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K. Miwa, J. Shinoda, H. Yano and T. Iwama

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## CASE REPORT

K. Miwa  
J. Shinoda  
H. Yano  
T. Iwama

# Relatively Decreased $^{11}\text{C}$ -Methionine Uptake within the Anaplastic Component of a Mixed-Grade Oligodendroglioma

**SUMMARY:** A 56-year-old woman presented with a mixed-grade oligodendroglioma. On  $^{11}\text{C}$ -methionine [MET]-positron-emission tomography images, heterogeneous uptake of MET was demonstrated in the mass lesion. The part of the lesion with higher MET uptake was identified as an ordinary oligodendroglioma, whereas the part of the lesion with lower MET uptake was an anaplastic component of oligodendroglioma. With oligodendrogliomas, we should be aware of the possibility that MET uptake decreases paradoxically with an increased anaplastic component of oligodendroglioma cells.

**P**ositron-emission tomography (PET) after injection of  $^{11}\text{C}$ -methionine (MET) shows that gliomas accumulate this amino-acid tracer.<sup>1,2</sup> Some articles have reported a correlation between MET uptake and histologic grade in gliomas.<sup>3-5</sup> However, no one to date has found a correlation between MET uptake and distinct features within a tumor that has several histologic components. We present a case of mixed-grade oligodendroglioma that had a combination of low- and high-grade malignant features and examine the histologic findings in the context of images obtained with MET-PET, MR imaging, and CT.

## Case Report

A 56-year-old woman was admitted to our hospital with a 2-month history of headache. CT demonstrated a cystic right frontal mass with calcification. A 1.5T MR imaging system (Signa Horizon LX; GE Healthcare, Waukesha, Wis) was used to obtain transaxial T1-weighted images. For contrast enhancement studies, 0.1 mmol/kg of body weight of gadolinium was injected intravenously. On MR imaging with gadolinium, an enhanced mass lesion with a large cyst was demonstrated in the right frontal lobe (Fig 1A). PET was carried out with an Advance NXi Imaging System (GE Medical Systems, Tokyo, Japan). After a 7-minute transmission scan was obtained, a dose of 370 MBq of MET was intravenously injected into a cubital vein within 1 minute. A 10-minute static PET scan was begun 20 minutes after MET injection. With MET-PET, high uptake of MET was demonstrated in the anterior right frontal lobe (Fig 1B, tumor area A: short arrow), moderate uptake of MET was demonstrated in the anteromedial right frontal lobe (Fig 1B, tumor area B: long arrow), and high uptake of MET was demonstrated in the posteromedial right frontal lobe (Fig 1B, tumor area C: arrowhead). MET uptake ratio was defined as the ratio of radioisotope count of MET in tumor to that in normal gray matter. MET uptake ratio was 3.9 for tumor area A, 2.1 for tumor area B, and 4.1 for tumor area C.

PET and MR imaging datasets were transferred to a SUN workstation (SPARC MP20; Sun Microsystems, Mountain View, Calif). Coregistration of MET-PET and MR imaging data used a commercial software package (Dr. View; Asahi Kasei Joho System, Tokyo, Japan).

On coregistered images, tumor area B demonstrated intensive gadolinium enhancement; however, there was no enhancement in areas A or C (Fig 1C). Tumor area C corresponded largely with the calcified lesion seen on CT scans (Fig 1D).

With reference to coregistered images, the tumor was totally removed with a neuronavigated surgical system (Brain LAB, Munich, Germany). Histologic examination was done with hematoxylin-eosin (H&E) staining. Within each tumor area, the degree of proliferative activity (Ki-67 index) was estimated. Tumor area A was a low-grade oligodendroglioma (Fig 2A). In tumor area B, histologic features consistent with high-grade (anaplastic) oligodendroglioma were evident (Fig 2C). Tumor area C was a low-grade oligodendroglioma with abundant calcification (Fig 2E). The Ki-67 index was 1.8% for area A, 7.6% for area B, and 2.2% for area C (Fig 2B, D, F). Histologic and neuroradiologic features for all of the areas are shown in the Table.

## Discussion

MET uptake by tumor tissue was first described in 1976 by Comar et al.<sup>6</sup> Previous reports have shown that MET uptake by gliomas depends on histologic grade.<sup>1,3,7,8</sup> Among glial tumors, oligodendrogliomas show high MET uptake.<sup>9</sup> It has been suggested that oligodendroglial tumors have a high rate of cell turnover,<sup>10</sup> which could enhance amino acid uptake and metabolism. High-grade oligodendrogliomas have been shown to have significantly higher MET uptake than low-grade tumors.<sup>9</sup>

However, no sophisticated correlation has been demonstrated between MET uptake and a histologic feature within an individual tumor that has combined low- and high-grade oligodendroglioma. In our patient, an exact local comparison of MET uptake and a histologic feature was performed using the neuronavigation system with reference to coregistered images. The oligodendroglioma in our case was separated in 3 tumor areas defined by different histologic features. We found a paradoxical result between MET uptake and histologic grade compared with previous

**Histologic and neuroradiologic features of tumor areas A, B, and C**

| Tumor Area | Histology | MIB-1 Index, % | MET Uptake Ratio | Gd  | Calcification |
|------------|-----------|----------------|------------------|-----|---------------|
| A          | O         | 1.8            | 3.9              | (-) | (-)           |
| B          | AO        | 7.6            | 2.1              | (+) | (-)           |
| C          | O         | 2.2            | 4.1              | (-) | (+)           |

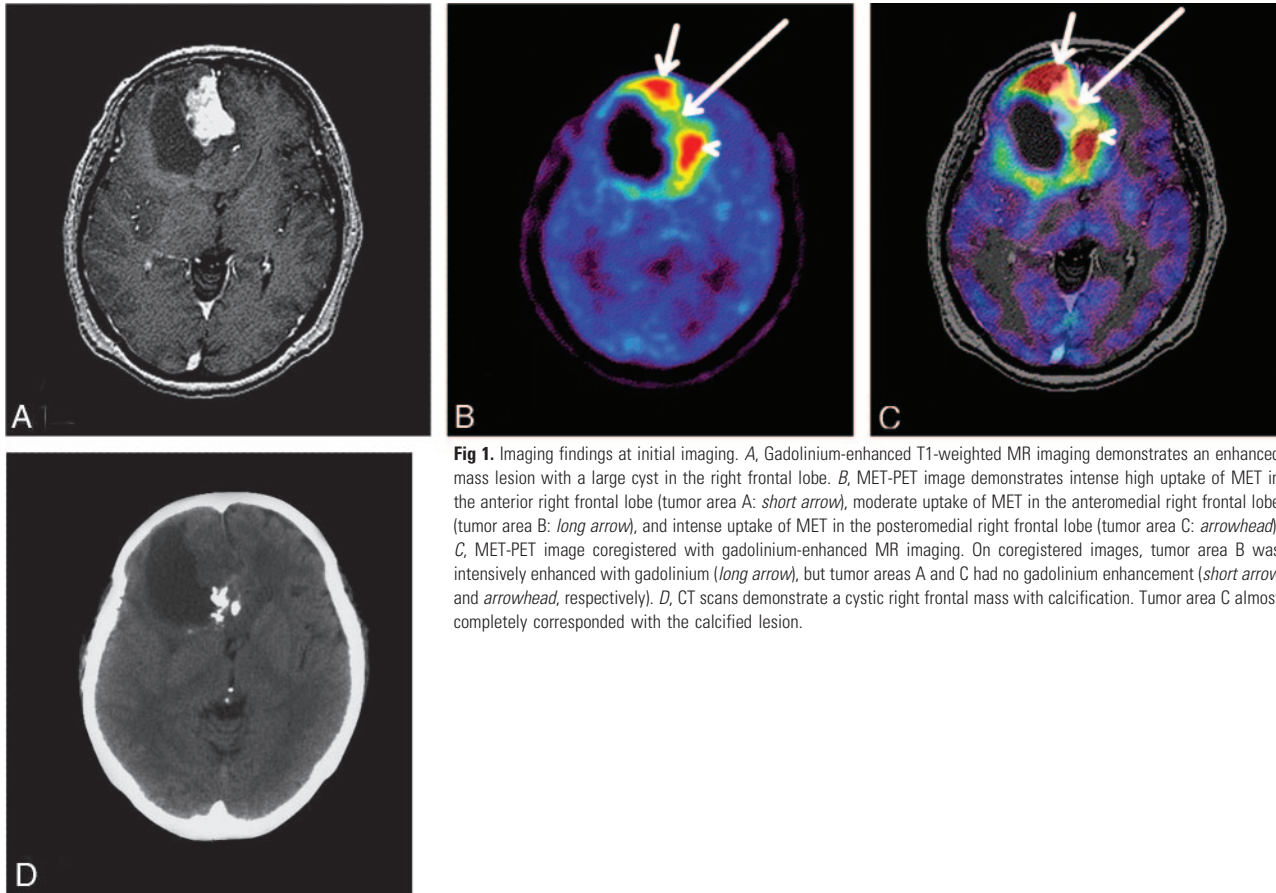
**Note:**—O indicates oligodendroglioma; AO, anaplastic oligodendroglioma; MET Uptake Ratio, the ratio of radioisotope count of MET in tumor to that in normal gray matter; Gd, gadolinium enhancement.

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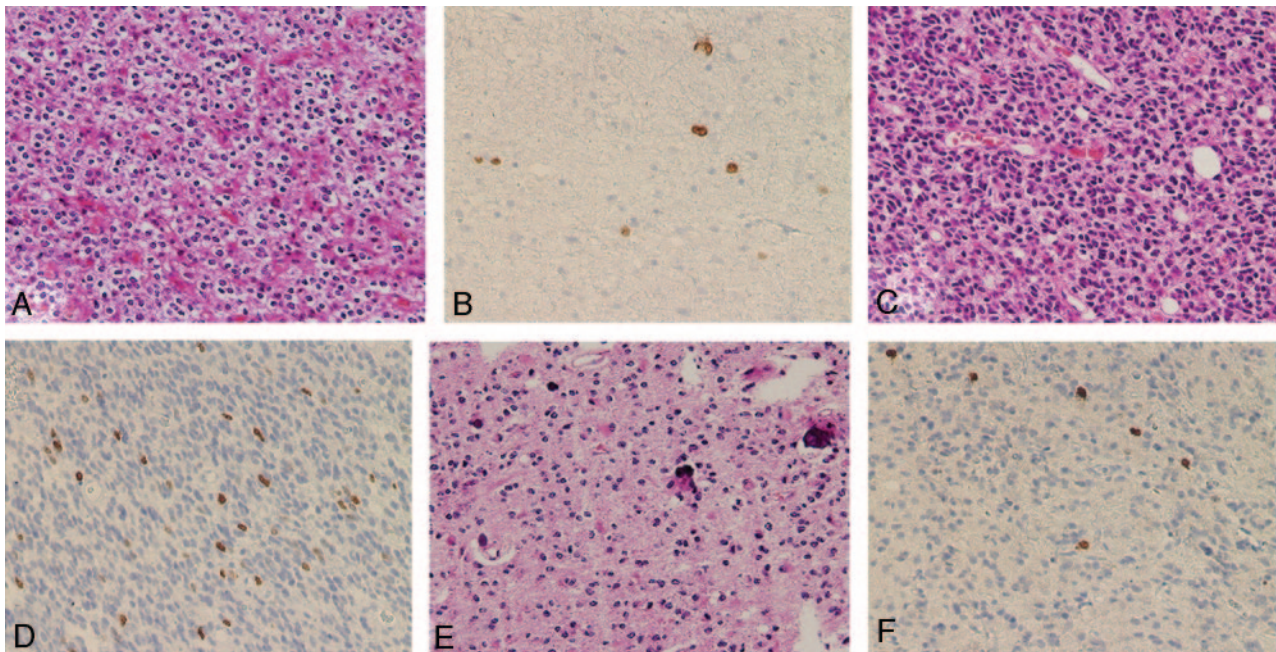
From the Chubu Medical Center for Prolonged Traumatic Brain Dysfunction (K.M., J.S.), Department of Neurosurgery, Kizawa Memorial Hospital, Gifu, Japan; Department of Neurosurgery (H.Y., T.I.), Graduate School of Medicine, Gifu University, Gifu, Japan.

Please address correspondence to Kazuhiro Miwa, Chubu Medical Center for Prolonged Traumatic Brain Dysfunction, Kizawa Memorial Hospital, 630 Shimokobi, Kobi-cho, Mino-kamo 505-0034, Japan; e-mail: doctor.3@jasmine.ocn.ne.jp

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**Fig 1.** Imaging findings at initial imaging. *A*, Gadolinium-enhanced T1-weighted MR imaging demonstrates an enhanced mass lesion with a large cyst in the right frontal lobe. *B*, MET-PET image demonstrates intense high uptake of MET in the anterior right frontal lobe (tumor area A: *short arrow*), moderate uptake of MET in the anteromedial right frontal lobe (tumor area B: *long arrow*), and intense uptake of MET in the posteromedial right frontal lobe (tumor area C: *arrowhead*). *C*, MET-PET image coregistered with gadolinium-enhanced MR imaging. On coregistered images, tumor area B was intensively enhanced with gadolinium (*long arrow*), but tumor areas A and C had no gadolinium enhancement (*short arrow* and *arrowhead*, respectively). *D*, CT scans demonstrate a cystic right frontal mass with calcification. Tumor area C almost completely corresponded with the calcified lesion.



**Fig 2.** Histologic findings of tumor area A (*A* and *B*), tumor area B (*C* and *D*), and tumor area C (*E* and *F*). (H&E,  $\times 200$  [*A*, *C*, and *E*], MIB-1 immunostaining, hematoxylin counterstaining,  $\times 200$  [*B*, *D*, and *F*].) *A*, Tumor area A is moderately cellular and composed of cells with rounded, homogeneous nuclei and a swollen, clear cytoplasm (honeycomb appearance), consistent with low-grade oligodendroglioma. *B*, Tumor area A has MIB-1 positive cells and an MIB-1 labeling index of 1.8%. *C*, Tumor area B shows increased cellularity, marked cytological atypia, and high percentage of mitotic activity, consistent with high-grade (anaplastic) oligodendroglioma. *D*, Tumor area B shows frequent MIB-1 positive cells and an MIB-1 labeling index of 7.6%. *E*, Tumor area C is moderately cellular and composed of cells with rounded, homogeneous nuclei with calcification, consistent with low-grade oligodendroglioma. *F*, Tumor area C shows MIB-1 positive cells and an MIB-1 labeling index of 2.2%.

studies. The lesion with higher MET uptake ratio (tumor areas A and C) had normal oligodendroglial cells, whereas

the lesion with lower MET uptake ratio (tumor area B) was composed of anaplastic oligodendroglial cells. The in-

creased Ki-67 index of tumor area B was consistent with the malignant features seen with H&E staining.

The reason for such a paradoxical result remains unclear, but we speculate that in a high-grade tumor, the cell is so deranged that its amino acid uptake mechanism no longer works and, hence, no MET uptake. On the other hand, anaplastic area was demonstrated with gadolinium-enhancement on MR imaging, which reflected disruption of the blood-brain barrier. We also suspect that MET uptake ratio does not always correlate with disruption of the blood-brain barrier. Only tumor area C demonstrated remarkable calcification independent of MET uptake ratio.

## Conclusions

We demonstrated the case of relatively decreased MET uptake within the anaplastic component of a mixed-grade oligodendroglioma. Our exceptional case is interesting because of its value in elucidating the histologic and metabolic value of oligodendroglioma.

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