Metastatic Merkel cell Carcinoma: Case Report

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Carcinoma de Células de Merkel Metastático: Relato de Caso

Carcinoma de Células de Merkel Metastásico: Relato de Caso

Nathielen Caroline Schoeler[1]; Thayse Fachin Cormanique Kayser[2]; Thalita Basso Scandolara[3]; Rodrigo Kern[4]; Fernanda Mara Alves[5]; Daniel Rech[6]; Carolina Panis[7]

ABSTRACT

Introduction: The Merkel cell carcinoma is a rare cutaneous neuroendocrine tumor that originates from cells responsible for tactile sensitivity, it has an aggressive character, fast evolution and difficult treatment. **Case report:** 49 years Caucasian male patient, with a painless nodule, infiltrating deep tissue, not ulcerated and located in left arm identified during the dermatological consultation. The result of the incisional biopsy was positive for Merkel cell carcinoma. After resection of the lesion, complementary exams revealed metastatic disease in the axilla and chest wall. The chemotherapy treatment brought an initial improvement with tumor reduction, however, it was not durable, because new areas with tumor metastases in upper regions of the body were revealed, the patient was submitted to another surgical procedure, after which a new chemotherapy regimen failed. **Conclusion:** At the time of the treatment of this patient, monoclonal antibodies, such as avelumab, were not available. Early diagnosis with immediate lesion excision surgery, before the involvement of other regions, remains the best option for a better prognosis. However, regardless of this, because of the limitations at the time of the treatment, the patient died.

Key words: Carcinoma, Merkel Cell; Merkel Cells; Neoplasm Metastasis; Skin Neoplasms; Case Reports.

RESUMO

Introdução: O carcinoma de células de Merkel é um raro tumor neuroendócrino cutâneo, que se origina das células responsáveis pela sensibilidade tátil, possui caráter agressivo, evolução rápida e difícil tratamento. **Relato do caso:** Paciente do sexo masculino, 49 anos, caucasiano, que, ao atendimento dermatológico, apresentou nódulo indolor, infiltrando tecidos profundos, não ulcerado e localizado na região do braço esquerdo. O resultado da biópsia incisional foi positivo para carcinoma de células de Merkel. Após ressecção da lesão, os exames complementares evidenciaram doença metastática na axila e parede torácica. Com o tratamento quimioterápico, houve um benefício inicial com redução tumoral, porém, não durável, uma vez que foram reveladas novas áreas com metástases tumorais em regiões superiores do corpo, sendo submetido a novo procedimento cirúrgico, o qual, após novo regime quimioterápico, não obteve sucesso. **Conclusão:** Na ocasião do tratamento desse paciente, os anticorpos monoclonais, como o avelumab, não estavam disponíveis. O diagnóstico precoce com cirurgia de exérese da lesão imediata, antes do acometimento de outras regiões, permanece sendo a melhor opção para um prognóstico favorável ao paciente. Contudo, a despeito disso, com as limitações à época do tratamento, o paciente evoluiu a óbito.

Palavras-chave: Carcinoma de Célula de Merkel; Células de Merkel; Metástase Neoplásica; Neoplasias Cutâneas; Relatos de Casos.

RESUMEN

Introducción: El carcinoma de células de Merkel es un tumor neuroendocrino cutáneo raro, que se origina en células responsables de la sensibilidad táctil, tiene un carácter agresivo, una evolución rápida y un tratamiento difícil. **Relato del caso:** Paciente masculino, de 49 años, caucásico, que en atención dermatológica encontró nódulo indoloro, infiltrando tejidos profundos, no ulcerados y ubicados en la región del brazo izquierdo. El resultado de la biopsia incisional fue positivo para el carcinoma de células de Merkel. Después de la resección de la lesión, los exámenes complementarios mostraron enfermedad metastásica en la axila y la pared torácica. Con el tratamiento de quimioterapia, hubo un beneficio inicial con la reducción del tumor, sin embargo, no es duradero, ya que se revelaron nuevas áreas con metástasis tumorales en las regiones superiores del cuerpo, que se sometieron a un nuevo procedimiento quirúrgico, que después de un nuevo régimen de quimioterapia no tuvo éxito. **Conclusión:** En el momento del tratamiento de este paciente, los anticuerpos monoclonales, como avelumab, no estaban disponibles. El diagnóstico temprano con cirugía para la escisión de la lesión inmediata, antes de la participación de otras regiones, sigue siendo la mejor opción para un pronóstico favorable para el paciente. Sin embargo, a pesar de esto, con las limitaciones al momento del tratamiento, el paciente falleció.

Palabras clave: Carcinoma de Células de Merkel; Células de Merkel; Metástasis de la Neoplasia; Neoplasias Cutáneas; Informes de Casos.

[1-7]Paraná West State University. Francisco Beltrão (PR), Brazil.
[1]E-mail: natyschoeler@gmail.com. Orcid iD: https://orcid.org/0000-0002-5501-1730
[2]E-mail: thayse-c@hotmail.com. Orcid iD: https://orcid.org/0000-0003-0774-8946
[3]E-mail: thalitascandolara@hotmail.com. Orcid iD: https://orcid.org/0000-0003-4709-9207
[4]E-mail: rodrigokern1@gmail.com. Orcid iD: https://orcid.org/0000-0003-3154-0088
[5]E-mail: fernandamaraalves@gmail.com. Orcid iD: https://orcid.org/0000-0001-8464-1646
[6]E-mail: dr.rech@gmail.com. Orcid iD: https://orcid.org/0000-0002-2654-4562
[7]E-mail: carolpanis@hotmail.com. Orcid iD: https://orcid.org/0000-0002-0104-4369
Corresponding author: Carolina Panis. Universidade Estadual do Oeste do Paraná. Laboratório de Biologia de Tumores. Rodovia Vitório Traiano km 2 - Água Branca. Francisco Beltrão (PR), Brazil. CEP 85601-010. E-mail: carolpanis@hotmail.com

INTRODUCTION

Merkel-cells discovered in 1875 are responsible for tactile sensitivity[1] and result from epidermal pluripotent stem-cells[2]. Rarely, these cells become neoplastic originating the Merkel-cell carcinoma (MCC)[3]. The neoplasm develops rapidly in the chronically sun damaged skin. Usually, the tumor grows as a hemisphere and centrifuge form, infiltrating in depth to the extent that the healthy epidermal is tensioned, reaching the tissues[2,4]. MCC is confounded with pulmonary small cells carcinoma metastasis, cells B lymphoma and anaplastic melanomas whose incidence remains rare[1], and appears to be related to conditions as immunosuppression, ultraviolet sun rays-induced damages and HIV-infection (human immunodeficiency virus) and Merkel-cell polyomavirus (MCPyV)[5].

Due to the disease rarity, this case report has the objective of describing a MCC case affecting a patient at an early age, not being usual to what the literature reports.

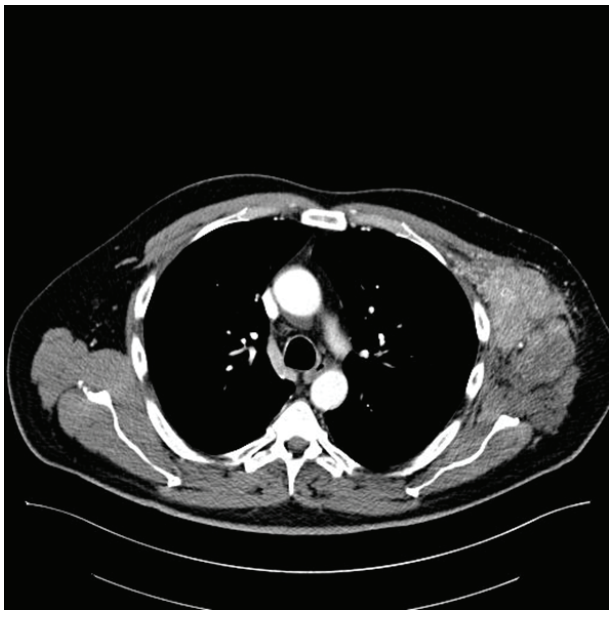

Figure 1. Image of computed tomography with axillary nodal masses at left.

CASE REPORT

One single individual case report selected due to the rarity of the neoplasm conducted at Cancer Hospital Francisco Beltrão (CEONC), Paraná, Brazil. After the Informed Consent Form was signed and the Institutional Review Board, CAAE number 34323220.8.0000.0107 approved the study, the investigation commenced. The chart was reviewed to obtain clinicopathological data and databases PubMed and SciELO were searched for literature review, including all the studies published in the period available. The patient's anonymity was protected.

Caucasian, 49 years-old male patient V.T, from Francisco Beltrão-PR, single, formerly healthy. In the beginning of 2014 sought dermatological consultation because of painless node infiltrating in deep tissues, non-ulcerated in the left arm region. At the occasion, thoracic computed tomography with contrast confirmed nodal mass at the left axillary region, measuring 13x9x6 cm (Figure 1). The exam revealed preserved pleural space, normal transparence of the parenchyma, absence of mediastinum or peri-hilar mass, pervious principal bronchi with normal situation, caliber, and borders. Yet the computed tomography of abdomen and pelvis did not identify signs of the target-lesion.

Incisional biopsy suggestive of MCC was indicated, considering the lack of neuroendocrine carcinoma history in another anatomic site. Immunohistochemical exam of the incisional biopsy was performed, the immunomarker was positive for cytokeratin 20 (CK20), which, together with the characteristics observed in the histopathological exam determined the diagnosis of MCC.

On February 2014, the patient was referred for resection of the lesion carried out at hospital A. C. Camargo, in São Paulo-SP. There are no clear records of widening of the margins and sentinel lymphadenectomy considering that lymph node infiltration in axillary region and homolateral supraclavicular were present earlier. Because of the suspicion of persistent disease, the patient was submitted to complementary tests which evidenced fusion status axillary nodes indicative of metastasis and infiltration in thoracic wall. Within this context of metastatic disease (M1), six cycles of chemotherapy with cisplatin and etoposide were indicated to begin on September 2014. At the end of the treatment, the benefit achieved reached optimal level with 25% reduction of the tumor.

On January 2015 a PET-CT showed anomalous concentration of 18F-FDG in craniocervical region (tonsillar pillar at left and bilateral cervical lymph nodes); thoracic (infraclavicular lymph node and voluminous expansive formation of axillary soft parts at left with infraclavicular extension and lateral thoracic wall) and skeletal (cutaneous densification in the posterior face of elbow at left).

In the following month, the patient was submitted to left supraclavicular and axillary lymphadenectomy associated to exeresis of the tumor mass. The mass in surgical monoblock measured 21x12x11.5 cm and weighted 1,890 grams, accompanied of striated muscle tissue. In the periphery, other ten node formations were

found, the largest with 2.8 cm. The anatomopathological report revealed small cells malignant carcinoma (MCC) with extensive necrosis areas, infiltrating ten dissected lymph nodes and compromising lymphoid, fibrous conjunctive and adipose tissues.

Clinicopathological data of the patient are described in Table 1.

Table 1. Clinicopathological characterization of the patient

Gender	Male
Age	49 years
Race or Color	Caucasian
Profession	Administrative assistant
Education	Complete university
Tobacco use	No
Alcohol use	No
Cancer family history	Yes
Anatomopathological	Axillary left clavicular lymphadenectomy (in monoblock): Merkel-cell carcinoma of small cells with extensive necrosis areas infiltrating dissected lymph nodes and compromising lymphoid, fibrous conjunctive and adipose tissues. Perineural invasion with neoplasm-free skin and muscleskelectal tissue
Puncture liquor aspiration	Oncotic negative cytology and for malignant cells with compatible cytologic aspects with inflammatory process
Treatment regimen	Cisplatin and etoposide Regimen CAV (cyclophosphamide, doxorubicin and vincristine)
Relapse	Yes, left axillary/thoracic region

Immunohistochemistry of the biopsy of the left axillary lymph node was conducted and based in the panel found (Table 2), metastatic MCC was detected.

On March 2015, the patient submitted to ultrasound when multiple nodular images were found in the transition of the cervicothoracic region at left and between the axillary medium and posterior lines, in addition to diffuse edema of the subcutaneous cell tissue of the regions investigated. Palliative chemotherapy with cyclophosphamide and vincristine (CAV) was prescribed. After the 4th cycle, the clear progression of the disease and low performance hindered the treatment completion.

Table 2. Immunohistochemical biopsy

Markers	Result
AE1/AE3	Positive
Chromogranin A	Positive
Synaptophysin	Positive
CK20	Positive
MCPyV	Positive
Melan-A	Negative

Note: Exam performed in 2015, conclusive for metastatic Merkel cell carcinoma.

DISCUSSION

MCC is an aggressive disease with rapid infiltration of tissues and early metastasis, affecting Caucasian older men, mostly in sites continuously exposed to ultraviolet rays as the upper limbs[6]. The epidemiological profile of the patient of this case is similar to what was reported in the literature – Caucasian males and upper limbs lesions – although the patient does not match the profile of older age (70 years or more)[7].

The clinical progression of 12-month survival approximately after lymph nodes metastasis were found has been already detected in other studies; patients with clinically proven lymph nodes metastasis have worse prognosis because they are classified in clinical stage IV where 5-years survival rate is below 25%[6,7].

Because of MCC suspicion, the immunohistochemical analysis is paramount for the diagnosis. The immunohistochemical positive result for MCPyV is consistent with the literature review, being associated to nearly 80% of the cases of MCC[8]. In addition, positive MCPyV tend to develop lesions in the extremities as the patient under investigation, as opposed to negative MCPyV patients with higher frequency of lesions in head and neck[9].

No information was found about why radiotherapy treatment together with primary surgery and resection was not done, considering that MCC is still a disease restricted to the origin anatomic site. In 2016, the Food and Drug Administration (FDA) approved the use of avelumab, a immunoglobulin G1 monoclonal antibody (IgG1) that binds to the programmed-death ligand protein 1 (PD-L1) inhibiting cells T CD 8, necessary for the tumor

proliferation and with this, slowing down the immune response involved in the pathogenesis of MCC, being effective for the treatment[2,10]. This therapy, however, was unavailable then.

The patient initiated chemotherapy after metastasis was evident with cisplatin + etoposide, reaching consistent results already found in the literature: initial benefit with tumor reduction, but non-durable, since few months later new metastatic areas were found spread in the upper body area, classified as stage IV. The chemotherapy CAV regimen usually for lung cancer was utilized for the relapse; but due to histopathological and cytochemical similarities, it was applied to the MCC although with palliative objective alone[7]. In despite of this, the chemotherapy regimen did not stop the progression of the disease, was discontinued and the patient died.

CONCLUSION

Considering the low incidence of this type of neoplasm and the considerable lack of information about an effective and well-established treatment in the literature, the therapies to be used in the treatment are extremely limited. The early diagnosis with urgent lesion exeresis prior to the compromise of other regions remains the best manner of favorable prognosis to the patient. In this case report, the main characteristics correspond to what was found in the literature, except the diagnosis which, as opposed to the statistics, was early.

CONTRIBUTIONS

All the authors contributed for the study conception and/or design, gathering, analysis and interpretation of the data, wording, critical review and approved the final version to be published.

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DECLARATION OF CONFLICT OF INTERESTS

There is no conflict of interests to declare.

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