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The authors reply: We thank Drs. Miller and Brealey[1] 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 Brealey[1] 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.

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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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Multivesicular bodies mimicking SARS-CoV-2 in patients without COVID-19

To the editor: It is now well known that patients with novel coronavirus disease 2019 (COVID-19) due to severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) commonly have kidney complications, including acute kidney injury, proteinuria, and hematuria. Recent publications in *Kidney International* used electron microscopy (EM) to detect the virus in autopsy or biopsy specimens of the kidney.[1,2] Most of the published images depicting the suspected virus are very similar, if not identical, to multivesicular bodies (MVBs). MVBs have been well-known since the 1960s and their appearance and occurrence is detailed in the classic monograph of Feroze Ghadially;[3] however, their exact significance and function is unclear. We suspect that the EM images of SARS-CoV-2 published to date are in fact MVBs.

To address this question, we examined the EMs of 11 current consecutive kidney biopsies and 10 kidney biopsies from the pre–COVID-19 era (Table 1). Every EM contained renal cortex with 1 to 2 glomeruli. MVBs were found in all 20 kidney biopsies, irrespective of the underlying kidney disease (Figure 1). To our surprise, MVBs were always identified in podocytes (1 to 4 podocytes per glomerulus), but we have not seen them in tubular epithelial cells. MVBs were occasionally seen in endothelial cells (mainly arterial or arteriolar) and in a parietal glomerular epithelial cell of 1 biopsy. MVBs theoretically may represent podocyte endocytosis with subsequent formation of intracytoplasmic microvesicles resembling viruses. Seeing an MVB by EM is just a snapshot and we do not know how and when they evolved or how long they remain. MVBs contain microvesicles. However, microvesicles are commonly "free floating" in the cytoplasm of many cell types, including tubular epithelial cells (frequently representing endocytotic vesicles). Su *et al.*[1] show such cytoplasmic microvesicles in tubular epithelial cells in their Figure 2, but the particles in Figure 2a may have come from an MVB after its membrane dissolved. While these "free floating" cytoplasmic microvesicles could represent viral particles, they are

Table 1 | Renal cells with MVB

Case no.	Year of biopsy	Age (yr)	Sex	Podocyte	Endothelial cell	Parietal epithelial cell	Diagnosis
1	2015	56	F	+	+		Membranous glomerulonephritis
2	2015	58	M	+	+		Minimal change disease
3	2015	56	M	+			Focal segmental glomerular sclerosis
4	2015	59	M	+			Immune complex glomerulonephritis with membranoproliferative pattern
5	2016	60	M	+			Immune complex glomerulonephritis focal crescents
6	2016	72	M	+			AL amyloidosis
7	2016	25	M	+			IgA nephropathy
8	2016	48	M	+			Cryoglobulinemic glomerulonephritis
9	2016	82	M	+		+	Oxalate nephropathy
10	2016	69	F	+			Thin basement membrane nephropathy
11	Current	32	F	+			Class V+III lupus nephritis (COVID-19–negative)
12	Current	80	F	+			Membranous glomerulonephritis
13	Current	52	M	+			Diabetic nephropathy
14	Current	80	M	+	+		Diabetic nephropathy
15	Current	66	F	+			Fibrillary glomerulonephritis
16	Current	79	M	+			IgA nephropathy
17	Current	26	M	+	+		Chronic active antibody-mediated rejection
18	Current	40	M	+	+		Chronic active antibody-mediated rejection
19	Current	54	F	+			Thrombotic microangiopathy
20	Current	86	F	+	+		Pauci-immune crescentic glomerulonephritis
21	Current	68	F	+			Acute tubular necrosis

AL, amyloid λ light chain amyloidosis; COVID-19, coronavirus disease 2019; MVB, multivesicular body.