Nodule on the left cheek

Often mistaken for a cyst or acneiform lesion, this lesion is actually quite aggressive—and worrisome.

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AN 85-YEAR-OLD MAN with a history of skin cancer presented to my dermatology practice (NT) for evaluation of a "pimple" on his left cheek that failed to resolve after 2 months (**FIGURE**). The patient noted that the lesion had grown, but that he otherwise felt well.

On examination, the lesion was plum colored, and the area was firm and nontender to palpation. The patient was referred to a plastic surgeon for an excisional biopsy to clarify the nature of the lesion.

- WHAT IS YOUR DIAGNOSIS?
- HOW WOULD YOU TREAT THIS PATIENT?

FIGURE

Plum-colored nodule on left cheek

PHOTO COURTESY OF NATHMAL S. TARFARE, MD

Diagnosis: Merkel cell carcinoma

A biopsy performed 2 weeks after the initial visit confirmed the clinical suspicion for Merkel cell carcinoma (MCC).

MCC is a cutaneous neuroendocrine malignancy. Although its name acknowledges similarities between the tumor cells and Merkel cells, it is now considered unlikely that Merkel cells are the actual cells of origin.[1]

The majority of MCCs are asymptomatic despite rapid growth and are typically red or pink and occur on UV-exposed areas, as in our patient.[2] A cyst or acneiform lesion is the single most common diagnosis given at the time of biopsy.[2]

The incidence of MCC is greatest in people of advanced age and in those who are immunosuppressed. In the United States, the estimated annual incidence rate rose from 0.5 cases per 100,000 people in 2000 to 0.7 cases per 100,000 people in 2013.[3] MCC increases exponentially with advancing age, from 0.1 (per 100,000) in those ages 40 to 44 years to 9.8 in those older than 85 years.[3] The growing cohort of ageing baby boomers and the increased number of immunosuppressed individuals in the community suggest that clinicians are now more likely to encounter MCC than in the past.

While UV radiation is highly associated with MCC, the major causative factor is considered to be Merkel cell polyomavirus (MCPyV).[1] In fact, MCPyV has been linked to 80% of MCC cases.[1,3] Most people have positive serology for MCPyV in early childhood, but the association between MCC and old age highlights the impact of immunosuppression on MCPyV activity and MCC development.[1]

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Clinical suspicion is the first step in diagnosing MCC

The mnemonic AEIOU highlights the key clinical features of this aggressive tumor[2,4]:

- **A**symptomatic
- **E**xpanding rapidly (often grows in less than 3 months)
- **I**mmune suppression (eg, chronic lymphocytic leukemia, solid organ transplant patient)
- **O**lder than 50
- **U**V exposure on fair skin.

If a lesion is suspected to be MCC, the next step includes biopsy so that a definitive diagnosis can be made. A firm, nontender nodule that lacks fluctuance should raise suspicion for a neoplastic process.

The differential is broad, ranging from cysts to melanoma

The differential diagnosis for an enlarging, plum-colored nodule on sun-exposed skin includes an abscess, a ruptured or inflamed epidermoid cyst, basal cell carcinoma, squamous cell carcinoma, and malignant melanoma.

An abscess is typically tender and expands within a matter of days rather than months.

A cyst can be ruled out by the clinical appearance and lack of an overlying pore.

Basal cell carcinoma can be characterized by a rolled border and central ulceration.

Squamous cell carcinomas often exhibit a verrucous surface with marked hyperkeratosis.

Melanoma manifests with brown or irregular pigmentation and may be associated with a precursor lesion.

Tx includes excision and consistent follow-up

Complete excision is the critical first step to successful therapy. Sentinel lymph node studies are typically performed because of the high incidence of lymph node metastasis. Frequent follow-up is required because of the high risk of recurrent or persistent disease.

Local recurrence usually occurs within 1 year of diagnosis in more than 40% of patients.[5] Distant metastasis can be treated with a programmed cell death ligand 1 blocking agent (avelumab) or a programmed cell death protein 1 inhibitor (nivolumab or pembrolizumab).[6]

Our patient was referred to a regional cancer center for sentinel lymph node evaluation, where he was found to have nodal disease. The patient was put on pembrolizumab and received radiation therapy but showed only limited response. Seven months after diagnosis, he passed away from metastatic MCC. JFP

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