Merkel Cell Carcinoma

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Case Presentation:

Patient: H.K. is a 97 year-old Caucasian female.

History of Present Illness: Patient presented from a personal care facility with a one month history of a rapidly enlarging and fungating mass on the left cheek. Excisional biopsy was performed and a diagnosis of Merkel cell carcinoma was established. After extensive family counseling, wide local excision was agreed upon as a course of action. On the day of the proposed surgery (within one month of the initial diagnosis) the lesion had recurred to the original size. On physical exam she was found to have pre-auricular, sub-mental, and anterior cervical lymphadenopathy. She also had a mild wound infection at the biopsy site. With the patient in poor health, and the possibility of local metastatic disease, the family elected hospice care.

Medical History: Dementia, dysphagia, hypothyroidism, congestive heart failure, type II diabetes, chronic kidney disease, chronic obstructive pulmonary disease

Family History: Unknown

Current Medications: Lorazepam, levothyroxine, fentanyl, acetaminophen, cephalexin/doxycycline (for wound infection)

Physical Examination: 2.3 x 1.5 x 1.2 cm hemorrhagic crusted exophytic tumor on the left cheek.

Biopsy: *CBL Path* (D12NY1-0414557, 12/28/2012) Left cheek: "Ulcerated dense multinodular dermal/subcuticular infiltrate of large poorly differentiated basaloid epithelial cells with 'salt and pepper' chromatin and high n:c ratios. Abundant mitotic activity is present. With immunostains, the lesional cells stain in a characteristic fashion with CK20, CK7 (rare), neurofilament, chromogranin, and synaptophysin (patchy and mild), and do not stain with TTF-1, LCA, or S100."

Reason for Presentation: Interest

Discussion:

Merkel cell carcinoma (MCC) is a rare and aggressive neuroendocrine tumor of the skin. Originally described by Toker in 1972, the exact origin of Merkel cells is still a matter of debate, with some hypothesizing an origin from neural crest stem-cells. At presentation, 66% of patients have local disease, 27% have nodal involvement, and 7% have distant metastases. The reported incidence has more than tripled over the last 20 years, with some authors contributing this increase to improved detection by the immunohistochemical marker cytokeratin-20 (CK20). Known risk factors include T-cell suppression and extensive prior sun exposure. This link to immune suppression led to the discovery of the Merkel cell polyomavirus (MCPyV) in 2008.

Current thought, through several experimental observations, suggests that tumor growth is dependent on contribution of the MCPyV and independent immune system involvement. MCPyV is incorporated into host DNA causing an integration mutation. A truncation mutation follows, eliminating viral replication, and allows persistent oncogenic function. Persistent viral antigen expression inactivates the retinoblastoma tumor suppressor protein allowing tumor growth. Independently, MCPyV evades the immune system by UV-mediated immune tolerance, chronic antigen exposure, downregulation of antigen expression, and immunosuppressive cytokines. The other critical tumor suppressor pathway that is altered in the course of tumor progression is p53. It is also believed that the MCPyV can inactivate the AKT-mTOR signaling pathway, thus promoting tumor growth.

Immune response is currently being studied as a prognostic indicator. The presence of MCPyV antibodies appears to correlate with tumor burden in MCC patients. High antibody titers, (>10,000), appears to result in better progression-free survival than low titers. High intratumoral infiltration of CD8+ cells may confer increased survival, compared to sparse or no infiltration. In the future, vaccination against MCPyV, or modification and enhancement of the host immune response, offers a promising role in the treatment of MCC.

Currently, there are no consensus guidelines for staging. (18)F-fluorodeoxyglucose positron emission tomography in conjunction with high resolution CT scan appears to offer the most accurate staging of disease. Surgery remains the mainstay of treatment with either wide local excision or treatment with Mohs surgery to ensure complete removal. Patients who are able to undergo sentinel lymph node biopsy are encouraged to do so. Radiation and chemotherapy may be used as adjuvant therapy.

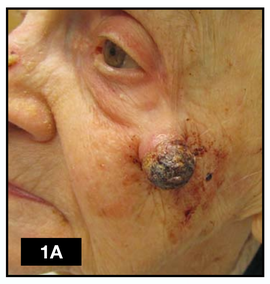

Figure 1A: December 2012: Hemorrhagic crusted exophytic tumor on the left cheek.

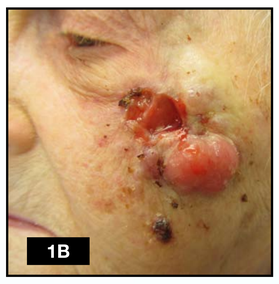

Figure 1B: January 2013: Four weeks s/p excisional biopsy showing recurrence.

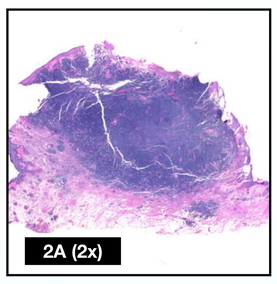

Figure 2A: H&E December 2012: Infiltrating dermal nodule.

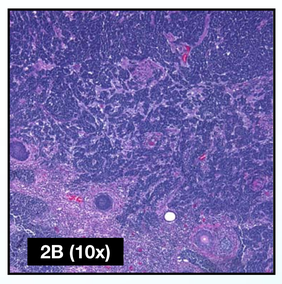

Figure 2B: H&E December 2012: Infiltrating cords of basaloid cells.

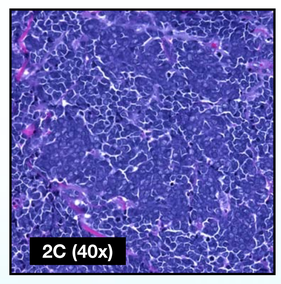

Figure 2C: H&E December 2012: Sheets of small basophilic cells in the dermis with vesicular nuclei.

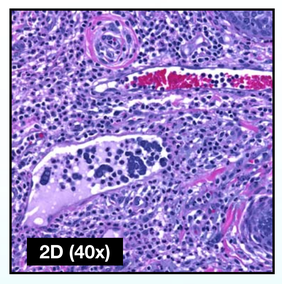

Figure 2D: H&E December 2012: Vascular invasion of tumor cells.

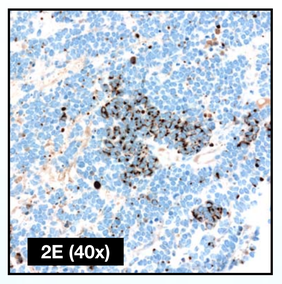

Figure 2E: December 2012: Positive perinuclear dot CK20 staining.

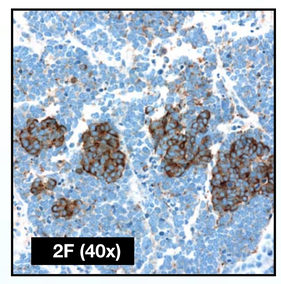

Figure 2F: December 2012: Chromogranin positive cells.

References:

1 Demetriou S, Ona-Vu K, Sullivan E, Dong T, Hsu SW, Oh D. Defective DNA repair and cell cycle arrest in cells expressing merkel cell polyomavirus t antigen. *Int. J. Cancer.* 2012;131:1818-1827.

2 Sihto H, Bohling T, Kavola H, Koljonen V, Salmi M, Jalkanen S, Joensuu H. Tumor infiltrating immune cells and outcome of merkel cell carcinoma: a population-based study. *Clin Cancer Res.* 2012;18(10):2872-2881.

3 Bhatia S, Afanasiev O, Nghiem P. Immunobiology of merkel cell carcinoma: implications for immunotherapy of a polyomavirus-associated cancer. *Curr Oncol Rep.* 2011;13:488-497.

4 Touze A, Le Bidre E, Laude H, Fleury M, Cazal R, Arnold F, Carlotti A, Maubec E, Aubin F, Avril MF, Rozenberg F, Tognon M, Maruani A, Guyetant S, Lorette G, Coursaget P. High levels of antibodies against merkel cell polyomavirus identify a subset of patients with merkel cell carcinoma with better clinical outcome. *Jour Clin Onc.* 2011;29(12):1612-1619.