v. 4, n. 13, 2024

International Journal of Health Science

MERKEL CELL CARCINOMA: A CASE REPORT

Alana Carla Albuquerque Sarmento
Department of Head and Neck Surgery at: ``Hospital do Câncer de Pernambuco``
Recife – Pernambuco
http://lattes.cnpq.br/1119624935920222

Danielle Patrícia de Morais de Azevedo
Department of Head and Neck Surgery at: ``Hospital do Câncer de Pernambuco``
Recife – Pernambuco
http://lattes.cnpq.br/1149175540276569

Daniele Martins de Sá Carneiro
Department of Head and Neck Surgery at: ``Hospital do Câncer de Pernambuco``
Recife – Pernambuco
http://lattes.cnpq.br/9100975013566916

Gabriela Silva De Almeida
Centro Universitário Maurício de Nassau
Recife – Pernambuco
http://lattes.cnpq.br/0897690141770177

Carlos Vinícius Goiana Pinto Simeão
Centro Universitário Maurício de Nassau
Recife – Pernambuco
http://lattes.cnpq.br/6425223313760837

Ísis Coutinho Albuquerque de Oliveira
Centro Universitário Maurício de Nassau
Recife – Pernambuco
http://lattes.cnpq.br/5369648333298968

Maria Fernanda Torres Modesto Pinheiro.
Faculdade Pernambucana de Saúde Recife – Pernambuco
http://lattes.cnpq.br/3308557648513459

Lucas Silvestre Araújo
Faculdade Pernambucana de Saúde Recife – Pernambuco
https://lattes.cnpq.br/9151149595740055

Abstract: Primary Neuroendocrine Carcinoma or Merkel Cell Carcinoma (MCC) is a rare and aggressive skin neoplasm that presents as an asymptomatic and rapidly growing skin lesion, affecting immunocompromised people and/or people over 50 years of age, with significant sun exposure. The diagnosis is made through biopsy, whether or not associated with immunohistochemistry. The treatment of choice is surgical excision with an adequate margin, associated with adjuvant radiotherapy and, depending on the stage, chemotherapy and/or immunotherapy. This study provided reports that can serve as evidence about the clinical history and hospital management of patients with MCC.
Keywords: Merkel Cell Carcinoma, Primary Neuroendocrine Carcinoma, Cutaneous Neoplasia

INTRODUCTION

Primary Neuroendocrine Carcinoma or Merkel Cell Carcinoma (MCC) is a rare and aggressive skin neoplasm, which has the highest number of fatal cases among skin tumors when compared to other aggressive skin cancers (1). Like melanoma, CCM is considered rare, as its annual incidence is 0.2-0.45 cases per 100,000 inhabitants, being 100 times less frequent than melanoma (2). It presents as an asymptomatic and rapidly growing skin lesion, affecting immunocompromised people and/or people over 50 years of age, with significant sun exposure. In this sense, more than half of Merkel cell carcinomas (MCC) occur in the head and neck of elderly people, in areas of actinically damaged skin due to sun exposure (1).

Regarding its cytological etiology, it is necessary to understand the uniqueness of Merkel cells, which have scant cytoplasm and a round or oval nucleus with fine,

evenly dispersed chromatin. In addition, it has desmosomal connections with the surrounding keratinocytes, intracytoplasmic aggregates of intermediate filaments and numerous dense central granules linked to the membrane - with changes in these connections facilitating diagnosis by electron microscopy by highly trained professionals (3)

The tumor often presents as a painless mass on the surface of the skin or just below it, assuming an erythematous or violet appearance with bleeding and superficial ulceration, which may be late findings suggestive of advanced disease. Furthermore, MCCs are found close to other lesions, most frequently adjacent to Squamous Cell Carcinoma, Basal Cell Carcinoma, solar keratoses and lentigo maligna, with 53% of MCCs in the head and neck region (4). This tumor, in addition to the high power of lymph node metastasis, presents as its main complications the involvement of the brain, bones, liver and lungs, with distant metastases - due to the high level of aggressiveness of the disease - being the main predictors of a fatal condition.

Diagnosis is through biopsy, associated or not with immunohistochemistry, but this is often used for diagnostic confirmation, whose main markers are NSE, low molecular weight cytokeratins and neurofilament protein (5). Imaging exams, in turn, are essential for defining appropriate staging and treatment, as they identify and locate metastases efficiently. The treatment of choice is surgical excision with an adequate margin, associated with adjuvant radiotherapy and, depending on the stage, chemotherapy and/or immunotherapy.

In terms of prevention, the ideal context would be to inhibit the main risk factor for skin cancer: sun exposure. Therefore, reducing exposure, using sunscreens and protective clothing are essential. Also avoiding exposure to indoor tanning and sun lamps are important measures to prevent CCM (6). This care, therefore, must be taken with greater care in patients with a personal history of skin cancer, as they have a high positive predictive factor for this specific type of cancer.

CASE REPORT

Female patient, 50 years old, referred to the head and neck clinic, presenting a solid nodular lesion in the right malar region, raised, smooth, brownish broncho, measuring 3.2 x 2.7 x 2.1 cm (TR x L. x AP) in Computed Tomography (CT). The resection of a soft tissue tumor was performed in the mentioned topography, the biopsy of which resulted in an "unidentified neoplasm". When the immunohistochemical examination was performed, bone exposure in the right malar region and infiltration in the floor of the ipsilateral orbit were identified and the suspicion of Merkel Cell Carcinoma was confirmed. Preoperative exams and a new CT scan were urgently requested.

In a new CT scan of the neck, face, chest, upper abdomen and pelvis, staging was performed and distant metastases, cervical, mediastinal, retroperitoneal lymph node enlargement, in the upper abdomen or pelvic cavity were ruled out. The tumor was located in the subcutaneous and muscular plane, however, with a cleavage plane with the adjacent cortical bone, without evidence of bone erosion.

After discussion at a round table, the procedure defined was right total maxillectomy with orbital exenteration and right partial parotidectomy with neck dissection from levels I to V and reconstruction using the temporal and middle frontal muscles. The intervention was carried out uneventfully and the patient was discharged from hospital on the second post-operative day.

The anatomopathological examination of the surgical specimen showed margins, parotid glands and lymph nodes free of

disease. After evaluation by the oncology team, the need for adjuvant chemotherapy was ruled out, however radiotherapy was indicated. Therefore, the patient underwent radiotherapy to the malar region and the tumor bed, obtaining a good response and improving the prognosis.

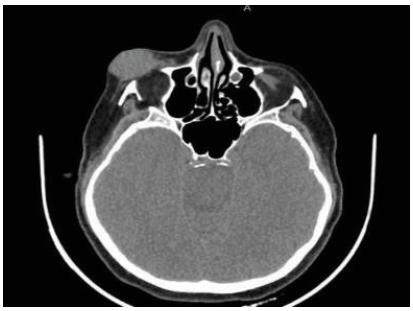

Figure 1: Solid nodule measuring 3.2 x 2.7 x 2.1 cm on CT, in topography of the right malar region.

Source: Authors' records

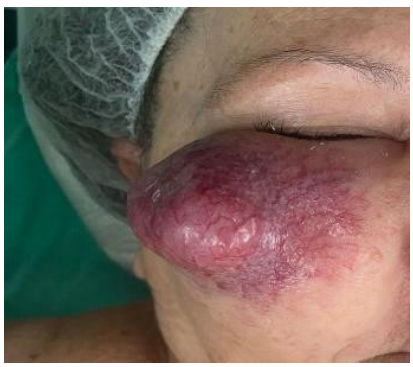

Figure 2: Record of a solid nodular lesion in the right malar region, elevated, smooth and brownish broncho before the first surgical intervention.

Source: Authors' records

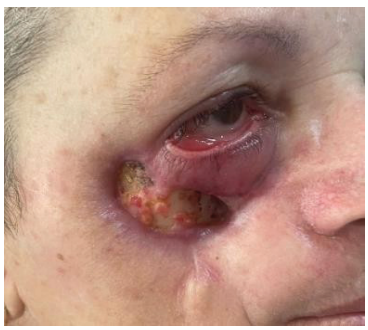

Figure 3: Return 2 months postoperatively in which the patient presented bone exposure and infiltration of the orbital floor.

Source: Authors' records

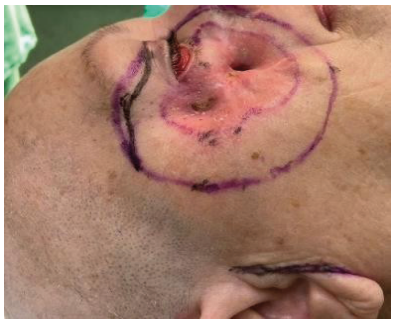

Figure 4: Pre-operative demarcation in the surgical suite, to perform right total maxillectomy with orbital exenteration and right partial parotidectomy with neck dissection.

Source: Authors' records

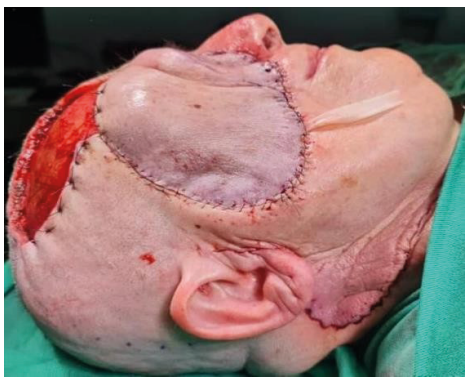

Figure 5: Immediate postoperative period, demonstrating reconstruction performed using a graft of the middle and frontal temporal muscles

Source: Authors' records

Figure 6: Result on the first day after surgery.

Source: Authors' records

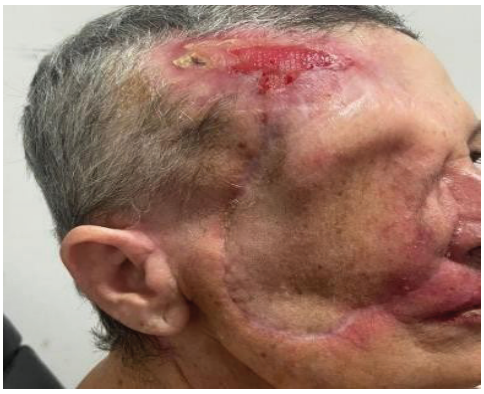

Figure 7: Result in the fourth month after surgery and after radiotherapy.

Source: Authors' records

DISCUSSION

Merkel Cell Carcinoma (MCC) is a disease with a low probability of survival, due to its aggressive dissemination nature. Local metastases recur in 44% of patients, while multiple local recurrences are less frequent, representing 15% of all patients. However, its manifestation is reported as painless, rapidly growing nodules, mainly in elderly Caucasians or young adults with ectodermal dysplasia syndrome. (1) The age of onset is on average 68 years old, with no gender preference observed. CCMs generally present as hardened plaques or violaceous (red or deep purple) nodules, solitary and dome-shaped with a shiny surface, telangiectasias and possible ulceration, measuring about 0.7 – 1.2 cm in diameter in the majority.

Based on therapies for the treatment of CCM, we can highlight two that are current in the international context. Firstly, pharmacological therapy is based on the monoclonal antibody anti-programmed death ligand –1 (Anti-PD-L1) and immunoglobulin G1 (IgG1), the medicine of which is called Avelumab (Bavencio), (8) Thus the approval of Avelumab was based on the open-label, single-arm, multicenter JAVELIN Merkel 200 study, carried out in 88 patients with histological confirmation of metastatic MCC and who experienced disease progression during or after administration of chemotherapy for distant metastatic disease. The overall response rate (ORR) reached 33% (29 patients), the partial response rate (PRR) was 22%, and the complete response rate (CRR) was 11%. Eight-six percent of tumor responses lasted at least 6 months (25 patients) and 45% lasted at least 12 months (13 patients) with duration of response (DOR) lasting from 2.8 to more than 23.3 months. (7)

In Brazil, however, surgical therapy is the most used in cases where the cure potential is high, with the decision to use this method based on the staging of the disease (11). The system used is the Yiengpruksawan, which divides patients into three stages of the disease, based on the size of the tumor and its dissemination (presence or absence of metastasis) (9). In this sense, the patient in this case was classified as stage II, but without distant metastases, which allowed surgical intervention with excision of the primary lesion and lymph node dissection due to the aggressiveness of the tumor to adjacent nodes.

MCC is a radiosensitive tumor, and radiotherapy is currently used as an adjuvant treatment. Most clinical studies demonstrate better local control rates when there is adjuvant radiotherapy after surgical excision, as irradiation of the primary site and primary lymph node drainage areas is essential for a better prognosis and is recommended in most cases, as an example the patient analyzed. (10)

CONCLUSION

As it is a rare and aggressive histological change, the knowledge obtained through observation of clinical reports with positive outcomes becomes essential for the collaboration of adequate therapeutic management of patients diagnosed with Merkel Cell Carcinoma.

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