Journal of Investigative Medicine High Impact Case Reports
Volume 8: 1–4

DOI: 10.1177/2324709620963714
journals.sagepub.com/home/hic
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An Aggressive Presentation of Merkel Cell Carcinoma: A Case Report

Zemni Ines, MD[1], Haddad Sabrine, MD[1], Fatma Saadallah, MD[1], Ayadi Mohamed Ali, MD[1], Charfi Lamia, MD[1], Chargui Riadh, MD[1], and Rahal Khaled, PhD[1]

Abstract

Merkel cell carcinoma (MCC) is a rare malignant neuroendocrine tumor more common in immunosuppressed old patients. It is characterized by a high frequency of local recurrence, regional nodal metastasis, distant metastasis, and low survival rate. The diagnosis of MCC is challenging due to its rarity and can be clinically mistaken for other skin cancer. We report a case of locally advanced MCC of the left groin with aggressive behavior that was finally controlled with a combined treatment and we collected data from the literature to discuss the appropriate therapeutic algorithm for the management of this uncommon skin tumor.

Keywords

Merkel cell carcinoma, neuroendocrine, surgery, systemic treatment

Introduction

Merkel cell carcinoma (MCC) is a rare malignant neuroendocrine tumor more common in immunosuppressed old patients. It is characterized by a high frequency of local recurrence, regional nodal metastasis, distant metastasis, and low survival rate.[1] This tumor rather affects the sun-exposed skin and especially the head and neck. The diagnosis of MCC is challenging due to its rarity and can be clinically mistaken for other skin cancer. The diagnosis is made after the tumor is biopsied for immunohistopathologic examination.[2,3] We report a case of locally advanced MCC of the left groin with aggressive behavior that was finally controlled with a combined treatment, and we collected data from the literature to discuss the appropriate therapeutic algorithm for the management of this uncommon skin cancer.

Case Presentation

A 60-year-old male patient was referred to our Department of Surgical Oncology in March 2015 for a painless swelling of about 3 month's duration in the left inguinal area that grew rapidly. Past medical history was remarkable for nasopharyngeal cancer diagnosed in 2008 and treated with chemoradiation. Local examination showed a hard fixed inguinal mass of about 11 ×10 × 5 cm in diameter. The overlying skin was at a pre-ulcer stage (Figure 1). The patient was completely asymptomatic and did not show clinical symptoms of carcinoid syndrome (flush, diarrhea, and wheezing).

Thoracoabdominal and pelvic computed tomography with contrast revealed a multilobular mass of approximately 12 × 11 × 5 cm in size with heterogeneous enhancement at the left inguinal region. The tumor infiltrated the iliopsoas muscle and compressed the left femoral pedicle. Pathologic inguinal lymph nodes and infracentimetric subcutaneous nodules were observed (Figure 2). Detectable distant metastasis or other suspicious lesions were excluded. A Tru-Cut biopsy from the inguinal mass was performed and histological examination concluded to the diagnosis of a primary MCC. The patient underwent a left inguinal dissection with wide local excision of the tumor with 2 cm margins and satellite lymph node dissection (Figure 3A and B). Macroscopic examination revealed a solid, yellow-tanned, and lobulated mass measuring 13 × 10.5 × 9.5 cm with clear lateral margins of 1 cm and narrow deep margins (<4 mm). Histological examination revealed a dermal and subcutaneous tumor with a diffuse growth pattern (Figure 4A). Tumor cells were

[1]Salah Azaiez Institute, University of Tunis El Manar, Tunis, Tunisia

Received April 6, 2020. Revised April 19, 2020. Accepted April 30, 2020.

Corresponding Author:
Zemni Ines, MD, Department of Surgical Oncology, Salah Azaiez Institute, Bab Saadoun Boulevard 9 Avril, Tunis 1006, Tunisia.
Email: ines.zemni@yahoo.fr

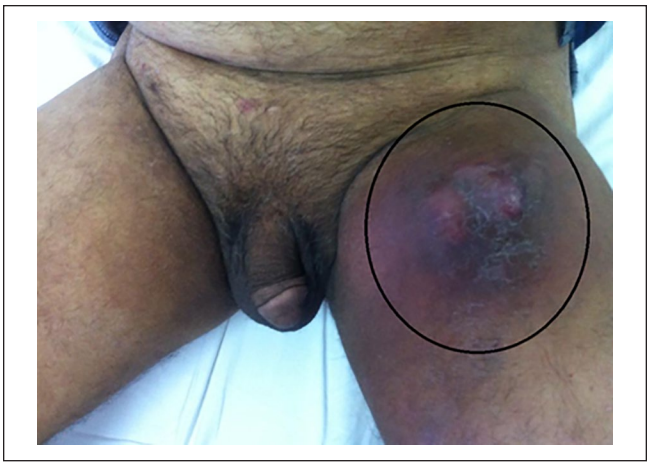

Figure 1. Hard fixed 8 × 6 × 5 cm left inguinal mass and overlying skin at a pre-ulcer stage.

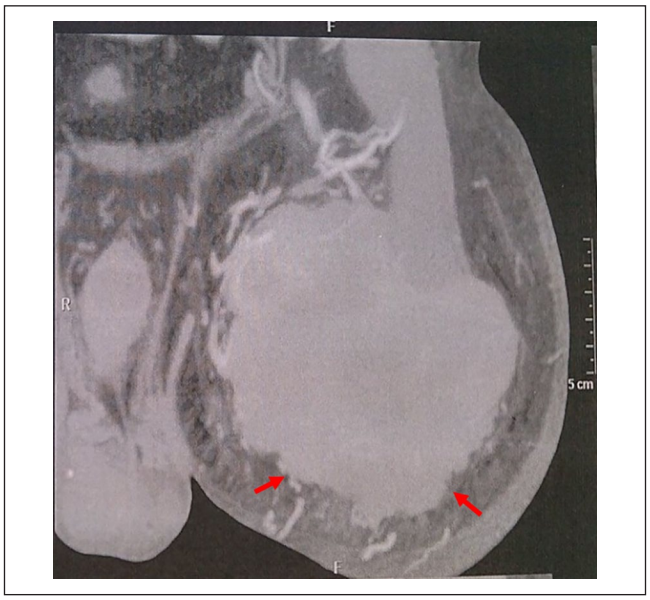

Figure 2. Computed tomography (CT) scan with contrast shows a 12 × 11 × 5 cm multilobular (↗) mass of the left inguinal region with heterogeneous enhancement.

monotonous and round with scant eosinophilic cytoplasmic rim, round and vesicular nuclei with finely granular and dusty chromatin. Frequent mitotic figures were observed (Figure 4B). Immunohistochemically, tumor cells were positive for cytokeratin 20 (CK20) in a perinuclear dot-like fashion (Figure 4C), chromogranin, and synaptophysin (Figure 4D). They were negative with thyroid transcription factor-1, cytokeratin 7 (CK7), leucocyte common antigen, and S-100.

The diagnosis of primary MCC was established and the patient was proposed to undergo radiotherapy. Two months later, during the follow-up period and before starting radiotherapy he was readmitted to the surgical department for local recurrence. Local excision of left inguinal nodes was achieved with safe margins. Around the third postoperative day, the patient presented a sudden active arterial bleeding from the inguinal incision. He underwent an immediate surgical procedure to stop the bleeding. Preoperative exploration revealed a tumoral invasion of the common femoral artery. A ligation of the femoral artery with excision of the tumoral tissue was performed with no possibility of arterial reconstruction. Fortunately, in postoperative follow-up, the enlargement of collateral circulation after ligation of the left common femoral artery allowed preserving the viability of the limb. The patient was discharged after 20 days in good shape and he had a regular follow-up in both cardiovascular and surgical oncology departments. The patient was considered as having a high-risk MCC and he received platinum-based chemotherapy (6 cycles carboplatin-etoposide) regimen. He was kept under close follow-up with physical examination every 3 months and a CT scan every 6 months within the first year and then a CT scan every year. He did not experience any locoregional or distant relapse 3 years after treatment.

Discussion

There is no clear algorithm for the treatment of MCC, and the results of retrospective studies showed that the best cure rates are achieved with multimodal therapy. Treatment with large excision and adjuvant radiotherapy demonstrated an improved locoregional control.[3] The current recommendation of the National Comprehensive Cancer Network and the Danish Guidelines is a wide local excision (WLE) with 1 to 2 cm peripheral margins and deep margins reaching to the level of the deep fascia.[4,5] However, MCC is characterized by a microscopic satellite extension to the main, something which has prompted some medical societies to recommend a microscopically controlled surgery as an alternative to WLE using a peripheral excision margin of 1 to 2 cm.[6] Sentinel lymph node biopsy is advised, and the indication depends on the tumor's stage and location.[4-7] Local adjuvant radiotherapy is advised as a final step in the curative treatment.[8]

In our case, we could not perform radiation therapy after the ligation of the femoral artery and we indicated systemic chemotherapy because our patient presented an aggressive form of MCC with a high risk of locoregional recurrence. Reports from retrospective studies evaluating potential histologic factors showed that infiltrative growth patterns, narrow tumor depth, and presence of lymphovascular invasion are significantly associated with worse specific disease survival.[1,2] When compared with monotherapy (surgery or radiotherapy), the combination of WLE with adjuvant radiotherapy improved locoregional control and disease-free survival with a statistically significant benefit.[9,10] Radiotherapy alone is preferred for locally advanced and unresectable tumors, and chemotherapy appears to be beneficial in metastatic MCC.[10] Although current data suggest that the adjunction of chemotherapy in patients at high risk of recurrence

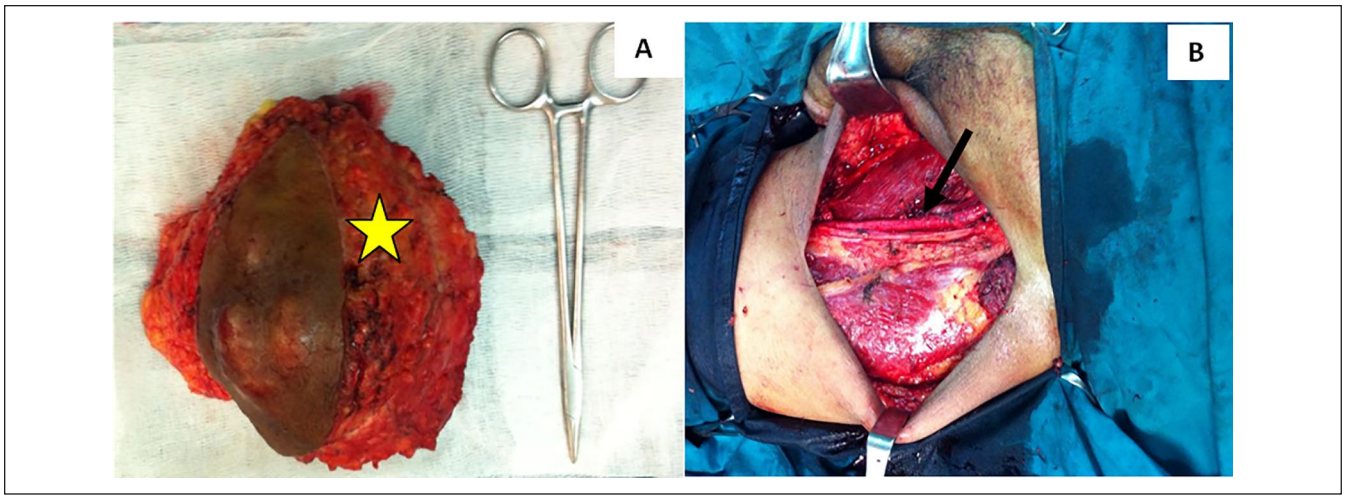

Figure 3. (A) Wide local excision of the tumor (☆) with peripheral margins of 2 cm. (B) Wide local excision with deep margins extending to the level of the deep fascia and an intact left femoral pedicle (↙).

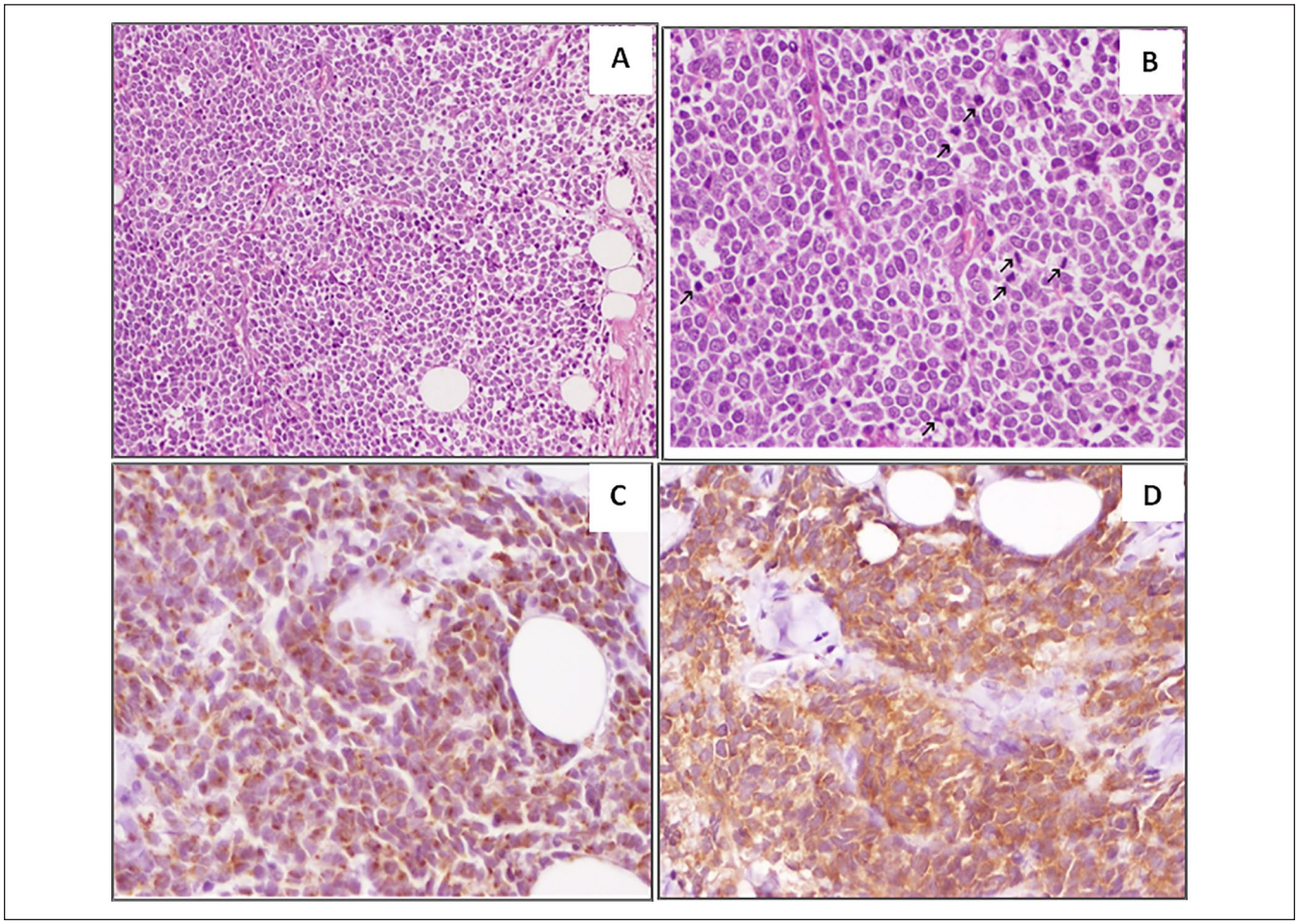

Figure 4. (A) Merkel cell carcinoma infiltrating subcutaneous fatty tissue (hematoxylin-eosin, original magnification ×200). (B) Small round cells with a round nucleus, dusty chromatin, and numerous mitotic figures (↗) (hematoxylin-eosin, original magnification ×400). (C) Para nuclear dot-like staining with cytokeratin 20 (immunoperoxidase staining, original magnification ×400). (D) Cytoplasmic staining with synaptophysin (immunoperoxidase staining, original magnification ×400).

(lymph nodes invasion, tumor >1 cm, and pathological surgical margins) do not improve locoregional control and survival rates, each case of MCC should be evaluated in a multidisciplinary cancer team in order to indicate adjuvant chemotherapy.[3,6] Immunotherapy has revolutionized the management of this orphan disease and preliminary data from non-randomized trials in patients with metastatic or recurrent locoregional MCC, demonstrate that avelumab, an anti-PDL-1 agent and pembrolizumab and nivolumab anti-PD-1 agents improved the rate of prolonged response, compared with cytotoxic therapy.[11-14] Unfortunately this therapy is not accessible in our country with limited resources, for advanced MCC and the locoregional recurrence in our patient was well managed with surgery and chemotherapy.

Conclusion

In summary, MCC is a very uncommon skin cancer in our routine clinical practice. This case allowed us to investigate its main features from available published data. Obviously it is difficult to establish a well codified and definitive therapeutic approach. However, an early aggressive multimodal treatment is needed to control this malignancy.

Author Contributions

Acquisition of data: Sabrine Haddad, Ines Zemni
Analysis and interpretation of data: Ines Zemni, Sabrine Haddad, Ayadi Mohamed Ali
Critical revision: Ines Zemni, Fatma Saadallah, Lamia Charfi
Drafting of the manuscript: Sabrine Haddad, Riadh Chargui, Khaled Rahal
Study conception and design: Ines Zemni, Sabrine Haddad, Ayadi Mohamed Ali
Final approval of the version to be published: All authors

Declaration of Conflicting Interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Funding

The author(s) received no financial support for the research, authorship, and/or publication of this article.

Ethics Approval

Our institution does not require ethical approval for reporting individual cases or case series.

Informed consent

Verbal informed consent was obtained from the patient(s) for their anonymized information to be published in this article.

ORCID iDs

Zemni Ines https://orcid.org/0000-0002-7244-8248
Chargui Riadh https://orcid.org/0000-0002-4518-4048

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