An Unusual Cause of AKI in a Kidney Transplant Patient with Merkel Cell Cancer

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Case Description
A 64-year old woman presented to the nephrology clinic with an 8-week history of a rapidly growing skin lesion in the right lower extremity. She had a background of familial IgA nephropathy, underwent right kidney transplantation 10 years ago, and had remained on post-transplant immunosuppression since. A raised, nontender pale nodule measuring 58×45 mm and situated 70 mm above the knee joint line in the right anteromedial thigh was found. Following surgical excision, microscopic examination identified lymphovascular invasion. Immunohistochemistry showed positive staining for cytokeratins MNF116, CAM5.2, and CD56 and paranuclear dot-like staining for cytokeratin-20 (CK20), confirming Merkel cell carcinoma (MCC).

The patient presented 2 weeks later with rightsided lower quadrant abdominal pain associated with dysuria and darkened urinary appearances. Initial laboratory evaluation was unremarkable. Ultrasound of the transplanted kidney displayed a normal-sized graft with no evidence of hydronephrosis or loss of renal cortex. Computed tomography (CT) scans of the chest, abdomen, and pelvis were performed, showing incident lymphadenopathies in the left neck, supraclavicular, para-aortic and inguinal regions, and areas surrounding the transplanted kidney. A 2-cm liver lesion at the confluence of the middle and right hepatic veins was detected.

The patient developed oliguric AKI with a peak serum creatinine of 4.6 mg/dl (admission serum creatinine was 1.7 mg/dl) 48 hours following admission. Initial concerns of a graft rejection prompted an urgent kidney biopsy. Microscopic examination of biopsied tissue showed infiltrations of a round, blue cell neoplasm (Figure 1A). Immunohistochemistry staining was strongly positive for CK20 dot-positivity staining (Figure 1B) and CAM5.2 membrane and focal dot-positivity staining (Figure 1C). CD45 and CK7 staining were negative. This suggested metastatic dissemination of MCC to the transplanted kidney and unlikely a post-transplant lymphoproliferative disorder.

A whole body fluorodeoxyglucose-position emission tomography revealed increased fluorodeoxyglucose intensity in the transplanted kidney, consolidating the diagnosis of stage IV metastatic disease. Unfortunately, the patient had further clinical deterioration and was deemed unfit to receive immunotherapy treatment. Palliative treatment was recommended, and the patient passed away during the same admission.

Discussion
MCC is a rare but aggressive neuroendocrine skin cancer found mostly in the sun-exposed areas of the head and neck (1). Since 2008, discovery of the Merkel cell polyomavirus strengthened claims of the link between MCC and immunosuppression. Classic histologic findings describe small blue cells with minimal cytoplasmic volume with high indexes for mitosis and apoptosis. Positive staining for CK20 and cytokeratin CAM5.2 in immunohistochemistry is highly sensitive for MCC (2).

Metastasis to the lymphatic system, brain, bone, liver, lung, and heart has been previously reported in patients with metastatic MCC. Kidney metastasis is less common and only recently reported with greater frequency (3). We describe a first-reported case of metastatic MCC to the transplanted kidney.

Historically, treatment of metastatic MCC is palliative. The use of immune checkpoint inhibitors such as Avelumab and Pembrolizumab in metastatic MCC achieved major breakthroughs from multicenter phase 2 clinical trials showing promising survival outcomes (4,5). Avelumab and Pembrolizumab have since been approved by the US Food and Drug Administration as first-line treatment for metastatic MCC.

Teaching Points
- Merkel cell carcinoma should be considered as a potential complication for patients requiring long term post-transplant immunosuppression.
- Metastatic Merkel cell carcinoma to the kidney is uncommon but increasingly reported in recent years.

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Immune checkpoint inhibitor treatments for patients with metastatic Merkel cell carcinoma have demonstrated promising results for survival outcomes.

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Author Contributions
H.H.L. Wu wrote the original draft; all authors reviewed and edited the manuscript; V. Jeyalan and A. Ponnusamy were responsible for data curation; A. Ponnusamy conceptualized the study; H.H.L. Wu agreed to be accountable for all aspects of the work; and all authors gave final approval before submission.

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Figure 1. | Light microscopy images from biopsy of the transplanted right kidney. High-powered view with hematoxylin and eosin staining showing cancer cells (round, blue cells) infiltrating the kidney parenchyma (Figure 1A); high-powered view of strongly positive CK20 (Figure 1B) and CAM5.2 (Figure 1C) immunohistochemistry staining suggestive of metastatic Merkel cell carcinoma.