Detection of Merkel Cell Carcinoma Polyomavirus in Mucosal Merkel Cell Carcinoma

Karen N. Wu, MD[1], Peter A. McCue, MD[1], Zi-Xuan Wang, PhD[1,2], and Agnieszka K. Witkiewicz, MD[1]

[1]Department of Pathology, Anatomy and Cell Biology, [2]Department of Surgery, Thomas Jefferson University, Philadelphia, PA.

Case Report:

A 61-year-old woman with a past medical history significant for hypertension, bipolar disorder, obstructive sleep apnea and chronic obstructive pulmonary disease presented with diffuse lymphadenopathy suspicious for lymphoma. A lymph node in her right groin was biopsied by fine needle aspiration and showed atypical cells, but was not diagnostic. An excisional biopsy of the 2 x 2 cm lymph node demonstrated metastatic Merkel cell carcinoma (MCC). No skin lesions were detected. A CT scan revealed the presence of a large nasopharyngeal mass that following surgical removal was diagnosed as MCC. Treatment with etoposide and cisplatin and radiation were instituted. The patient went on to develop radiation-induced pneumonitis and cystitis, fungal sepsis, and deep vein thromboses. The patient was later transferred to a long-term acute care facility.

Pathologic Findings:

The microscopic examination of the nasopharyngeal tumor and the lymph node metastases showed a monotonous population of small- to intermediate-sized, round blue cells with vesicular nuclei and finely granular and dusty chromatin with multiple nucleoli. Immunohistochemistry revealed perinuclear staining in a dot-like pattern with cytokeratins AE1/AE3 and CK20. The cells were positive for c-kit and chromogranin and negative for LCA and S-100. This morphology and immunohistochemical profile were characteristic of MCC. MCC was recently shown to harbor a novel polyomavirus, Merkel Cell Polyomavirus (MCPyV), in the majority of cases (1). PCR analysis using the same primers as published (1) for T-antigen LT1 and LT3 was performed on formalin-fixed, paraffin-embedded (FFPE) tissue blocks from the patient's primary nasopharyngeal tumor and lymph node metastasis. MCPyV was detected in the primary tumor and metastasis from 200ng of genomic DNA extracted from FFPE specimens.

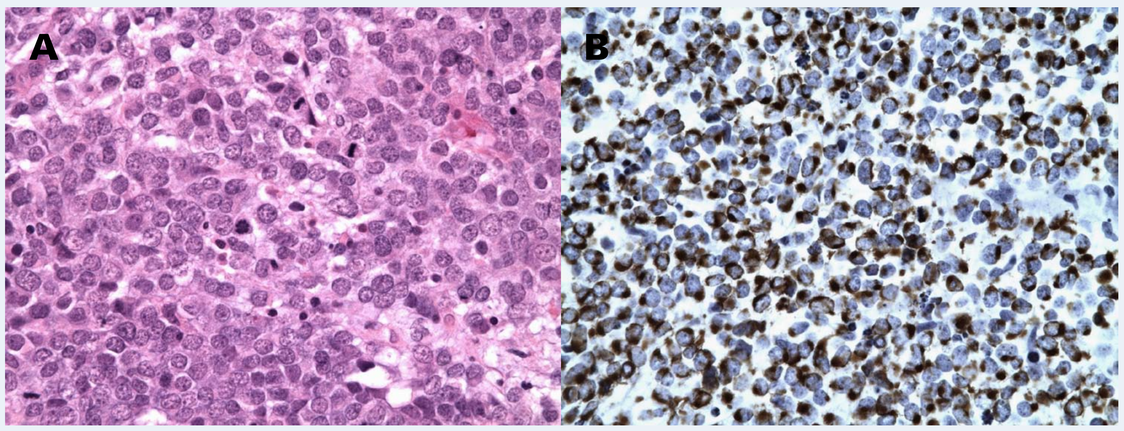

Figure 1. Primary nasopharyngeal MCC (A) Mucosal involvement of tumor H&E (40x). (B) Perinuclear dot-like staining with CK20 (40x).

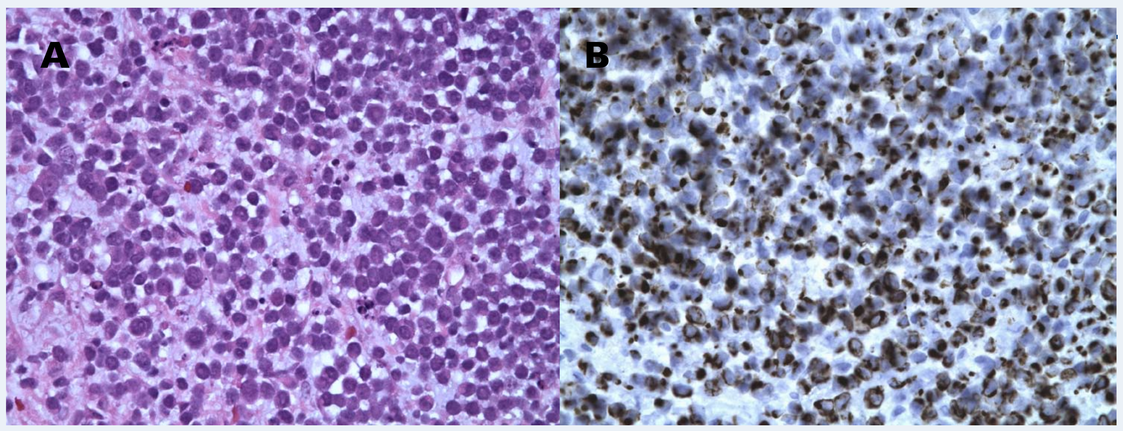

Figure 2. Metastatic MCC (A) Lymph node involvement of tumor cells, H&E (40x). (B) Perinuclear dot-like staining with CK20 (40x).

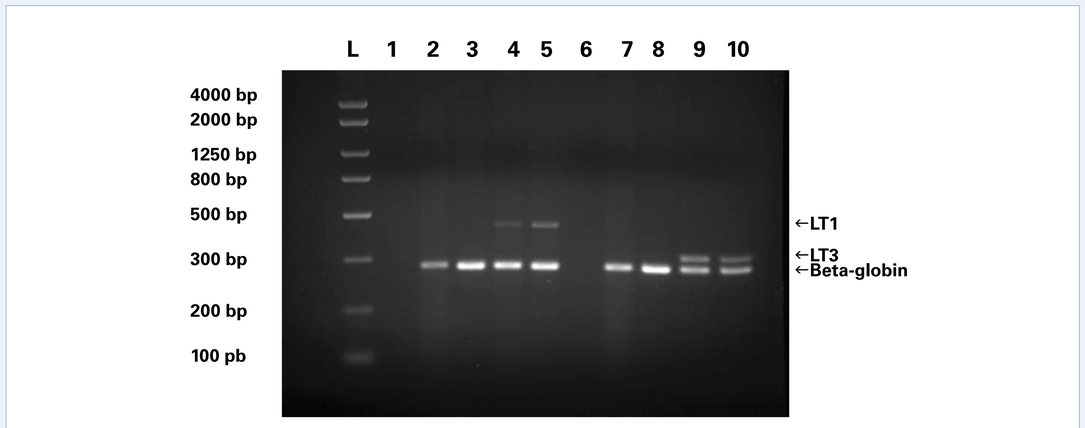

Figure 3. PCR result for detection of MCPyV from primary and metastatic MCC tumor specimens.

PCR was performed using the ApliTaq Gold (ABI), dNTP at 200 uM, primers at 200 nM in 25 ul volume. The cycling conditions were: 95 °C for 10 min, 35 cycles consisting of 30 sec at 94 °C, 30 sec at 55 °C, and 30 sec at 72 °C, then 72 °C for 7 min. L, molecular weight ladder. Lanes 1 to 5 are multiplex PCR for LT1 viral gene (440 bp) and beta-globin housekeeping gene. 1, water control; 2 and 3, two colorectal cancer specimens as negative controls for the MCPyV; 4, primary nasopharyngeal MCC; 5, metastatic MCC. Lanes 6 to 10 are multiplex PCR for LT3 (309 bp) and beta-globin genes; 6, water control; 7 and 8, two colorectal cancer specimens; 9, primary nasopharyngeal MCC; 10, metastatic MCC.

Conclusion:

Our report adds to the recent literature supporting a role for MCPyV in MCC. In addition, this is the first report to demonstrate presence of MCPyV in MCC arising in a mucosal site and in the metastatic foci.

Reference:

[1] Feng H, Shuda M, Chang Y, Moore P. Clonal integration of a polyomavirus in human Merkel cell carcinoma. *Science.* 2008;319:1096-1100.