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CASE REPORT

Merkel cell carcinoma and delayed diagnosis: a clinical alert

Carcinoma de células de merkel e diagnóstico tardio: um alerta clínico

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Abstract

Merkel cell carcinoma (MCC) is a rare but highly aggressive neuroendocrine skin cancer with a mortality rate higher than melanoma. It primarily affects elderly patients with risk factors such as chronic sun exposure, immunosuppression, or previous skin cancers. This case describes an 80-year-old male with multiple ulcerated skin lesions and widespread metastasis, diagnosed at an advanced stage (stage IV). Due to the disease's extent, curative treatment was not possible, and palliative chemotherapy was initiated but discontinued due to severe toxicity. This case highlights the rapid progression of MCC, the challenges in early diagnosis, and the critical importance of timely recognition to allow for more effective treatment and improved patient survival.

Keywords: Merkel cell carcinoma. Skin neoplasm. Early diagnosis. Elderly. Metastasis. Immunohistochemistry.

Resumo

O carcinoma de células de Merkel (CCM) é um câncer de pele neuroendócrino raro, porém altamente agressivo, com taxa de mortalidade superior à do melanoma. Afeta principalmente pacientes idosos com fatores de risco como exposição solar crônica, imunossupressão ou histórico de neoplasias cutâneas. O caso descrito envolve um paciente de 80 anos com múltiplas lesões cutâneas ulceradas e metástases disseminadas, diagnosticado em estágio avançado (estágio IV). Devido à extensão da doença, o tratamento curativo foi inviável, sendo iniciada quimioterapia paliativa, posteriormente interrompida por toxicidade significativa. Este caso evidencia a rápida progressão do CCM, os desafios no diagnóstico precoce e a importância crucial do reconhecimento oportuno para possibilitar terapias mais eficazes e melhorar a sobrevida do paciente.

Palavras-chave: Carcinoma de células de Merkel. Neoplasia cutânea. Diagnóstico precoce. Idoso. Metástase. Imuno-histoquímica.

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Introduction

Merkel cell carcinoma (MCC) is a rare but highly aggressive cutaneous neuroendocrine neoplasm originating from Merkel cells in the epidermis, which are responsible for sensory functions[1]. Although its incidence is relatively low, its lethality is disproportionate, surpassing that of melanoma in terms of skin cancer-specific mortality[2]. In recent decades, a significant increase in MCC incidence has been observed, attributed to factors such as population aging, increased ultraviolet radiation exposure, and broader use of immunosuppressants[3].

Clinically, MCC typically presents as a rapidly growing, painless papule or nodule, red, bluish, or skin-colored, and is often mistaken for benign lesions or other malignant neoplasms[4]. This non-specific appearance contributes to diagnostic delays, which negatively affect prognosis. Given MCC's high metastatic potential and aggressive behavior, early diagnosis is essential to improve disease control and patient survival[5].

Early identification allows for surgical interventions with appropriate margins and, when indicated, the use of adjuvant therapies such as radiotherapy and immunotherapy, which have been shown to improve clinical outcomes[6]. Furthermore, early recognition of the Merkel cell polyomavirus (MCPyV) role in the pathogenesis of most cases has contributed to advances in molecular diagnostics and the development of targeted therapies[7].

Therefore, due to MCC's aggressiveness and rapid course, this case report is justified by the importance of raising awareness among health-care professionals about the clinical features of the disease and the early use of biopsy and complementary examinations as crucial strategies for proper disease management.

Case report

An 80-year-old male patient with a medical history of squamous cell carcinoma (SCC) and basal cell carcinoma (BCC) presented in December 2024 with multiple ulcerated, indurated nodular skin lesions diffusely distributed across the integument. The lesions had emerged approximately 2 months prior, exhibiting progressive enlargement and ulceration. On dermatological examination, the following were described:

- Ulcerated erythematous nodules, 2-3 cm, fixed and firm, located on the left supralabial region, left sternal area, and right flank (Fig. 1).

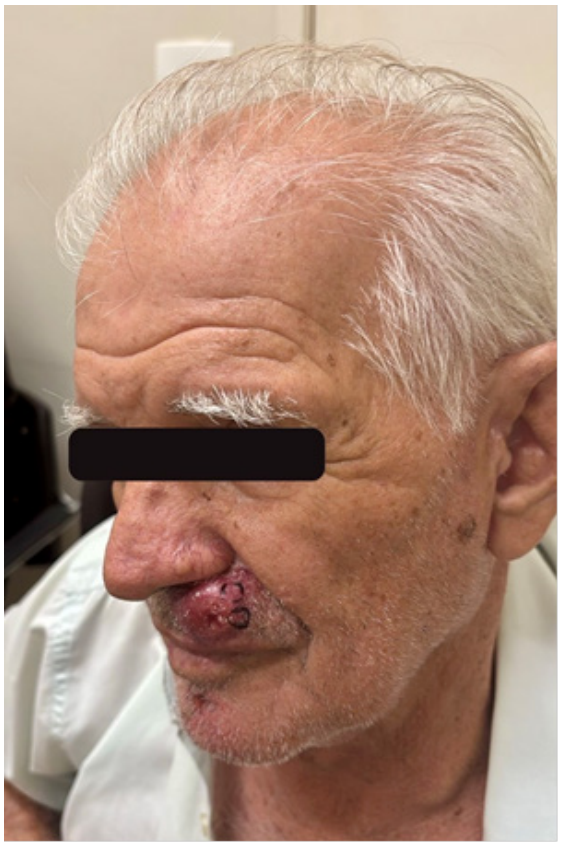

Figure 1. Initial lesion on the left supralabial region, nodular and erythematous, without apparent ulceration.

- Indurated, fixed masses ranging from 4 to 6 cm in the left cervical region, right upper scapular region (with surface telangiectasia), and right lower scapular region.

An incisional biopsy of the supralabial lesion was performed for initial investigation, along with laboratory tests, computed tomography (CT) of the chest and abdomen, and magnetic resonance imaging (MRI) of the brain and neck.

In January 2025, approximately 1 month later, the patient returned for a result evaluation. Physical examination revealed a new ulcerated, erythematous, fixed nodular lesion in the right inframammary region (Fig. 2).

Chest CT revealed right axillary (2.9 × 3.6 cm), pericardial (3 × 4 cm), and left supraclavicular lymphadenopathy. Abdominal CT showed multiple solid nodules in the subcutaneous tissue, the largest in the right gluteal region (4 cm), in addition to lesions compatible with secondary implants in the right subphrenic region, right iliac fossa, left pelvic cavity, and left mesenteric region (largest nodule measuring 5.3 cm).

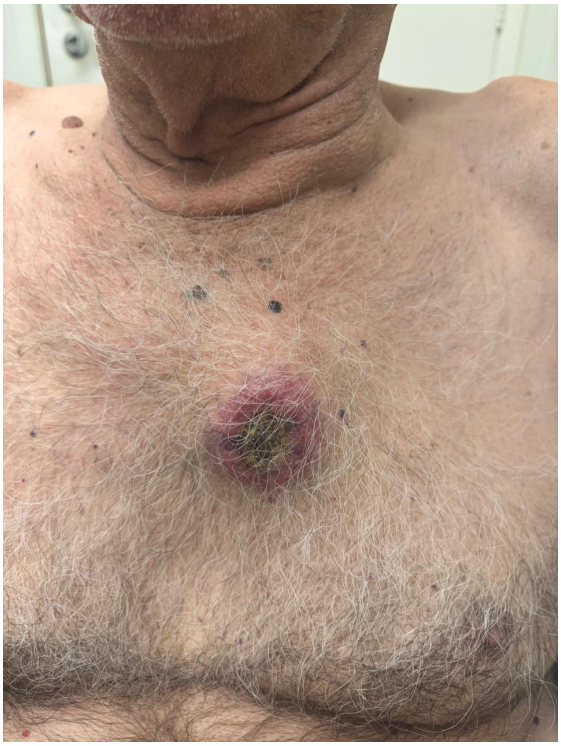

Figure 2. Disease progression with the appearance of new ulcerated cutaneous lesions on the anterior thoracic region (left sternal area).

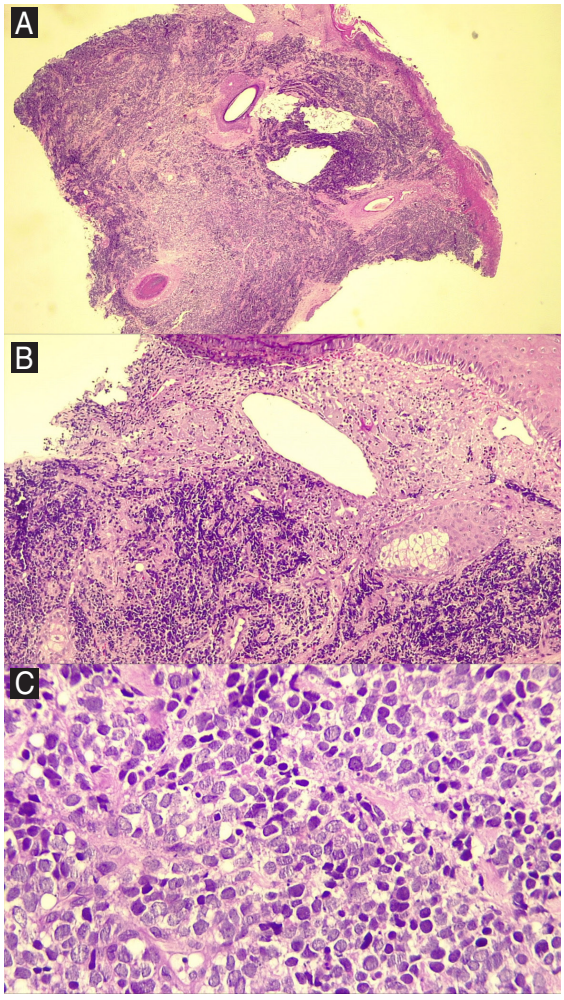

Figure 3. Histological sections of the lesion stained with hematoxylin and eosin (H&E) at **A**: 25×, **B**: 100×, and **C**: 400×. The findings are consistent with Merkel cell carcinoma, showing a dermal infiltrate composed of small, round neoplastic cells with hyperchromatic nuclei, "salt-and-pepper" chromatin, and scant cytoplasm.

Neck MRI revealed nodular lesions with heterogeneous contrast enhancement located in the upper lip, left supraclavicular, and parasternal regions, with features suggestive of neoplastic etiology. Brain MRI did not show relevant alterations.

The supralabial lesion biopsy demonstrated an undifferentiated malignant neoplasm, with special stains negative for fungi and mycobacteria (Fig. 3). The patient was referred to clinical oncology and oncologic surgery services, and immunohistochemical analysis was requested.

In February 2025, during follow-up, clinical progression of the skin lesions was evident. An immunohistochemical study confirmed the diagnosis of MCC (Figs. 4 and 5), staged as clinical stage IV (M1a), with subcutaneous, lymph node, and retroperitoneal metastases.

Due to the extent of the disease, curative surgical treatment was ruled out. Palliative chemotherapy with carboplatin and etoposide was initiated. However, after the first cycle, the patient developed significant toxicity (asthenia, weight loss, and mental confusion), which led to a transition to palliative care focused on symptom control. The patient passed away in late April 2025.

Discussion

MCC is a rare but highly aggressive cutaneous neuroendocrine neoplasm with a higher mortality rate than melanoma[3]. This case illustrates the aggressive clinical behavior of the disease, with rapid evolution, multiple skin lesions, and lymphatic and visceral dissemination in a short period.

Most MCC cases occur in elderly male patients with chronic sun exposure, immunosuppression, or a history of previous skin cancers such as SCC and BCC – all of which were present in this patient[2,8]. Infection with MCPyV is also associated with approximately 80% of

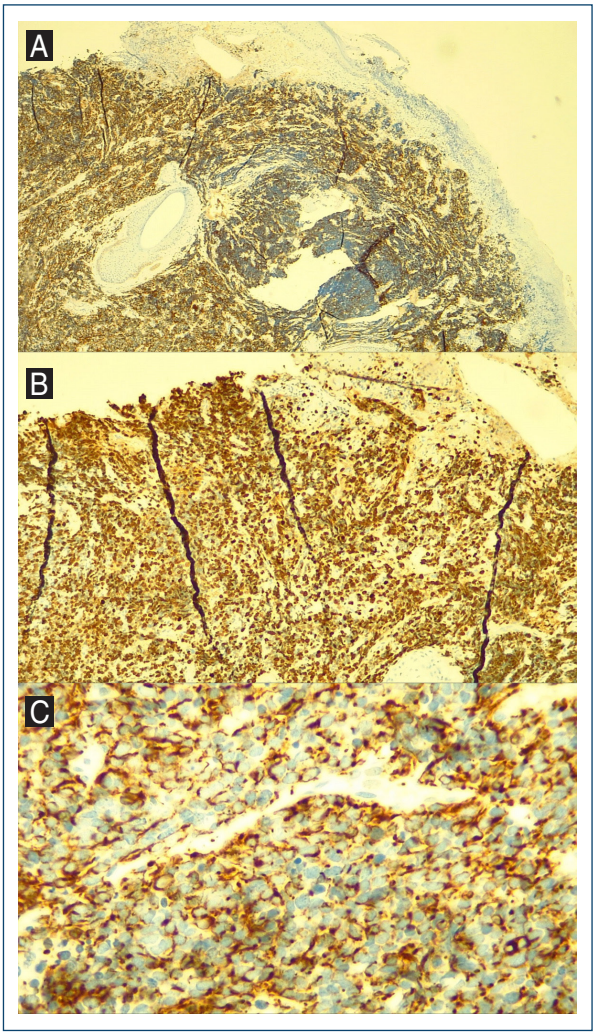

Figure 4. Immunohistochemical panel showing positive staining for **A**: CAM 5.2, **B**: Ki-67, and **C**: CK20. This staining pattern supports the diagnosis of Merkel cell carcinoma (MCC).

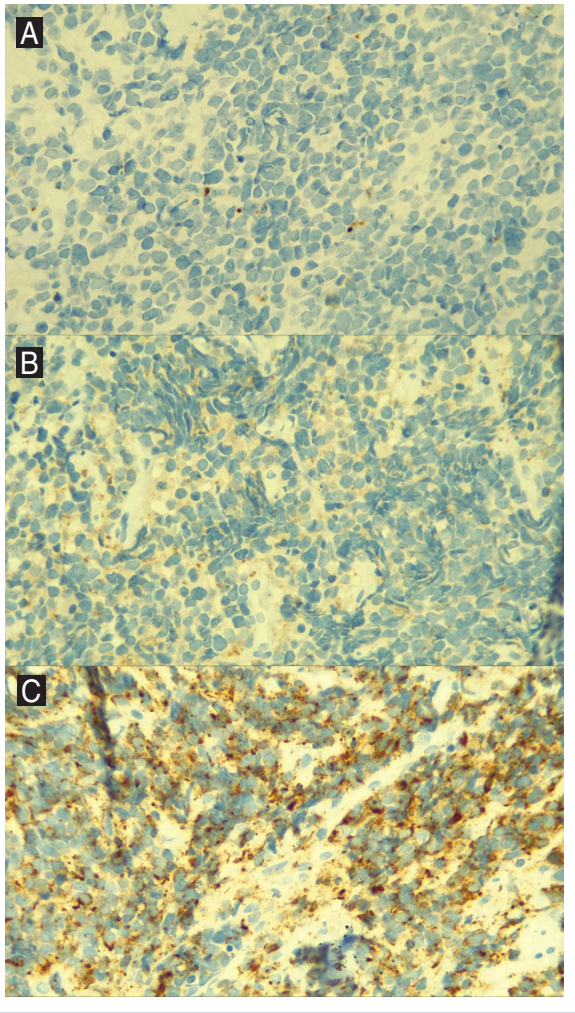

Figure 5. Immunohistochemical panel showing negative staining for neurofilament **(A)** and synaptophysin **(B)**, and positive staining for chromogranin **(C)**. This staining pattern supports the diagnosis of Merkel cell carcinoma.

cases and contributes to oncogenesis, especially in individuals with immunosenescence[7].

Clinically, MCC may present as painless, firm, rapidly growing cutaneous nodules prone to ulceration – as described in this patient – and is often mistaken for other etiologies such as SCC, sarcomas, or granulomatous infections[4]. The broad differential diagnosis in this case reflects this initial diagnostic challenge. Diagnosis requires biopsy and immunohistochemistry, typically showing cytokeratin 20 positivity in a perinuclear dot-like pattern, along with neuroendocrine markers such as chromogranin and synaptophysin[4].

The advanced stage (M1a, stage IV), with subcutaneous, nodal, and retroperitoneal metastases, ruled out curative surgical treatment. Palliative chemotherapy was indicated. Platinum-based regimens (e.g., carboplatin + etoposide) have traditionally been used, although responses are typically short-lived and associated with significant toxicity in elderly patients[9]. This was evidenced by the rapid clinical deterioration observed after the first cycle, leading to the decision for exclusive palliative care.

Conclusion

In recent years, immunotherapy with checkpoint inhibitors, such as avelumab and pembrolizumab, has emerged as a therapeutic alternative with higher response rates and a more favorable safety profile, particularly in metastatic cases[10]. However, its use

depends on clinical factors, availability, and patient condition, which may have limited its application in this case.

Given MCC's aggressiveness and the limited efficacy of treatments in advanced stages, early diagnosis is critical to offer therapeutic options with curative potential. Loss of follow-up during the pandemic may have contributed to delayed diagnosis in this patient, highlighting the importance of continuous care for high-risk patients.

Funding

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Conflicts of interest

None.

Ethical considerations

Protection of humans and animals. The authors declare that no experiments involving humans or animals were conducted for this research.

Confidentiality, informed consent, and ethical approval. The authors have followed their institution's confidentiality protocols, obtained informed consent from patients, and received approval from the Ethics Committee. The SAGER guidelines were followed according to the nature of the study.

Declaration on the use of artificial intelligence. The authors declare that no generative artificial intelligence was used in the writing of this manuscript.

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