Impact of SARS-CoV-2 on Fetal Malformation During Pregnancy: A Case Report of Fetal Autopsy

Yuping Guo
Renmin Hospital of Wuhan University: Wuhan University Renmin Hospital
Jiacai Ren
Renmin Hospital of Wuhan University: Wuhan University Renmin Hospital
Jingping Yuan
Renmin Hospital of Wuhan University: Wuhan University Renmin Hospital
Di Lei
Renmin Hospital of Wuhan University: Wuhan University Renmin Hospital
Nawsherwan .
Wuhan University
Ying Yu
Renmin Hospital of Wuhan University: Wuhan University Renmin Hospital
Cuifang Fan (fancuifang@whu.edu.cn)
Renmin Hospital of Wuhan University: Wuhan University Renmin Hospital https://orcid.org/0000-0001-7052-4529
Suqing Wang
Wuhan University

Case report

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Abstract

Background: Little is known about the impact of SARS-CoV-2 on fetal anomalies.

Case presentation: We described a case report of fetal anomalies during second-trimester (25^{+3} weeks) pregnancy. The fetal autopsy was found with abnormal heart anatomy (including ventricular septal defect, oval hole valve missing, and pericardial effusion), polycystic kidney, and acute chorioamnionitis.

Conclusions: SARS-CoV-2 infection in second-trimester pregnancy not the direct factor resulted in congenital defects, and multiple risk factors contribute to these changes.

Background

In December 2019, the coronavirus disease 2019 (COVID-19), caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), has become a global public health emergency (1). Many previous studies have been reported the impact of COVID-19 on pregnancy outcomes. However, there is limited data about COVID-19 and congenital defects. To know, if COVID-19 has an effect on congenital defects in middle pregnancy, we conducted a case report of a pregnant woman with laboratory-confirmed COVID-19 pneumonia admitted to a hospital of Wuhan, Hubei, China.

Case Presentation

A 36 years old pregnant woman (gravida 2, para 1) diagnosed with COVID-19 at 16^{+1} weeks of pregnancy. She worked as a doctor in a hospital of Wuhan, Hubei province. After a range of treatments including antiviral (Arbidol), antibiotic (Azithromycin), Chinese patent medicine (Lianhua qingwen capsule) and oxygen support during 39 days of hospitalization, she recovered from COVID-19 and was discharged home at 21^{+1} weeks of pregnancy. Reviewing her clinical characteristics, we found the pregnant woman had positive results of IgG antibodies of cytomegalovirus and Epstein-Barr virus, which suggests that she had a history of previous infections with these two viruses. She had no history of adverse pregnancy outcomes, history of consanguinity, family history of congenital defects or adverse drug intake, and had regular antenatal care since conception. Down's screening and fetal nuchal translucency screening results were normal. No structural abnormalities were detected in the first trimester ultrasonographic screening. However, four-dimensional color doppler ultrasound examination at 25^{+3} weeks of pregnancy revealed multiple fetal malformation, including multiple cardiac malformations, bilateral renal cystic changes, short nasal bones, accompanied by low amniotic fluid (the maximum depth of amniotic fluid is 3.17 cm, amniotic fluid index is 5.68 cm), and the impedance of the uterine artery blood flow increased. Furthermore, ultrasound measurement of fetal only 23^{+1} weeks of gestation. The woman chose to medically terminate the pregnancy due to severe fetal anomalies. Induction of labor was done with rivanol and delivered a stillbirth (female, 560 g) along with placenta via vaginal route.

Later fetal autopsy was performed; Fig. 1 shows the gross morphology of the dead female fetus. On examination, the fetus was small for gestational age, as observed in the obstetric ultrasound reported above. In terms of gross findings, head facies and limbs of the fetus were normal. The heart measured 3 × 2.5 × 2 cm, but abnormal anatomical structure appeared in the heart, which manifested as ventricular septal defect, oval hole valve missing and pericardial effusion. Moreover, polycystic changes were observed in both kidneys. Placenta measured 11 × 8 × 5 cm, the gross appearance of the placenta was normal, however, maternal neutrophils was noted on microscopy in the connective tissues of the chorionic plate and membranous chorioamnion, which can be defined as maternal inflammatory response, stage 2 (intermediate) acute chorioamnionitis (Fig. 2). No other obvious pathological changes were noted. Using quantitative RT-PCR, the placenta, cord blood, amniotic fluid, and vaginal secretions were found negative for SARS-CoV-2.

Discussion And Conclusions

A substantial number of fetal losses are caused by fetal malformations, which manifested as different patterns and may indicate specific etiopathogenesis or associated syndromes. Congenital heart diseases and congenital abnormalities of the genitourinary tract are common phenotype of fetal malformation(2, 3). Genetic factors, environmental factors, and maternal complications or a combination of the three are often involved(4). Especially, maternal infection is an important factor to cause fetal malformations (5, 6). Several reports confirmed the possibility of vertical transmission of SARS-CoV-2 during pregnancy (7, 8), but no evidence exist about SARS-CoV-2 and fetal malformation. Previous studies suggested that during Asian influenza pandemic of 1957, the influenza virus increased the risk of several adverse fetal outcomes including congenital defects (9, 10). The human cytomegalovirus is the leading cause of congenital birth defects(11). Furthermore, SARS-CoV infection during pregnancy may result in fetal growth restriction(12). In our report, the fetal was observed small for gestational age, which suggests that it may be affected by SARS-CoV-2 infection. Moreover, the mother had previous history of cytomegalovirus and Epstein-Barr virus infections, but it is unknown whether she infected during pregnancy.

According to Shi L et al.(13), the impact of viral infection on the fetus may be secondary to the maternal inflammatory response, rather than the direct effect of the virus. Maternal inflammatory response can be manifested as histological chorioamnionitis or leukocyte infiltration into the chorion and amniotic membrane in utero(14). Groome et al. (15) reported that chorioamnionitis was associated with an increased risk of intraventricular hemorrhage. In our case report, mother had a transient high fever (> 39℃) during the course of COVID-19. Besides, mother was found with acute chorioamnionitis, which may be caused by intrauterine injection of rivanol rather than SARS-CoV-2.

In this case report, fetus was found with abnormal heart structure and bilateral renal cystic changes at 25^{+3} weeks of gestation. The mother had a history of viral infection (SARS-CoV-2, cytomegalovirus, and Epstein-Barr virus) and antiviral drugs (Arbidol) in the second-trimester of pregnancy. In addition, the woman was 36-year-old, which is a high-risk factor of birth defect(16). However, these findings did not

exclude a multifactorial pathogenesis which led to fetal malformations. We speculate that multiple risk factors contributed to the formation of fetal malformation in this case. SARS-CoV-2 infection contribute to maternal inflammation, which can adversely affect the fetus. Further genetic studies are required to identify the genotype of the fetus.

Abbreviations

COVID-19, Corona Virus Disease 2019;

SARS-CoV-2, Severe acute respiratory syndrome coronavirus 2;

Ig G, Immunoglobulin G.

Declarations

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Conflict of Interest

On behalf of all authors, the corresponding author states that there is no conflict of interest.

Ethical approval and consent to participate

This study was approved by the institutional ethics board of Renmin Hospital of Wuhan University (WDRY2020-K015). Written informed consent was obtained from the patient who recruit in our study.

Consent for publication

Written informed consent for publication was obtained from all participants.

Availability of data and material

The processed data required to reproduce this finding cannot be shared at this time as the data also forms part of an ongoing study.

Authors' contributions

Protocol/project development: Cuifang Fan, Suqing Wang

Yuping Guo, Jiacai Ren: Data Collection, Manuscript writing

Jingping Yuan, Di Lei, Ying Yu: Data collection

Nawsherwan: Manuscript writing

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Figures

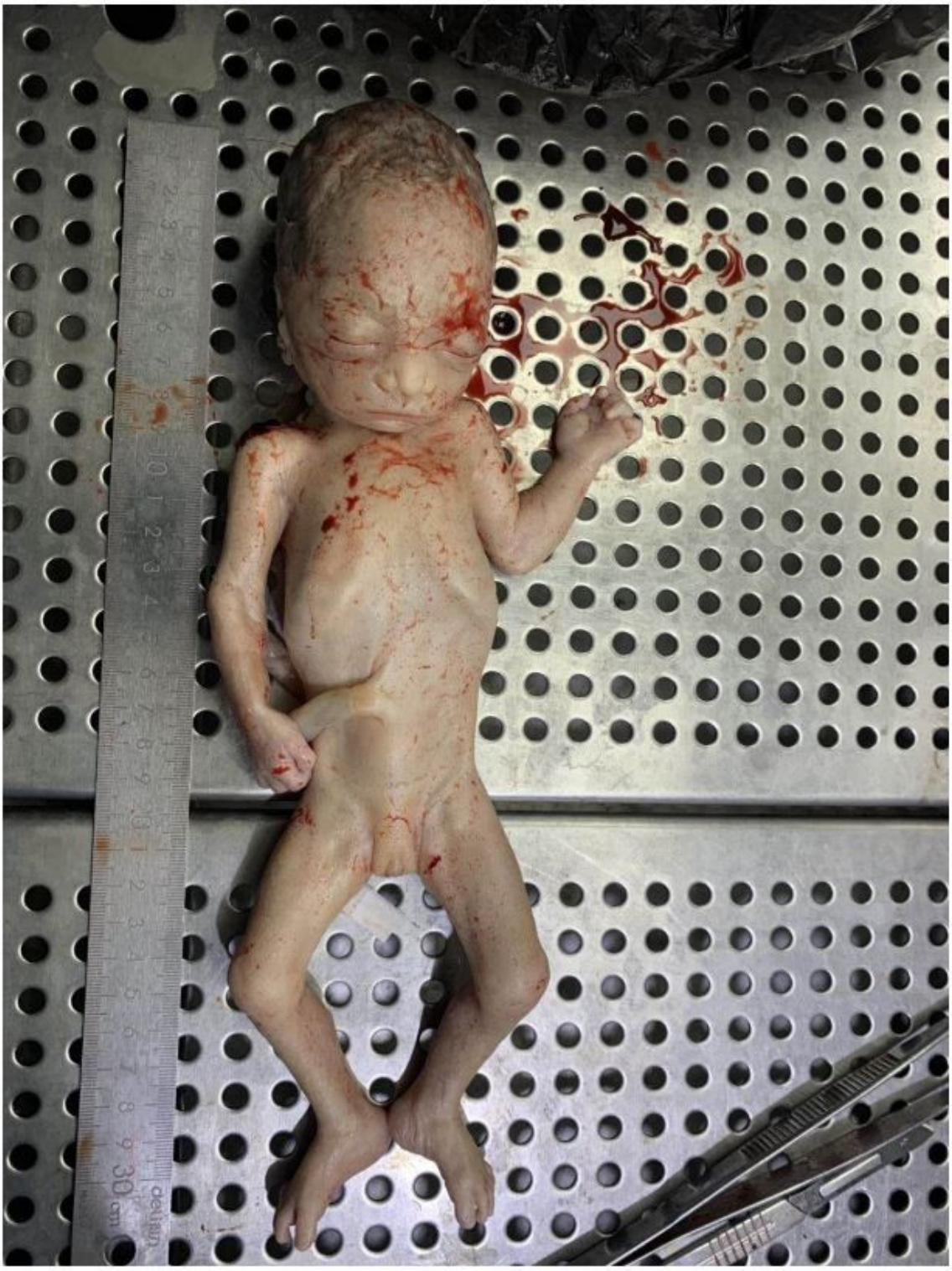
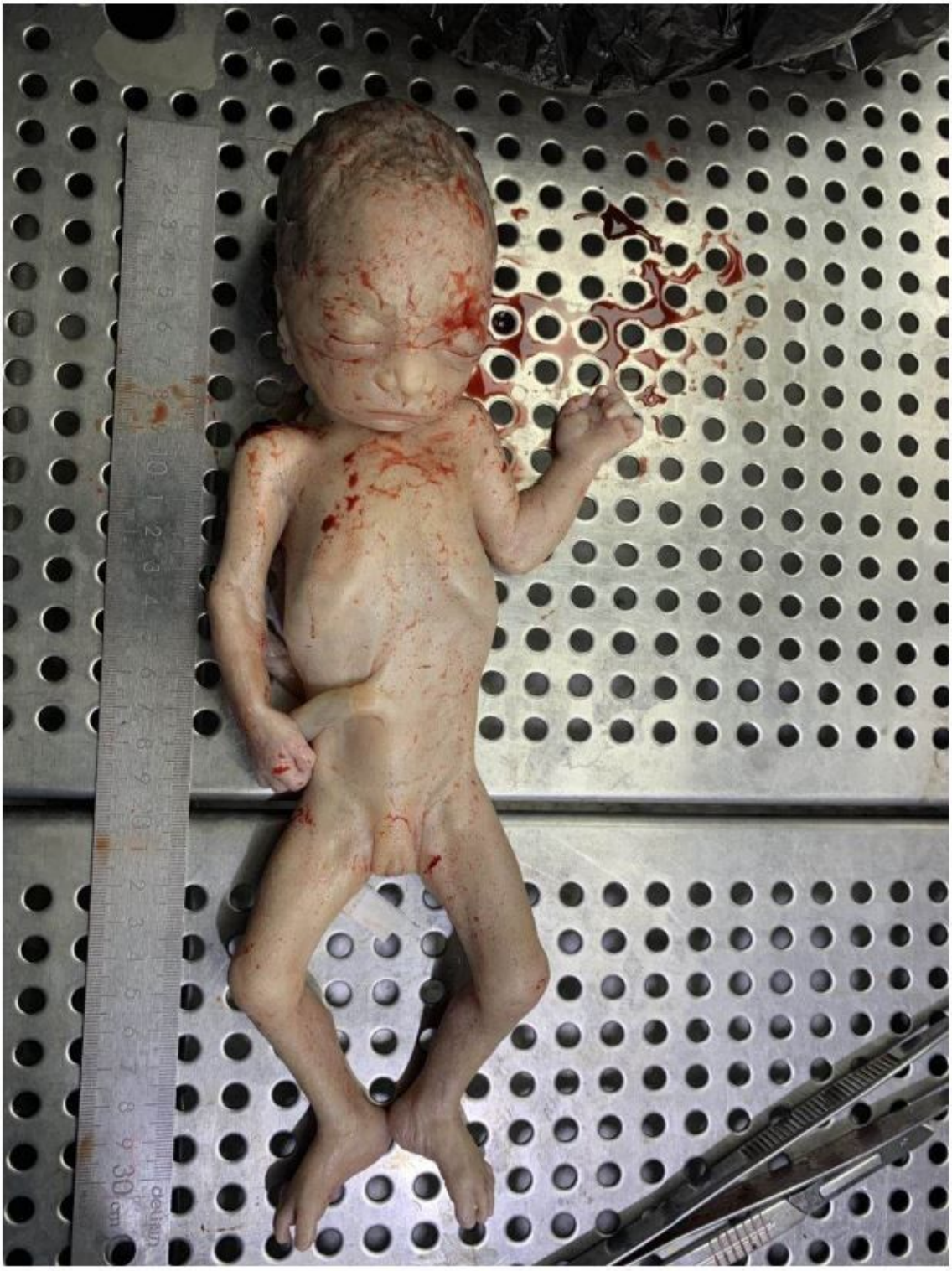


Figure 1

The gross morphology of the dead female fetus. No obvious abnormalities in gross view of the fetus, head facies and limbs of the fetus were normal.



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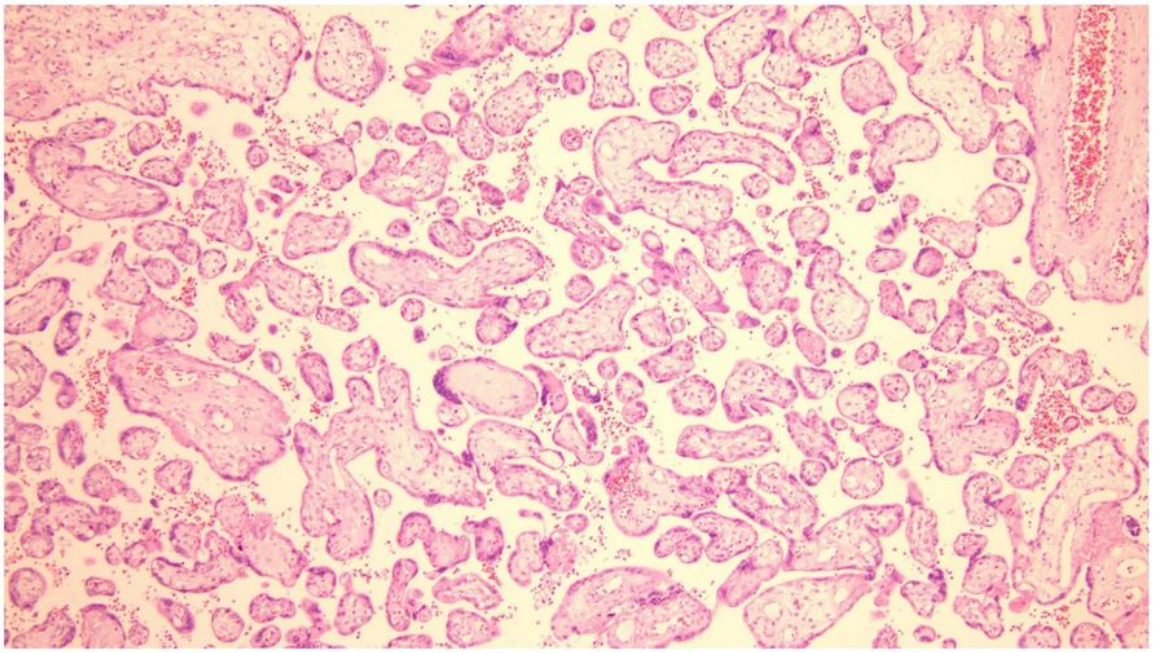


Fig 2A

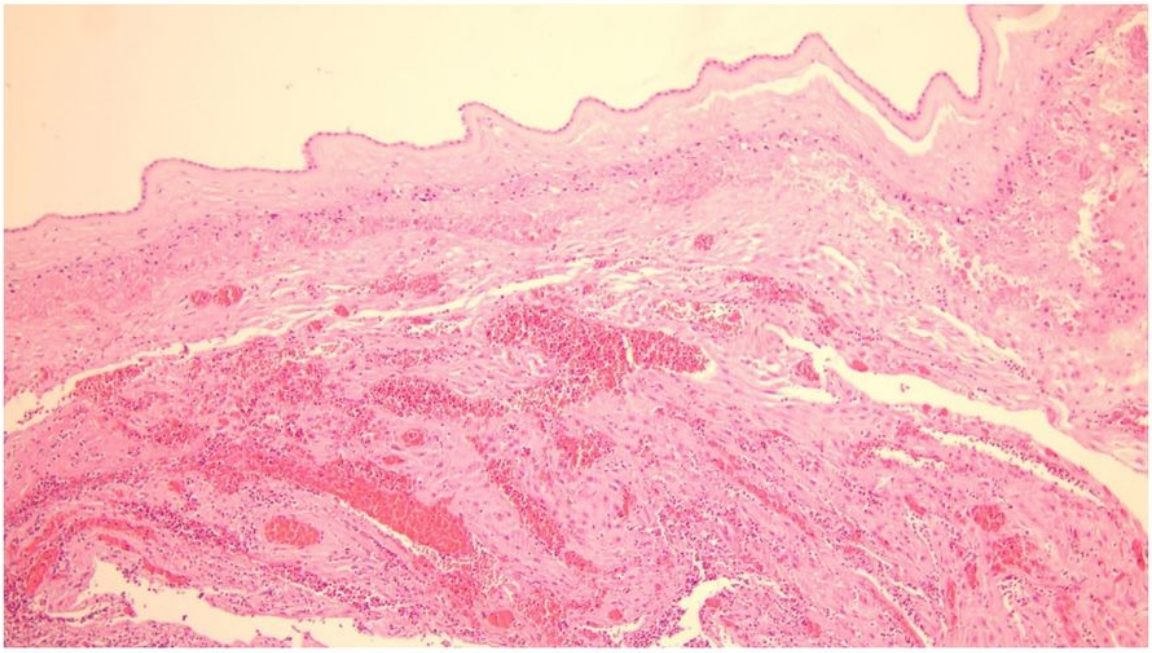


Fig 2B

Figure 2

Hematoxylin-eosin staining and microscopy of the placental disk. A. The microscopy of chorionic plate on the maternity side. Normal vessels of stem villi and terminal villi at second-trimester pregnancy (H&E, 10X, 40X). B. The microscopy of chorionic plate on the fetal side. Neutrophils was noted on microscopy in the connective tissues of the chorionic plate and membranous chorioamnion (H&E, 10X, 40X).

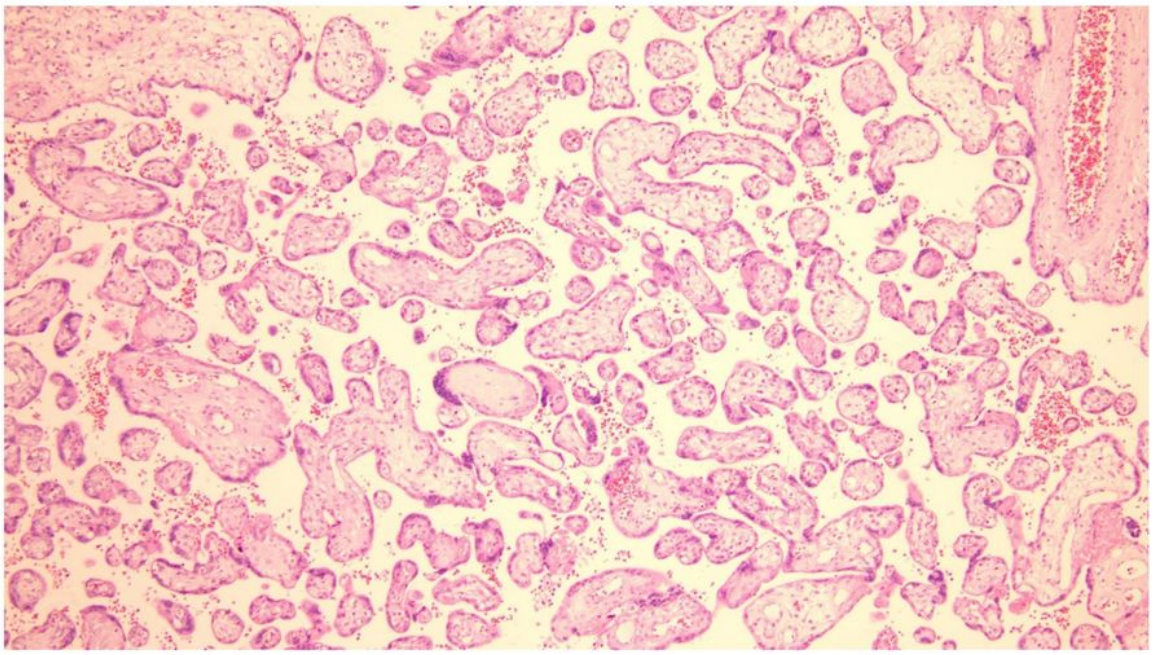
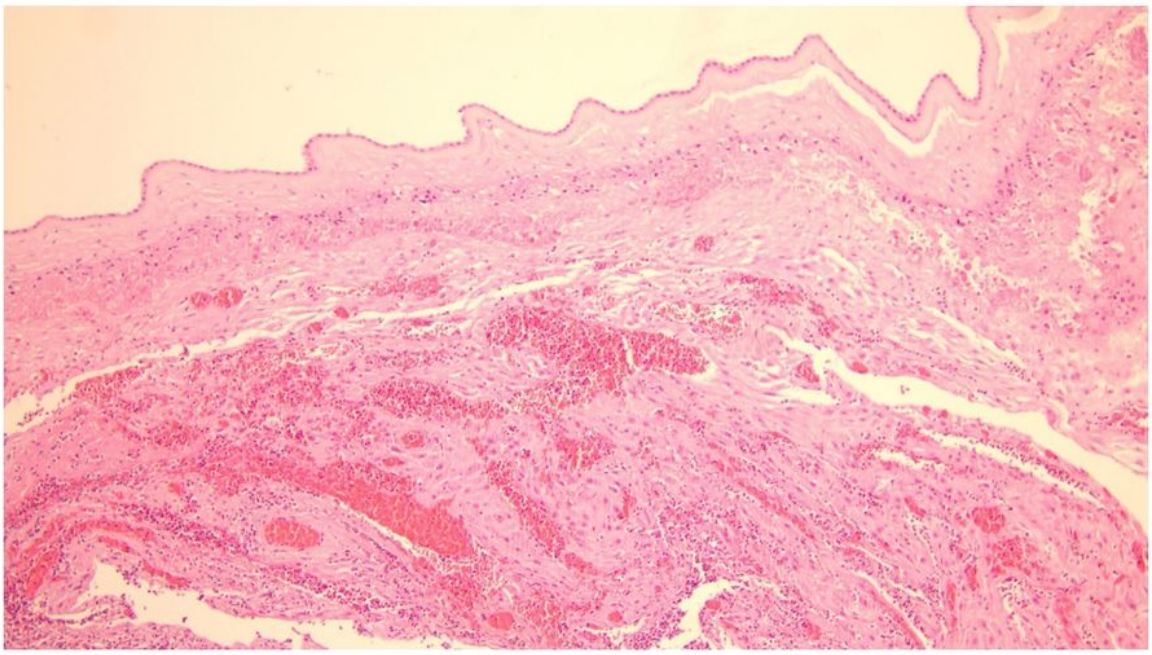


Fig 2A



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