Widespread Metastatic Involvement in a Patient with Merkel Cell Carcinoma on 68Ga-DOTATATE PET/CT: Case Report

Merkel hücre karsinomuzun yaygınlığı ve metastatik involvementi.

**ABSTRACT** Merkel cell carcinoma (MCC) is an uncommon but very aggressive form of neuroendocrine tumor. It locates in the skin, in the basal layer of the epidermis, and it has higher mortality than melanoma with a high tendency to metastatic disease. Surgery is a principle treatment modality at the local stage. However, most patients are treated with palliative radiochemotherapy because of metastatic disease. In this case, we report the benefit of somatostatin receptor imaging with 68Ga-labeled somatostatin analog in the evaluation of disease spread and its impact on therapy management.

**Keywords:** Carcinoma, merkel cell; receptors, somatostatin; 68Ga-DOTATATE; positron-emission tomography


**Anahtar Kelimeler:** Karsinom, merkel hücreli; reseptörler, somatostatin; 68Ga-DOTATATE; pozitron emisyon tomografi

Merkel cell carcinoma (MCC) is a rare and very aggressive cutaneous neoplasm. It arises from neuroendocrine cells within the basal layer of the epidermis and has a tendency to lymph node recurrence and distant metastases. It has higher mortality than melanoma with a high rate of 5-year–specific mortality (46%). Surgery is a principle treatment modality at the local stage. However, most patients are treated with palliative radiochemotherapy because of metastatic disease. There is no standardized consensus in the treatment of the disease.

Contrast-enhanced computed tomography (ceCT) is generally used to evaluate the extent of disease. Nevertheless, it has some limitations such as lower detection rate for nodal disease, especially at the initial stage. Somatostatin receptor

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(SR) imaging might be an option to evaluate the spread of disease because of the neuroendocrine component. In the literature, there is a limited number of reports about SR scintigraphy with $^{111}$In (Indium-111)-labeled somatostatin analog in MCC. According to these reports, SR scintigraphy added no extra data to conventional imaging.\(^5\) Positron-emission tomography (PET) with $^{68}$Ga (Gallium-68)-labeled somatostatin analogs is more accurate than conventional SR imaging.\(^6\) Nowadays, $^{68}$Ga-labeled somatostatin analogs are preferred to SR scintigraphy. Molecular imaging with somatostatin analogs also has the advantage of being able to serve as a guide for peptide receptor radionuclide therapy (PRRT).

In this case, we report the benefit of SR-PET imaging in the evaluation of disease spread and its impact on therapy management.

## CASE REPORT

A man aged 79 years presented with swelling and skin color change in the left leg. Excisional biopsy from the skin lesion resulted in MCC with extensive lymphovascular invasion and tumor-positive surgical margins. Metastatic disease was not detected by concurrent thoracoabdominal ceCT. At the end of the one-year follow-up period, enlargement in the left inguinal region was detected and fine needle aspiration biopsy revealed recurrence of MCC. Accordingly, the patient was referred to the Nuclear Medicine Department for restaging of disease using $^{68}$Ga-DOTATATE PET/CT. Widespread intense uptake was shown in whole-body (Figure 1a) and lower-extremity (Figure 1b) maximum intensity projection (MIP) images. Pathologic uptakes were observed in mediastinal (Figure 2a), abdominal (Figure 2b), and pelvic (Figure 2c) enlarged lymph nodes, and in subcutaneous lesions in the lomber region (Figure 2d) and left lower extremity (Figure 2e) during evaluation of axial-fused images. Palliative radiotherapy (3600 cGy) was applied to the left inguinal metastatic region. Additionally, chemotherapy was started but the patient died of tumor burden soon afterwards.

This case report has been prepared in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki and its later amendments. All subjects in the study gave written informed consent.

## DISCUSSION

Merkel cell carcinoma is an aggressive neuroendocrine tumor of the skin. Sentinel lymph node biopsy (SLNB) is recommended for the initial evaluation of all patients with no evidence of lymph node metastasis. Gupta et al. reported that the recurrence rate was three times higher in patients who were SLNB positive compared with an SLNB-negative group.\(^7\) Interestingly, a statistically significant association was found between SLNB status and recurrence and survival in the largest single-center study.\(^8\) Fields et al. reported that the presence of lymphovascular invasion was a strong predictor of SLNB positivity.\(^9\) In the present case, extensive lymphovascular invasion was seen histopathologically at the diagnosis. Unfortunately, SLNB was not performed at this stage.

Imaging methods are important in the management of MCC because of the increased trend towards metastasis. Due to limitations of anatomic imaging methods, molecular imaging procedures such as SR imaging and $^{18}$F (Fluorine-18)-FDG (fluorodeoxyglucose) PET imaging have been used. According to these reports, conventional SR scintigraphy (with $^{111}$In-octreotide) added no extra data to conventional imaging.\(^6\) Lu et al. also stated that $^{18}$F-FDG PET/CT had better results than conventional SR scintigraphy for the detection of MCC.\(^9\) In a recent meta-analysis, the sensitivity and specificity of $^{18}$F-FDG PET/CT in the diagnostic performance with MCC was reported as 90% and 98%, respectively.\(^10\) $^{18}$FDG-PET/CT has a role in the evaluation of the MCC because of the high incidence of regional and metastatic disease. Nowadays, SR imaging with $^{68}$Ga-labeled somatostatin analogs are preferred to conventional SR scintigraphy owing to the high resolution of PET imaging. In the present case, we initially preferred SR imaging with $^{68}$Ga DOTATATE instead of $^{18}$F-FDG because of the patient’s neuroendocrine history. Widespread intense uptake was shown by $^{68}$Ga-DOTATATE PET/CT. Unfortunately, we did not
have the chance to compare the results with ¹⁸FDG PET imaging. Abgral et al. reported that FDG PET was more sensitive than the SR scintigraphy for staging of metastatic well-differentiated endocrine carcinoma with a high Ki-67 index.⁵ In a small study, Belhocine et al. concluded that normal FDG PET findings could rule out MCCs with low Ki-67 indexes.¹¹ Again unfortunately, we did not have the Ki-67 index of the tumor so we could not evaluate the relationship between Ki-67 index and FDG uptake. However, ⁶⁸Ga-⁶⁸ PET imaging has an advantage because it serve as guide for peptide receptor radionuclide therapy, although PRRT could not used in this case. We report an uncommon case of MCC with widespread somatostatin receptor expression detected in ⁶⁸Ga DOTATATE PET/CT. This case suggests a place for SR imaging in patients with neuroendocrine tumors to accurately stage and determine therapy management.

Conflict of Interest
Authors declared no conflict of interest or financial support.

Authorship Contributions

FIGURE 1: a) Maximum intensity projection (MIP) image of whole-body ⁶⁸Ga-DOTATATE PET/CT b) Maximum intensity projection (MIP) image of lower-extremity ⁶⁸Ga-DOTATATE PET/CT

FIGURE 2: a) Intense ⁶⁸Ga-DOTATATE uptake in mediastinal enlarged lymph nodes, b) Intense ⁶⁸Ga-DOTATATE uptake in abdominal enlarged lymph nodes, c) Intense ⁶⁸Ga-DOTATATE uptake in pelvic enlarged lymph nodes, d) Intense ⁶⁸Ga-DOTATATE uptake in subcutaneous lesions in the lomber region, e) Intense ⁶⁸Ga-DOTATATE uptake in left lower extremity.
REFERENCES


