

Upper Urinary Tract Urothelial Cell Carcinoma in Two Macaques

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Introduction

- Urothelial cell carcinomas (UCCs) have been rarely reported in non-human primates in the urinary bladder or in the upper urinary tract.^{1,2} Here we describe two cases of urothelial cell carcinoma arising from the renal pelvis and kidney of a rhesus macaque (*Macaca mulatta*) and a cynomolgus macaque (*Macaca fascicularis*).
- Case 1: A 22-year-old rhesus macaque presented to the clinical veterinarians for hindlimb osteoarthritis.
- Case 2: A 24-year-old cynomolgus macaque presented for chronic unresolving diarrhea.
 - > No clinical signs associated with the urinary tract were reported in either animal.
 - > At necropsy, the kidneys of the cynomolgus macaque were described as spongy. No mass effects were observed in the kidneys or other tissues in either case.
 - > Major organs from both animals were submitted for histopathology, and processed and routinely stained with H&E.
 - > IHC for Uroplakin III, a urothelial-specific marker, was performed at Michigan State University.

Results

- In both cases, a neoplastic population of urothelial cells forms a well-circumscribed mass arising at the renal pelvis and expanding into the adjacent renal medulla. In Case 1, the neoplastic cells are present in patchy areas spreading into renal tubules extending from the renal pelvis to the bulk of the cystic mass (intratubular spread). Neoplastic cells are arranged in anastomosing trabeculae and papillary projections extending into a central cystic space supported by fine fibrovascular stroma. Neoplastic cells are polygonal, have distinct cell borders, moderate to abundant amounts of eosinophilic and variably vacuolated cytoplasm. Nuclei are ovoid containing coarsely stippled chromatin and 0-1 distinct nucleoli. Anisokaryosis and anisocytosis are minimal, and up to 2 mitotic figures are observed in 10 HPF (2.37 mm²). The neoplastic cells were rarely focally infiltrative to the surrounding parenchyma.
- Both tumors exhibited positive immunoreactivity for Uroplakin III (UPIII), with variable perimembranous labeling.

Results

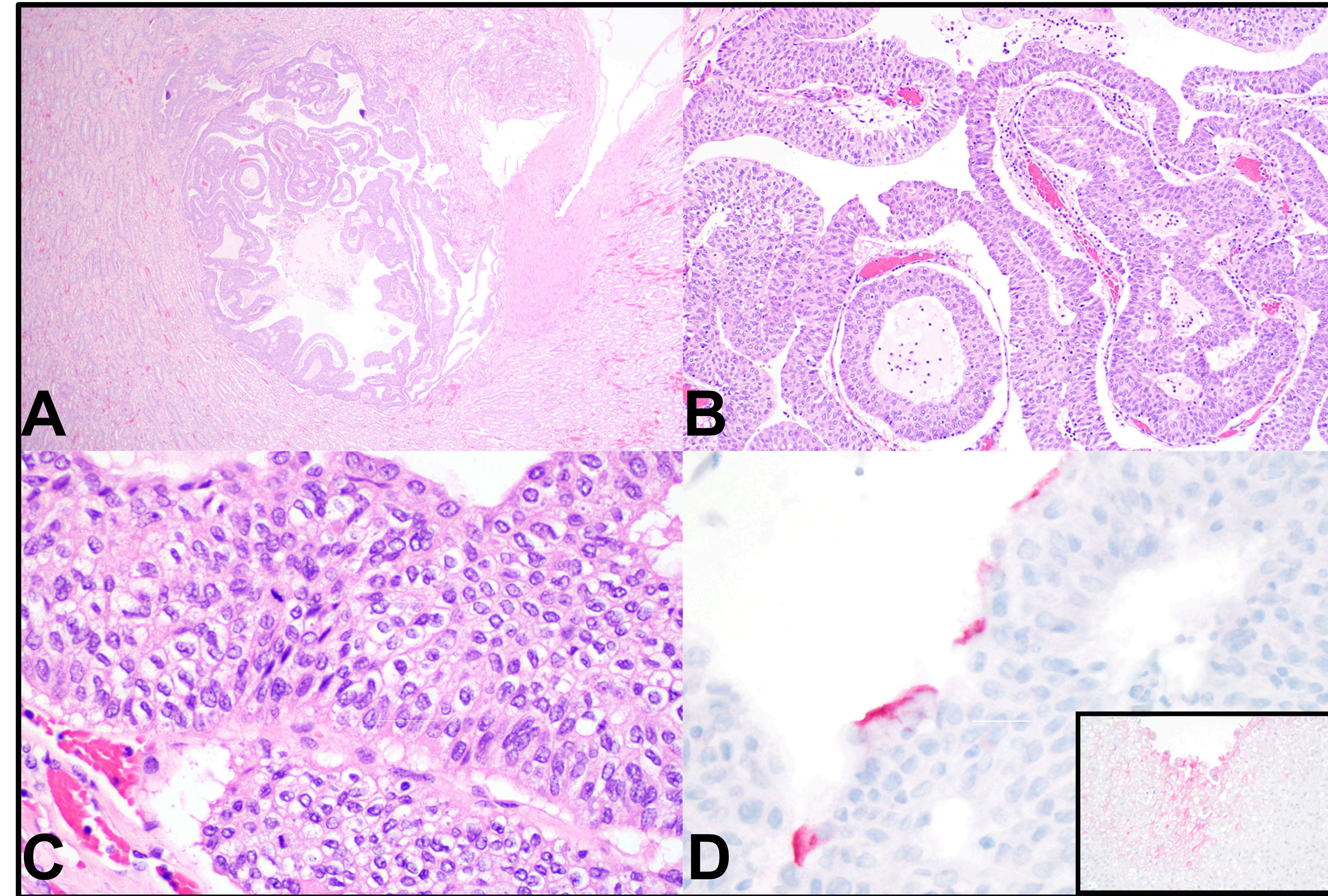


Figure 1. Kidney from Case 1 (A-C, H&E stain; D – UPIII IHC stain)

A: Mass arises in the renal pelvis and exhibits intratubular spread. **B:** Neoplastic cells form anastomosing trabeculae and papillary projections. **C:** Mitotic figures were rare. **D:** Neoplastic cells display variable positive apical perimembranous labeling for UPIII. Inset: Normal renal pelvis urothelium

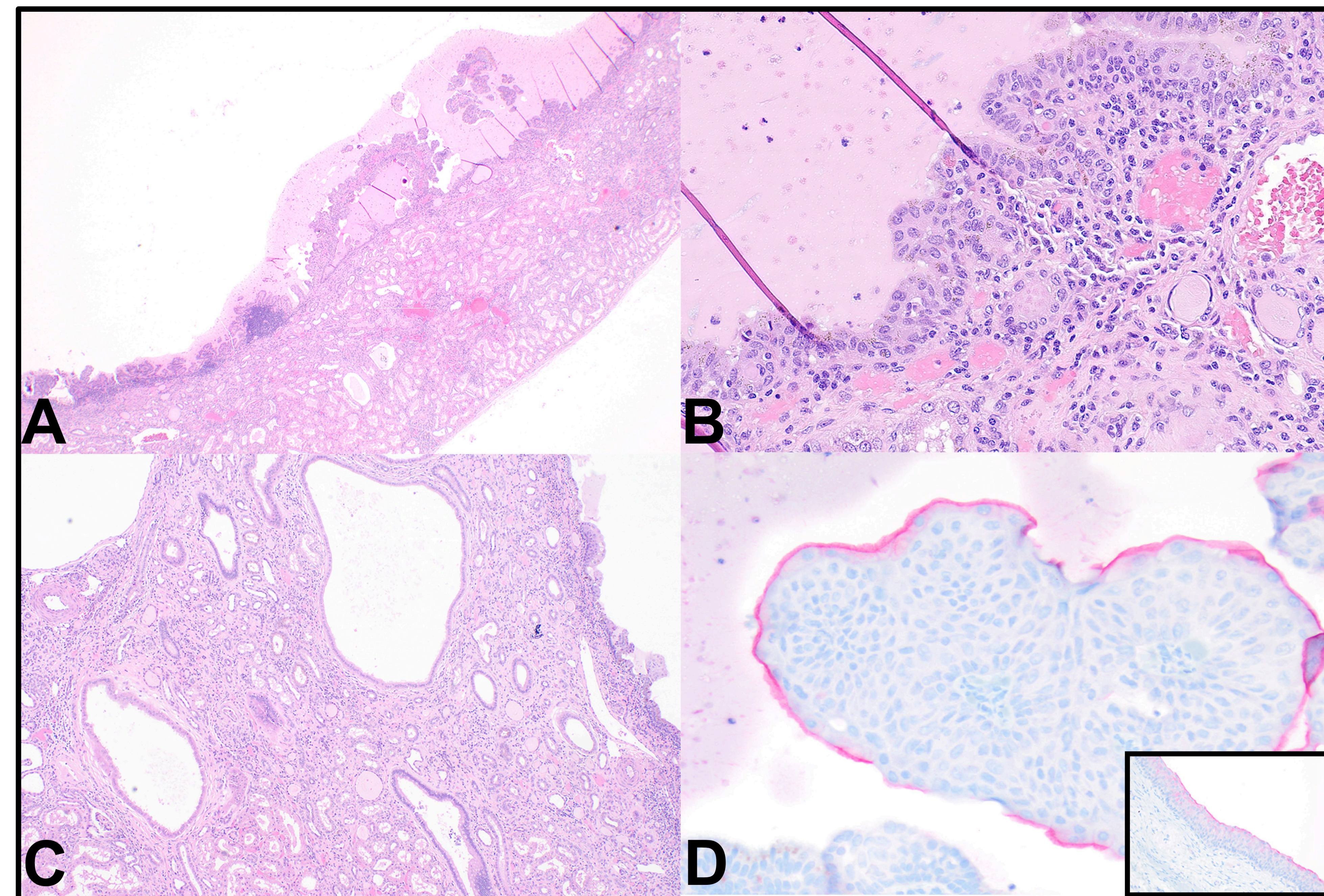


Figure 2. Kidney from Case 2 (A-C, H&E stain; D – UPIII IHC stain)

A: The mass forms a cystic structure within the renal medulla. **B:** The neoplastic cells form small papillary projections and rarely infiltrate the adjacent parenchyma. **C:** The adjacent renal interstitium is infiltrated by plasma cells and lymphocytes, and non-neoplastic tubules are mildly dilated. **D:** Neoplastic cells display variable positive apical perimembranous labeling for UPIII. Inset: Normal renal pelvis urothelium

Discussion

- UCCs are rarely described in non-human primates, despite being the tenth most common human neoplasm throughout the world, and the sixth most incident neoplasm in the USA.³
- Upper urinary tract UCCs are uncommon in humans. This entity in humans frequently exhibits retrograde intratubular spread, as observed in Case 1.⁴
- UCCs in humans are divided into papillary and non-papillary variants.⁵
- Both masses are most consistent with a low-grade papillary urothelial carcinoma based on the 2022 WHO Classification.⁶

Conclusions

- Urothelial cell carcinomas may be seen in cercopithecine non-human primates, with tumors occurring in the upper urinary tract, and neoplastic cells often forming papillary projections and a central cystic cavity.
- Neoplastic cells display variable perimembranous Uroplakin III reactivity, consistent with a urothelial origin.
- These two cases expand the current understanding of spontaneous neoplasia in rhesus and cynomolgus macaques as potential comparative oncology models for age-related neoplasia.

Acknowledgments

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