Merkel cell carcinoma
By Abdulhadi Jfri, MD, MSc, FRCPC, FAAD, and Catherine Pisano, MD, FAAD

<table>
<thead>
<tr>
<th>Merkel cell Causes</th>
<th>Location</th>
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<tbody>
<tr>
<td>Receptor of light touch in the basal layer</td>
<td>Merkel cell polyomavirus 80%</td>
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<td>UV signature mutations 20%</td>
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<td>Head and neck (most common)</td>
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<td>Extremities</td>
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<td>Buttock</td>
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Clinical features
Rapidly growing painless pink-red to violaceous dome shaped nodule.
- Asymptomatic
- Expanding
- Immunosuppression
- Older than 50
- UV exposed site

Metastatic Merkel of unknown primary 4%
Merkel metastasis at time of diagnosis 40%

Risk factors:
- Age
- Cumulative sun exposure
- Immunosuppression (10%)

Histologic features
Diffuse uniform small round blue cells primarily seen in the dermis with possible epidermal and/or subcutaneous involvement.

- **Stains:**
  - CK20 (perinuclear dot)
  - CK 5/6
  - CK7
  - CD56
  - Neuroendocrine: synaptophysin, chromogranin, somatostatin, calcitonin, vasoactive intestinal peptide (VIP)

- **Stains:**
  - S100 (+ve in melanoma)
  - TTF1 (+ve in small cell lung ca)
  - CD20, CD45, CD3 (+ve in lymphoma)

Path patterns:
Small blue round cells, sheet like, nested and trabecular

Clinical ddx
Basal cell carcinoma, squamous cell carcinoma, amelanotic melanoma, cutaneous lymphoma, cutaneous metastasis, angiosarcoma, dermatofibrosarcoma protuberans, keratoacanthoma, neuroblastoma, adnexal tumors, and neural tumors (neuroma, schwannoma).
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AJCC 8th T staging

| Tis: | In situ |
| T1: | ≤ 2 cm |
| T2: | > 2 cm ≤ 5 cm |
| T3: | > 5 cm |
| T4: | Muscle, fascia, cartilage, or bone |

AJCC 8th clinical (cTNM)

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<tr>
<th>St.</th>
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<tr>
<td>0</td>
<td>Tis</td>
<td>cN0</td>
<td>M0</td>
</tr>
<tr>
<td>I</td>
<td>T1</td>
<td>cN0</td>
<td>M0</td>
</tr>
<tr>
<td>IIA</td>
<td>T2-T3</td>
<td>cN0</td>
<td>M0</td>
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<tr>
<td>IIB</td>
<td>T4</td>
<td>cN0</td>
<td>M0</td>
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<tr>
<td>III</td>
<td>T0-T4</td>
<td>cN1-3</td>
<td>M0</td>
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<tr>
<td>IV</td>
<td>T0-T4</td>
<td>Any N</td>
<td>M1</td>
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AJCC 8th pathological (pTNM)

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<tbody>
<tr>
<td>0</td>
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<tr>
<td>I</td>
<td>T1</td>
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<tr>
<td>IIA</td>
<td>T2-T3</td>
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<td>IIB</td>
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<tr>
<td>IIIA</td>
<td>T1-T4</td>
<td>N1a(sn)</td>
<td>M0</td>
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<tr>
<td>IIIB</td>
<td>T1-T4</td>
<td>N1b-3</td>
<td>M0</td>
</tr>
<tr>
<td>IV</td>
<td>T0-T4</td>
<td>Any N</td>
<td>M1</td>
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Management

• Surgical excision with 1-2 cm margin
• Sentinel lymph node biopsy
• Radiation of the Merkel site and draining node basin if needed
• PET CT scan or CT chest/abdomen/pelvis to search for distant metastasis

Patient not a surgical candidate?
Radiation alone
(Merkel is very radiosensitive)

Patient has metastatic Merkel?
Immunotherapies (pembrolizumab, nivolumab, or avelumab)

Markers to follow-up response to treatment

• MCPyV oncoprotein antibodies (AMERK) at baseline, if positive, serial titers may be drawn to monitor response to treatment and help to predict recurrent disease/increased tumor burden
• Circulating tumor DNA (ctDNA) (FDA approved for monitoring colon cancer post-surgery, under investigation in MCC)

Prognosis: 5-year overall survival (OS):

- Local: 51%
- Nodal: 35%
- Distant: 14%

Poor prognostic factors:

- Size: > 2 cm
- Location: head & neck
- Male
- Immunosuppression

Path

- Increased P63
- Sheet-like pattern
- Negative CK20
- Negative Merkel polyomavirus

Special thanks to Manisha Thakuria, MD, FAAD, director of the Merkel Cell Carcinoma Clinic Center of Excellence at Dana-Farber Cancer Institute, for reviewing this Boards Fodder chart.

References: