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Rate of growth of Merkel cell carcinoma: a unique photographic evidence

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Abstract

Merkel cell carcinoma (MCC) is a rare, aggressive neuroendocrine skin tumor, mainly linked to *Merkel Cell Polyomavirus* (MCPyV) and less often to ultraviolet exposure. Additional risk factors include advanced age and immunosuppression. Although MCC is known to grow rapidly, its exact growth rate has not been described yet. We report a case of a 73-year-old man who developed *de novo* MCC on the lower eyelid while undergoing immunotherapy with nivolumab. Clinical photographs document the absence of disease in March 2024 and the appearance of a 7 mm papule in October 2024. Histology confirmed the diagnosis. This case represents rare visual evidence of MCC's rapid progression, suggesting an estimated growth rate of approximately 1 mm/month. A controversial aspect is that MCC developed despite ongoing treatment with a PD-1 checkpoint inhibitor, currently recommended for this cancer. Although anecdotal, this case highlights MCC's progression and the need for further research and new therapies.

Introduction

Merkel cell carcinoma (MCC) is a rare but aggressive neuroendocrine skin tumor that mostly arises from *Merkel Cell Polyomavirus* (MCPyV) infection, while a minority of cases are linked to ultraviolet-induced genetic damage. Additional risk factors include advanced age and immunosuppression. Although it is known that MCC is a rapidly growing tumor, its exact growth rate has not been described yet. In this article, we report the development of MCC *ex novo* in a patient while undergoing immunotherapy with a unique visual documentation of the tumor's progression and estimation of the tumor growth rate.^{1,2}

Case Report

We report the case of a 73-year-old man with a complex oncological history of multiple malignancies. He underwent right nephroureterectomy for urothelial carcinoma of the renal pelvis in 2020; in November 2023, he was diagnosed with low-grade bladder carcinoma, yet awaiting transurethral resection (TURB); in July 2023, he was diagnosed with choroidal melanoma in the right eye and received proton therapy. In August 2024, Positron Emission Tomography (PET) detected lung metastases; therefore, immunotherapy with nivolumab (240 mg every 2 weeks) was started in September 2024.

During a dermatological visit in March 2024, a pT1a melanoma on the left nasal wing was detected and excised, followed by routine re-excision only (Figure 1A). At the subsequent dermatological follow-up in October 2024, the patient presented a *de novo* papule on the lower left eyelid (Figure 1B), measuring 7 mm in diameter, which was not documented in clinical photographs seven months

earlier. Dermoscopy (Figure 1C) showed an erythematous non-specific background pattern with shiny white lines.

An excisional biopsy was performed, and histological examination of hematoxylin-eosin (H&E) sections revealed a dense nodular dermal infiltrate composed of round to oval small basophilic cells with vesicular nuclei, multiple nucleoli, scant cytoplasm, and many mitoses (Figure 2). Immunohistochemical staining confirmed the diagnosis of MCC since it showed positivity for cytokeratin 20 (CK20), chromogranin, and synaptophysin but negativity for thyroid transcription factor-1 (TTF-1). A subsequent excision for safety peripheral surgical margins was performed, and in the same procedure, a sentinel lymph node biopsy was attempted. Unfortunately, no lymph node with contrast enhancement was identified, necessitating re-excision; however, N staging could not be performed. A multidisciplinary meeting concluded with the decision to continue nivolumab without adjuvant radiotherapy. The last PET follow-up in June 2025 revealed stable disease; additionally, dermatological follow-up was negative.

Discussion

This case represents a rare visual documentation of the rapid growth of an MCC. Comparison between photographs shows no clinical sign of the disease in March 2024 and a papule with a diameter of 7 mm seven months later. Upon a close examination of the March 2024 photo, a small telangiectasia can be observed at the site where the papule appeared, and it may possibly be the first subclinical sign of the future MCC. If this were the case, we could estimate a growth rate of this MCC of about 1 mm/month. To our knowledge, no studies to date have precisely quantified the growth rate of MCC, highlighting the uniqueness and educational contribution of this report.

A controversial aspect of this case report is that the patient was receiving nivolumab, a PD-1 checkpoint inhibitor currently recommended for the treatment of advanced and metastatic MCC, at the time the MCC developed. Several clinical trials have proved the efficacy of PD-1 checkpoint inhibitors, such as nivolumab and pembrolizumab, in the treatment of MCC. KEYNOTE-017, a phase II study testing pembrolizumab monotherapy on advanced unresectable MCC, showed an overall response rate of 58%, with 30% of complete responses.³ The ADMEC-O phase II trial, which compared adjuvant nivolumab to observation in patients with completely resected MCC, showed an absolute risk reduction of 9% (1-year disease-free survival [DFS]) and 10% (2-year DFS) in the nivolumab group as compared to observation.⁴ Additionally, CheckMate 358, a phase I/II trial evaluating neoadjuvant nivolumab in virus-positive MCC patients, reported a 24-month recurrence-free survival rate of 68.5%.⁵ These figures are promising, yet they also underly that a substantial

portion of patients still experience disease progression, as approximately 50% do not respond to PD-1 checkpoint inhibitors.⁶

In our case report, despite ongoing immunotherapy, nivolumab did not prevent the development of a new MCC, further highlighting the need for additional therapeutic strategies. Alternative therapeutic strategies, including tyrosine kinase inhibitors (TKIs) and somatostatin analogs (SSAs), have shown promising results in improving clinical responses and reducing tumor volumes. Moreover, there is increasing interest in the pathological role of *MCPyV*, and it is possible that, in the near future, a vaccine targeting this virus may be developed and administered to individuals at risk of developing MCC.^{1,2}

Conclusions

In conclusion, this case report highlights the rapid growth of MCC and underscores the importance of clinical and photographic monitoring for high-risk patients. While ours is an anecdotal observation, it offers a unique visual documentation of the tumor's progression and estimates the potential tumor growth rate. Further investigations, including case series and prospective studies, are needed.

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Figure 1. **A)** On the left nasal pigmented irregular macule (melanoma T1a): absence of lesion on the lower left eyelid. **B)** At the subsequent dermatological follow-up in October 2024, the patient presented a *de novo* papule on the lower left eyelid, measuring 7 mm in diameter. **C)** Dermoscopy showed an erythematous non-specific background pattern with shiny white lines.

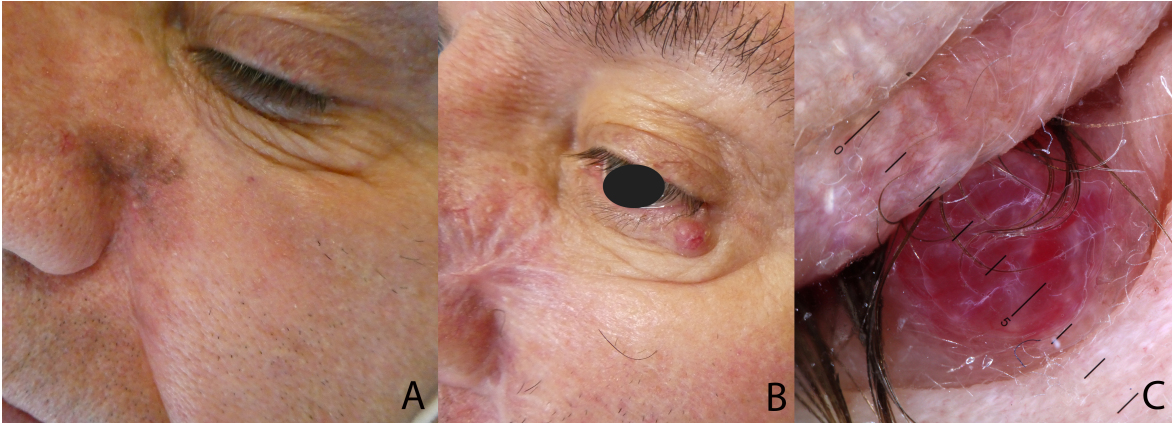


Figure 2. **A)** A dense nodular infiltrate is present in the dermis (H&E, 10X). **B)** Sheets of round to oval small basophilic cells with vesicular nuclei, multiple nucleoli, and scant cytoplasm. Many mitoses are present (H&E, 400X). **C)** positivity for CK20 (200X). **D)** positivity for chromogranin (200X). **E)** positivity for synaptophysin (200X). **F)** negativity for TTF-1 (200X).

