Clinical interpretation of residual uptake in ^{11}C -methionine positron emission tomography after treatment of basal ganglia germ cell tumors: report of 3 cases

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Although ^{11}C -methionine (MET)–PET has been used to diagnose intracranial germ cell tumors (GCTs) arising in the basal ganglia, whether this imaging technique is useful in assessing treatment response and residual tumor is still unclear. The authors report 3 cases of basal ganglia GCTs in which the residual MET uptake at the end of treatment did not develop into a relapse, even without additional treatment. Case 1 is a 22-year-old man who had a second relapse of a left basal ganglia germinoma with diffuse dissemination on the walls of both of his lateral ventricles. MET-PET revealed high MET accumulation around tumors and their surroundings (maximum standardized uptake value [SUVmax] 3.3). After all treatments, MET-PET demonstrated mild tracer accumulation in both basal ganglia (SUVmax 2.2). Progression-free survival was 56 months from the second relapse without any further treatment. Case 2 is a 17-year-old boy with a left basal ganglia germinoma that showed increased MET uptake (SUVmax 4.2). After treatment, MET-PET revealed residual MET uptake (SUVmax 2.4) along the left posterior limb of the internal capsule. Progression-free survival was 52 months from the start of treatment. Case 3 is a 7-year-old boy with a left basal ganglia choriocarcinoma with increased tumor MET uptake (SUVmax 2.5). A minor enhanced mass remained on MRI after treatment with residual MET accumulation (SUVmax 1.4). Progression-free survival was 44 months. Treatment strategies based on MET uptake on PET should be carefully designed in patients with basal ganglia GCTs to avoid overtreatment and complications.

<http://thejns.org/doi/abs/10.3171/2015.3.PEDS14458>

KEY WORDS intracranial germ cell tumors; methionine PET; basal ganglia; residual accumulation; oncology

BASAL ganglia are the third most common site for intracranial germ cell tumors (GCTs) to develop, following the pineal region and neurohypophysis.⁸ The extent of GCTs in the basal ganglia is difficult to evaluate compared with those in other regions because the former show only a subtle signal change on MRI, especially at an early stage. ^{11}C -methionine (MET) is an amino acid tracer widely used in PET not only to evaluate the metabolic activity of brain tumors but also to detect tumors not found on conventional neuroimaging.⁶ Although MET-PET has been reported to be beneficial in diagnos-

ing and localizing precise biopsy targets in basal ganglia GCTs,^{1,2,9} whether this imaging technique is useful in assessing the tumor treatment response remains unclear. We report 3 cases of basal ganglia GCTs with residual MET uptake at the end of the treatment that did not develop into a relapse, even without additional treatment.

PET/CT Imaging

PET/CT imaging was performed 20 minutes after MET administration, with a scan duration of 600 sec/bed using

ABBREVIATIONS AFP = α -fetoprotein; CARE = carboplatin and etoposide; GCT = germ cell tumor; HCG = human chorionic gonadotropin; ICE = ifosfamide, cisplatin, etoposide; MET = ^{11}C -methionine; SUVmax = maximum standardized uptake value; T/N = tumor/normal.

SUBMITTED August 27, 2014. **ACCEPTED** March 18, 2015.

INCLUDE WHEN CITING Published online July 3, 2015; DOI: 10.3171/2015.3.PEDS14458.

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

dedicated PET/CT scanners (Biograph 6 and 16, Siemens Japan Ltd.). Different MET doses were injected according to age: 0–4 years, 91 MBq; 5–9 years, 180 MBq; 10–14 years, 271 MBq; 15 years and older, 6 MBq/kg. The CT acquisition parameters were 5-mm-thick transaxial images at 130 kV and 120 mA for the head and neck and 130 kV and 50 mA for the body.

Images were reconstructed using a combination of Fourier rebinning and the ordered subset expectation maximization at iteration 3 with 8 subsets. The PET images were corrected for attenuation based on CT data. Volumes of interest were set manually on the brain regions. We evaluated the MET uptake of the lesion as the maximum standardized uptake value (SUVmax) and tumor/normal (T/N) gray matter ratio.

On posttreatment assessment, the patients underwent PET scanning within 1 month after the final chemotherapy course.

Case Reports

The diagnoses, tumor characteristics, and outcomes in our 3 patients are shown in Table 1. Progression-free survival was defined as the probability of being alive and free of progression or relapse.

Case 1

A germinoma in the left basal ganglia had been diagnosed in a 14-year-old boy. At the time, he was solely treated with chemotherapy consisting of carboplatin (450 mg/m²/day) on Day 1 and etoposide (150 mg/m²/day) on Days 1–3 (carboplatin and etoposide [CARE] regimen), but the tumor recurred after 1 year. He received extended local radiotherapy of 46 Gy for the recurrent tumor. However, generalized seizures developed and a second relapse occurred when the patient was 22 years old. Brain MRI revealed a diffuse enhanced lesion along the walls of both of his lateral ventricles (Fig. 1A). Serum human chorionic gonadotropin (HCG) and α -fetoprotein (AFP) levels were within normal limits, although the concentration of free HCG β -subunit in CSF was elevated to 0.15 ng/ml. MET-PET revealed high tracer uptake (SUVmax 3.3 and T/N ratio 1.4) at the enhanced lesion and its surroundings

(Fig. 1B and C). He received 6 courses of conventional chemotherapy, including 1 course of the CARE regimen and 5 courses of 900 mg/m² ifosfamide, 20 mg/m² cisplatin, and 60 mg/m² etoposide for 5 consecutive days (ICE regimen), followed by high-dose chemotherapy consisting of cyclophosphamide (1500 mg/m²/day) on Days –8 to –5 and melphalan (60 mg/m²/day) on Days –4 to –2 and autologous stem cell transplantation (Day 0). Treatment response was clearly observed as a marked decrease in tumor size after the first course of chemotherapy (Fig. 1D) and disappearance of the tumor after the third course (Fig. 1E). MET-PET after all the treatments still demonstrated a mild accumulation of MET in the bilateral basal ganglia (SUVmax 2.2, T/N ratio 1.0; Fig. 1F). However, even without any additional treatment, the patient did not experience any further recurrence for 56 months from the second relapse.

Case 2

A 17-year-old boy was admitted to our hospital with the chief complaint of right hemiparesis. Brain MRI showed a large tumor (6 cm) in the left basal ganglia that extended to the temporal subcortical area. His serum total HCG level was elevated to 105.6 mIU/ml, although his serum AFP level was not elevated. He underwent partial removal of the tumor via craniotomy, and the pathological diagnosis was germinoma. MET-PET showed increased tracer uptake (SUVmax 4.2, T/N ratio 2.1; Fig. 2A–C) after the operation. Brain MRI after the first course of chemotherapy revealed significant shrinkage of the tumor (Fig. 2D), and the patient’s serum HCG level had decreased to normal levels. He underwent 3 courses of the CARE regimen and whole-brain radiotherapy (total 24 Gy). After completion of the treatments, MET-PET revealed residual accumulation (SUVmax 2.4, T/N ratio 1.0) along the left posterior limb of the internal capsule, although the tumor had disappeared on MRI, except for an unenhanced scar in the left temporal subcortical area (Fig. 2E and F). The patient was in complete remission for 52 months from the start of treatment.

Case 3

Choriocarcinoma occurred in a 7-year-old boy who

TABLE 1. Basal ganglia GCT cases with assessment on MET-PET

Authors & Year	Diagnosis	Pretreatment		Posttreatment		Outcome (mos after treatment)
		SUVmax	T/N Ratio	SUVmax	T/N Ratio	
Kawai et al., 2009	Germinoma	1.6	1.74	1.62	1.31	No recurrence (36)
	Mixed GCT	2.26	1.55	1.94	1.39	ND
	Germinoma	1.79	2.45	2.33	1.68	ND
Lee et al., 2009	Germinoma	2.26	ND	1.5	ND	No recurrence (28)
	Germinoma	1.9	ND	1.5	ND	ND
	Germinoma	1.9	ND	1.03	ND	ND
Present study						
Case 1	Germinoma	3.3	1.4	2.2	1.0	No recurrence (44)
Case 2	Germinoma	4.2	2.1	2.4	1.0	No recurrence (46)
Case 3	Choriocarcinoma	2.5	3.4	1.4	1.2	No recurrence (30)

ND = no data.

FIG. 1. Case 1. **A:** Axial contrast-enhanced T1-weighted MR image obtained at the second relapse, showing a diffuse enhanced lesion along the bilateral ventricle walls. **B and C:** MET-PET images showing high accumulation in the lesion in accordance with the enhanced lesion on MRI and its surroundings. **D:** Axial contrast-enhanced T1-weighted MR image obtained after the first course of chemotherapy, showing significant shrinkage of the enhanced lesion. **E:** Axial contrast-enhanced T1-weighted MR image obtained after treatment, showing disappearance of the enhanced lesion. **F:** MET-PET image obtained after all treatments, showing mild accumulation in the bilateral basal ganglia (arrows). Figure is available in color online only.

developed precocious puberty within 3 months. Although he had undergone total removal of the tumor at another hospital, the lesion recurred 3 months later because he had not received any postoperative chemotherapy and/or radiotherapy. He was referred to our hospital, and MRI at that time demonstrated a circular enhanced lesion in the left basal ganglia (Fig. 3A). MET-PET revealed increased MET uptake by the tumor (SUVmax 2.5, T/N ratio 3.4; Fig. 3B). His serum HCG level was elevated to 464 mIU/ml from the start of treatment. He had a significant reduction in tumor size and normalization of the tumor marker after the first course of chemotherapy (ICE regimen) and radiotherapy (craniospinal radiation 30 Gy, local boost radiation 60 Gy total; Fig. 3C). Although he received 8 courses of the ICE regimen and his clinical course was uneventful, the minimally enhanced mass showed no changes on MRI from the end of the third chemotherapy course to the completion of treatment (Fig. 3D). MET-PET uptake by residual lesion was observed (SUVmax 1.4, T/N ratio 1.2; Fig. 3E). However, the patient was free of any signs of recurrence without further treatment for 44 months from the start of treatment. Follow-up MET-PET studies showed no significant changes in radiological findings at 1 month (SUVmax 1.2, T/N ratio 1.05) or 4 months (SUVmax 1.7, T/N ratio 1.16) after the end of treatments.

Discussion

In this report, we describe 3 cases of basal ganglia GCT with residual uptake of MET on PET that did not indicate tumor residue. Several previous studies have reported the usefulness of MET-PET in the diagnosis of basal ganglia GCTs.^{1,2,4,9} Sudo et al.⁹ described a patient with a basal ganglia germinoma who developed slowly progressive hemiparesis. The apparent MET uptake on PET allowed for a precise biopsy, although MRI had shown only a minor signal change on T2-weighted imaging and no enhancement of the lesion. Hence, MET-PET may be able to detect a more exact extent of basal ganglia GCTs than MRI.

Nonetheless, whether MET-PET is useful for the post-treatment assessment of basal ganglia GCTs remains uncertain. In fact, MET uptake remained in the lesion after treatment in many of the previously reported cases.^{3,4,9} The residual MET uptake may indicate disorders other than residual tumor. Several disorders such as cerebral infarction⁵ or radiation necrosis⁷ also show signs of high MET uptake because the tracer accumulates in the lesion of inflammatory change and reactive gliosis.⁷ Because basal ganglia are one of the most important regions of the brain in which several neuronal pathways penetrate, overtreatment of tu-

FIG. 2. Case 2. **A:** Axial contrast-enhanced T1-weighted MR image obtained on admission, showing a huge tumor with multiple large cysts located in the left basal ganglia. There is also a cystic lesion in the left caudate head. **B and C:** Postoperative MET-PET images showing high accumulation on the tumor extending to the left caudate head along the left internal capsule. **D:** Axial contrast-enhanced T1-weighted MR image obtained after the first course of chemotherapy, showing marked tumor shrinkage. **E:** Axial contrast-enhanced T1-weighted MR image obtained after completion of the treatment, showing disappearance of the tumor with the scar in the left temporal lobe. **F:** MET-PET image obtained after the completion of treatment, showing residual accumulation on the left internal capsule (arrow). Figure is available in color online only.

FIG. 3. Case 3. **A:** Axial contrast-enhanced T1-weighted MR image obtained after admission to our hospital, showing an enhanced mass (size 22 mm) in the left basal ganglia. **B:** MET-PET image showing significant MET accumulation on this lesion. **C:** Axial contrast-enhanced T1-weighted MR image obtained after the first course of chemotherapy and radiotherapy, showing a significant reduction in tumor size (arrow). **D and E:** Axial contrast-enhanced T1-weighted MR image obtained after the completion of treatment, showing minor enhancement (arrow), and an MET-PET image showing uptake on the lesion (arrow). Figure is available in color online only.

mors in this area should be avoided, especially additional radiotherapy, including stereotactic radiotherapy or radiosurgery, which can directly affect a patient's quality of life. MET uptake does not necessarily correspond to tumor residue when posttreatment assessment of basal ganglia GCTs is performed, especially in cases when a tumor's response to treatment is clearly observed.

Treatment strategies based on MET uptake should be carefully designed in patients with basal ganglia GCTs to avoid overtreatment and its complications. The T/N ratio may be a more reliable indicator of tumor activity than SUVmax or visual assessment given that T/N ratios in 2 of our 3 cases were normalized after treatment (Table 1). Efforts that allow the detection of minimal residual disease in intracranial GCTs should be continued.

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Conception and design: Fukuoka, Yanagisawa, Suzuki, Nishikawa. Acquisition of data: Fukuoka, Watanabe, Kuji. Analysis and interpretation of data: Fukuoka, Watanabe, Kuji. Drafting the article: Fukuoka. Critically revising the article: Yanagisawa, Kuji, Nishikawa. Reviewed submitted version of manuscript: Fukuoka. Approved the final version of the manuscript on behalf of all authors: Fukuoka. Administrative/technical/material support: Watanabe, Suzuki. Study supervision: Yanagisawa, Suzuki, Matsutani, Kuji, Nishikawa.

Supplemental Information

Previous Presentation

Portions of this work were presented in abstract form as proceedings at the Third International CNS Germ Cell Tumor Symposium, Cambridge, UK, April 17, 2013.

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