FDG-PET/CT for Spontaneous Regression of Metastatic Merkel Cell Carcinoma: Friend or Foe?

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Merkel cell carcinoma (MCC) is a rare, aggressive, neuroendocrine carcinoma. It is a skin cancer of sun-exposed areas, especially the head and neck. It affects mostly elderly Caucasians and there is a slight male predominance. It has a tendency for lymph node metastases and local recurrence [1]. The estimated incidence is 0.6 per 100,000 persons in the United States. It is highly fatal, with a 5-year survival rate of 25% when metastases are present and 75% when they are not [1]. Yet, several reports have reported spontaneous regression in this aggressive cancer [2]. Currently, this phenomenon is rare and unpredictable.

FDG-PET/CT (2-deoxy-2 fluoro-D-glucose positron emission tomography/computed tomography) is becoming widely available as a powerful imaging modality, combining the ability to detect active metabolic processes and their morphologic features in a single study. Previous case series have demonstrated the high impact of FDG-PET/CT use in the treatment of primary lesions, nodal disease and distant metastases of MCC. FDG-PET/CT was found to be a valuable staging tool in MCC management, reaching a sensitivity of 95.5% and specificity of 89.1% [3].

We present a case of Merkel cell carcinoma of the eyelid, which had metastasized to the parotid gland and to the ipsilateral cervical lymph nodes (level 2). Parotid and nodal metastases were demonstrated by CT and magnetic resonance imaging (MRI). In addition, FDG uptake in these areas was intense. Preoperative tissue diagnosis of the parotid mass was made by ultrasound-guided fine needle aspiration (FNA). Two weeks later, the patient underwent a parotidectomy with neck dissection during which the tumor was found, unexpectedly, to have spontaneously regressed. We present and discuss the role of FDG-PET/CT in rapid MCC regression.

PATIENT DESCRIPTION

An 87 year old white female presented to the Ophthalmology Department with a tan cystic growth over her left upper eyelid margin. The growth had recently appeared and had reached the size of a few millimeters in diameter. The patient was treated with deralin for high blood pressure and coumadin for atrial fibrillation. Complete resection was performed. The specimen was composed of small blue basaloid cells with a foamy appearance [Figure 1A]. Immunohistochemistry was positive and showed a dot-like and membranous staining with chromagranin [Figure 1B] and with cytokeratin-20 [Figure 1C], but not with CD56. There was an abundance of mitotic figures. The morphology was consistent with Merkel cell tumor. There was no adenopathy at the time (sentinel lymph node biopsy was not performed), and all routine blood tests were normal. The patient was advised to attend serial follow-up. Five months later, she presented to the otolaryngology head & neck surgery clinic with ipsilateral lymphadenopathy and a painless swelling in her left parotid gland. Neck CT, MRI, and FDG-PET/CT [Figure 2] showed a 23 mm mass in the parotid gland and several suspicious enlarged cervical nodes (level 2). The FDG-PET/CT maximal standardized uptake value was 10.6. The parotid mass was positive for MCC on cytological analysis. Two weeks later total parotidectomy with unilateral selective neck dissection was performed. Although there was some reduction in the size of the parotid mass, it was still palpable at the time at surgery. The recovery was uneventful, and the pathology report revealed all specimens to be free of cancer [Figure 3]. The area of the parotid mass was identified and

Figure 1. Left eyelid. **[A]** Classical nuclear washed-out pattern (x400 magnification) of Merkel cell carcinoma on H&E staining, **[B]** peri-nuclear stippling of chromogranin, and **[C]** cytokeratin-20 (CK-20)

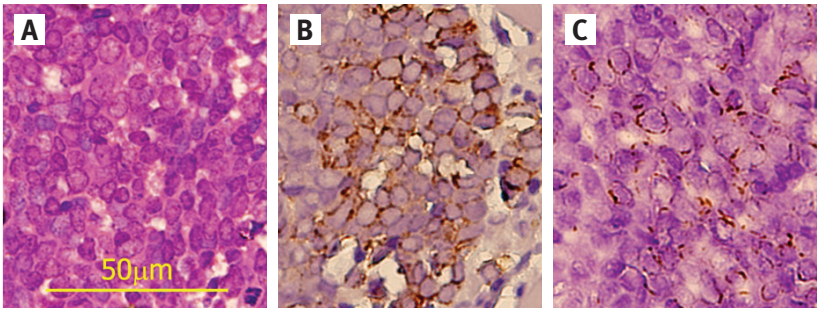

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Figure 2. Left parotid gland with 23 mm mass demonstrated on **[A]** CT scan, **[B]** MRI, and **[C]** FDG-PET/CT (standardized uptake value of 10.6)

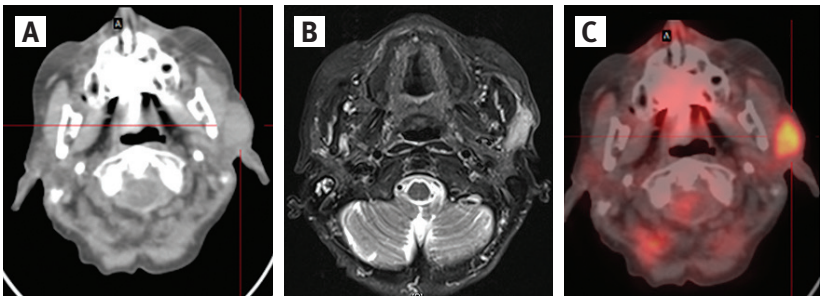
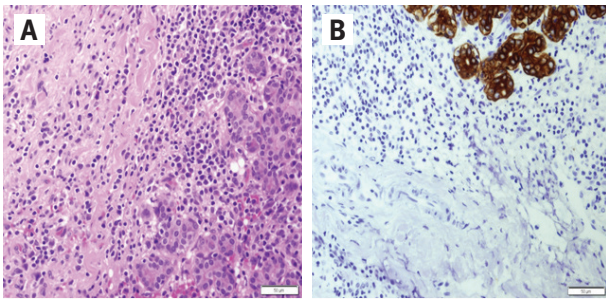


Figure 3. Histological workup demonstrating (x200 magnification) **[A]** wide fibrotic areas with mild chronic inflammation (H&E) and **[B]** preserved CK positive acinar glands



comprised a fibrous scar of the same size as the original mass. After 3 years follow-up, the patient is free of disease.

COMMENT

Merkel cell carcinoma, also known as neuroendocrine or primary small cell carcinoma of the skin, trabecular cell carcinoma, and anaplastic cancer of the skin, is a rare highly malignant neoplasm. It has a high propensity for local, regional, and distant spread often involving the lymph nodes, skin, lung, central nervous system, and bone. It occurs mostly in the sun-exposed areas of the skin. Half of all cases occur in the head and neck region and 10% in the sun-exposed upper eyelid. Its incidence has risen in recent years, possibly due to the increased aging population and incidence of sun exposure [2]. It is more commonly found in immunocompromised patients, especially in those with chronic lymphocytic leukemia [3].

A Merkel cell carcinoma of the eyelid is a rare entity, previously described by Atamney et al. [5]. Prognostic factors appear to be the size and depth of tumor invasion and presence of metastasis, as well as the gender of the patient, with women having a better prognosis [1]. Aggressive treatment includes wide local excision with negative margins sometimes with adjuvant radiotherapy, which decreases local recurrence but has no effect on overall survival [2]. Complete MCC spontaneous regression has been well documented in the medical literature [2]. None of these published cases have reported recurrence or metastasis after regression. There are no recognized epidemiological, clinical or imaging findings, or cytological parameters that can predict the enigma of tumor regression.

A strict preoperative workup is required in every MCC case. Lately, FDG-PET/CT has been widely used in a variety of cancer patients including MCC. FDG-PET/CT can demonstrate areas of increased glucose metabolic activity, as in rapidly dividing tumors [4]. Its ability to image the whole body allows simultaneous assessment of nodal regions and sites of potential metastatic disease. However, a number of physiologic and non-neoplastic conditions may also be associated with the focal accumulation of FDG and can cause false-positive results.

In our 87 year old patient, a total parotidectomy and selective neck dissection clearly carried risks such as permanent facial nerve palsy and the risk of general anesthesia. Unfortunately, different imaging modalities, including bio-function modality, have failed to identify a rapid (2 weeks) spontaneous MCC regression. Since Merkel cell carcinoma is an aggressive and sometimes lethal disease, our strict management resulted in an unnecessary operation.

We present, to the best of our knowledge for the first time, a Merkel cell carcinoma that showed high radionucleotide uptake (max SUV 10.6) on FDG-PET/CT 2 weeks prior to complete regression of the tumor. Positive FDG uptake can be secondary to a rapid tumor regression or to a significant fibrotic process; both are characterized by a high metabolic rate. Since the maximum standardized uptake was relatively high, we assumed that the FDG uptake, like the cytological analysis, was indicative for tumor. Nevertheless, the high uptake may have been associated with the complete tumor regression as a result of an intensive inflammatory process. We highlight the importance of FDG-PET/CT in treating Merkel cell carcinoma, noting that a positive scan may be misleading and confusing in the diagnosis of rapid tumor regression.

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