Merkel cell carcinoma (MCC) of the left auricle

Pathology Quiz Case 2: Diagnosis

**Diagnosis:** Merkel cell carcinoma (MCC) of the left auricle

Merkel cell carcinoma, which is an uncommon, aggressive cutaneous neoplasm, was first described in 1972. Although MCCs were originally thought to originate from neuroendocrine mechanoreceptor cells, it is now believed that they are derived from pluripotent neural crest cells. Nearly half of all MCCs present in the head and neck area. Facial areas, including the cheeks, nose, mouth, and eyelids, are the most common sites, while auricular MCC is extremely rare. Merkel cell carcinoma exhibits rapid growth and aggressive lymphatic spread, and 25% of patients will have local or distant spread at initial presentation. An additional 30% will develop local or distant spread during the disease course. On physical examination, MCC lesions appear as pink or violaceous subcutaneous nodules. Ulceration is a rare finding.

Although rare, the incidence of MCC has tripled in the past 15 years. This increase may be the result of improved recognition as well as of an aging population and more sun exposure. Risk factors include age (average age at diagnosis, 70 years), male sex, sun exposure, and immunosuppression. Merkel cell carcinoma seems to be disproportionately associated with other neoplasms, including skin, hematologic, ovarian, and breast adenocarcinomas.

The pathogenesis of MCC is multifactorial. Mast cells may mediate several aspects of neoplastic proliferation through several mechanisms, including immunosuppression, angiogenesis stimulation, extracellular matrix degradation, and mitogenesis. The presence of mast cells on microscopic examination of the MCCs can be correlated with an increased risk of death. Merkel cell polyomavirus has been found in a high percentage of MCCs in several series. Merkel cell polyomavirus integrates into the genome, and 2 oncogenes, *LT* and *ST*, are expressed. Acting similarly to the human papillomavirus E6 and E7 proteins, *LT* inactivates p53 and pRb; *ST* disrupts a protein phosphatase complex that has been implicated in cellular adhesion. Also, deletions and unbalanced translocations have been identified in the short arm of chromosome 1.

On microscopic examination, MCC exhibits small round cells arranged in sheets and trabeculae. Infiltration into surrounding dermal lymphatics is common and indicative of the aggressive nature of this disease. Cytoplasmic granules show similarities to cells of neuroendocrine and amine precursor uptake decarboxylation cell lineage. Intercellular junctions, vesicular nuclei with fine chromatin, high nuclear to cytoplasm ratio, and spindly processes are all characteristic cytologic features.

Immunohistochemical analysis can aid the pathologic diagnosis, with MCC demonstrating characteristic perinuclear dot-like immunopositivity for CK20. Often morphologically similar to metastatic small cell carcinoma of the lung, MCC notably lacks a recently identified marker known as achaete-scute complex–like 1. Furthermore, small cell carcinoma of the lung is typically positive for thyroid transcription factor 1, whereas MCC is negative. The absence of S-100 protein and homatropine methylbromide helps rule out malignant melanoma. Immunohistochemical analysis can also serve a prognostic role, with p63 expression associated with (1) a more aggressive clinical course; (2) nuclear expression of the antiapoptotic protein survivin, which is associated with higher mortality and rates of metastasis; and (3) overexpression of matrix-metalloprotein 7, which has been shown to be associated with increased metastasis. Other pathologic characteristics associated with a worse prognosis include lymphocytic infiltration and a high mitotic index.

After a pathologic diagnosis, presurgical staging should include a clinical examination and may include a PET scan. A PET scan may contribute useful information about the presence of metastatic lesions, but normal findings on the PET scan do not rule out metastatic disease. Computed tomography is not accurate for detecting nodal disease. Wide local excision with 2- to 3-cm margins is the initial treatment of choice. However, such large margins are often difficult to obtain in the head and neck area. With respect to auricular lesions, auriculectomy may be nec-

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Sentinel lymph node biopsy has been used but is limited by the dense and irregular lymphatic drainage pattern in the head and neck region. Identification of nodal spread is important for prognostication and adjuvant treatment. However, owing to the high rate of clinically apparent micrometastases, elective regional lymphadenectomy is often considered. Gamma probe-guided lymphadenectomy may help identify the nodes that should undergo rigorous pathologic examination (analysis of fine sections and immunohistochemical staining) for micrometastatic disease. Lymphadenectomy has been shown to decrease regional recurrence and its associated morbidity but does not seem to increase survival. There are no consistent recommendations regarding lymphadenectomy. Chemotherapy has a limited role as a palliative measure only and may actually worsen prognosis in patients with local nodal spread. It has never been shown to improve survival. Although controversial, radiotherapy should be considered. Merkel cell carcinomas are radiosensitive, and radiation monotherapy has been shown to be effective in inoperable stage I tumors. At least 1 single-institution study has demonstrated effective local control with postoperative adjuvant radiotherapy. Radiation is usually applied to the primary site and the draining regional lymph node bed. Reported rates of local recurrence are around 30%, and for regional recurrence, the rate is approximately 59%. Lymph node involvement is the most robust predictor of survival and distant metastasis. Five-year survival rates range from 40% to 68%.

REFERENCES


