Merkel cell carcinoma.

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Merkel cell carcinoma is a rare and highly aggressive cutaneous neuroendocrine carcinoma that, in most cases, is caused by Merkel cell polyomavirus (approximately 80% of cases). The tumor usually arises on sun-exposed skin of elderly patients, particularly on the head and neck and extremities. There is a slight female preponderance and an increased risk in individuals who are immunosuppressed. Clinically, the tumors are often indistinguishable from other skin cancers and typically present as a firm, painless, rapidly growing nodule. They may be flesh-colored, red, or blue tumors that typically vary in size from 0.5 cm to more than 5 cm (average, 2 cm). When they have a reddish nodular appearance, they may be mistaken for angiosarcoma or granulation tissue.

The expected 5-year survival rate is more than 80% if the tumor is less than 2 cm and has not metastasized. Once a tumor has metastasized regionally, the 5-year survival rate drops to about 50%. Local recurrences occur in about one-third of cases. The tumor spreads to the regional lymph nodes in up to 75% of cases, and distant metastasis with eventual death occurs in one-third or more.

Initial treatment includes complete surgical excision along with sentinel lymph node biopsy (lymph node dissection is indicated if lymph nodes are clinically or biopsy proven positive). Sentinel lymph node biopsy is a challenge in head and neck sites, as there are frequently multiple lymph node drainage regions affected or with crossover. A sentinel lymph node biopsy detects metastasis in one-third of patients who might otherwise have been clinically and/or radiographically understaged, resulting in undertreatment.

Adjuvant radiotherapy has been shown to be effective in reducing the rate of recurrence and increasing survival. Patients with no distant metastases and a negative sentinel lymph node have a very good prognosis when treated with surgery and radiotherapy (approximately 90% survival rate at 5 years).

The tumor is composed of uniform, small, round to oval cells arranged in sheets and solid nests, usually infiltrating the entire dermis (figure 1) and sometimes extending into the subcutaneous adipose tissue. Epidermal involvement is uncommon. Focal necrosis may be seen, and mitoses and apoptotic bodies are usually numerous. The neoplastic cells have a very high nuclear-to-cytoplasmic ratio, with nuclei that are delicate and prone to crush artifacts. The nuclear chromatin is delicate, even with a salt-and-pepper distribution (figure 2). Nucleoli are small but easily identified. Mitoses are greatly increased and include atypical forms. Cannibalism of cells is noted.

Figure 1. The epidermis is intact and separated from the dermal neoplastic proliferation. The tumor fills the dermis, arranged in sheets and nests. Crush artifact is seen.

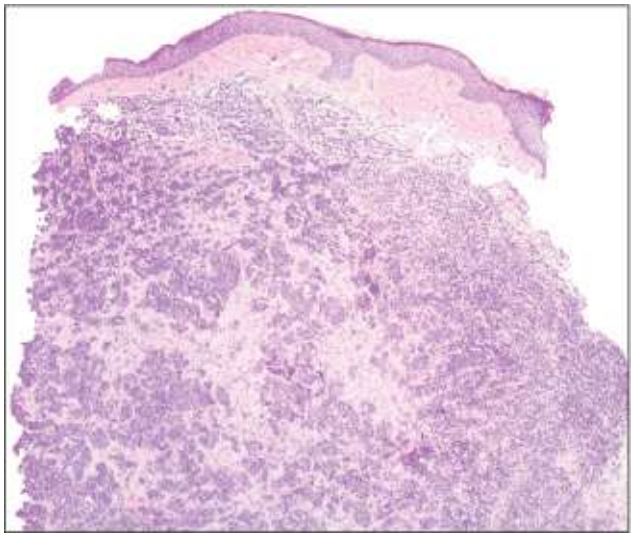
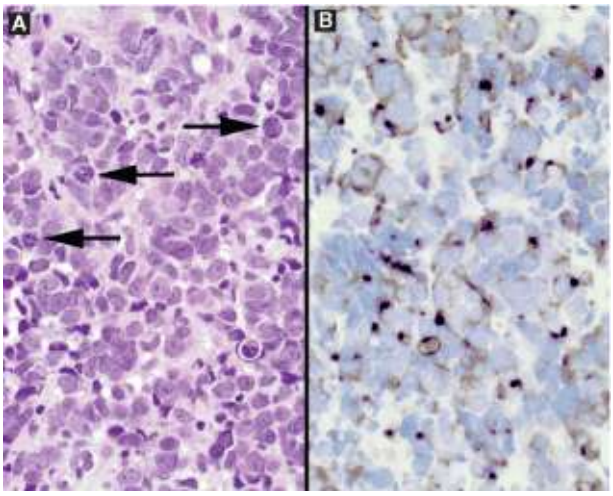


Figure 2. *A*: The neoplastic cells have a high nuclear-to-cytoplasmic ratio. The nuclear chromatin is stippled. Mitoses are common (arrows). *B*: A Golgi paranuclear dot-like positive reaction with CK20 immunohistochemistry helps to confirm the diagnosis of Merkel cell carcinoma.



The histopathologic differential diagnosis mainly includes basal cell carcinoma, lymphoma, melanoma, and metastatic small cell carcinoma. Merkel cell carcinoma reacts positively for neuroendocrine markers such as synaptophysin and chromogranin, showing a characteristic perinuclear dot-like staining pattern with pan-cytokeratin and CK20 immunohistochemistry (figure 2). CK20 is a particularly useful marker, as metastatic small cell carcinomas are negative for this marker.

Suggested reading

1. Donepudi S, DeConti RC, Samiowski WE. Recent advances in the understanding of the genetics, etiology, and treatment of Merkel cell carcinoma. Semin Oncol 2012; 39 (2): 163-72.

2. Han SY, North JP, Canavan T ,et al. Merkel cell carcinoma. Hematol Oncol Clin North Am 2012; 26 (6): 1351-74.
3. Pellitteri PK, Takes RP, Lewis JS Jr. ,et al. Merkel cell carcinoma of the head and neck. Head Neck 2012; 34 (9): 1346-54.

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Ear Nose Throat J. 2014 March;93(3):100-102.