention was inducing the childbirth, but as this procedure did not work hysterectomy was performed at two days of admission. The decision was made as a result of altered maternal health. The patient presented with persistent hypoxia, tachypnoea and to prevent acute respiratory decompensation the patient was transferred to the intensive care and intubated. Despite maximum ventilator support, she suffered a cardiopulmonary collapse and died within 24 hours of intubation after all failed resuscitation efforts. The patient was not vaccinated against COVID-19 and did not present other TORCH infectiousdiseases.The presented case highlights the importance of testing for COVID-19 in pregnancy.

Keywords: Sars Cov2, Covid 19, pregnant women, birth

1. INTRODUCTION

Various infectious agents encountered during pregnancy are important because they affect both the health of the mother and the fetus and can cause birth defects in the fetus by crossing the placental barrier. Pregnancy-related physiological changes suppress immunity for a period of time and therefore increase susceptibility to infectious agents. Infections grouped by the acronym TORCH or TORCH panel are T- Toxoplasma Gondii, O- other infections such as viral hepatitis B, viral hepatitis C, Parvovirus B19, HIV / AIDS, Zika virus infection, Chickenpox, Chlamydia, group B streptococci, Gonococci Infec , Listeriosis, Syphilis, SarsCov 2 Virus, R - Rubella, C - Cytomegalovirus, H - Herpes Simplex).

Of these, Toxoplasma gondii, rubella and cytomegalovirus (CMV) are the most common.

The COVID-19 disease, determined by the SARS CoV-2 virus is mainly transmitted through Flugge droplets, yet some cases of perinatal transmission have been described. Although it is not clear whether this transmission occurred through placenta or other routes [1, 2] there are multiple examples into the literature. Most of the pregnant women infected with SARS CoV-2 develop mild forms of the disease, but there are a few cases of severe maternal morbidity and mortality or perinatal deaths [3]. According to the published studies, placental infection occurs at a low rate, estimated in 21% of pregnancies, but only 2% of newborns become SARS CoV-2 infected [4].

Infectious diseases can be transmitted from mother to fetus through the placenta, whether the mother contracted the disease before pregnancy or even during it. Maternal-fetal transmission has significant consequences on the product of conception, the transmission can be achieved antenatal, perinatal and postnatal.

2. PRESENTATION OF CASE

We will consider the case of 26-year-old woman, obese (BMI 30.5 kg / m2, at the third pregnancy, without comorbidities or complications. She presented at theEmergency Room (ER) at 25 weeks of gestation with vaginal bleeding and abdominal pain. For the last 24 hours she experienced shortness of breath, rhinorrhea, myalgia, anorexia, nausea and diarrhea. For the last three days she also presented fever (39.0 Celsius degrees).

The pregnancy went well until the moment of presentation to the ER. Until then all routine prenatal laboratory tests and fetal ultra-sounds were normal.

At the present episode the patient presented with: fever (39.2 Celsius degrees, Normal -36 - 37.5 degrees Celsius), pulse = 115 / min (Normal - 60 to 100 beats per minute), respiratory rate = 20 / min (the average number of breaths in an adult is 16-18 breaths per minute), blood pressure = 16 5 × 100 mmHg (normal blood pressure in pregnant women - systolic - less than 140 mmHg, diastolic less than 90 mmHg) and SpO2 = 94%. The membranes were intact, and the clinical obstetrical examination showed no signs of imminent premature birth. The fetal heartbeats were absence. At the obstetric ultrasound the fetal death was confirmed, the amniotic fluid was in normal quantity and placenta was of normal appearance.

RT-PCR nasopharyngeal swabs collected at the moment of admission were positive for SARS CoV-2. Chest X-ray revealed significant blurred opacity with an aspect of polished glass distributed in the lower 1/3 of the right hemithorax and in the lower 2/3 of the left hemithorax (organic lung damage in viral context for 50%). Laboratory tests revealed increased hepatic transaminases, marked thrombocytopenia , increased urinary protein, all suggestive for the diagnosis of preeclampsia. Prolonged partial time of thromboplastin and low fibrinogen were suggestive for disseminated intravascular coagulation. The laboratory test are detailed into Table 1.
They were performed every day since the patient deceased

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Table1. Laboratory analysis.

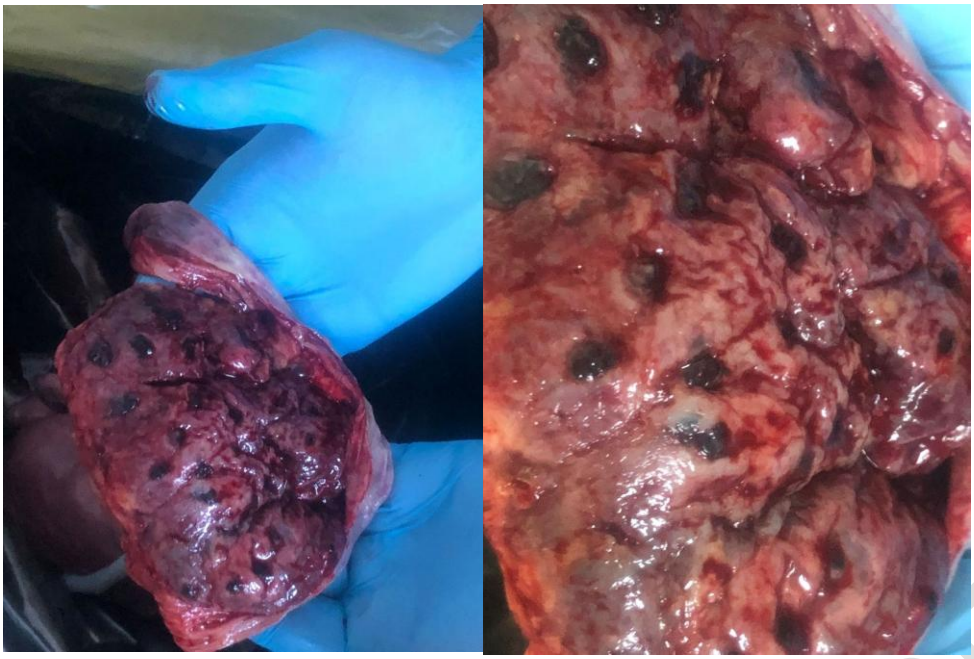
LABORATORY TEST	The first day/ Value	The second day/ Value	Thefourth day/ Value	Reference values Value/UM
APTT *	26.50	28.50	34.00	24.00 – 35.00

				seconds
PT **	11.30	11.90	12.70	11.00 – 14.50 sec
Aspartate aminotransferase	65.24	180.34	290.42	5.00 – 32.00 UI/L
Alanine aminotransferase	37.35	145.90	265.43	5.00 – 33.00 UI/L
C-reactive protein	24.80	56.03	101.00	0.00 – 5.00 mg/L
Cervical culture	absent pathogenic microbial flora, absent yeast			absent pathogenic microbial flora, absent yeast
D - dimmer	2.48	2.70	5.90	0.00 – 0.50 ug/ml
Direct serum bilirubin	1.15	1.58	1.56	0.00 – 0.20 mg/dl
INR ***	0.84	1.20	3.70	0.82 – 1.18 INR
Fibrinogen	442.00	196.00	138.00	200.00 – 400.00 mg/dl
Glucose	122.46	108.20	136.70	74.00 – 109.00 mg/dL
Hemoglobin	12.30	11.10	10.50	11.70 – 15.00 g/dL
Hematocrit	35.70	32.50	30.40	36.00 – 48.00
Lactate dehydrogenase	245.00	968.00	1113.00	135.00 – 214.00 UI/L
Lymphocyte	0.56	10.10	7.8	1.50 – 4.50 *1000/uL
Platelets	149.00	101.00	98.00	150.00 – 450.00 *1000/uL
Proteinuria	200	400	420	Negativ. 0-30 mg/dL
Serum lipase	12.90	16.90	24.70	>18 years: <60.00
Serum uric acid	8.69	8.40	5.20	2.40 – 5.70 mg.dl
Serum creatinine	0.31			0.50 – 0.90 mg/dl
Serum ferritin	482.00	849.00	924.00	15.00 – 150.00 ng/dl
Serum urea	4.91	10.28	19.07	16.60 / 48.50 mg/dL
Total serum bilirubin	28.50	32.80	46.90	0.00 – 1.20 mg/dl
Urinalysis	Have been developed < 1.000 CFU / ML			Absent CFU/ML
WBC****	7.26	10.45	7.2	4.00/11.00 *1000/uL

**APTT - Partial thromboplastin time activated ** PT - Protrombine Time*
**** INR- International normalized ratio **** WBC - white blood cells*

The patient was admitted in the delivery room and administration of Amoxicillin trihydrate - Potassium clavulanate 1 gram at 12 hours, enoxaparin sodium 0.6 IU per day and Paracetamol intravenous 1 gram at 6 hours began. Remdesivir was administered 200 mg on the first day, (100mg twice a day) and then only 100mg daily along with oxygen therapy. The first intention was inducing the childbirth with Misoprostol, but as this procedure did not work hysterectomy was performed at two days of admission. The decision was made as a result of altered maternal health (SpO2 = 74%). The female fetus, non-macerated, 330 grams, was extracted. The post-mortem examination did not detect any fetal malformation. Histopathological examination of the placenta indicated an acute infection and ischemia. Figure 1. The family did not accept the fetal autopsy.

Figure 1. Placenta after extraction



After hysterectomy the patient presented persistent hypoxia, tachypnoea and to prevent acute respiratory decompensation the patient was transferred to the intensive care and intubated. Her antibiotic treatment was changed to vancomycin and meropenem, and enoxaparin sodium was administered twice daily.

Despite maximum ventilator support, she suffered a cardiopulmonary collapse and died within 24 hours of intubation after all failed resuscitation efforts. The patient was not vaccinated against COVID-19 and did not present other symptoms suggestive for TORCH infectious diseases.

3. DISCUSSION

Intrauterine transmission is one of the most serious complications of viral diseases that occur during pregnancy. Maternal-fetal transmission of viral diseases (with the exception of the herpes virus) is usually on the hematogenous route in which the virus circulating in the maternal bloodstream penetrates the placenta, reaches the tree of chorionic villi and fetal blood vessels, and is transmitted to the fetus [5, 8]. Intrauterine and perinatal transmission of COVID-19 infection is possible [9]. There is evidence that mother-to-child transmission is possible, although the number of publications supporting this situation is currently low [10].

The presented case highlights the association between COVID-19 and pregnancy, with associated placental inflammation.

Future efforts to correctly diagnose and identify the processes underlying the SARS CoV-2 infection associated with pregnancy are essential for targeting patient care and advising pregnant women during the pandemic.

A plus in our case is the evidence of the laboratory confirmation of the pregnant woman for SARS CoV-2 infection and the histopathological exam of the placenta. The laboratory diagnosis for COVID-19 was performed by Real-Time polymerase chain reaction (PCR) assay with manual nucleic acid extraction technique (MasterPure™ Complete DNA and RNA Purification Kit, Lucigen, Middleton, WI, USA) and RNA detection and quantification with “genesig®Real-Time PCR assay” (Primer Design™ Ltd., Camberley, UK), in vitro Real-Time PCR diagnostic test for Coronavirus (COVID-19), targeting RNA dependent RNA polymerase (RdRp) on a Real-Time PCR LightScanner 32 (LS32) (IdahoTechnology, Salt Lake City, UT, USA).

A limitation of the study is that we did not collect amniotic fluid and placental samples for RT-PCR. Another limitation is that, due to the lack of family consent, we could not perform fetal autopsy. According to previous studies regarding the necrotic diagnosis of the placenta, there have been reported several fetal deaths associated with inflammatory and ischemic placental damage [11]

But although the stage of placenta pathology has been interpreted as inflammatory by some authors, Debelenko et al. have focused their attention on necrosis of the trophoblast and the acute and chronic component of the inflammatory infiltrate [12], and our case meets this description.

The exact mechanisms of intrauterine SARS-CoV-2 transmission are not clear, but there are two hypotheses . Angiotensin that converts enzyme 2 (ACE2), a possible sensitive surface receptor for cells infected with SARS-CoV-2, is expressed in human placentas. This could explain placental infection with SARS CoV-2 virus [13]. Another possible explanation for intrauterine infection is by affecting the placental barrier by severe maternal hypoxemia in women with COVID-19 [14].

4. CONCLUSION

Having COVID-19 during pregnancy is a new condition and it is important to report and research all the cases of possible maternal-fetal transmission as long with all the complications associated with this disease.

Determining the mortality rate and the risk of severe morbidity in pregnancy requires rigorous population surveillance data in many countries. However, the case we have presented here suggests that maternal mortality caused by COVID-19 has to be considered.

The presented data is important to inform patients and healthcare providers about the possible danger of transmission, and to help develop appropriate management protocols for testing the pregnant women for COVID-19 infection. We recommend that pregnant women should be vaccinated against COVID-19.

Early recognition and detection of TORCH infections in both mother and fetus are an important part of prenatal care, there are a large number of pregnant women who are poorly informed about the possibility of transmitting infections to the fetus before, after or even during birth. We believe the testing and information are a good mean of preventing in these cases.

CONSENT (WHEREEVER APPLICABLE)

All authors declare that ‘written informed consent was obtained from the patient (or other approved parties) for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editorial office/Chief Editor/Editorial Board members of this journal.

ETHICAL APPROVAL (WHEREEVER APPLICABLE)

The Ethics Committee of the Hospital of Obstetrics and Gynecology, Ploiești, Romania issued approval 14325
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REFERENCES

[1] Alzamora MC, Paredes T, Caceres D, Webb CM, Valdez LM, La Rosa M - SevereCOVID-19 during pregnancy and possible vertical transmission, *Am. J. Perinatol.*2020 Jun;37(8):861-865. doi: 10.1055/s-0040-1710050

[2] Blumberg DA, Underwood MA, Hedriana HL, Lakshminrusimha S - Vertical transmission of SARS-CoV-2: what is the optimal definition? *Am. J. Perinatol.*2020 Jun;37(8):769-772 doi: 10.1055/s-0040-1712457.

[3] Zaigham M, Andersson O - Maternal and perinatal outcomes with COVID-19: a systematic review of 108 pregnancies. *ActaObstetGynecol Scand.* 2020 Jul;99(7):823-829. doi: 10.1111/aogs.13867

[4] Sharps MC, Hayes DJL, Lee S , Zou Z, Brady CA, Almoghrabi Y , et al - A structured review of placental morphology and histopathological lesions associated with SARS-CoV-2 infection. *Placenta*. 2020 Nov;101:13-29. doi: 10.1016/j.placenta.2020.08.018

[5] Nita I, Nitipir C, Toma SA, Limbău AM , Pîrvu E, Bădărău IA , Suciu I , Suciu G, Manolescu LSC - Histological Aspects and Quantitative Assessment of Ki67 as Prognostic Factors in Breast Cancer Patients: Result from a Single-Center, Cross Sectional Study.*Medicina* (Kaunas). 2020 Nov; 56(11): 600 doi:10.3390/medicina56110600.

[6] Manolescu LSC, Temereanca A, Diaconu CC, Ruta S - Correlation between resistance profile and immunosuppression in heavily treated HIV-1 infected Romanian patients. *Rom Biotechnol Lett.* 2011 Aug; 16(4): 6439–6449https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3237115/

[7] Dragomirescu CC, Lixandru BE, Coldea IL , Palade AM, Baltoiu M, Dinu S , Cristea VC, Manolescu LSC , Popa MI - Comparative analysis of different phenotypic and molecular methods used for the taxonomic identification of Corynebacterium spp. isolated from clinical samples in Romania. *Antibiotics* 2020, 9(1), 31; https://doi.org/10.3390/antibiotics9010031

[8] Dragomirescu CC, Lixandru BE, Coldea IL, Cornelia ON , Pana M , Palade AM, Cristea VC, Suciu I, Suciu G , LSC Manolescu, Popa GL, Popa MI - Antimicrobial Susceptibility Testing for Corynebacterium Species Isolated from Clinical Samples in Romania, *Antibiotics* (Basel). 2020 Jan 16;9(1):31. doi: 10.3390/antibiotics9010031

[9] Juan J , Gil MM , Rong Z ,Zhang Y , Yang H, Poon LC - Effects of coronavirus disease 2019 (COVID-19) on maternal, perinatal and neonatal outcomes: a systematic review. *Ultrasound Obstet Gynecol*. 2020 Jul;56(1):15-27. doi: 10.1002/uog.22088

[10] Radu MC, Boeru CA, Marin M, Manolescu LSC - SARS-CoV-2 infection in seven childbearing women at the moment of delivery, a Romanian experience. *Cureus.* 2021 Jan 20;13(1):e12811. doi: 10.7759/cureus.12811

[11] Richtmann R , Torloni MR, Otani ARO, Levi JE, Tobara MC, Silva CA , et al - Fetal deaths in pregnancies with SARS-CoV-2 infection in Brazil: a case series. Case Rep *Womens Health*. 2020 Jul; 27: e00243 doi: 10.1016/j.crwh.2020.e00243

[12] Debelenko L, Katsyv I, Chong AM, PeruyeroL ,Szabolcs M, Uhlemann A-C - Trophoblast damage with acute and chronic intervillositis: disruption of placental barrier by SARS-CoV-2. *Hum Pathol.* 2021 Mar;109:69-79. doi: 10.1016/j.humpath.2020.12.004

[13] Lukassen S, Chua RL, Trefzer T, Kahn NC, Schneider MA, Muley T, et al - ARSCoV-2 receptor ACE2 and TMPRSS2 are primarily expressed in bronchial transient secretory cells. *EMBO J*. 2020 May 18;39(10):e105114. doi: 10.15252/embj.20105114

[14] Wang C, Zhou YH, Yang HX, Poon LC - Intrauterine vertical transmission of SARSCoV-2: what we know so far. *Ultrasound Obstet Gynecol*. 2020 Jun;55(6):724-725. doi: 10.1002/uog.22045