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The authors reply: We thank Drs. Miller and Brealey¹ for their comments and fully acknowledge their expertise in the field of electron microscopy. We also acknowledge our uncertainties regarding the exact nature of the particles seen in the podocytes in our patient’s kidney biopsy, and we were cautious in the interpretation of these findings. Following Drs. Miller and Brealey’s comments,¹ we have modified our letter before its final publication in the journal to further underline that these particles may correspond to nonviral entities.

However, the particles detected in our patient’s biopsy are rather similar to the ones reported in the first documentation of severe acute respiratory syndrome coronavirus 2.² Besides, the appearance of intracellular viral inclusions appears to be quite variable from one publication to another.^{3,4} To our opinion, it remains, therefore, possible that the particles observed in our patient are of viral origin. Nevertheless, we totally agree with Drs. Miller and Brealey¹ that the definite proof for the presence of viral inclusions in cells requires an immunostaining with specific antibodies, whether in cultured cells or in tissue samples.

Our knowledge of coronavirus disease 2019 is rapidly evolving and caution is of the utmost importance.



The authors reply: We have carefully read and considered the letter from Prof. Miller and Dr. Brealey,¹ distinguished experts of electron microscopy (EM), and appreciate that they pointed out the limitations of our study.²

We agree with Miller and Brealey’s point and recognize that there are inherent difficulties in discrimination of cellular vesicles from viral particles solely by morphological evidence, especially in routine EM processing of autopsy tissues. These conditions differ markedly from the *in vitro* negative staining of body fluids or cell culture, which are the techniques usually utilized for optimal visualization of viral structure. However, EM is still an essential tool and a front-line evaluation method in the search for unknown pathogens in outbreaks or epidemics. For example, the causative agents of the outbreak of severe acute respiratory syndrome (SARS) in China in 2003 and human monkey pox in the United States in 2003 were both first identified by EM. In addition, with our immunofluorescence staining for SARS-coronavirus (CoV) nuclear protein as we presented in our paper (Figure 3d)² and the recent publications of ultrastructural feature of SARS-CoV-2,^{3,4} we consider the structures as possible, but not definitively proven, CoV. We have therefore prudently changed the description in the preprint version of our article of “viral particle” to “coronavirus-like particle.” Ideally, immuno-EM or *in situ* hybridization studies to assess local protein or RNA levels of CoV will further clarify the possibility of direct kidney parenchymal infection. Such a combination of ultrastructural images and molecular data could then definitively identify viral-like particles as SARS-CoV-2.

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