⁶⁸Ga-DOTATOC-PET/CT–guided resection of a primary intraosseous meningioma: technical note

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Primary intraosseous meningiomas (PIMs) are rare tumors that present with a variable radiological appearance and a clinical behavior that is considerably different from that of intracranial meningiomas. Treatment of PIMs consists of complete resection, which may be difficult to achieve due to the lack of clear tumor margins on conventional imaging studies. PET/CT using ⁶⁸Ga-DOTA–conjugated peptides has been used for the diagnosis and treatment planning of different types of meningiomas due to these tracers' affinity to somatostatin receptors, which are found in most meningiomas. However, this imaging modality's use as an intraoperative adjunct has not been reported for PIMs. In this technical note, the authors describe a [⁶⁸Ga-DOTA⁰-Tyr³]octreotide (⁶⁸Ga-DOTATOC)-PET/CT–guided resection of a PIM. In this case, the area of increased uptake in the ⁶⁸Ga-DOTATOC-PET/CT study extended well beyond the tumor margins identified on MRI. The patient's pathology report confirmed the presence of tumor cells within peripheral bone, which macroscopically appeared normal. The authors propose ⁶⁸Ga-DOTATOC-PET/CT as a valuable adjunct in the surgical management of PIMs and offer a reasonable justification for its use based on current evidence. Its use for intraoperative image guidance may aid neurosurgeons in achieving a complete resection, thus minimizing the risk of recurrence of this complex pathological entity.

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P RIMARY extradural meningiomas are infrequently occurring neoplasms, representing less than 2% of all meningiomas. These tumors arise from outside the subdural compartment and may involve bone, scalp, or nasopharynx; other rare locations have also been reported in the literature.¹ Primary intraosseous meningiomas (PIMs) are a subtype responsible for up to two-thirds of these cases and typically arise from within the bone of the skull. Their clinical manifestations and overall prognosis differ from those of intracranial meningiomas.^{2,3} Radiologically, PIMs may present as hyperostotic, osteolytic, or mixed lesions, with a variable appearance on MRI.⁴

PET/CT using ⁶⁸Ga-DOTA–conjugated peptides as tracers has gained considerable popularity in the evaluation and management of meningiomas with or without osseous invasion.^{5,6} These tracers act as a ligand for somatostatin receptors,⁷ which have reportedly been found in variable degrees in virtually all meningiomas.^{5,6,8} The use of PET/CT using ⁶⁸Ga-DOTA–conjugated peptides in

PIMs has not been widely reported due to these tumors' low frequency; however, existing evidence suggests the imaging technique might be as useful for PIMs as it is for intracranial meningiomas.⁹

Since PIMs may be viewed as an entity different from intracranial meningiomas both clinically and radiologically, they represent a diagnostic and therapeutic challenge. In this paper, we describe the use of [⁶⁸Ga-DOTA⁰-Tyr³]octreotide (⁶⁸Ga-DOTATOC)-PET/CT in the evaluation and management of a calvarial PIM at our center and describe the surgical technique that we used to effectively remove the lesion and confirm the diagnosis. Informed consent was obtained from the patient for the publication of this work.

Illustrative Case

This 30-year-old man presented to our clinic with headache associated with a growing scalp lesion. The patient had a 1-year history of a mixed nonseminomatous germ

ABBREVIATIONS ¹⁸F-FDG = ¹⁸F-fluorodeoxyglucose; ⁶⁸Ga-DOTATOC = [⁶⁸Ga-DOTA⁰-Tyr³]octreotide; PIM = primary intraosseous meningioma.

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cell tumor in the left testis, which had been treated with radical orchiectomy followed by adjuvant chemotherapy. Remission status had been achieved at the time of the patient's first visit to our center. On examination, a firm, painful mass was found in the patient's left parietal region. The findings of the neurological examination were unremarkable. Since the man did not accept gadolinium administration, MRI was performed without a contrast agent. Imaging displayed a heterogeneous intradiploic lesion in the left parietal bone. Despite the fact that the patient was considered to have clinical and biochemical remission, a whole-body ^{18}F -fluorodeoxyglucose (^{18}F -FDG) PET/CT study was performed to rule out metastatic disease. Interestingly, the lesion did not display significantly increased uptake of the tracer, and no other lesions were identified on the scan. Due to the suspected diagnosis of an intraosseous meningioma, a ^{68}Ga -DOTATOC-PET/CT study was performed. This showed increased uptake of the tracer within the lesion as well as within the bone a few centimeters around the lesion. Preoperative images obtained in this patient are displayed in Fig. 1. Due to a concern of potential invasion into the periphery of the main lesion, the patient underwent a ^{68}Ga -DOTATOC-PET/CT-guided resection of the lesion.

Surgical Technique

The patient was positioned prone with his head fixed by a Mayfield three-pin head clamp. Using neuronavigation equipment (Curve, Brainlab), the preoperative MRI and ^{68}Ga -DOTATOC-PET/CT images were automatically fused, and registration was performed using external anatomical landmarks. A horseshoe-shaped incision was planned to expose the entirety of the affected skull. The main lesion (identified during preoperative MRI) was intraoperatively seen to be a fragile, slightly exophytic mass protruding from the calvarial bone with findings suggestive of previous bleeding. The adjacent affected bone, which displayed increased uptake of the tracer in the preoperative ^{68}Ga -DOTATOC-PET/CT, macroscopically appeared normal. Using ^{68}Ga -DOTATOC-PET/CT navigation for delineation (Fig. 2), two concentric circumferential craniotomies were made surrounding the main lesion and the affected bone, respectively. The outer bone flap was elevated first to gain control over potential adhesions between the main lesion and the underlying dura mater. Because of the potential of microscopic invasion, the inner bone flap (containing the lesion) was removed along with the underlying dura mater and the overlying pericranium to enhance a radical resection. On visual inspection, the dura mater appeared macroscopically normal. Both bone flaps and the underlying dura mater were sent to the pathology laboratory in separate samples. A watertight duraplasty was made by using a free flap of autologous pericranium, a cranioplasty was performed using a tailored titanium mesh implant, and the scalp was closed in a standard layered fashion. The surgical technique is broadly illustrated in Fig. 3. A postoperative CT scan confirmed complete resection of the affected bone (Fig. 4).

Postoperative Course and Follow-Up

The patient was discharged home 2 days after the pro-

cedure and presented no postoperative complications. The pathology examination demonstrated an intraosseous fibroblastic meningioma in both the inner and outer bone flaps, with no apparent invasion of the underlying dura mater, confirming the diagnosis of a PIM with tumor invasion into surrounding bone. As of his last outpatient visit at the 1-year follow-up, the patient remained asymptomatic with no tumor recurrence.

Discussion

Due to their relatively low incidence, evidence regarding the management and outcome of PIMs has not been as extensively reported as that for intracranial meningiomas. The available evidence suggests these tumors display a behavior different from intracranial meningiomas and should thus be treated as a distinct pathological entity.^{1,3,10,11} However, one thing they share in common is the goal of surgical treatment, which is achieving a complete resection in order to minimize the risk of recurrence.^{2,12,13}

For intracranial meningiomas, the extent of resection and histopathological grade have been closely associated with tumor recurrence.^{12,14} On the other hand, PIMs display a more aggressive behavior than intracranial meningiomas. Some studies have shown PIMs to harbor atypical or malignant features more frequently than intracranial meningiomas, especially when the lesions are osteolytic, which is less frequently found.^{1,2,10} As expected, these cases are also associated with a higher risk of recurrence than benign PIMs.¹⁰ Accordingly, a complete resection should be attempted in PIM cases whenever possible, with removal of any affected tissue that might harbor tumor cells. In the illustrated case, the underlying dura mater was also removed because dural involvement has been proven by pathological reports, even in cases of PIM with macroscopically normal dura mater.¹³

Contrary to intracranial meningiomas, PIMs do not always display clearly identifiable margins, which may hamper achieving a complete resection. Furthermore, findings on contrast-enhanced MRI may not always represent the complete lesion, because tumor invasion may extend well beyond macroscopic structural lesions.^{5,9}

Due to its affinity for somatostatin receptor type 2, PET/CT with ^{68}Ga -DOTA-conjugated peptides offers particular value in the workup of certain patients in whom the diagnosis is uncertain—for instance, patients with atypical lesions or those with multiple differential diagnoses. Even though positive findings are not specific for meningiomas and may represent a wide variety of lesions,^{6,7,15} their interpretation must be tailored to each clinical scenario. In this case, a metastatic lesion was the primary differential diagnosis due to the patient's past medical history. Therefore, ^{18}F -FDG-PET/CT was initially performed as the metastatic workup. However, once metastasis was considered less likely, due to the radiological findings, and a PIM was suspected, we performed ^{68}Ga -DOTATOC-PET/CT to support the diagnosis, which was further confirmed by the pathology report. There have been other cases of PIM discovered during metastatic workups reported in the literature,^{13,16,17} highlighting the importance of an individualized approach to narrow down the broad range of differential diagnoses.

FIG. 1. Axial (*left*), coronal (*center*), and sagittal (*right*) preoperative imaging studies. **A:** An osteolytic intradiploic lesion is seen on CT scans. **B:** No apparent involvement of intracranial structures is seen on MRI studies. **C:** ^{18}F -FDG-PET/CT scans display a mild tracer uptake within the lesion. **D:** Significantly increased tracer uptake is seen within the lesion and in surrounding bone on ^{68}Ga -DOTATOC-PET/CT scans.

FIG. 2. Navigation software displaying preoperative ^{68}Ga -DOTATOC-PET/CT images is used to delineate the tumor margins. The anterior (A) and lateral (B) limits of the affected bone can be seen.

The value of PET/CT with ^{68}Ga -DOTA-conjugated peptides may be further emphasized in the delineation of meningiomas. Previous studies have shown these tests to display a high accuracy for tumor delineation, in some cases even surpassing that of contrast-enhanced MRI,^{5,6,15} especially for bone-related components of intracranial meningiomas.^{9,18} Furthermore, previous pathological studies have confirmed the presence of tumor cells in areas displaying increased uptake.^{6,9,19} In the present case, bone invasion seen on ^{68}Ga -DOTATOC-PET/CT scans extended well beyond the lesion seen on MRI. This encouraged us to pursue a PET/CT-guided resection to include poten-

tially affected tissue within the surrounding bone. The histopathological demonstration of tumor cells within the outer bone flap confirmed the value of this technique for achieving a complete resection, which could not have been possible if attempted by conventional means.

Whether the routine use of this image-guidance method may improve surgical and clinical outcomes still remains to be determined. To illustrate this caveat, Fig. 5 displays the case of another patient with meningiomatosis who was treated at our center and harbored a highly similar calvarial PIM. Increased tracer uptake in that case was limited only to the area corresponding to the

FIG. 3. Photographs of the surgical technique. **A:** Exposure of the affected skull. The main lesion can be seen as a small protruding mass in the left parietal bone (arrow). **B:** Two circumferential craniotomies were performed. This view shows the outer bone flap elevated. **C:** The inner bone flap is removed along with the underlying dura mater. **D:** Cranioplasty with a tailored titanium mesh implant.

structural lesion identified on contrast-enhanced MRI, adding little value to the surgical plan and thus making the use of ^{68}Ga -DOTATOC-PET/CT for image guidance unnecessary for a complete resection. Nonetheless, given the uncertain extension of these tumors, PET/CT with ^{68}Ga -DOTA-conjugated peptides may be justified as part of the preoperative evaluation of PIMs to appropriately select patients who may benefit from this surgical adjunct.

The use of PET/CT with ^{68}Ga -DOTA-conjugated peptides has been widely described for treatment planning in cases of meningiomas, specifically for radiotherapy target delineation.^{6,18,20} Some authors have also proposed this method for image-guided resection of complex intracranial meningiomas (e.g., skull base or recurrent meningiomas).^{5,18} However, its use in PIMs is not universally adopted, and, to our knowledge, it has not been reported as an intraoperative

FIG. 4. Postoperative CT scans. Tumor margins from the preoperative ^{68}Ga -DOTATOC-PET/CT study (red lines) were fused with the postoperative CT scans. Postoperative axial (A), coronal (B), and sagittal (C) CT images confirm a complete resection.

FIG. 5. Second case used as a comparison. Axial (left), coronal (center), and sagittal (right) preoperative contrast-enhanced MR images (A) and ^{68}Ga -DOTATOC-PET/CT images (B) in a patient with meningiomatosis. A left parietal intraosseous meningioma is evident. In this case, the increased tracer uptake is limited to the area corresponding to the lesion seen on MRI. Notice the presence of a small en plaque meningioma in the right frontal region, which also displays increased tracer uptake (asterisk in B).

adjunct for the resection of this type of tumors. Structural image guidance (e.g., MRI or CT) in the surgical treatment of PIMs is far from novel; however, the illustrated case we present offers evidence supporting an added “molecular” image guidance from ^{68}Ga -DOTATOC-PET/CT based on the biology of meningiomas. This multimodal approach can reasonably improve spatial orientation during surgery, especially when clear macroscopic landmarks are absent. The pathology report of tumor invasion in the surrounding bone confirmed the value of this test for surgical planning and intraoperative image guidance for the successful treatment of this patient. This report may pioneer future studies aimed at enhancing a radical resection of these complex and often underestimated lesions; however, large series or comparative studies may be difficult to carry out due to the low prevalence of these tumors.

Conclusions

The illustrated case highlights the utility of ^{68}Ga -DOTATOC-PET/CT in the general management of PIMs and suggests its potential role as an adjunct in their surgical treatment in order to achieve a complete resection. This could include otherwise macroscopically normal tissue that could potentially harbor tumor cells and give rise to a recurrence. Although evidence supporting its routine use is lacking, we believe the distinct behavior of PIMs makes the use of this adjunct appropriate in their surgical management.

References

- Lang FF, Macdonald OK, Fuller GN, DeMonte F. Primary extradural meningiomas: a report on nine cases and review of the literature from the era of computerized tomography scanning. *J Neurosurg*. 2000;93(6):940–950.
- Elder JB, Atkinson R, Zee C-S, Chen TC. Primary intraosseous meningioma. *Neurosurg Focus*. 2007;23(4):E13.
- Liu Y, Wang H, Shao H, Wang C. Primary extradural meningiomas in head: a report of 19 cases and review of literature. *Int J Clin Exp Pathol*. 2015;8(5):5624–5632.
- Chen TC. Primary intraosseous meningioma. *Neurosurg Clin N Am*. 2016;27(2):189–193.
- Rachinger W, Stoecklein VM, Terpolilli NA, et al. Increased ^{68}Ga -DOTATATE uptake in PET imaging discriminates meningioma and tumor-free tissue. *J Nucl Med*. 2015;56(3):347–353.
- Galldiks N, Albert NL, Sommerauer M, et al. PET imaging in patients with meningioma-report of the RANO/PET Group. *Neuro Oncol*. 2017;19(12):1576–1587.
- Virgolini I, Ambrosini V, Bomanji JB, et al. Procedure guidelines for PET/CT tumour imaging with ^{68}Ga -DOTA-conjugated peptides: ^{68}Ga -DOTA-TOC, ^{68}Ga -DOTA-NOC, ^{68}Ga -DOTA-TATE. *Eur J Nucl Med Mol Imaging*. 2010;37(10):2004–2010.
- Menke JR, Raleigh DR, Gown AM, et al. Somatostatin receptor 2a is a more sensitive diagnostic marker of meningioma than epithelial membrane antigen. *Acta Neuropathol*. 2015;130(3):441–443.
- Kunz WG, Jungblut LM, Kazmierczak PM, et al. Improved detection of transosseous meningiomas using ^{68}Ga -DOTATATE PET/CT compared with contrast-enhanced MRI. *J Nucl Med*. 2017;58(10):1580–1587.
- Kwon SM, Ko Y, Bang SS. Primary intraosseous osteolytic meningioma: a case report and review of the literature. *BMC Neurol*. 2019;19(1):176.
- Gokce E, Beyhan M, Acu L. Cranial intraosseous meningiomas: CT and MRI findings. *Turk Neurosurg*. 2020;30(4):542–549.
- Goldbrunner R, Minniti G, Preusser M, et al. EANO guidelines for the diagnosis and treatment of meningiomas. *Lancet Oncol*. 2016;17(9):e383–e391.
- Bassiouni H, Asgari S, Hübschen U, et al. Dural involvement in primary extradural meningiomas of the cranial vault. *J Neurosurg*. 2006;105(1):51–59.
- Hwang WL, Marciscano AE, Niemierko A, et al. Imaging and extent of surgical resection predict risk of meningioma recurrence better than WHO histopathological grade. *Neuro Oncol*. 2016;18(6):863–872.
- Afshar-Oromieh A, Giesel FL, Linhart HG, et al. Detection of cranial meningiomas: comparison of ^{68}Ga -DOTATOC PET/CT and contrast-enhanced MRI. *Eur J Nucl Med Mol Imaging*. 2012;39(9):1409–1415.
- Yener U, Bayrakli F, Varderele E, et al. Intradiploic meningioma mimicking calvarial metastasis: case report. *Turk Neurosurg*. 2009;19(3):297–301.
- Tang V, Lam M, Lai A. Intraosseous meningioma mimicking a metastasis. *BMJ Case Rep*. 2014;2014:bcr2014207633.
- Cornelius JF, Langen KJ, Stoffels G, et al. Positron emission tomography imaging of meningioma in clinical practice: review of literature and future directions. *Neurosurgery*. 2012;70(4):1033–1042.
- Marcus H, Schwindack C, Santarius T, et al. Image-guided resection of sphenoid-orbital skull-base meningiomas with predominant intraosseous component. *Acta Neurochir (Wien)*. 2013;155(6):981–988.
- Gehler B, Paulsen F, Oksüz MO, et al. [^{68}Ga]-DOTATOC-PET/CT for meningioma IMRT treatment planning. *Radiat Oncol*. 2009;4:56.

Disclosures

The authors report no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper.

Author Contributions

Conception and design: all authors. Acquisition of data: Martínez-Manrique, Guinto-Nishimura, Kerik-Rotenberg, Uribe-Pacheco. Analysis and interpretation of data: all authors. Drafting the article: Martínez-Manrique, Guinto-Nishimura, Gómez-Amador, Uribe-Pacheco, Sangrador-Deitos. Critically revising the article: all authors. Reviewed submitted version of manuscript: all authors. Approved the final version of the manuscript on behalf of all authors: Martínez-Manrique. Statistical analysis: Gómez-Amador. Administrative/technical/material support: all authors. Study supervision: Martínez-Manrique, Guinto-Nishimura, Gómez-Amador, Kerik-Rotenberg.

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