
The Complementary Role of ^{68}Ga -DOTATATE PET/CT in Diagnosis of Recurrent Meningioma

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Contrast-enhanced brain MRI is the imaging modality of choice in diagnosis and posttreatment evaluation, but its role is limited in distinguishing recurrent lesions from postoperative changes. ^{68}Ga -DOTATATE is a somatostatin analog PET tracer that has high affinity to meningioma expressing somatostatin receptor. **Methods:** In this case series review, we describe 8 patients with brain MRI showing suspected recurrent meningioma who underwent focused ^{68}Ga -DOTATATE PET/CT for radiation treatment planning. **Results:** The combined brain MRI and PET/CT improved the conspicuity of the lesions and aided radiation treatment planning. The time from the initial surgery to PET/CT varied widely, ranging from 1 to 12 y. Three patients underwent PET/CT shortly after the initial surgery (1–3 y) and underwent targeted radiation therapy. Subsequent imaging showed no evidence of recurrence. Four patients had a prolonged time between the PET/CT and the initial surgery (7–12 y), which showed an extensive tumor burden. All 4 patients died shortly after the last PET/CT scan. **Conclusion:** ^{68}Ga -DOTATATE PET shows a promising complementary role in detection and treatment planning of recurrent meningioma.

Key Words: meningioma; somatostatin receptor; DOTATATE; octreotide

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Meningioma is the most common primary tumor of the central nervous system, accounting for approximately 27% of all intracranial tumors (1–3). On the basis of histologic features and its local aggressiveness, meningiomas are grouped into 3 grades (I–III) on the World Health Organization (WHO) scale. Although most meningiomas are grade I, factors such as mitoses and aggressive histology can predict a higher rate of recurrence (4). The most common locations of meningioma are the sites of dural reflection, including falx cerebri, tentorium cerebelli, and venous sinuses (5). Certain locations are associated with increased morbidity and mortality and pose challenges in treatment, regardless of grade.

The standard treatment for symptomatic meningioma is surgical resection, with complete removal of the tumor being the main determinant of its prognosis. Meningioma recurrence

requiring a second operation is a poor prognostic factor, along with malignant degeneration of the recurrent tumors (6,7). Radiation therapy is another treatment option for malignant and recurrent meningioma, although its role in benign meningioma remains controversial (7). Despite these therapeutic options, the overall 10-y survival of benign meningioma is 87%, and the 10-y survival for malignant meningioma remains approximately 60% (8).

Contrast-enhanced (CE) MRI is the imaging modality of choice in diagnosis, treatment planning, and postoperative evaluation of meningioma. However, CE MRI has a limited role in distinguishing recurrent tumor from postoperative changes. (9) Meningiomas exhibit strong somatostatin receptor expression, especially type 2, which can be detected by octreotide-based scintigraphy (^{111}In -octreotide SPECT [OctreoScan; Mallinckrodt Pharmaceuticals]) (10,11). In the last decade, ^{68}Ga -labeled somatostatin analog PET tracers have been used in the diagnosis and staging of gastroenteropancreatic neuroendocrine tumor. Among them, ^{68}Ga -DOTATATE has gained growing popularity in imaging of meningioma given its high specificity and nearly 10-fold increased affinity to somatostatin receptor 2 (SSTR-2) compared with ^{111}In -octreotide SPECT. ^{68}Ga -DOTATATE PET/CT plays a complementary role in imaging meningioma, including recurrent and residual lesions (10,12–15).

In this article, we report our initial experience in using combined brain CE MRI and ^{68}Ga -DOTATATE PET/CT to identify recurrent meningioma and aid radiation therapy. We also discuss the potential theragnostic application of ^{68}Ga -DOTATATE in management of recurrent or nonresectable meningioma.

MATERIALS AND METHODS

This study was conducted under the approval of the institutional review board. Patients who were diagnosed with recurrent meningioma or were suspected of having recurrent meningioma in 2017–2021 were retrospectively identified.

Surveillance CE MRI with ^{68}Ga -DOTATATE PET/CT was performed on all patients. Brain MRI was performed on 1.5-T or 3-T scanners under a routine MRI brain tumor protocol with multiple sequences consisting of 3-dimensional T1-weighted, T2-weighted, fluid-attenuated inversion recovery, diffusion-weighted, gadolinium CE 3-dimensional T1-weighted, and T1-weighted spoiled gradient echo. Dedicated brain MR images were interpreted by fellowship-trained neuroradiologists. To further define the tumor burden and

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TABLE 1
Demography of Meningioma Patients

Patient no.	Sex	WHO grade	Age (y)	Initial location	Onset	Treatment history	PET/CT time (y)	PET/CT findings	Follow-up therapy	Outcome
1	F	1	69	Right frontal	2005	Craniotomy × 3, CyberKnife embolization	12	Positive	Bevacizumab, octreotide	Died
2	F	2	82	Right sphenoid	2016	Craniotomy × 2	1	Positive × 2	Proton beam therapy	Survived
3	M	2	72	Bifrontal	2009	Craniotomy × 3, radiation therapy	8	Positive	Octreotide	Died
4	M	2	59	Left skull base	2008	γ-knife	10	Positive	Octreotide	Died
5	M	2	77	Bifrontal	2012	Radiosurgery, craniotomy × 2	7	Positive	Octreotide, bevacizumab	Died
6	M	2	72	Left frontoparietal	2015	Craniotomy × 1, radiation therapy	3	Positive	Proton beam therapy	Survived
7	F	3	47	Right frontal	2008	Craniotomy × 1	12	Negative × 2	Surveillance	Survived
8	F	1	68	Right skull base	2021	Partial resection	1	Positive	Radiation therapy	Survived

guide the subsequent treatment strategy, patients with suggestive focal enhancement on post-CE MR images underwent ⁶⁸Ga-DOTATATE PET/CT.

⁶⁸Ga-DOTATATE PET/CT of the head was performed 40 min after intravenous injection of 185 (±10%) MBq of ⁶⁸Ga-DOTATATE, with additional bone algorithm reconstruction CT images. Head PET/CT images were sent to an independent workstation (MIM Software, Inc.) for interpretation by nuclear radiologists who were dually board-certified (American Board of Radiology and American Board of Nuclear Medicine).

The ultimate diagnosis of meningioma recurrence was based on imaging: on CE MRI, a dura-based enhancing focus at the surgical bed or a new enhancing meningeal focus at other meningeal regions, and on ⁶⁸Ga-DOTATATE PET/CT, focal meningeal radiotracer uptake with a corresponding dura-based mass on unenhanced CT.

The head PET/CT data were subsequently coregistered with high-resolution 3-dimensional spoiled gradient echo brain MRI sequences for further localization.

RESULTS

Eight patients with a histopathologically proven meningioma after surgical resection were identified (Table 1). Each underwent CE MRI and ⁶⁸Ga-DOTATATE PET/CT as a part of the postsurgical surveillance.

One patient showed no evidence of disease recurrence on 2 consecutive PET/CT scans after surgical resection (patient 7) and remained well as of his last clinic visit, without evidence of recurrence. The remaining 7 patients had PET-positive recurrent lesions corresponding to the findings visualized on CE MRI.

The time from the initial surgery to obtaining the PET/CT scans varied widely, ranging from 1 to 12 y (mean, 6.75 y). Three patients (patients 2, 6, and 8) underwent the PET/CT in a relatively short period from the initial surgery (1, 3, and 1 y, respectively), and both PET and MRI showed recurrence. Plans for proton beam therapy and stereotactic radiation therapy were adjusted on the basis of the PET/CT findings. The adjustments included changes in the radiation beam entry point and the trajectory of the radiation. The patients showed improvement in tumor burden on subsequent follow-up CE MRI and were doing well as of the last clinical follow-up visit, without evidence of recurrence.

Four patients (patients 1, 3, 4, and 5) underwent PET/CT after a longer time from the initial surgery (12, 8, 10, and 7 y, respectively). Although octreotide

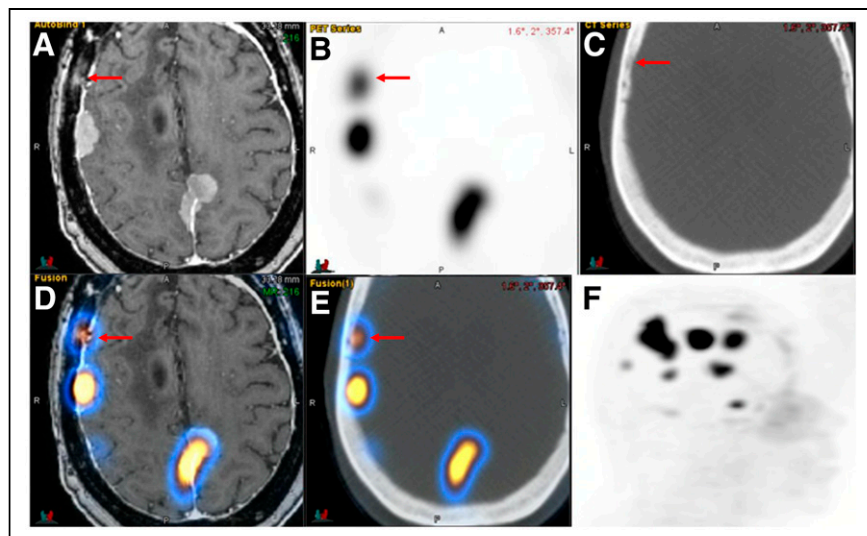


FIGURE 1. Multiple variable-sized, dura-based enhancing lesions exhibit somatostatin receptor positivity on ⁶⁸Ga-DOTATATE PET/CT. One tracer-avid bone marrow focus on right frontal bone is concerning for meningioma transosseous infiltration (arrows). Maximum-intensity projection exhibits extensive tumor burden of recurrent meningioma. Shown are CE MR image (A), ⁶⁸Ga-DOTATATE PET image (B), low-dose CT image (C), PET/MR image (D), PET/CT image (E), and PET maximum-intensity projection (F).

therapy was initiated on the basis of the PET/CT findings, all 4 patients showed an extensive tumor burden on the initial PET/CT images and died shortly afterward.

Patient 1

A 69-y-old woman had a clinical history of recurrent WHO grade 1 meningiomatosis and had undergone 3 craniotomies and 1 course of CyberKnife (Accuray) therapy. CE MRI revealed multiple recurrent meningiomas. To accurately evaluate the recurrent tumoral burden, ^{68}Ga -DOTATATE PET/CT was performed. The combined brain MR and PET images depicted multiple variably sized CE, somatostatin receptor-positive meningiomas. The patient received embolization therapy followed by bevacizumab and octreotide and died from disease progression 1 y after the PET/CT scan (Fig. 1).

Patient 2

An 82-y-old woman had a history of WHO grade 2 atypical meningioma with invasion of the right temporalis muscle, calvarium, and dura and had undergone subtotal resection. A large, enhancing mass was confirmed on CE MRI. After surgical resection of the tumor, ^{68}Ga -DOTATATE PET/CT was performed and showed recurrent disease at the surgical bed. This recurrence was not identified on CE MRI because of surrounding postsurgical changes. The ^{68}Ga -DOTATATE PET/CT findings led to repeat craniotomy and definitive proton beam therapy and were used to assist planning of the proton beam therapy. The patient remained free of residual tumor after the radiotherapy (Fig. 2).

Patient 6

A 72-y-old man had a history of left frontal–parietal atypical meningioma (WHO grade 2) and had undergone total tumor resection. The ^{68}Ga -DOTATATE PET images showed 2 recurrent foci at the vertex, which were not seen well on CE MRI given their locations. Radiation therapy planning was adjusted on the basis of the PET/CT findings, including changes in the radiation beam trajectory. The patient received 6,000 cGy of external beam therapy and has been symptom free since then (Fig. 3).

DISCUSSION

CE MRI is the imaging method of choice in the diagnosis of recurrent and residual meningioma. However, its role is limited as it cannot accurately distinguish viable tumors from posttreatment changes. Somatostatin receptor is a G-protein-coupled cell membrane receptor and can be activated by somatostatin or its synthetic analogs. In the brain, expression of SSTR-2 has been observed in meningioma (11,16). Although ^{111}In -octreotide SPECT is a traditionally complementary imaging modality in surveillance of meningioma in posttreatment patient populations, ^{68}Ga -DOTATATE PET/CT is shown to be more effective in imaging meningioma given its high specificity and robust affinity to SSTR-2, with a 10-fold increase compared with ^{111}In -octreotide SPECT (10,17,18). Accumulating literature has shown that PET/CT ligated to ^{68}Ga -DOTA analogs, including DOTATOC,

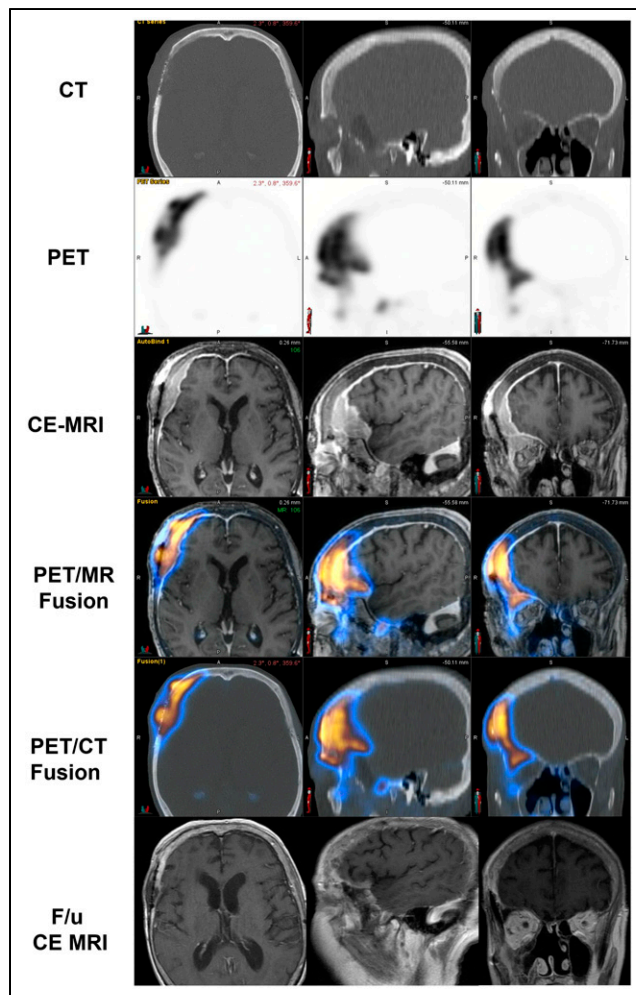


FIGURE 2. ^{68}Ga -DOTATATE PET/CT/MRI series, adapted for radiation therapy planning for proton beam therapy, showed enhancing lesions centered at right temporal craniectomy site, indicating residual tumor after subtotal resection. Three-year follow-up CE MRI showed decreased size of tumor, indicating favorable response to radiation therapy. F/u = follow-up.

DOTANOC, and DOTATATE, has a promising role in identifying and localizing meningioma and may play a complementary role in guiding therapy and predicting survival in select patients (12–15,19–23).

^{68}Ga -DOTATATE uptake can be seen in other primary and secondary brain tumors besides meningioma, including hemangiopericytoma and intracranial metastatic neuroendocrine tumor. The pituitary gland also demonstrates physiologic SSTR-2 expression, which could limit evaluation of an adjacent meningioma in the skull base (24–26). Combined molecular imaging with CE MRI is extremely helpful in this setting, as it may help define the tumor margin and avoid unnecessary exposure of the patient to radiation. We implemented a bone reconstruction algorithm in our PET/CT protocol to aid visualization of osseous tumoral infiltration, given its superiority in detecting subtle transosseous involvement (27).

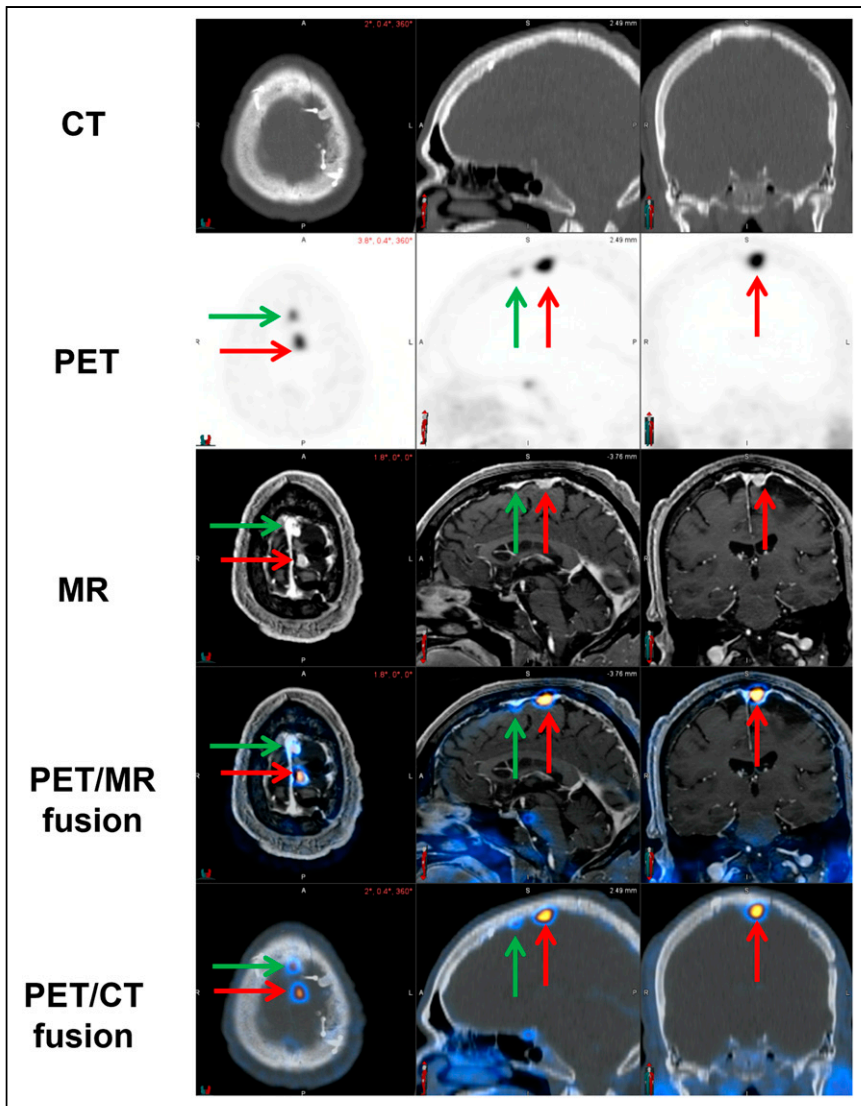


FIGURE 3. In ^{68}Ga -DOTATATE PET/CT/MRI series, CE MRI demonstrated enhancing focus at parietal vertex, which exhibited PET avidity (red arrows). PET/CT was able to identify another PET-avid focus at parasagittal left frontal region, indicative of recurrence (green arrows).

Our single-center experience with fusion of ^{68}Ga -DOTATATE PET/CT and CE MRI in a small cohort concurred with prior work that demonstrated the vital role of a complementary ^{68}Ga -DOTATATE PET/CT scan in identifying recurrent meningioma. For example, in patient 2—the patient who had a WHO II meningioma that recurred after initial craniotomy—follow-up ^{68}Ga -DOTATATE PET/CT demonstrated focal uptake suggestive of recurrence despite no evidence of recurrence on CE MRI. This finding prompted repeat craniotomy and targeted proton beam therapy. The patient was clinically well as of the last visit, without evidence of recurrence on follow-up CE MRI.

^{68}Ga -DOTATATE PET may also provide therapeutic potential in patients for whom surgery has a limited role. The somatostatin receptor-targeted treatments consist of

octreotide and a peptide receptor radionuclide. Clinical trials have shown the role of long-acting somatostatin analogs in inhibiting proliferation of meningiomas. Schulz et al. used 30 mg of octreotide to treat 8 patients with a progressive residual skull base meningioma after surgery. The investigators found that octreotide stabilized the progression of a recurrent skull base meningioma despite no convincing imaging evidence of tumor regression (28). In our small cohort, 4 patients received octreotide therapy, with ^{68}Ga -DOTATATE PET/CT being used to identify potential candidates for this pharmacologic therapy. Unfortunately, all 4 patients died shortly after initiation of the therapy, probably because of a limited octreotide therapy response due to the already extensive tumor burden at the time of diagnosis. Perhaps the treatment approach with the greatest potential for recurrent meningioma is somatostatin receptor-targeted peptide receptor radionuclide therapy, which is a novel theragnostic approach using either β -emission ^{90}Y or ^{177}Lu agents. Clinical trials for nonresectable and recurrent meningiomas have confirmed that peptide receptor radionuclide therapy has a promising role in the treatment of unresectable meningioma, with improved progression-free status, and may be an alternative approach for patients with an unfavorable response to traditional therapy (29–33).

Our small retrospective case series had several limitations. Histopathologic correlation of the ^{68}Ga -DOTATATE PET/CT findings was not available for any of our patients, and the diagnosis was based solely on visual inspection of brain CE MRI and ^{68}Ga -DOTATATE PET/CT images. We did not apply SUVs to aid the diagnosis, since no standard imaging protocol for meningioma has been established among the different institutions. Use of an SUV_{max} cutoff of 2.3, as applied by Rachinger et al., to differentiate tumor from tumor-free tissue is one example of what can be tried in future studies (15). Another limitation is lack of a direct comparison of the diagnostic performance of brain MRI and ^{68}Ga -DOTATATE PET/CT in lesion detection, given the lack of histopathologic evidence as a gold standard and the nature of the study. Future large-scale, prospective investigations of ^{68}Ga -DOTATATE PET/CT in diagnosis of recurrent meningioma need to overcome the shortcomings of this study.

CONCLUSION

⁶⁸Ga-DOTATATE PET/CT is a promising complementary molecular imaging tool in the detection of recurrent meningioma. It may improve diagnostic accuracy and confidence in guiding clinical management, particularly in surgically challenging patients. ⁶⁸Ga-DOTATATE PET/CT also serves a vital role in radiation therapy planning. With somatostatin receptor–targeted therapy on the horizon, ⁶⁸Ga-DOTATATE PET/CT may aid in selection of appropriate patients for peptide receptor radionuclide therapy, an emerging therapeutic approach in the management of meningioma.

DISCLOSURE

No potential conflict of interest relevant to this article was reported.

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KEY POINTS

QUESTION: What is the role of ⁶⁸Ga-DOTATATE PET/CT in imaging meningioma?

PERTINENT FINDINGS: For recurrent meningioma, combined use of ⁶⁸Ga-DOTATATE PET/CT may enhance diagnostic accuracy and further guide clinical management. It has great potential to improve treatment outcomes and life expectancy.

IMPLICATIONS FOR PATIENT CARE: ⁶⁸Ga-DOTATATE PET and brain MRI play a complementary role in imaging of complicated recurrent meningioma.

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