CASE REPORT

Active surveillance after complete spontaneous regression of a metastatic Merkel cell carcinoma of the head

Alvaro Sanabria1,2*, Iván Vega3, Lizeth Sánchez4

Abstract

Complete spontaneous regression (CSR) of Merkel cell carcinoma (MCC) is a known phenomenon. There are no reports of an active decision to avoid resection or adjuvant treatment and keep surveillance after CSR of MCC in the literature. An 84-year-old Caucasian male patient with a 6×5 cm MCC on the left forehead, with evidence of satellite nodules and a lymph node conglomerate in the left parotid region compatible with metastasis and confirmed by 18F-FDG PET-CT, presented CSR of the neoplasm. The use of PET-CT and non-operative active surveillance strategy can assist with monitoring response, thus avoiding unnecessary resections.

Keywords: Merkel cell carcinoma; spontaneous neoplasm regression; active surveillance; 18F-FDG PET-CT.

Introduction

Merkel cell carcinoma (MCC) is an rare aggressive neuroendocrine tumor of the skin. It is commonly presented as an asymptomatic violet or pink nodule of rapid growth, usually located in sun exposed areas of the head and neck. It usually occurs in Caucasian, older, immunocompromised patients. Almost a third of patients present with metastatic regional lymph nodes and have a high potential of local recurrence and systemic metastasis. The accepted treatment is surgical resection with wide margins and lymphadenectomy of the appropriate nodal basins. Adjuvant radiation therapy (RT) is usually added, resulting in increased overall survival for early stage tumors. Chemotherapy has not been proved beneficial1.

Complete spontaneous regression (CSR) is a known phenomenon that occurs in some tumors such as melanoma. Few cases of CSR of the primary tumor in MCC after biopsy or resection have been reported. The number of cases of CSR of metastatic disease is smaller, with only seven reports to date2. Most cases have occurred after unresectable late recurrence, with treatment denial by the patient or because of the physician’s decision due to comorbidities.
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and surgical risks; however, there are no reports of an active decision to avoid resection or adjuvant treatment and keep surveillance in the literature. This last option is currently a possibility due to the availability of positron emission tomography–computed tomography (PET-CT), which has been used for monitoring response in other tumors with immunologic mediated mechanisms.

We present a documented case of MCC metastatic to regional lymph nodes where medical decision of active surveillance was taken supported by PET-CT evidence of CSR of the neoplasm.

Case report

An 84-year-old Caucasian male patient, with chronic kidney disease (stage 3B) and a previous history of multiple resections of basal and squamous cell carcinomas of the face, presented with a highly vascularized, fast-growing, 6×5 cm nodule on the left forehead associated with perilesional small nodules in April 2018. Additionally, an increase in volume of the left parotid region was identified. An incisional biopsy was performed and revealed “suspicion for neuroendocrine tumor”. Pathological review confirmed a neoplasm of round and small cells with granulated chromatin in the nucleus, with an infiltrative pattern. Immunohistochemistry demonstrated characteristics of MCC (positivity for AE1-AE3, CAM5.2, CK20, chromogranin, synaptophysin; negativity for CK7, TTF1, LCA) with a Ki 67 proliferation index of 60%, lymphovascular invasion, >10 mitosis/field, and >6 mm depth. The patient was evaluated in a Head and Neck Clinic in July 2018 after biopsy. At the first evaluation, a mobile exophytic nodular 5 cm mass was found on the left forehead invading the eyebrow, but not the eyelid, with evidence of satellite nodules in an area of approximately 7 cm (Figure 1). A lymph node conglomerate of approximately 4 cm in the left parotid region and a palpable lymph node (level II) of 2.5 cm on the neck were also found. As part of disease staging, brain, thorax and head and neck CT scans were performed, and confirmed clinical findings without bone invasion of the skull or lung metastases. In addition, an 18F-fluorodeoxyglucose positron emission tomography–computed tomography (18F-FDG PET-CT) scan was performed in order to rule out systemic compromise, and showed hypermetabolic foci on the forehead and in the left parotid region (Figure 2). The case was presented in a multidisciplinary meeting for consideration of therapeutic alternatives, where surgery, fully human monoclonal antibody (Avelumab), and palliative RT were discussed. Finally, the patient was scheduled to undergo wide local resection plus left total parotidectomy, left supraomohyoid neck dissection, and skin graft reconstruction. Due to the patient's age and comorbidities, a complete preoperative evaluation that included blood tests, spirometry, and echocardiography was conducted. All these administrative and clinical processes took three weeks. Four weeks after the first visit and one day before the surgical procedure, the patient was reevaluated, and the family reported that the red nodules had become black and had shrunk, with evidence of these changes confirmed by cell phones photographs (Figure 1). Due to the possibility of spontaneous regression of the tumor, the surgery was suspended. The attending surgeon decided to present published evidence of CSR to the patient, analyze the risks and benefits of delaying resection, and involve the patient and his family in the decision making process. Finally, an active surveillance strategy with photographic follow-up every three days and
weekly clinical evaluation was agreed. The follow-up demonstrated progressive shrinking of the neoplasm due to dry necrosis of the primary tumor with disappearance of the parotid gland and neck lymph nodes, spontaneous scarring of the original margins of the tumor, and eventual CSR of the tumor and metastasis. In November 2018, a follow-up PET-CT scan was performed, and showed lack of metabolic activity in previous locations of tumor and metastasis (Figure 2). In the last clinical evaluation conducted in January 2020, there was no evidence of tumor (https://youtu.be/dg0F2ndIFUE).

Figure 1. Clinical evolution of the Merkel cell carcinoma of the forehead.

Figure 2. Imaging for evaluation of locoregional stage. A and B - ¹⁸F-FDG PET-CT performed at disease staging; on the left, a PET-CT 3D body scan and PET-CT axial and coronal slices; at the top, presence of abnormal metabolic activity in the lesions on the left frontal and parotid regions (arrows); there is no other tumor evidence in the body. C and D - Follow-up with another ¹⁸F-FDG PET-CT scan performed after 12 weeks shows no evidence of previously known lesions.
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Discussion

Incidence of MCC is still low, but it has been progressively growing due to population aging and advance in diagnostic techniques. MCC is an aggressive neuroendocrine tumor with an early potential for regional lymph nodes and distant metastasis. Most tumors occur in the head and neck region of elderly Caucasian individuals. Although most tumors are discovered as resectable nodules in the skin, the finding of locoregional nodal compromise worsens prognosis and survival.

Surgical resection with neck dissection is the preferred treatment when patient medical conditions allow it. Often, adjuvant RT is offered without significant advantages to disease or overall free survival, and recent trials using Avelumab have presented acceptable results in a selected group of patients.

Spontaneous regression is a relatively common phenomenon in melanoma, but CSR is very rare in these tumors. CSR of regional metastatic MCC is an extremely rare event (1-3% of all regressions), and only seven cases have been reported in literature, four of them only after biopsy\(^2\). However, these tumors present rapid growth after onset (1-5 months), and when this occurs, the long-term prognosis is good, with identification of small number of late recurrences in case series\(^2,3\).

There are no clinical factors that enable prediction of CSR. CSR is probably mediated by a T-cell immune reaction linked to activation of a response stimulated by the surgical intervention and apoptosis. Histological findings of surgical specimens have shown infiltration by foamy macrophages, fibrosis, and CD3+, CD4+ and CD8+ T-lymphocytes. Some authors have suggested that this reaction could be a consequence of the surgical trauma produced by the biopsy, but most patients undergo this procedure, and only a minimal number have presented CSR.

Most reported cases of CSR occurred after biopsy or after an attempt to primary resection with an early recurrence. Connelly et al.\(^4\) and Richetta et al.\(^5\) reported cases similar to this, with metastasis to the parotid gland and the neck, but neither suggested an active surveillance based on clinical evaluation and imaging monitoring without specific treatment.

Although the number of cases is small, the reports published support the existence of the CSR phenomena and allow a close and active surveillance protocol for patients with clinical evidence of regression. For instance, Richetta et al.\(^5\) aborted systemic treatment after clinical evidence of tumor regression and Ahmadi Moghaddam et al.\(^2\) suspended surgery after findings of regression. We opted for active surveillance based on objective photographic evidence of regression, but under close monitoring to detect progression. Another factor involved the suspicion that a new surgical procedure could cause immunosuppression and thus interrupt the ongoing immune response.

In contrast, pathological evidence of total regression is not necessary if the clinical findings can be confirmed by other tests. Ahmadi Moghaddam et al.\(^2\) reported single necrotic cells after resection of the face primary tumor and sentinel lymph nodes; Ciudad et al.\(^3\) reported lymphocyte infiltration after resection of a regressing nodule on the cheek; Richetta et al.\(^5\) reported that parotidectomy after complete clinical and
radiological regression of lymph node metastases only identified fibrosis, vascular congestion, and lymphocyte infiltrate. In our case, surgical procedures were avoided based on the findings of a second PET-CT scan that showed complete disappearance of hypermetabolic foci, extrapolating results of monitoring with other tumors. Currently, 18F-FDG PET-CT is of primordial value in the management of different types of cancer. In the initial stage, behavior after an 18F-FDG PET-CT scan can be modified in 36% of cases, and this raises to 39% when the monitoring therapy is conducted through this diagnostic method.

However, close follow-up is necessary, because some cases of complete locoregional regression have presented systemic recurrence after a few months.

In conclusion, CSR of MCC is a phenomenon that can occur, and surgeons should be aware of it. Although the number of these cases is small, if there is a clinical suspicion for CSR, an active surveillance strategy can be offered to the patient under strict follow-up conditions. The use of PET-CT scans, due to their capability to assess metabolic activity, and the experience with other tumors, can assist with monitoring response, thus avoiding unnecessary resections.

References


