v. 4, n. 14, 2024

International Journal of Health Science

METASTATIC MERKEL CELL CARCINOMA IN INTRAPAROTID LYMPH NODE WITH OCCULT PRIMARY: CASE REPORT

Rafael Scarpari
Hospital São Vicente de Paula - Guarapuava/ PR - Department of Head and Neck Surgery
Guarapuava – PR
https://lattes.cnpq.br/1196455167437122

Andressa Lima da Silva
Centro Universitário Campo Real
Guarapuava – PR
https://lattes.cnpq.br/7788238136619043

Isabela Cequinel
Centro Universitário Campo Real
Guarapuava – PR
http://lattes.cnpq.br/3001970546571084

Abstract: Representing 1% of skin malignancies, Merkel carcinoma is a rare neuroendocrine skin cancer with significant metastatic potential. Its incidence is higher in elderly males, Caucasians and immunosuppressed people, with risk factors being infection by Merkel cell polyomavirus and exposure to the sun. We report a case of an elderly patient with intraparotid lymph node metastasis with an occult primary, which according to the literature, is a rare manifestation (0.8%) of Merkel carcinoma - by not knowing the origin of the metastasis, the diagnostic and therapeutic challenge increases.
Keywords: Merkel Carcinoma, Occult Primary Neoplasm, Skin Neoplasm, Merkel Cell, skin cancer.

INTRODUCTION

Merkel carcinoma (MCC) was initially described as "trabecular carcinoma" by Cyril Toker. But, after neurosecretory granules were found in tumor cells, very similar to Merkel cells, the name was changed to CCM (DELLAMBRA, E. et al., 2021).

Representing only 1% of cutaneous malignancies CCM is a rare aggressive neuroendocrine skin cancer (GAUCI, M.L., et al., 2022) whose 5-year survival rate is between 48 and 63% (DELLAMBRA, E. et al., 2021; GAUCI , M.L., et al., 2022). The incidence is higher in elderly, white, immunosuppressed and male individuals (DELLAMBRA, E. et al., 2021; GAUCI, M.L. et al., 2022; PULIDO, C.F. et al., 2022; SIQUEIRA et al., 2023).

Merkel cell polyomavirus (MCPyV) infection and sun exposure are two of the main molecular pathogenic pathways for MCC due to their high mutational rates (DELLAMBRA, E. et al., 2021; GAUCI, M.L. et al., 2022).

The pathogenesis of this tumor is not well known, but it is known that the two factors (MCPyV infection and UV radiation) disrupt cellular repair mechanisms through the expression of viral proteins or the high frequency of DNA damage, respectively (DELLAMBRA, E. et al., 2021; GAUCI, M.L. et al., 2022).

CASE REPORT

Male patient, 64 years old, previously hypertensive, presenting for 8 months with a well-defined nodule, located in the superficial pole of the right parotid, measuring 1.8 cm x 1.5 cm and without lymph node enlargement. After 8 months, on physical examination, the nodule was 2 cm well defined, mobile, painless, without recent growth and without signs of facial paralysis. In the complementary ultrasound examination (USG), an 8 mm thyroid nodule and a 2 cm parotid nodule were found, without lymph node enlargement. FNAB - fine needle aspiration biopsy - was requested and a benign nodule was found in the thyroid and pleomorphic adenoma in the parotid gland. Due to the size of the lesion, surgery was indicated.

Upon performing partial parotidectomy in oncology, a 3 cm nodule was found in the lower region of the superficial pole of the right parotid (figure 1). The facial nerve was without particularities - therefore preserved - and there was no presence of suspicious lymph nodes enlargement**.**

The patient evolved well, without complications or sequelae. In the pathological anatomy of the surgery, a poorly differentiated neoplasm was identified, metastatic to one lymph node of eleven isolates, without extracapsular extension and histologically preserved parotid. Diagnostic complementation was then requested with an immunohistochemical test, which demonstrated compatibility with CK20 +/3, Pan CK AE1/AE3 +++/3, Synaptophysin +++/3, confirming Merkel Cell Carcinoma.

Post-operative PET CET (figure 2) did

not demonstrate metabolic signs of active neoplasia. Since it was a single lymph node metastasis - with no evidence of primary - and absence of distant disease, treatment with adjuvant radiotherapy was chosen. Currently, the patient is being followed up with no signs of recurrence.

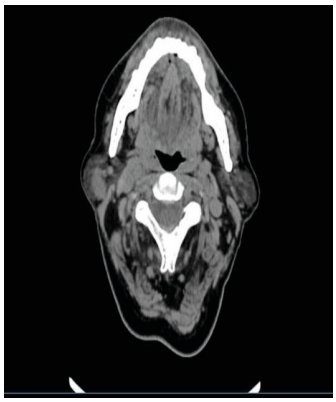

Figure 1 - CT scan demonstrating injury in the right parotid.

Source: own authorship.

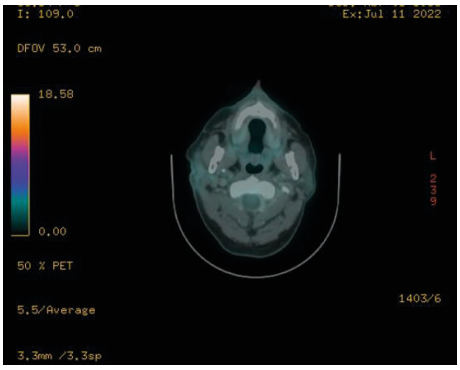

Figure 2 - Post-operative PET CET without metabolic signs of active neoplasia.

Source: own authorship.

DISCUSSION

Merkel Cell Carcinoma is a rare skin tumor with great metastatic potential and a poor prognosis. The common presentation of CCM occurs from the primary manifestation of a firm plaque or nodule, whose main location is in sun-exposed areas - such as extremities (36.9-45%), head and neck (29-43.9%) - and rarely in areas that are protected - such as thighs and abdomen (5-10%) (GAUCI, M.L. et al., 2022). This lesion has a skin-like or red color, increases in size quickly and can develop ulcerations (GAUCI, M.L. et al., 2022). This tumor has a high frequency of metastases in lymph nodes and distal organs, such as liver, bones, pancreas, lung and brain, while the oral mucosa and parotid gland are rarely affected (DELLAMBRA, E. et al., 2021; GAUCI, M.L. et al., 2022).

In 0.8% to 14% of cases there is no known primary tumor and the disease manifests itself through metastases in distant organs or lymph nodes (GAUCI, M.L. et al., 2022). Thus, the reason for the rarity of the reported case is shown. The patient did not present the primary manifestation common to occur in MCC, but rather a metastatic neoplasm to the lymph node identified in the pathological anatomical examination of the surgery.

In these cases, immunohistochemistry is used to verify the presence of important biomarkers for confirming the diagnosis and differentiating MCC from other tumors. MCC is often confused with other malignant tumors (basal cell carcinoma or squamous cells) and benign lesions, as its clinical presentation is nonspecific, therefore it is important that suspicious lesions are biopsied and their diagnosis verified (DELLAMBRA, E. et al., 2021; GAUCI, M.L. et al., 2022).

The biopsy can be performed by puncture, incision or excision. The histological characteristics are nests of small undifferentiated blue, round, uniform cells, with scant cytoplasm, large lobulated nucleoli, high mitotic rates and, occasionally, necrotic cells (GAUCI, M.L. et al., 2022). Immunohistochemistry is important for differential diagnosis (DELLAMBRA, E. et al., 2021).

The most common mutations found in CCM are the p53 and Rb proteins, but they are not specific to CCM. Among the most

important biomarkers used in differentiation are cytokeratin (CK) AE1/AE3, synaptophysin and CK20 - a pathognomonic biomarker (DELLAMBRA, E. et al., 2021; GAUCI, M.L. et al., 2022). Immunohistochemistry tests performed on the patient revealed a pattern corresponding to the pathognomonic markers of MCC, which confirmed Merkel Cell Carcinoma with an occult primary.

For diagnosis with unknown primary tumor, MCC will be negative for thyroid transcription factor 1 (TTF-1, a marker present in small cell lung cancer), S-100 and HMB-45 (melanoma) (GAUCI, M.L. et al, 2022).

Despite the knowledge of markers and mutations, the cell of origin of the carcinoma remains unknown. The most likely candidates are pre-B cells, epidermal stem cells and, in recent evidence, interfollicular basal keratinocytes. Extracutaneous sites, such as the parotid, reported in the case, are rarely involved (approximately 0.5% of cases) (GAUCI, M.L. et al., 2022).

Due to the aggressive profile of MCC, therapeutic choices for advanced cancer generally involve a combination of surgery, radiotherapy, chemotherapy and immunotherapy (DELLAMBRA, E. et al., 2021). First-line treatment combines surgical excision with margins and adjuvant radiotherapy (GAUCI, M.L. et al., 2022), and this was the treatment chosen for the patient described in the case.

Spontaneous regressions have been recorded, although rare, and most come with a good prognosis. Although the restitution mechanisms are unknown, there is a chance that the lesions caused by biopsies and partial excisions caused a local anti-tumor inflammatory response that culminated in the elimination of the tumor (GAUCI, M.L. et al., 2022). This injury-regression relationship generates the hypothesis that the patient's primary tumor may have disappeared after an injury or unintentional local inflammatory response, leaving only the parotid tumor.

REFERENCES

DELLAMBRA, E. et al. **Merkel Cell Carcinoma**. **Biomedicines**, v. 9, n. 7, p. 718–718, 23 jun. 2021. Disponível em: https://doi.org/10.3390/biomedicines9070718

GAUCI, M.L. et al. **Diagnosis and treatment of Merkel cell carcinoma: European consensus-based interdisciplinary guideline – Update 2022**. E**uropean Journal of Cancer**, v. 171, p. 203–231, 1 ago. 2022. Disponível em: https://doi.org/10.1016/j.ejca.2022.03.043

PULIDO, C.F. et al. **Clinicopathological features, MCPyV status and outcomes of Merkel cell carcinoma in solid-organ transplant recipients: a retrospective, multicentre cohort study. Journal of the European Academy of Dermatology and Venereology**, v. 36, n. 11, p. 1991–2001, 14 jun. 2022. Disponível em: https://onlinelibrary.wiley.com/doi/10.1111/jdv.18256

SIQUEIRA, S. et al. **Merkel cell carcinoma: epidemiology, clinical features, diagnosis and treatment of a rare disease**. **Anais Brasileiros de Dermatologia**, v. 98, n. 3, p. 277–286, 1 maio 2023. Disponível em: https://doi.org/10.1016/j.abd.2022.09.003