doi:10.1017/S1431927622005608
Microsc. Microanal. 28 (Suppl 1), 2022

Detection and Identification of SARS-CoV-2 in Placental and Neonate Tissues

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Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection during pregnancy has been of concern throughout the COVID-19 pandemic. While most neonates born to SARS-CoV-2 positive people test negative after birth, some neonates do test positive for SARS-CoV-2 and still others show evidence of SARS-CoV-2 infection of the placenta. Transmission electron microscopy (EM) evidence of SARS-CoV-2 infection in neonates and placental tissues has been rare. The Infectious Diseases Pathology Branch at CDC utilized formalin-fixed paraffin embedded (FFPE) tissues to detect and identify coronavirus particles in SARS-CoV-2 positive neonate and placental tissues. Areas of interest from FFPE blocks were selected based on results from SARS-CoV-2 immunohistochemistry (IHC) and in situ hybridization (ISH), enabling a targeted approach to finding the virus by EM. Samples for EM were deparaffinized using xylene, rehydrated, and post-fixed in 2.5% glutaraldehyde. Samples were then post-fixed with 1% osmium tetroxide, en-bloc stained with uranyl acetate, dehydrated, and embedded in Epon-Araldite resin.

In neonate tissues, coronavirus-like particles were observed by EM in respiratory and myocardial tissues. Intracellular vacuolar accumulations of coronavirus particles were found within pneumocytes and ciliated cells. Extracellular viral particles were identified in association with cilia of respiratory epithelial cells and near collagen in the heart. Areas with EM evidence of coronavirus corresponded to areas positive for SARS-CoV-2 RNA and proteins by ISH and IHC. Positive SARS-CoV-2 immunohistochemical staining was also observed in the syncytiotrophoblasts of placental tissues. EM analysis revealed an abundance of coronavirus-like particles within cytoplasmic vacuoles in the syncytiotrophoblasts, although no extracellular viral particles were apparent. While these results are suggestive of SARS-CoV-2 replication in the placenta, the timing of SARS-CoV-2 infection in neonates has been and remains difficult to determine. Larger, systematic studies with robust ISH, IHC, and EM evidence of SARS-CoV-2 localization in placental, fetal, and neonate tissues will be necessary to fully understand the impacts of SARS-CoV-2 infection on pregnancy outcomes.