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Merkel Cell Carcinoma: Diagnostic and Therapeutic Challenges

—A Case Report with Literature Review

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Abstract

Merkel cell carcinoma (MCC) is a rare and aggressive cutaneous neuroendocrine tumor predominantly affecting elderly and immunocompromised patients. It is characterized by a high propensity for local recurrence, regional lymph node involvement, and distant metastasis, leading to poor outcomes. Diagnosis remains challenging due to its rarity and nonspecific presentation, often leading to misdiagnosis. We report a case of locally advanced MCC originating in the gluteal region, exhibiting aggressive behavior. In the Moroccan context, where access to immunotherapy is limited, the patient was managed with chemotherapy, achieving transient disease control within a multimodal treatment strategy. This case report is accompanied by a literature review to discuss current therapeutic strategies and to underscore the challenges in managing MCC in resource-limited settings.

Keywords

Merkel Cell Carcinoma, Neuroendocrine Tumor, Gluteal Region, Chemotherapy, Resource-Limited Settings, Immunotherapy

1. Introduction

Merkel cell carcinoma (MCC) is a rare, aggressive cutaneous neuroendocrine malignancy with a rising global incidence, primarily affecting elderly and immunosuppressed individuals [1] [2]. Major etiological factors include ultraviolet radia-

tion exposure and Merkel cell polyomavirus infection [3].

Due to its rarity and nonspecific clinical features, MCC is frequently mistaken for more common skin cancers, resulting in diagnostic and therapeutic delays [4].

The disease follows an aggressive course, with high risks of local recurrence, regional lymph node metastasis, and distant spread, contributing to a poor prognosis in advanced stages [5]. Definitive diagnosis relies on histopathological examination supported by immunohistochemistry, particularly the characteristic perinuclear dot-like expression of cytokeratin 20 (CK20) [6].

Recent years have seen a paradigm shift with the introduction of immune checkpoint inhibitors (ICIs) targeting the PD-1/PD-L1 pathway, which have become the standard of care for advanced MCC due to significant improvements in survival [7] [8]. However, in many resource-limited regions, access to these therapies remains restricted, and cytotoxic chemotherapy—despite its limited durability—continues to be a primary treatment option [9].

We present a case of locally advanced MCC in the gluteal region, managed in Morocco without initial access to immunotherapy. This report highlights the diagnostic and therapeutic challenges encountered in real-world practice and emphasizes the need for context-adapted management strategies [10].

2. Case Presentation

2.1. Patient Information and Clinical History

A 57-year-old woman with no significant past medical history presented with a one-year history of a progressively enlarging mass in the right gluteal region. The lesion was painful and associated with local inflammatory signs, including erythema and warmth. Initially, it was managed as a gluteal abscess, and the patient underwent surgical drainage followed by antibiotic therapy. Due to the absence of clinical improvement, she subsequently sought medical consultation in the private sector.

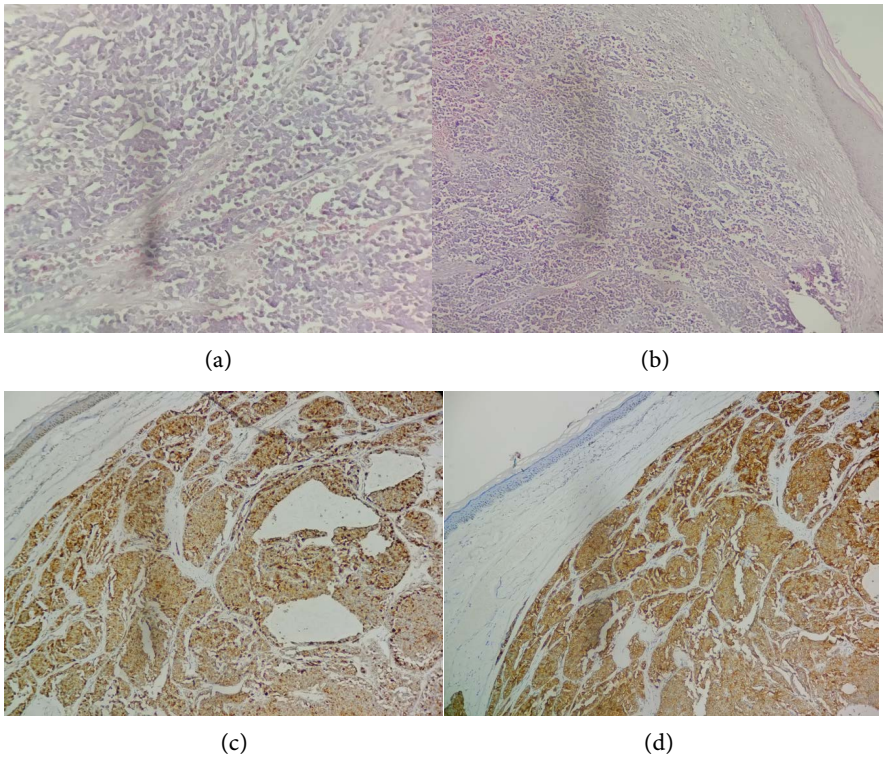
2.2. Diagnostic Assessment

Magnetic resonance imaging (MRI) of the soft tissues performed on October 30, 2021, revealed a right gluteal soft tissue lesion with imaging characteristics suggestive of a cystic lesion with myxoid content. Surgical excision of the mass was performed on December 6, 2021.

Histopathological examination of the excised specimen revealed a malignant tumor proliferation arranged in sheets and nodules, with extensive areas of necrosis. Hematoxylin and eosin staining showed clusters of undifferentiated tumor cells. Immunohistochemical analysis demonstrated positivity for chromogranin and synaptophysin, supporting neuroendocrine differentiation, with weak expression of cytokeratin 20 (CK20). Further immunohistochemical staining showed negativity for thyroid transcription factor-1 (TTF-1) and cytokeratin 7 (CK7), arguing against a pulmonary or visceral neuroendocrine primary tumor (**Figure 1**).

A thoraco-abdomino-pelvic CT scan showed no evidence of an alternative pri-

mary tumor, thereby supporting the diagnosis of primary cutaneous Merkel cell carcinoma. Based on the tumor location and the immunohistochemical findings, Merkel cell carcinoma was established as the final diagnosis.



(a) (b)

(c) (d)

Figure 1. (a) Skin tissue infiltrated by tumor proliferation arranged in sheets and nodules (H&E, ×100); (b) Skin tissue infiltrated by tumor proliferation arranged in sheets and nodules (H&E, ×100); (c) Immunohistochemical study showing chromogranin expression; (d) Immunohistochemical study showing synaptophysin expression.

To assess the locoregional and distant extent of the disease, staging imaging was performed.

A thoraco-abdomino-pelvic computed tomography (CT) scan performed on December 23, 2021, showed a soft tissue lesion measuring 14 × 10 mm at the upper part of the surgical incision, suspicious for residual or recurrent disease, as well as a left inguinal lymph node measuring 15 mm in short-axis diameter. No distant metastases were identified. At this stage, the disease was clinically classified as cT2N0M0, corresponding to AJCC stage II.

A pelvic MRI performed on January 8, 2022, confirmed the presence of a suspicious residual soft tissue lesion adjacent to the surgical scar in the right gluteal region, measuring 20 × 14 mm.

2.3. Therapeutic Interventions

A wide local excision was performed on January 27, 2022, at a tertiary care center. Histopathological examination confirmed the diagnosis of Merkel cell carcinoma. Surgical margins were close, measuring 6 mm on one margin, greater than 15 mm

on another, 1.5 mm on a third margin, and 1.9 mm at the deep margin.

In March 2022, pelvic ultrasound revealed a suspicious right inguinal lymphadenopathy measuring 25 mm in short-axis diameter. Sentinel lymph node biopsy was not performed due to technical limitations in our setting. Right inguinal lymph node dissection was performed on April 29, 2022, and histopathological analysis demonstrated metastatic involvement in 2 out of 4 lymph nodes by a poorly differentiated malignant tumor, consistent with nodal metastasis of Merkel cell carcinoma. The pathological stage was therefore pT2N1M0, corresponding to AJCC stage III.

The patient subsequently received adjuvant radiotherapy to the right gluteal surgical scar and the regional lymphatic basins, including the inguinal and paraaortic lymph node areas, in accordance with recommendations for high-risk Merkel cell carcinoma with nodal involvement. A total dose of 50 Gy was delivered between August 16 and September 18, 2022, using conventional fractionation (2 Gy per fraction).

2.4. Follow-Up and Outcomes

In October 2022, one month after completion of radiotherapy, the patient developed epigastric pain. Abdominal CT imaging revealed bulky metastatic lymphadenopathies in the hepatic hilum and retro-duodeno-pancreatic regions, forming a confluent mass, as well as multiple small indeterminate hepatic lesions, consistent with metastatic disease progression (Figure 2). This evolution corresponded to metastatic disease classified as cT2N1M1 (AJCC stage IV).

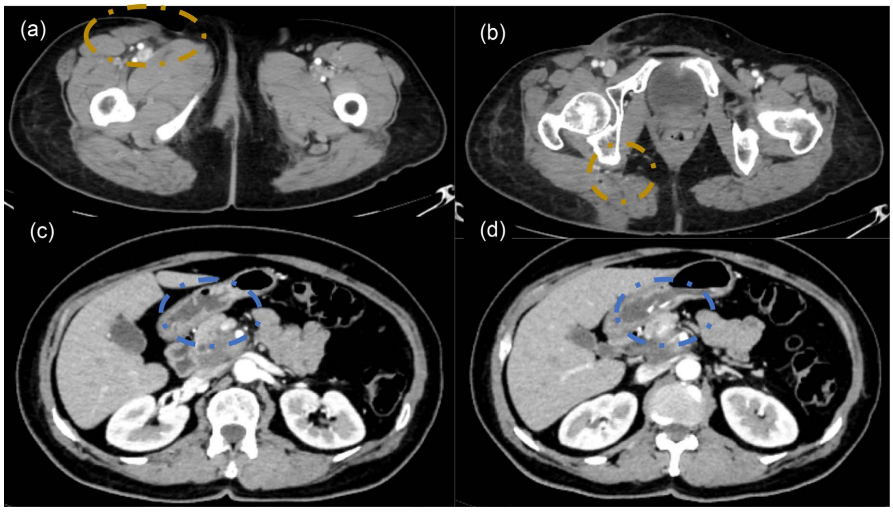


Figure 2. Contrast-enhanced computed tomography (CT) images. (a, b) Axial pelvic CT sections showing a right gluteal subcutaneous soft-tissue lesion at the primary tumor site (yellow dashed circle), raising the differential diagnosis between postoperative fibrotic changes and residual tumor; (c, d) Axial abdominal CT sections demonstrating a conglomerate ("magma") of enlarged upper mesenteric lymph nodes in the precaval region (blue dashed circle), consistent with metastatic lymphadenopathy in the context of Merkel cell carcinoma.

Given the unavailability of immunotherapy at that time, the patient was treated with platinum-based chemotherapy using a cisplatin-etoposide regimen. At treatment initiation, the patient had a good performance status (ECOG 0). The chemotherapy was generally well tolerated, with grade 2 nausea and vomiting effectively managed with antiemetic medication, and no dose reduction was required. After four cycles, radiological reassessment demonstrated a partial response, with a decrease in the size of upper mesenteric and pre-caval lymphadenopathies and stability of the remaining lesions (Figure 3). The patient ultimately received eight cycles, achieving temporary disease control.

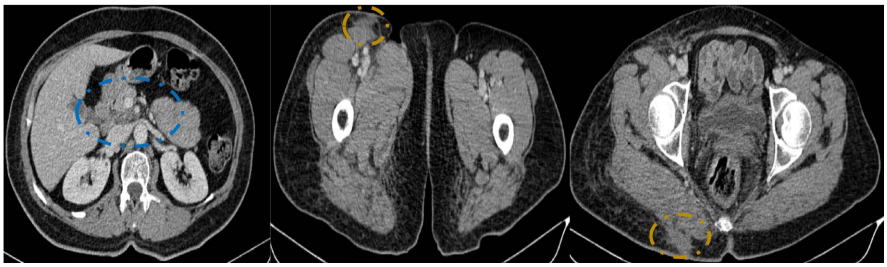


Figure 3. Follow-up contrast-enhanced CT scan performed after four cycles of cisplatin-etoposide chemotherapy, showing a partial radiological response with a reduction in the size of the conglomerate of metastatic upper mesenteric lymphadenopathies in the precaval region (blue dashed circle). The right gluteal subcutaneous soft-tissue lesion remains stable in appearance (yellow dashed circle).

A follow-up CT scan performed on August 24, 2023, demonstrated an increase in the size of a right adrenal lesion, while the remainder of the disease, including pre-caval infiltration and intra- and retroperitoneal lymphadenopathies, remained stable. Stereotactic radiotherapy was therefore delivered to the right adrenal metastasis.

In October 2023, imaging showed progression of metastatic disease involving the right adrenal gland and celiac-mesenteric lymph nodes, leading to compression of the biliary tract with dilation of the common bile duct and intrahepatic bile ducts. The case was discussed in a multidisciplinary setting, and the patient underwent endoscopic retrograde cholangiopancreatography (ERCP) with papillotomy and placement of a plastic biliary stent on October 30, 2023.

Further disease progression was documented in January 2024. The patient was started on lanreotide and received two injections without clinical or radiological benefit. Following the eventual availability of immunotherapy, pembrolizumab was initiated, and the patient received two doses. However, she experienced rapid deterioration in general condition before treatment response evaluation could be performed.

The patient died during hospitalization in April 2024 due to progressive metastatic disease.

3. Discussion

MCC is an aggressive malignancy with a high metastatic potential, posing signif-

icant management challenges. Our case underscores several key issues: diagnostic delay, the transient benefit of chemotherapy, the critical importance of timely immunotherapy, and the realities of practice in resource-limited settings.

The initial misdiagnosis as an abscess is not uncommon, reflecting MCC's ability to mimic benign conditions and leading to critical delays [4]. Imaging findings are often nonspecific, underscoring the indispensable role of histopathology and immunohistochemistry (e.g., CK20, synaptophysin, chromogranin) for definitive diagnosis [6].

Despite optimal locoregional therapy—including wide excision, lymph node dissection, and adjuvant radiotherapy—our patient experienced rapid regional and distant recurrence. This aligns with the known aggressive biology of MCC and highlights the limitations of local modalities in controlling systemic disease [5] [11].

3.1. Chemotherapy: A Temporary Solution

In the pre-immunotherapy era, platinum-etoposide regimens were the standard for advanced MCC, yielding high initial response rates (50% - 60%) but with a median duration of only 3 - 6 months and no proven survival benefit [9]. Our patient's course mirrors this pattern: a meaningful partial response to cisplatin-etoposide, followed by inevitable progression. This underscores chemotherapy's role as a palliative, temporizing measure rather than a curative strategy.

3.2. Immunotherapy: A Missed Opportunity

Immune checkpoint inhibitors such as avelumab and pembrolizumab have revolutionized the treatment of advanced Merkel cell carcinoma, demonstrating high response rates, durable disease control, and improved overall survival [7] [8]. Recent real-world studies and long-term follow-up data have confirmed the sustained benefit of ICIs, particularly when used in the first-line setting, leading to their adoption as the preferred initial systemic therapy in contemporary clinical guidelines [12]-[16]. In our case, the absence of timely access to pembrolizumab likely profoundly impacted the outcome. Immunotherapy was initiated late, after multiple lines of treatment and clinical deterioration, a context in which therapeutic efficacy is often reduced. This contrast with modern evidence underscores the critical importance of early integration of immunotherapy in MCC management [10].

3.3. Managing Oligoprogression and Late-Stage Challenges

The use of stereotactic radiotherapy for an isolated adrenal metastasis provided transient local control, illustrating a potential strategy for oligoprogressive disease [12]. However, without effective systemic control, such approaches are of limited value. The lack of benefit from lanreotide aligns with the scant evidence for somatostatin analogs in MCC and underscores the need for evidence-based approaches.

3.4. Clinical Implications and Lessons

This case highlights the stark efficacy gap between chemotherapy and immunotherapy in MCC. It also exposes the inequities in global cancer care, where limited access to novel therapies can dictate patient outcomes. Efforts to improve early diagnosis, multidisciplinary management, and—critically—access to immunotherapy are essential to change the trajectory of this aggressive disease, especially in underserved regions.

4. Conclusion

MCC is a diagnostically challenging and biologically aggressive tumor. This case illustrates its rapid metastatic potential despite standard locoregional therapies and the transient nature of chemotherapy benefit. The delayed introduction of immunotherapy, now the cornerstone of advanced disease management, likely contributed to the poor outcome. Ensuring timely access to effective systemic therapies is paramount to improving survival, particularly in resource-limited settings where diagnostic and therapeutic bottlenecks persist.

Ethics and Declarations

Written informed consent was obtained from the patient for publication of this case report and accompanying images. Ethics committee approval was not required for this type of study in accordance with institutional policy. No funding was received for this work.

Conflicts of Interest

The authors declare no conflicts of interest.

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