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Letter to the editor – brief communication

HISTOLOGICAL CHARACTERIZATION OF PLACENTA IN COVID19 PREGNANT WOMEN

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Dear Editor,

The outbreak of SARS-CoV2 infection between the end of 2019 and the beginning 2020 has now involved most of the countries and represents a global challenge for health management (1).

Pregnant women are considered a susceptible category because of the limited data on maternal and neonatal outcomes of pregnant women with SARS-CoV2 infection (1).

In viral infections, histological examination of the placenta usually shows lesions that are characteristic for the different types of viruses with overlapping features.

This is a descriptive study of histological alterations in a series of placenta from pregnant women with documented SARS-CoV2 infection.

Nine patients who delivered between March and April 2020 at Fondazione IRCCS Ca' Granda – Ospedale Maggiore Policlinico (Milan), with SARS-CoV2 infection documented by nasopharyngeal swab test were enrolled in this study. Clinicopathological characteristics are shown in Figure 1 – Table section.

Clinically, one case (case #4) presented with fever up to 37.5° C and cough and another case (case #9) suffered from fever up to 38,5° C and bilateral interstitial pneumonia documented by chest X-ray which conditioned a severe respiratory distress; the remaining cases were asymptomatic.

Five histological samples for each case were paraffin-embedded and stained with Haematoxylin & eosin including umbilical cord sections, amnio-chorial membranes, and three sections of the parenchyma.

The histochemical staining Giemsa and PAS and the immunohistochemical staining for CD3, CD20, CD4, CD8, CD14, CD15, CD31 were performed to evaluate the inflammatory infiltrate and the structural alterations.

Reports were in accordance with the recently published guidelines (2).

Maternal vascular malperfusion of the placental bed

Distal villous hypoplasia was detectable in 2 out of 9 cases (22%), with a variation in villous diameters, formation of villous clusters, distal and peripheral villous hypoplasia. There was fewer fetal arterioles and those remaining showed hypertrophy of the media.

Distal villous immaturity was seen in association with distal villous hypoplasia, with an increased number of enlarged distal villi, stromal cells and villous macrophages.

Delayed villous maturation

Five/9 cases (55%) showed a delayed villous maturation that is characterized by a monotonous population of chorial villi with a reduction in the number of syncytial vascular membranes as well as the presence of a continuous coating of cytotrophoblasts and central capillaries in the villi.

Perivillous fibrin deposits, calcifications and intimal hyperplasia of truncular and intermediate vessels were present in 8/9 (88%), 6/9 (67%) and 4/9 (44%) cases, respectively.

Other lesions

One case showed villous immaturity and one presented meconium on the chorial plate, free or incorporated in macrophages.

In one case, a leukocitoclasic vasculitis without evidence of vascular thrombi in small, medium and terminal villi and with acute intervillitis was found.

Immuno- and histochemical results

No significant T- and B-cell infiltrate was observed.

Only one case, with Giemsa staining, showed focal changes related to thrombotic vascular disease in a vascular malperfusion background.

Our results show the high rate of chronic hypoxy-related morphological alterations of the placental parenchyma such as delayed villous maturation associated with perivillous fibrin deposits, calcifications and intimal hyperplasia.

One case (case #5) displayed a marked infiltration of the vascular tree by neutrophils and lymphocytes, with the characteristics of acute vasculitis.

During labour just two fetuses suffered from alterations in the cardiotocogram, one of them also with a reduction of the fetal movements. The Apgar scores of the newborn babies was of 9 and 10 at 5 and 10 minutes in most of the cases, newborn and placental weights were coherent for gestational age and all the newborn swap test were negative, predicting a good outcome of the pregnancies and indicating that there was no evidence of vertical transmission of SARS-CoV2 from infected pregnant mothers to newborns.

In conclusion, our results are like those showed in the only one reported study in literature and available in PubMed regarding placenta morphological analysis from SARS-CoV2 infected women, where no specific histological alterations were detectable (3-5), as these finding are common in other maternal conditions such as gestational diabetes or hypertension. Further studies will be needed to best understand the possible role of placenta in a potential vertical transmission and in the clinical outcome of the newborns.

AUTHOR CONTRIBUTIONS

Fulvia Milena Cribiù and Giorgio Alberto Croci drafted the manuscript, Enrico Iurlaro, Marta Tondo and Anna Viscardi provided and analyzed clinical data, Alessandro Del Gobbo and Tommaso Rizzuti analyzed histological data, Silvano Bosari, Stefano Ferrero revised the manuscript and supervised the work.

CONFLICTS OF INTEREST

The authors declare they have no conflicts of interest.

Declaration of interests

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Case #	Age	Comorbidities	Gestational age	Gestational age at swab test	Placental weight (g)	Newborn weight (g)	Apgar score (5–10 min)	Labour events	Newborn swab test
1	31	None	38+6	38+1	550	3160	9-10	None	Negative
2	25	Gestational diabetes	38	38	500	3870	9-10	None	Negative
3	21	None	35+5	35+4	500	2410	4-7	Alterations in cardiotocogram and reduction in fetal movements	Negative
4	34	None	37+3	37+2	580	2770	9-10	None	Negative
5	40	None	40	40	420	3000	9-10	None	Negative
6	41	None	33	33	300	2200	8-8	None	Negative
7	34	None	40	40	380	3250	9-10	None	Negative
8	27	None	37+5	36+5	490	2840	9-10	Alterations in cardiotocogram	Negative
9	34	Severe respiratory distress	35+4	35+1	440	2380	9-10	None	Negative

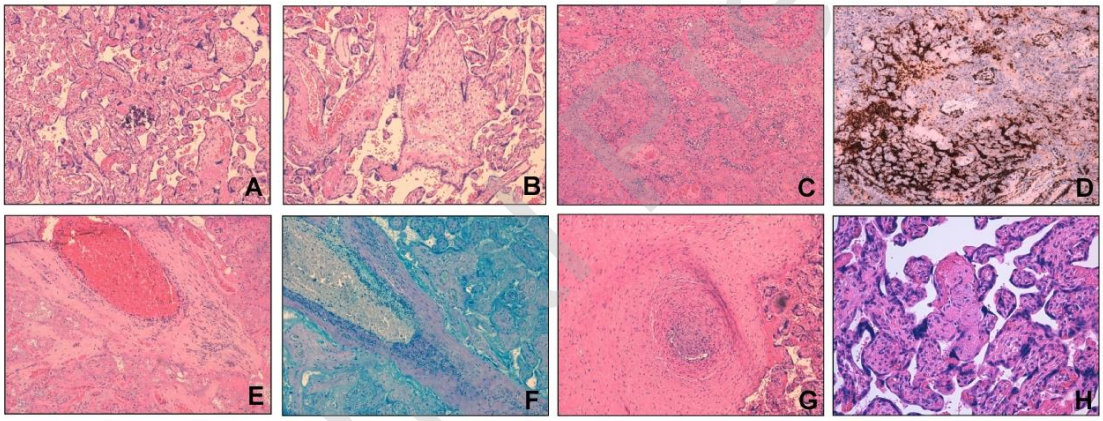

Figure 1 – Morphological alterations of the placenta: (A) Perivillous calcification associated with perivillous and intravillous fibrin deposits (H&E, original magnification: 100x); (B) villous immaturity, characterized by loose reticular stroma with capillaries in the center of the villi (H&E, original magnification: 100x); (C and D) Acute intervillitis, characterized by marked neutrophils infiltrate in the perivillous space, highlighted with anti-CD15 immunohistochemical staining (C, H&E, original magnification: 50x and D, anti-CD15 antibody (Dako®), original magnification:

100x); (E and F) Acute leukocytoclasic vasculitis, with neutrophils migrating from the lumen to the vessel wall, better shown with histochemical Giemsa staining (E, H&E, original magnification: 100x and F, Giemsa, original magnification: 100x, case #5); (G) Chronic recanalized arthery with marked hypertrophy of the wall (H&E, original magnification: 100x); (H) A small cluster of thrombotic villi, with fibrotic and avascular stroma (H&E, original magnification: 100x).