BRIEF ARTICLES

61-Year-Old White Female with a Non-Healing Ulcerated Ankle Mass

Christopher Lowther, MD MRCP[1], Troy Fiddler, MD PHD[2], Ian A. Whitcroft, MBChB MRCP[3], Juanita Sapp, MD[4], Etan Marks, DO[5], Clay Cockerell, MD[5]

[1]Edin, Big Horn Basin Skin Center, Cody Wyoming
[2]Frontier Cancer Ctr., St. Vincent Healthcare, Billings, Montana
[3]Weston General Hospital, Weston-Super- Mare, United Kingdom
[4]Heritage Healthcare, Powell, Wyoming
[5]Cockerell Dermatopathology, Dallas, Texas

ABSTRACT

Merkel cell carcinoma is a rare cutaneous carcinoma from the tactile Merkel cells. With fewer than half the patients surviving more than one year and fewer than 20% surviving beyond five years. These tumors are rarely suspected until the biopsy results return. Polyoma virus is associated with up to 80% of the tumors. 53% present on the head and neck and 35% present on the extremities while larger lesions are exceedingly rare in either location. Recently, A newly approved drug, Avelumab, has shown tumor response in patients with some patients experiencing complete remission.

HISTORY

A 61-year-old white female presented with a four month history of a 3.5 cm in diameter non-healing ulcerated mass on her right ankle.

PHYSICAL EXAMINATION

The patient also had two small lesions, both on her right lower leg measuring 5 mm in diameter. Her ankle was painfully inflamed. Lymphadenopathy was noted in the right inguinal area. The rest of her physical exam was unremarkable. All three lesions on her right leg underwent biopsy.

LABORATORY DATA

The only abnormal laboratory tests were a hemoglobin of 10.9 g/dL and ferritin of 9 ng/ML (eight - 252 ng/ML). Pre-biopsy impression was a metastatic squamous cell carcinoma or Pyoderma gangrenosum. The patient had a strong family history for colon cancer without a history of prior inflammatory bowel disease.

HISTOPATHOLOGY

All three lesions were biopsied and demonstrated a malignant basophilic neuroendocrine neoplasm, either primary or metastatic. Immunoperoxidase stains showed strong positivity for cytokeratin 20

and synaptophysin with a negative cytokeratin cocktail and TTF-1. A neuroendocrine carcinoma was diagnosed, likely a Merkel cell carcinoma, possibly metastatic.

CLINICAL COURSE

Computerized axial tomography revealed 6 mm non-calcified pulmonary nodules. There was a small 7 mm abnormality in the liver. However, a complete body PET imaging was performed. Focal hypermetabolic activity was noted at the left base of the tongue, with no hypermetabolic activity in the lungs. There was no evidence of mediastinal or hilar lymphadenopathy.

Liver, gallbladder, spleen, pancreas, adrenal glands, kidney and vessels were unremarkable. There was right inguinal lymphadenopathy, with the largest lymph node measuring 19 x 21 mm, with hypermetabolic activity and a maximum SUV value of 4.1. This was suspicious for metastasis.

Additionally, lymph nodes were seen along the right mid-thigh and medial lower leg with hypermetabolic activity. Diffuse soft tissue thickening around the distal tibia and fibula around the ankle with a soft tissue defect and hypermetabolic activity with a maximum SUV value at 9.4 at the lateral ankle which were also suspicious for known carcinoma. A subsequent biopsy of the right inguinal lymph node demonstrated Merkel cell carcinoma.

DIAGNOSIS

Metastatic Merkel Cell Carcinoma, Staging T2, N3, MO equating to stage IIIB. The case was presented at St. Vincent Healthcare tumor board. The recommendation was to proceed with systemic therapy without surgery due to the extent of disease.

The newly approved PD-L1 drug for Merkel cell carcinoma, Avelumab was started. With the start of cycle four, the right ankle had almost completely resolved. The treatment was tolerated without any complications. There was no dose modification. Follow-up axial tomography of the chest, abdomen and pelvis and right lower leg was ordered and is currently pending.

Figure 1. Ulcerated Mass and two biopsy sites

Figure 2. Merkel Cell Ulcerated Mass

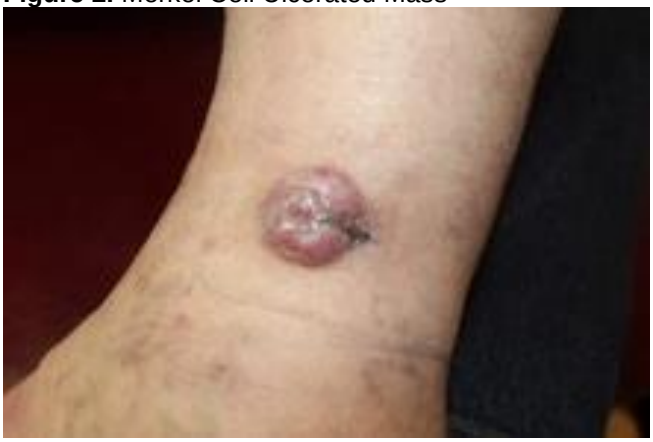
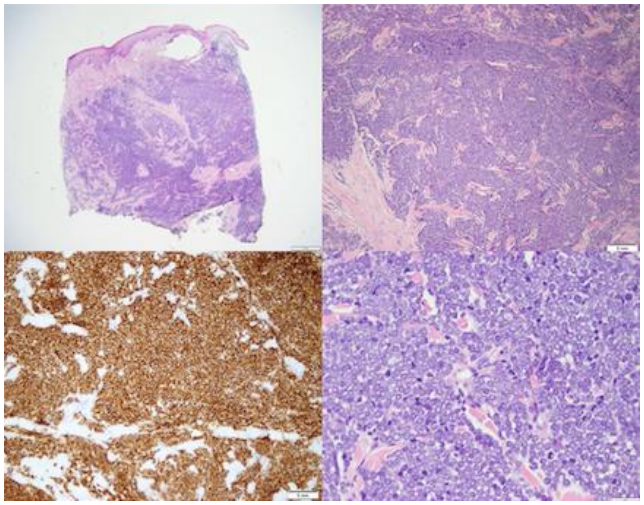


Figure 3. Composition of low and high power showing classic Merkel cell features of a dermal infiltration with monotonous round tumor cells with vesicular nuclei with finely granular and dusty chromatin and multiple nucleoli. Also there are several apoptotic nuclei and frequent mitotic figures. Additionally, a stain for cytokeratin 20 is diffusely positive.



POINTS OF EMPHASIS

Certain sweat gland carcinomas of the skin, first described by Toker in 1972 were later found to have dense corps granules of the tactile Merkel cells.[1,2,3,4] Upon presentation 66% of patients had local disease, 27% nodal involvement and 7% distant metastasis.[2,4] The majority of patients with Merkel cell carcinoma are 70 years or older with an increased incidence in renal transplant patients, chronic lymphocytic leukemia and HIV.[1] Polyomavirus is associated with up to 80% of tumors.[4] The primary lesion of Merkel cell carcinoma is often absent of distinctive clinical characteristics and is rarely suspected at the time of biopsy. It often presents as a rapidly growing reddish blue dermal papule or nodule.[5]

Avelumab, the human anti-PD-L1 antibody, is the first immunotherapy approved for metastatic Merkel cell carcinoma for adult and pediatric patients 12 years and older. Metastatic Merkel cell carcinoma is a rare and aggressive skin cancer with fewer than half the patients surviving more than one year and fewer than 20% surviving beyond five years.[6] Immunochemistry is extremely helpful as Merkel cells are almost impossible to see on light microscopy. Without immunohistochemical stains the tumor is nearly impossible to differentiate from other neuroendocrine carcinomas, such as metastatic small cell carcinoma of the lung.[5] CK 20 is the predominant tool used by pathologists and stains approximately 80 to 90% of all Merkel cell carcinomas with a distinctive perinuclear dot–like pattern.[5,7]

Approximately 53% of Merkel cell carcinomas occur in the head and neck; 35% occur in the extremities.[8] In the Javelin Merkel 200, a phase 2 clinical trial, at the median follow-up of 16.4 months, of which 88 patients had been enrolled and treated with Avelumab, there was an overall response rate of 33%(29 patients). The partial response was 22% with a complete response rate of 11%. 86% of tumor responses lasted at least six months(25 patients) and 45% lasted at least 12 months (13 patients).[8]

Conflict of Interest Disclosures: None

Funding: None

Corresponding Author:
Christopher Lowther, MD MRCP
chrislowther@qwestoffice.net

References:

1. Toker C. Trabecular carcinoma of the skin. Arch of Dermatol 1972; 105:107 – 110.
2. Han S, North J, Canavan T, et al. Merkel cell carcinoma. Hematol Oncol Clin N Amer. 2012; 26:1351 – 1374

3. Goessling, W, Mckee P, Mayer R. Merkel cell carcinoma. J Clin Oncol. 2002; 20:588 – 598.
4. Oram C , Bartus C S, Purcell S. Merkel cell carcinoma: A review. Cutis. 2016 Volume 97, 4 to 90 – 295
5. Wang T, Byrne, P, Et al, Semin Cutan Med Surg. 2011 Mar:30 (1) 48-56
6. Lemos B, Storer B, Lyer J, et al. Pathologic nodal evaluation approves prognostic accuracy and Merkel cell carcinoma; J Amer Acad Derm. 2010; 63(5): 751 – 761.
7. Bobos M, Hytiroglou P, Kostopoulos I, et al. immunohistochemical distinction between Merkel cell carcinoma and small cell carcinoma of the lung. Dermatopathol. 2006; 28:99 – 104. (Pub Med)
8. Pearson, J , Meyers, A Skin cancer – Merkel cell carcinoma, Medscape updated March 27, 2017