OASIS DERMATOLOGY GROUP

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Merkel Cell Carcinoma

Merkel cell carcinoma (MCC) is a rare but highly aggressive neuroendocrine skin cancer that primarily affects elderly individuals. It is characterized by rapid growth, high potential for metastasis, and a poor prognosis when diagnosed at advanced stages. MCC is more prevalent in fair-skinned individuals and is particularly common in older adults, with a higher incidence in men. The cancer's association with ultraviolet (UV) light exposure and immunosuppression underscores its importance in dermatologic and oncologic care.

Epidemiology and Risk Factors

MCC predominantly occurs in individuals over the age of 50, with the highest incidence observed in elderly Caucasians. The condition is slightly more common in men than in women. Several risk factors contribute to the development of MCC, many of which overlap with those of other skin cancers, particularly nonmelanoma skin cancer. These include older age, fair skin, and exposure to ultraviolet (UV) radiation, either through natural sun exposure or tanning beds. Immunosuppression is another significant risk factor, with individuals who have HIV, chronic lymphocytic leukemia (CLL), or organ transplant recipients being particularly vulnerable to developing MCC.

Recent studies have highlighted the importance of the Merkel cell polyomavirus (MCPyV) in the pathogenesis of MCC, particularly in immunocompetent individuals. The virus integrates into the DNA of Merkel cells, potentially contributing to the oncogenic process. However, while MCPyV infection is common in MCC, the role of UV radiation in inducing mutations in the tumor suppressor gene TP53 is also well established as a contributing factor.

Clinical Presentation

MCC typically presents as a painless, rapidly expanding, firm, dome-shaped nodule, often with a pink, red, or violaceous-blue hue. These lesions are usually asymptomatic but grow quickly, often within three months of onset. The tumors typically range from 0.5 cm to 5 cm in size and are most commonly located on sun-exposed areas, such as the head, neck, arms, and legs. However, unlike melanoma, MCC can also arise on areas of the skin that are not typically exposed to UV radiation, including the buttocks, abdomen, and thighs.

The clinical features of MCC can be summarized using the mnemonic AEIOU, which helps clinicians identify patients who may have the disease:

- **A**symptomatic or painless

- **E**xpanding rapidly (within 3 months)
- **I**mmunosuppression (e.g., HIV, organ transplant, CLL)
- **O**lder than 50 years of age
- **U**ltraviolet light-exposed skin

The presence of three or more of these clinical features should raise suspicion for MCC, and biopsy of the lesion is recommended to confirm the diagnosis.

Diagnosis

The diagnosis of MCC is made through biopsy of the lesion, with histopathologic examination showing small, round cells with neuroendocrine differentiation. Immunohistochemistry is often used to identify markers characteristic of MCC, such as chromogranin A, synaptophysin, and cytokeratin 20 (CK20). A characteristic feature of MCC is the presence of perinuclear staining of CK20. PCR testing can also be performed to detect Merkel cell polyomavirus DNA in the tumor, which is present in approximately 80% of MCC cases.

In addition to the biopsy, staging of the disease is essential. Sentinel lymph node biopsy is performed to assess regional lymph node involvement, which is critical for determining the extent of the disease and informing treatment decisions. Imaging studies, such as CT scans or PET scans, may be used to assess for distant metastasis.

Treatment

The treatment of MCC is complex and requires a multimodal approach. Wide surgical excision with clear margins is the treatment of choice for localized disease. Given the high rate of recurrence and regional spread, sentinel lymph node biopsy is performed to assess the involvement of regional lymph nodes. If positive, additional lymph node dissection may be necessary, though the role of lymph node dissection remains debated due to the high morbidity associated with the procedure.

Adjuvant therapies are commonly used to reduce the risk of recurrence and metastasis. These include:

- ***Radiotherapy****:* Radiation therapy is often administered following surgical excision, especially for high-risk cases with positive lymph nodes or margins. It is used to target any remaining microscopic disease and reduce local recurrence.
- ***Chemotherapy***: Given the aggressive nature of MCC, chemotherapy is frequently used in advanced or metastatic cases. Common regimens include cisplatin or carboplatin in combination with etoposide, which has shown efficacy in metastatic MCC.

Emerging therapies for MCC focus on immune checkpoint inhibitors. Recent clinical trials have demonstrated that PD-1 inhibitors (such as pembrolizumab) and PD-L1 inhibitors (such as avelumab) have shown promising results in treating metastatic MCC. Avelumab, in particular, has

been approved by the FDA for the treatment of MCC, specifically for metastatic or locally advanced disease.

Prognosis

Merkel cell carcinoma has a poor prognosis, especially when diagnosed at later stages. The overall survival rates for MCC depend on the size of the tumor and the presence of metastasis. For tumors smaller than 2 cm, the 5-year relative survival rate is approximately 66%. For tumors larger than 2 cm, this rate drops to 51%. The prognosis worsens significantly if regional lymph nodes are involved, with a 5-year relative survival rate of 39%. When the disease has spread beyond the lymph nodes to distant organs, the 5-year survival rate is as low as 18%. Recurrence is common, with most cases reappearing within 3 years of diagnosis. Therefore, close monitoring is essential, with skin and lymph node examinations recommended every 3 months for the first year, every 6 months for the second year, and annually thereafter.

Conclusion

Merkel cell carcinoma is a rare, aggressive skin cancer that requires early diagnosis and prompt treatment. It is primarily associated with older age, immunosuppression, UV light exposure, and, in many cases, Merkel cell polyomavirus infection. The clinical presentation often includes a painless, rapidly expanding nodule on sun-exposed skin. Treatment involves surgical excision with negative margins, sentinel lymph node biopsy, and adjuvant therapies such as radiation and chemotherapy. The prognosis remains poor for advanced-stage MCC, though the introduction of immune checkpoint inhibitors has improved outcomes for patients with metastatic disease. Continuous monitoring and early intervention are essential to manage recurrence and metastasis in MCC patients.

References

- Dummer, R., Liu, W., & Terness, P. (2021). Merkel cell carcinoma: Current treatment algorithms. *American Journal of Clinical Dermatology*, 22(4), 471-480. https://doi.org/10.1007/s40257-021-00554-x
- Gara, S. K., Lee, S. L., & McLaughlin, C. (2021). Merkel cell carcinoma: Clinical updates and emerging therapies. *Oncology Reports*, 45(5), 2052-2062. https://doi.org/10.3892/or.2021.8090
- Harms, P. W., Vats, P. K., & Palanisamy, N. (2020). Merkel cell carcinoma: Pathogenesis and molecular mechanisms. *Journal of Investigative Dermatology*, 140(8), 1504-1514. https://doi.org/10.1016/j.jid.2020.01.010
- Husain, N., Yeboah, E., & Thomas, S. (2021). Surgical management and adjuvant therapies in Merkel cell carcinoma. *Journal of Surgical Oncology*, 124(2), 248-256. https://doi.org/10.1002/jso.26329
- Kippen, L. M., Canner, J. K., & Bhatia, S. (2020). Merkel cell carcinoma: Risk factors, clinical presentation, and therapeutic strategies. *Cancer Management and Research*, 12, 1865-1875. https://doi.org/10.2147/CMAR.S276249
- Mendiratta, R., Kumar, A., & Rosenberg, M. (2021). Chemotherapy and immunotherapy in the treatment of Merkel cell carcinoma: An updated review. *OncoImmunology*, 10(1), 193-202. https://doi.org/10.1080/2162402X.2020.1859632