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Merkel Cell Carcinoma: Case Report and Bibliographic Review

Renata de Oliveira Belo Custódio dos Santos[1], Danielle da Silva Pinto[1], Flávya Muniz Souza[1], Ana Carla de Oliveira Johnen[1] and João Kleber de Almeida Gentile[2]*

[1] Graduation in Medical School of São Paulo City University (FM-UNICID), São Paulo/SP-Brazil

[2] Digestive Surgeon, Fellow of American College of Surgeons (FACS), Assistant of Discipline of Surgical Technique and Surgical Habilities of Faculdade de Medicina da Universidade Cidade de São Paulo (FM-UNICID), São Paulo/SP-Brazil

ABSTRACT

Introduction: Merkel cell carcinoma (MCC) is characterized as a malignant trabecular neoplasm of the skin. The most common sites of lesions are areas frequently exposed to the sun, thus regions such as head, neck and upper limbs. The aim of this study is to report the clinical case of a female patient assisted in a Teaching Hospital in the State of São Paulo, with a lesion in the left gluteal region, unusual to what is found in the literature.

Case Report: An 87-year-old female patient, who underwent excisional biopsy of a lesion on her left buttock, with an anatomopathological (AP) diagnosis of MCC, was also submitted to a control image, which showed a new lesion in the lymph node chain, and underwent a new surgical procedure, which was unsuccessful.

Discussion: Most patients have local disease, but MCC has a high rate of metastasis, with the main sites of secondary lesions being skin (28%), regional lymph nodes (27%), liver (13%), lung (10%), bone (10%), and brain (6%). As evident in the literature, the diagnosis of the patient was made by immunohistochemical analysis, through the positive expression of CK20, chromogranin and synaptophysin, and the extent of disease evaluated by computed tomography. Wide local excision and adjuvant radiotherapy remain the mainstay of MCC treatment, but many studies show promising results with the use of monoclonal antibodies, such as avelumab, which was not used in the case reported. Although MCC is rare, despite the high recurrence rate and poor prognosis, early diagnosis and treatment are essential to prevent and combat the progression of metastatic disease, the main factor in the decrease in overall survival of patients.

Conclusion: MCC is still a challenge for the medical field, since this neoplasm has a high potential for recurrence and metastasis. However, late diagnosis and limited and delayed treatment contribute to a higher lethality rate.

***Corresponding author**

João Kleber de Almeida Gentile, Department of Surgical Technique and Surgical Abilities of the Faculty of Medicine of the University of São Paulo (FM-UNICID). Rua Padre Estevão Pernet, 180-Tatuapé, São Paulo/SP-Brazil. Telephone No: 55(11) 2093-1303; E-mail: joaokleberg@gmail.com

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Introduction

Merkel cells are receptors of mechanical stimuli in the basal layer of the epidermis connected to nerve terminals and hair follicles, and are slowly adapting tactile sensors of glabrous and hairy skin [1,2]. They are intensely sensitive and play an important role in localization, determination of texture, detail, pressure and even in painful sensitivity [3,4]. These mechanoreceptors are part of less than 5% of the total epidermal cells and are distributed mainly on the palms of the hands, fingers, feet and sun-exposed regions. However, they are found in mucosal tissue in smaller quantities, especially in the oral mucosa, clitoris, foreskin and esophagus [1].

Merkel cell carcinoma (MCC) has been characterized as a malignant trabecular skin neoplasm since its discovery in 1972 by Cyril Toker, chief of surgical pathology at the University of Maryland School of Medicine [5-8]. Currently, it is also known to be a rare and aggressive neuroendocrine tumor that tends to present with lymphatic and distant metastases, recurrences, and a high risk of developing other types of cancers, such as melanoma or hematologic neoplasms [1,5].

The pathophysiology of MCC has not yet been fully established, however, evidence suggests that its accelerated and ungoverned growth arises from the basal layer of the epidermis, where Merkel cells are normally located. However, other studies suggest its origin through totipotent stem cells of the dermis, which acquire neuroendocrine characteristics during their maturation [7-9].

The increased incidence of MCC in recent years has been related to the higher population life expectancy, with the peak incidence being around the seventh decade of life [5,7-13]. Besides advanced age, risk factors are male gender, fair skin, exposure to ultraviolet (UV) radiation, immunosuppression, other neoplasms and, recently, some studies have described Polyomavirus infection in

more than 80% of cases [1,7-9,12-15]. The most common sites of lesions are areas frequently exposed to the sun, thus being regions such as head, neck and upper limbs [5,9,12-15].

The aim of this study is to report the clinical case of a female patient assisted in a Teaching Hospital in the State of São Paulo, with a lesion in the left gluteal region, uncommon to what is found in the literature.

Case Report

An 87-year-old female patient with a personal history of hypertension, gastroesophageal reflux disease, and Chagas megaesophagus, a former smoker, and a former alcoholic. He performed diagnosis and follow-up in a teaching hospital in the State of São Paulo.

Performed an excisional biopsy of the lesion on the left buttock in September 2018 with an anatomopathological diagnosis (AP) of MCC, undergoing a margin increase in February 2019. In August 2019, a new lesion was observed near the operative wound, and underwent excision in November 2019, with carcinoma, and proposed margin enlargement performed in February 2020. Control imaging was also done, which showed a new lesion in the lymph node chain.

Computed tomography (CT) scan of the abdomen performed on January 22, 2021, the presence of left inguinal lymphadenomegaly measuring 2.5 cm and another performed on April 20, 2021 showing heterogeneous superficial inguinal and left external iliac lymphadenomegaly measuring up to 2.7x2.0 cm and no characterization of lymphadenomegaly in other chains.

AP exams characterized on September 26, 2018 X KI-67 positive in 80% of cells, MX chromogranin positive, X CK 20 positive dot pattern, MX AE1/AE3 positive diagnosis MCC; AP on February 1, 2019 larger tumor size 1.2 cm, thickness 0.5 cm, level of subcutaneous tissue involvement, intratumoral lymphocytes present, not prominent and nodular growth pattern; on November 1, 2019 tumor size 0. 7 cm, level of hypodermis involvement, mitotic index up to 6 mitoses in 10 high magnification fields (6/10 CGA), intratumoral lymphocytes rare; on February 28, 2020, tumor size 8.0 cm, thickness 0.7 cm, mitotic index 1/CGA, Mx synaptophysin positive, cell proliferation index greater than 50% and on February 11, 2021 infiltration by MCC.

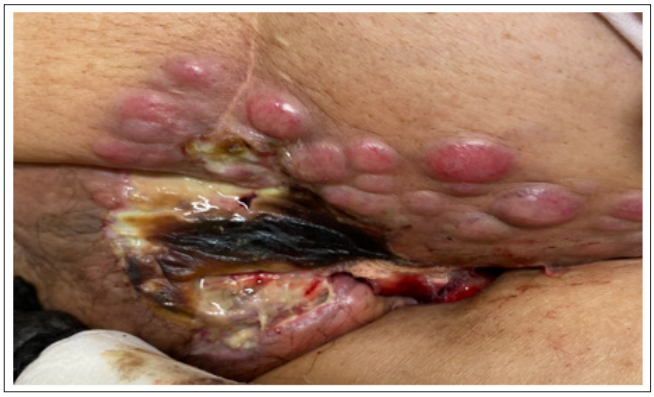

Figure 1: left inguinal region showing the clinical presentation of MCC in the form of multiple subcutaneous nodular lesions and a necrotic area.

Discussion

MCC is a rare and aggressive tumor of the skin that presents as a nodule of purple to reddish color, with an average size of 20 mm, painless, firm consistency, smooth surface and often bright, accompanied or not by telangiectasia [1,6,7,12,15]. It has rapid growth, being a single or multifocal lesion, which mainly affects regions most exposed to the sun, such as head and neck (more than 50% of cases), limbs and trunk, and more rarely in non-exposed areas, such as the buttocks [5,7,10]. Our patient had a lesion in the gluteal region, one of the few cases reported.

Most patients have local disease, but MCC has a high rate of metastasis, with the main sites of secondary lesions being skin (28%), regional lymph nodes (27%), liver (13%), lung (10%), bone (10%), and brain (6%) [5,15]. The acronym AEIOU was created to describe the characteristics of MCC: asymptomatic, rapid expansion over weeks to months, immunosuppression, advanced age (older), and UV exposure [1,8]. However, due to the variable and nonspecific presentation, MCC can be confused with other more common lesions such as basal cell carcinoma, amelanotic melanoma, squamous cell carcinoma, and lymphoma. [5,8,15].

The literature considers immunohistochemical analysis as the definitive diagnosis. The expression of cytokeratins (CK20) and neuroendocrine markers (neuron-specific enolase, intermediate filament, chromogranin and synaptophysin) is highly suggestive of MCC and helps distinguish it from small cell lung carcinoma [5-8,15]. In 95% of cases, the KIT receptor tyrosine kinase (CD117) is also expressed [15]. In addition, expression of CK7, common leukocyte antigen (CLA), S-100, TTF-1, CD45, MASH-1 HMB-45, Melan-A, desmin and myogenin are absent in MCC, allowing differential diagnosis to be made [1,8,12,13,15]. Histologically, MCC presents three patterns: 1- nodular/solid: irregular clusters of cells, similar to lymphoma (most common pattern); 2- diffuse: infiltrate of small cells in sheets, intense mitotic activity and necrosis, similar to small cell carcinoma of the lung; 3- trabecular: cords of well-defined cells and fibrous stroma (rarer pattern) [5,12].

Other exams are useful: blood count and serum electrolytes; sentinel lymph node biopsy and ultrasound-guided fine needle aspiration (FNAB) in case of suspected regional lymph node dissemination; and radiological evaluation to detect metastases. Among the imaging exams, Computed Tomography (CT) and Positron Emission Computed Tomography (PET-CT) are used to search for lesions in the thorax and abdomen, and Magnetic Resonance in regions difficult to access by ultrasonography [5,15]. Through diagnosis, staging was proposed based on the TNM classification (T: primary tumor; N: regional lymph nodes; M: distant metastasis), defined by the seventh edition of the American Joint Committee on Cancer (AJCM) [5].

Surgical treatment and adjuvant radiotherapy form the basis of MCC management, and follow-up with examinations is necessary due to the high rates of metastasis and recurrence. Surgery is performed by wide local excision with 1-2 cm margins, although some studies show that Mohs microsurgery is an option for head and neck tumors to ensure desired margins [1,5,7]. Adjuvant radiotherapy for lymph nodes is used in all cases, except in patients with negative sentinel lymph node, according to recommendations of the National Comprehensive Cancer Network [5].

Currently, patients with unresectable disease are candidates for chemotherapy as a form of palliative treatment. The most commonly used drugs are carboplatin, cisplatin, etoposide, cyclophosphamide, 5-fluorouracil, doxorubicin, and vincristine, similar to those for the treatment of small cell lung carcinoma [5,6,16]. Many studies have shown results regarding immunotherapy for metastatic MCC, and in 2017, the Food and Drug Administration (FDA)

approved avelumab, an IgG1 monoclonal antibody that binds to programmed death ligand 1 (PD-L1) protein on the surface of tumor cells, preventing their proliferation by inhibiting CD-8+ T cells [6,8,11,14]. However, many patients do not show durable responses or are not candidates for treatment, and further studies are needed to demonstrate promising results and complete response rate by immune checkpoint inhibitors [16].

Prognostic factors are tumor size, mitotic index, locoregional or distant metastasis, Breslow depth, and initiation of treatment [1,6,7,9]. MCC has a high recurrence rate within 2 years and the overall 5-year survival is 40-62% for early stage patients and 13-17% for those with distant metastasis. Some studies have proposed techniques to predict prognosis and treatment response, such as neuron-specific enolase (NSE), suggested as a biomarker able to assess disease extension and progression, and 18F-FDG PET/CT (fluordeoxyglucose), indicated in patients with suspected lymph node involvement within 2 years of diagnosis or recurrence, justified by bringing changes in staging and impact on disease management [16,17]. Despite this, early diagnosis and treatment are still essential, as MCC has recurrent negative outcomes, and our patient is one of many examples found in the literature.

Conclusion

The present study represents a case report unusual to that found in the literature, since the identified lesion is found on the left buttock of the patient, an area not usually exposed to UV rays. In addition, a new lymph node chain lesion, three recurrences and an operative wound infection accompanied by CPLA were evidenced, demonstrating a poor prognosis. The treatments were surgical, according to what the literature addresses about more effective therapies: exeresis of the gluteal lesion with a safety margin and left inguinal lymphadenectomy. Even so, the patient died after the beginning of treatment. Therefore, we can conclude that MCC is still a challenge for the medical field, since this neoplasm has a high potential for recurrence and metastasis, as observed in our patient and in several other publications. However, late diagnosis and limited and delayed treatment contribute to higher lethality rates, which were also verified in the reported case. The best way to achieve the most adequate result continues to be an early and accurate diagnosis, together with an adequate and multidisciplinary management of the patient, in this case, with the collaboration of the pathologist, radiologist, oncologist and surgeon [9,15].

Research Ethics Committee Approval: We declare that the patient approved the study by signing an informed consent form. The study followed the ethical guidelines established by the Declaration of Helsinki.

References

1. Fraga JS, Johnson LF, Freire AN, Andrade AB, Bocanegra RE, et al (2018) Carcinoma de células de Merkel: relato de caso e revisão bibliográfica. Rev. Científica HIS 2: 21-23.
2. Abraham J, Mathew S (2019) Merkel Cells: A collective review of current concepts. Int J App Basic Med Res 9: 9-13.
3. Hall JE (2017) Tratado de fisiologia médica. Tradução de Guyton & Hall. 13. ed. Rio de Janeiro: Elsevier.
4. Hahn JM, Combs KA, Lloyd CM, McFarland KL, Boyce ST, et al (2019) Identification of Merkel cells associated with neurons in engineered skin substitutes after grafting to full thickness wounds. PLoS ONE 14: e0213325.
5. Uchoa RS, Nogueira FR, Costa ML, Goes AC (2017) Merkel cell carcinoma: literature review. Fortaleza: Rev Med UFC 57: 44-49.
6. Harms PW, Harms KL, Moore PS, DeCaprio JA, Nghiem P, et al. (2015) The biology and treatment of Merkel cell carcinoma: current understanding and research priorities. Nature Reviews Clinical Oncology 763-776.
7. Selma K, Abdellah A, Soufiane B, Mouna K, Sanaa E, et al. (2017) Merkel cell carcinoma occurring in a black woman: a case report. Journal of Medical Case Reports 11:25.
8. Nicholas M, Alberto C, Armand A, Philip X (2019) Merkel cell carcinoma: a case report and literature review. Journal of Surgical Case Reports 11:1-3.
9. Carneiro C, Sbalchiero JC, Neto BR, Bracco G, Graziosi, et al. (2013) Merkel cell carcinoma: clinical presentation, prognostic factors, treatment and survival in 32 patients. Rio de Janeiro: Rev. Brasileira Cir. Plástica 28: 196-200.
10. Bellot T, Baez C, Almeida S, Venceslau M, Zalis M, et al. (2017) Molecular prevalence of Merkel cell polyomavirus in nonmelanoma skin cancer in a Brazilian population. Clinical and Experimental Dermatology 42: 390-394.
11. Garcia-Zamora E, Ganuza MV, Martin-Alcaldea J, Medrano RM, Moraleda FP, et al. (2021) Carcinoma de células de Merkel: estudio descriptivo de 11 casos. Actas Dermosifiliogr 112: 63-68.
12. Llombart B, Requena C, Cruz J (2017) Actualización en el carcinoma de células de Merkel: Epidemiología, etiopatogenia, clínica, diagnóstico y estadificación. Actas Dermosifiliogr 108: 108-119.
13. Berto J, Cuenca A, Diaz-Martinez B, Pena ML, Ruiz-Fernandez P, et al. (2005) Carcinoma de células de Merkel. Estudio de cinco casos. Actas Dermosifiliogr 96: 106-110.
14. Schoeler NC, Kayser TF, Scandolara TB, Kern R, Alves FM, et al. (2021) Metastatic Merkel cell Carcinoma: Case Report. Revista Brasileira de Cancerologia 67: e-091107.
15. Poulsen M (2004) Merkel-cell carcinoma of the skin. The Lancet Oncology 593-599.
16. Linde M, Bertolli E, Korse CM, Klop WM, Tesselar ET, et al. (2021) The Clinical Utility of Neuron-Specific Enolase (NSE) Serum Levels as a Biomarker for Merkel Cell Carcinoma (MCC). Annals of Surgical Oncology 28: 1019-1028.
17. Prior VL, Cussac BL (2021) The role of F18-FDG PET/CT in the management of Merkel cell carcinoma: The experience of 51 studies in our institution. Revista Española de Medicina Nuclear e Imagem Molecular 40: 139-148.