SARS-CoV-2 in the Kidneys- Postmortem Renal Histopathologic Findings in 3 Patients with COVID-19

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INTRODUCTION

As the mortality rate of coronavirus disease 2019 (COVID-19) continues to rise, forensic pathology has been integral in providing information on the pathogenesis of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) through postmortem examination. New onset acute kidney injury (AKI) and proteinuria have been observed in hospitalized patients with COVID-19 and no medical history of kidney disease. Various mechanisms for kidney injury have been proposed, including hypoperfusion, inflammatory injury secondary to cytokine storm and direct infection by the virus. The angiotensin-converting enzyme II (ACE2) serves as a functional receptor for the spike glycoprotein of the human coronavirus HCoV-NL63, SARS-CoV and SARS-CoV-2[1]. Evidently, the ACE2, essential for viral uptake by host cells, is highly expressed on podocytes and tubule epithelial cells[2]. Electron microscopy has been utilized as a direct approach to demonstrate the renal involvement of the virus. In this case series, the postmortem renal histopathologic and ultrastructural findings in three patients with COVID-19 are reported and discussed.

CLINICAL INFORMATION

Table 1- Summary of clinical information for the 3 patients with COVID-19

ID	Age/Sex	Medical history of HTN, HF, CAD, DM, ESRD, CKD, cancer	Reason for Admission	RT-PCR SARS-CoV-2 testing	Cr (mg/dL)	BUN (mg/dL)	eGFR (mL/min)	WBC (K/uL)	ALC (K/uL)	Proteinuria?	Critical Interventions	Hospital Stay (Days)
1	53 M	HTN	Acute type A aortic dissection	Detected	7.57	164	7	31.9	0.7	N/A	-Mechanical ventilation -Intravenous antihypertensive therapy -Continuous renal replacement therapy (CRRT)	11 days
2	79 F	HTN, ESRD (s/p renal transplant), CKD, DM	Altered mental status, lethargy and vomiting	Detected	2.73	55	16	12.5	0.6	2+	N/A	13 days
3	52 M	CAD, DM, HF (s/p LVAD)	Supratherapeutic INR and symptomatic anemia	Not detected (x2)	1.85	51	41	15.9	0.6	1+	-Mechanical ventilation -Vasopressor support	16 days

ALC- absolute lymphocyte count; BUN- blood urea nitrogen; CAD- coronary artery disease; Cr- creatinine; CKD- chronic kidney disease; DM- diabetes mellitus; eGFR- glomerular filtration rate; ESRD- end stage renal disease; HTN- hypertension; HF- heart failure; ID- patient ID; LVAD- left ventricular assist device; N/A- not available; s/p- status post

The cause of death for the three patients was acute respiratory distress syndrome (ARDS) secondary to COVID-19 infection. Although patient 3 tested negative for COVID-19 on multiple attempts, his clinical course and postmortem microscopic findings in the sampled lung and renal tissue support the diagnosis of COVID-19 infection.

RESULTS

Table 2- Summary of postmortem, light & electron microscopy kidney findings for the 3 patients with COVID-19

ID	Gross findings	Light microscopy findings	Electron microscopy findings
1	Normal left and right kidney	Proximal tubular isometric vacuolization; sloughed tubular epithelium	Abundant viral forms within tubular epithelial cells isolated to the areas of isometric vacuolization, Mature appearing viruses predominately located within the cytoplasm, focally organized into small arrays
2	Atrophic native left and right kidneys; diffusely coarse and granular with thin (<3 mm) cortical surfaces. Normal transplanted kidney	Native kidneys- thyroidization and vascular thickening Transplanted kidney- thickening of vessels; focal area in medulla with large, multinucleated, discohesive cells with foamy cytoplasm.	Intracellular virus morphologically consistent with SARS-CoV-2 in renal tubular epithelial cells as well as glomerular podocytes
3	Normal left and right kidney	Nodular glomerulosclerosis with scarred glomeruli. Rare glomerular microthrombi.	Intracellular virus morphologically consistent with SARS-CoV-2 in renal tubular epithelial cells as well as glomerular podocytes

ID- patient ID

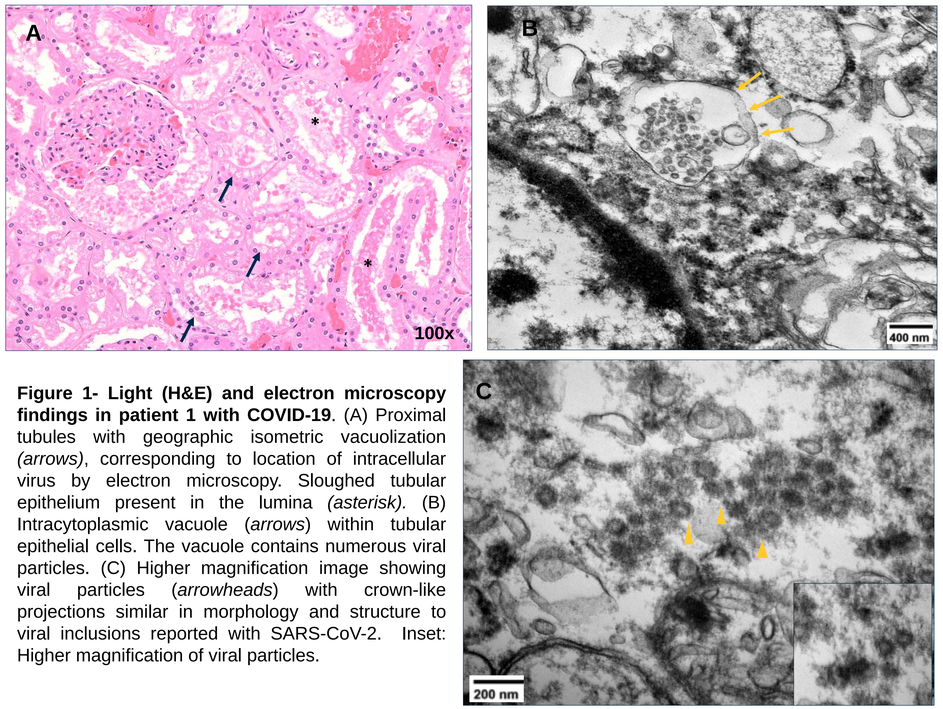

Figure 1- Light (H&E) and electron microscopy findings in patient 1 with COVID-19. (A) Proximal tubules with geographic isometric vacuolization *(arrows)*, corresponding to location of intracellular virus by electron microscopy. Sloughed tubular epithelium present in the lumina *(asterisk)*. (B) Intracytoplasmic vacuole (*arrows*) within tubular epithelial cells. The vacuole contains numerous viral particles. (C) Higher magnification image showing viral particles (*arrowheads*) with crown-like projections similar in morphology and structure to viral inclusions reported with SARS-CoV-2. Inset: Higher magnification of viral particles.

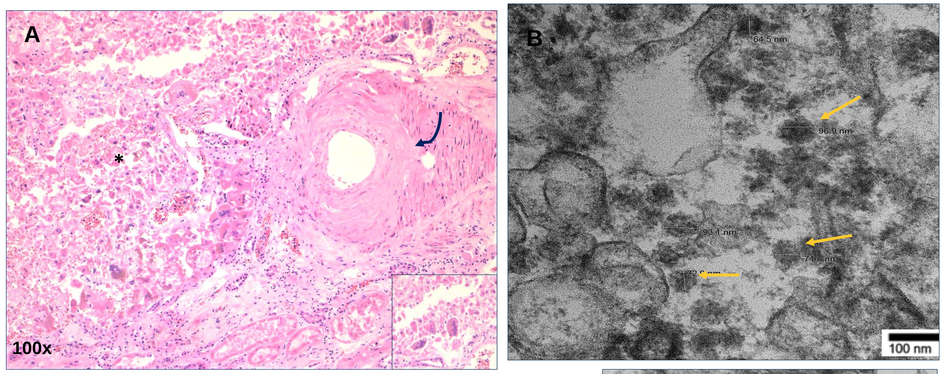

Figure 2- Light (H&E) and electron microscopy findings in patient 2 with COVID-19. (A) Section of transplanted kidney demonstrates vessel thickening (*curved arrow*). Focal area in medulla (*asterisk*) containing large discohesive cells with foamy cytoplasm. Inset: Multinucleated giant cells in medulla. (B) Intracellular virus (arrows) morphologically consistent with SARS-CoV-2 in renal tubular epithelial cells; measuring approximately 65 to 97 nm. (C) Higher magnification image of viral particles.

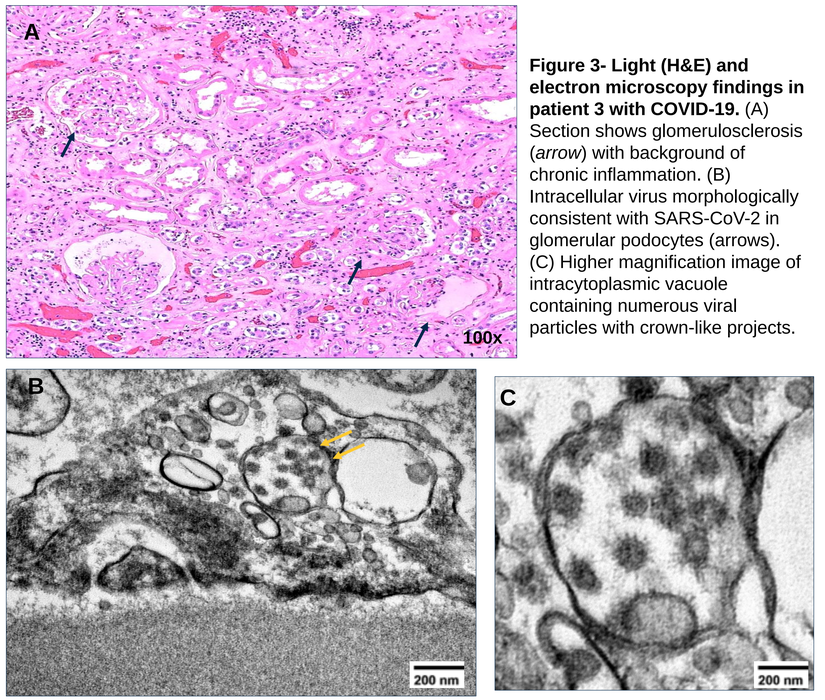

Figure 3- Light (H&E) and electron microscopy findings in patient 3 with COVID-19. (A) Section shows glomerulosclerosis (*arrow*) with background of chronic inflammation. (B) Intracellular virus morphologically consistent with SARS-CoV-2 in glomerular podocytes (arrows). (C) Higher magnification image of intracytoplasmic vacuole containing numerous viral particles with crown-like projects.

CONCLUSION

- Light microscopy results for the 3 patients showed non-specific findings of kidney injury including glomerulosclerosis, mild arteriosclerosis, sloughing of tubular epithelium and proximal tubular isometric vacuolization.
- Ultrastructural examination by electron microscopy demonstrated viral particles with crown-like projections characteristic of coronavirus in proximal tubular epithelial cells and glomerular podocytes. The overall structure of the virus is similar to previously reported cases of SARS-CoV-2 in the kidneys[3].
- Overall, these findings provide a strong evidence for SARS-CoV-2 invasion of the kidneys contributing to the onset of acute renal failure. It is important to recognize other more common causes that contributed to AKI in these patients including co-morbidities, hypoperfusion, sepsis, coagulopathy, and possible drug interaction. Therefore, the patients' cause of renal failure was multifactorial, with hypoperfusion injury likely being the primary cause and further complicated by direct viral infection.
- Further research is still needed for a comprehensive understanding of COVID-19, including its effects on the kidney.

REFERENCES

1. ACE2 Angiotensin I Converting Enzyme 2 [Homo Sapiens (Human)] - Gene - NCBI." National Center for Biotechnology Information, U.S. National Library of Medicine, www.ncbi.nlm.nih.gov/gene/?term=59272.
2. Durvasula R, Wellington T, McNamara E, Watnick S. COVID-19 and Kidney Failure in the Acute Care Setting: Our Experience From Seattle. Am J Kidney Dis. 2020;76(1):4-6. doi:10.1053/j.ajkd.2020.04.001
3. Su H, Yang M, Wan C, et al. Renal histopathological analysis of 26 postmortem findings of patients with COVID-19 in China. Kidney Int. 2020;98(1):219-227. doi:10.1016/j.kint.2020.04.003
4. Evan A. Farkash, Allecia M. Wilson, Jeffrey M. Jentzen. Ultrastructural Evidence for Direct Renal Infection with SARS-CoV-2. JASN Aug 2020, 31 (8) 1683-1687; DOI: 10.1681/ASN.2020040432

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