***** there was no patient handout for this one*****

Merkel cell carcinoma

Synopsis

Merkel cell carcinomas (MCCs, also known as cutaneous neuroendocrine carcinomas) are rare skin malignancies that demonstrate both neuroendocrine and epithelial differentiation. They are so named for their histological similarity to normal Merkel cells, which reside in the basal layer of the epidermis in the skin. They most frequently occur on the head and neck but can also be seen elsewhere on the body.

MCC occurred in 0.6 per 100 000 individuals in the United States in 2009. MCC favors older adults with a median age of 75-80 years old at the time of diagnosis. It is more common among individuals of Northern European descent than those of African, Asian, or Hispanic descent. MCC is also more common in the immunocompromised population. Two important etiologic factors for MCC are the Merkel cell polyomavirus and ultraviolet (UV) exposure. Patients with MCC who are polyomavirus negative have more aggressive tumors.

Affected individuals will typically present with an asymptomatic solitary nodule. Patients with metastatic disease may demonstrate weight loss, fatigue, and lymphadenopathy. Despite aggressive treatment, recurrence rates are high, metastases are common, and 5-year relative survival is approximately 60% in the United States based on data from a national database from 1973-1999.

Codes

ICD10CM:
C4A.9 – Merkel cell carcinoma, unspecified

SNOMEDCT:
253001006 – Merkel cell carcinoma

Look For

Pink, bluish-red, or reddish-brown cutaneous to subcutaneous firm nodules. The overlying skin is usually intact and may be shiny with telangiectasias or even appear normal in color. Ulceration is rare. Size normally ranges from 0.5-5.0 cm, and most are solitary.

Of MCCs, 50% arise in the head and neck region; the remainder occur on the extremities, buttocks, and trunk.

Regional lymphadenopathy is a sign of more advanced disease.

The mnemonic AEIOU (for asymptomatic, expanding rapidly, in an immunosuppressed patient, older than 50, and on UV-exposed skin) has been proposed to summarize the clinical associations of MCC, but these features are not specific and may also be present in other skin cancers, such as squamous cell skin cancer.

Diagnostic Pearls

MCCs have an increased incidence in the immunosuppressed and have been documented to occur in areas of erythema ab igne (areas of damage and discoloration from chronic heat exposure).

Differential Diagnosis & Pitfalls

- **Melanoma**
- **Lymphoma**
- **Metastatic carcinoma**
- **Squamous cell carcinoma**
- **Basal cell carcinoma**
- **Atypical fibroxanthoma**
- **Dermatofibroma**
- **Keratoacanthoma**
- **Kaposi sarcoma**
- **Pseudolymphoma**
- **Cutaneous lymphoid hyperplasia**
- Peripheral neuroepithelioma
- **Adnexal neoplasms**

Best Tests

- Biopsy
- Ultrasonography of draining lymph node basin
- Chest radiography may be helpful in ruling out lung metastases
- Staging CT or MRI may aid in planning treatment

Histopathology Findings:
Common features

- Poorly circumscribed monotonous dermal proliferation of basophilic cells
- Cells arranged in cords, nodules, or in a diffuse (sheet-like) pattern
- High nuclear-cytoplasmic ratio
- Nuclei with coarse chromatin ("salt-and-pepper pattern") and vesicular appearance
- Numerous mitoses among neoplastic cells
- Necrosis en masse and/or necrosis of individual neoplastic cells
- Admixed lymphocytes and plasma cells
- Solar elastosis
- Paranuclear dot staining with CK20, CAM5.2, and/or neurofilament immunostains

Occasional features

- Extension of the neoplastic infiltrate into the subcutis
- Tumor cells infiltrate the epidermis and adnexal structures (in situ)
- Spindle-shaped neoplastic cells
- Invasion of lymphatic vessels
- Increased vascularity
- Stromal sclerosis
- Extracellular deposits of amyloid

Management Pearls

Early referral to surgical, medical, and radiation oncology is important.

Very rarely, cases of MCC have been known to spontaneously regress.

Therapy

Wide local excision, if feasible. Sentinel lymph node biopsy and complete (prophylactic) lymph node dissection have been performed in select patients. Radiation is indicated as adjuvant therapy or for unresectable lesions.

MCC is chemosensitive, but no chemotherapeutic regimen has yet been shown to impact survival.

In March 2017, avelumab, a monoclonal antibody against PD-L1, received US Food and Drug Administration (FDA) approval for treatment of metastatic MCC in patients 12 years and older (including patients who have not received prior chemotherapy).

A phase 2 study with pembrolizumab, a monoclonal antibody against PD-1, has shown promise in advanced MCC.

Drug Reaction Data

Below is a list of drugs with literature evidence indicating an adverse association with this diagnosis. The list is continually updated through ongoing research and new medication approvals. Click on Citations to sort by number of citations or click on Medication to sort the medications alphabetically.

Medication	Citations
adalimumab	2
alemtuzumab	1
Antimetabolite	1
fludarabine	1
hydroxyurea	1
Monoclonal antibody	7
rituximab	3