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Case Report

Merkel cell carcinoma of an atypical presentation: A case report and literature review

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ABSTRACT

Merkel cell carcinoma (MCC) is a primary cutaneous neuroendocrine carcinoma. It is a rare and aggressive tumor characterized by a high frequency of local recurrence, regional nodal metastasis, distant metastasis, and a low survival rate. Its diagnosis is challenging due to its rarity and it may be clinically mistaken for other skin cancers. It requires an incisional biopsy and confirmation by histology and immunohistochemical staining. This case illustrates an uncommon presentation of MCC in a 53-year-old young adult in an unexposed area of the right gluteal region. It is a rare cutaneous tumor that should be diagnosed and treated precociously given the aggressive nature of MCC and the limited therapeutic options for metastatic tumors. Herein, we urge physicians to suspect this diagnosis in front of any rapidly growing skin tumor, even in an unusual location, to provide the patient with appropriate treatment and improve the overall survival rate.

Keywords: Merkel cell carcinoma; Unexposed skin areas; Neuroendocrine tumors; Cytokeratin-20 Introduction

INTRODUCTION

Merkel cell carcinoma (MCC) is a rare and aggressive primary cutaneous neuroendocrine carcinoma [1]. It is characterized by a high frequency of local recurrence, regional nodal metastasis, distant metastasis, and a low survival rate [2]. Its incidence has increased over the last thirty years. It affects elderly Caucasian males in their seventies and eighties and occurs in sun-damaged skin, commonly on the head and neck. It may present at an earlier age in immunocompromised patients, such as organ transplant recipients, HIV-infected individuals, and those with B-cell lymphoid malignancies [3]. Merkel cell polyomavirus (MCPyV) causes up to 80% of MCC tumors in North America and Europe, yet an advanced age, exposure to UV radiation, and an immunosuppressed state are important risk factors. It most often presents itself as an erythematous or violaceous nodule or plaque and its clinical presentation is non-specific and varied [4]. Its diagnosis is challenging due to its rarity and it may be clinically mistaken for other skin cancers. It requires an incisional or excisional biopsy and confirmation by histology and immunohistochemical staining. This paper reports an uncommon case of rapidly progressive Merkel cell carcinoma diagnosed in a 53-year-old young adult in an unexposed area of the right gluteal region.

CASE REPORT

Herein, we report the case of a 53-year-old patient, a chronic smoker, with no notion of immunosuppression or a history of radiotherapy. He presented with an ulcerated and budding lesion in the right gluteal region (Fig. 1), increasing in size progressively and rapidly, evolving for the previous seven months. A biopsy was performed, suspecting the diagnosis of sarcoma,

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squamous cell carcinoma, or high-grade B lymphoma. Histological analysis of the skin specimen after HES staining revealed a proliferation of blue, round cells infiltrating the dermis and hypodermis (Figs. 2a – 2c). The tumor cells were monotonous with round and vesicular nuclei with finely granular and salt-and-pepper chromatin patterns. Numerous mitotic figures were observed as well as reduced eosinophilic cytoplasm. On immunohistochemical staining (Figs. 3a and 3b), the tumor cells stained for low-molecular-weight cytokeratins (AE1/AE3 and CK20) with a characteristic perinuclear, dot-like pattern for CK20, as well as chromogranin A and synaptophysin. Lymphoid markers, TTF1 and CK7, were negative. In the light of these morphological and immunohistochemical findings, the diagnosis of Merkel cell carcinoma was reached. A large surgical excision (Fig. 4) was performed with clear margins followed by radiotherapy.

DISCUSSION

Merkel cell carcinoma is a primary cutaneous neuroendocrine carcinoma first described by Friedrich Sigmund Merkel in 1875 as a nondendritic, non-keratinocyte, epidermal "tastzellen" (or "touch cell") that functions as a tactile skin receptor [5]. It most commonly arises in the elderly and has a predilection for the upper body, although the trunk and lower limbs may be involved as well. Its clinical differential diagnosis is nonspecific. The prognosis of the tumor has been variable. However, in most cases, these are aggressive neoplasms with a tendency to recur and eventually metastasize. It affects elderly Caucasian males in their seventies and eighties and occurs in sun-damaged skin, commonly on the head and neck [6,7]. This is different from our patient, who was younger (53 years old), did not have immunosuppression, and his tumor had developed in a non-sun-damaged skin area (gluteal region). This unusual clinical presentation was a source of clinical misdiagnosis, thinking instead of sarcoma, high-grade B-cell lymphoma, or squamous cell carcinoma. The biopsy that was communicated to us revealed skin tissue in which the dermis was infiltrated by a proliferation of round, blue cells with typical histopathologic and immunohistochemical characteristics of Merkel cell carcinoma. Histologically, Merkel cell carcinoma is composed of nests of round, blue, small-to-medium, monotonous cells. They characteristically display a fine, granular, salt-and-pepper chromatin pattern with reduced cytoplasm. Mitotic figures and apoptotic bodies are frequent [1,8]. Immunohistochemically, the tumor cells are positive for neuroendocrine markers (chromogranin A, synaptophysin, and CD56), epithelial markers (CK AE1/AE3, EMA), and CK20 typically stains in a perinuclear, dot-like pattern due to the clumping of the intermediate filaments. TTF1 and lymphoid marker staining is negative, which distinguishes them from small-cell lung carcinoma and lymphoma, respectively [1,9]. The antibody anti-MCPyV detects the presence of MCPyV large T antigen of Merkel cell polyomavirus

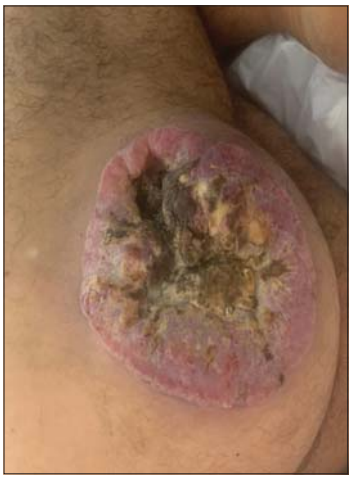

Figure 1: Ulcerated and budding lesion in the right gluteal region.

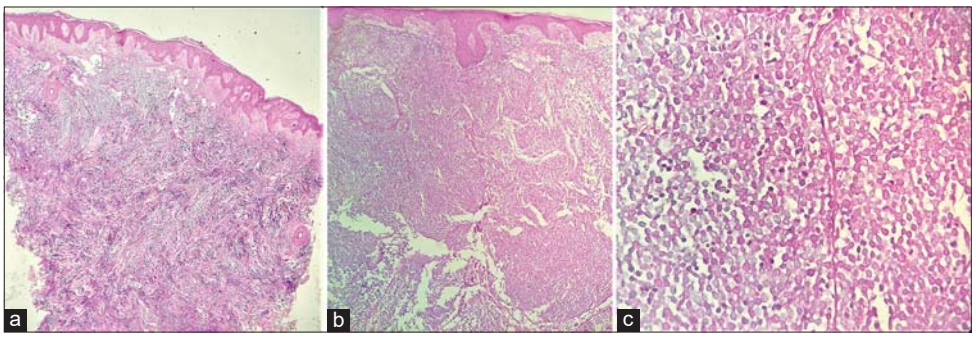

Figure 2: (a) Dermis infiltration by the small, round, blue cell, undifferentiated tumor (H&E, 40×). (b) Dermis infiltration by nests of small, round, blue, monotonous cells (H&E, 100×). (c) Tumor cells displaying a fine, granular, salt-and-pepper chromatin pattern with reduced cytoplasm and frequent mitotic figures and apoptotic bodies (H&E, 400×).

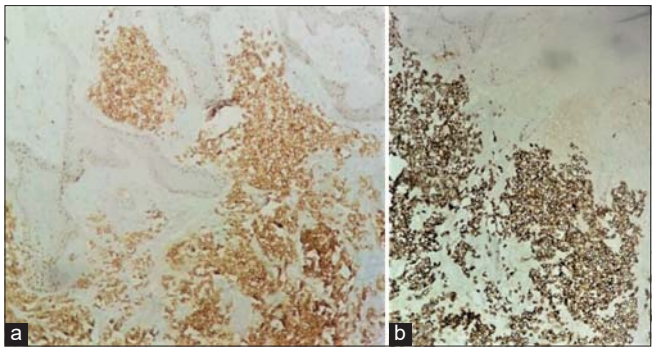

Figure 3: (a) Tumor cells immunostaining for chromogranin A. (b) Tumor cells immunostaining for cytokeratin 20 in a perinuclear, dot-like pattern.

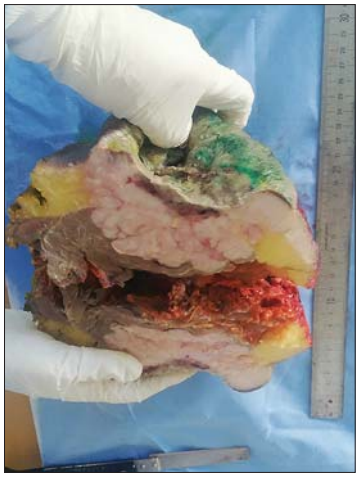

Figure 4: Surgical excision specimen: the macroscopic appearance of an ulcer, a budding tumor, with a whitish and homogeneous pattern.

with nuclear staining. Unfortunately, we did not have this antibody to confirm MCPyV in our gluteal Merkel cell carcinoma [10]. Surgical management with clear margins is the gold standard of treating Merkel cell carcinoma, as well as adjuvant radiotherapy [11]. The sentinel lymph node (SLN) is recommended for all patients to detect lymph nodal involvement and indicate a regional lymph node dissection. However, the current NCCN recommendations [12] on management and treatment remain based on clinically detectable nodal involvement because of conflicting evidence on the survival benefit of SLN in patients without clinical nodal involvement. Chemotherapy is reserved for metastatic cases with single or combined agents. While immunotherapy has revolutionized the management of Merkel cell carcinoma, preliminary data from non-randomized trials in patients with metastatic or recurrent locoregional MCC demonstrated that anti-PDL-1 agents and anti-PD-1 agents improve the rate of a prolonged response when compared to chemotherapy [13].

CONCLUSION

This case illustrates an uncommon presentation of Merkel cell carcinoma in a 53-year-old young adult in an unexposed area of the right gluteal region. It is a rare primary cutaneous tumor that should be diagnosed and treated precociously given the aggressive nature of MCC and the limited therapeutic options for metastatic tumors. Herein, we have urged physicians to suspect this diagnosis in front of any rapidly growing skin tumor, even in an unusual location, to provide the patient with appropriate treatment and improve the overall survival rate.

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