Whole body FDG-PET Diagnosis of primary central nervous system lymphoma

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Purpose

Primary central nervous system lymphoma (PCNSL) is less common than gliomas, the incidence of which is increasing in both immunosuppressed and immunocompetent individuals [1-5]. Pretreatment differentiation between PCNSL and other brain tumors is essential for therapeutic decision-making (Fig. 1 on page 2).

The clinical utility of FDG-PET for malignant lymphoma is well-established in the diagnosis, pretreatment staging or therapeutic effect evaluation with its very avid FDG accumulation. The usefulness of whole body FDG-PET has also been shown in the staging of PCNSL [6]. Several researchers have reported the diagnostic value of the difference of FDG uptakes between PCNSL and high grade glioma [7-10]. Considering these previous studies, the whole body FDG-PET is expected to play a role in the diagnosis of PCNSL by excluding the possibility of other diseases, such as brain metastases, infectious diseases, or cerebrovascular disorders.

The purpose of this study was to investigate the diagnostic accuracy of whole body FDG-PET for PCNSL among patients with undiagnosed brain tumors.

Images for this section:
Fig. 1: In the management of brain tumor, the nature of the tumor should be evaluated, by which the diagnostic strategy is decided. However, this evaluation can be sometimes difficult, especially when the differentiation of lymphoma and glioma is demanded.
Methods and Materials

Materials

We reviewed retrospectively the medical records of 27 patients who received FDG PET scans for the purpose of characterization of the brain tumors. Three patients who had history of malignancy, one whose serum glucose exceeded 130mg/dl, and one who was under 20 years old were excluded. Finally, 22 patients were included into this study. Age and sex of patients examined were as follows: age, 68 ± 12 years; male/female, 12/10.

Final diagnosis was determined by histopathologic examination or clinical follow up. Surgery in 10 patients and biopsy or CSF cytology in 10 patients was performed with histopathological confirmation. For the remaining 2 patients, the final diagnosis was based on clinical follow up. All available information, including follow up MRI and/or cerebrospinal fluid cytology, was used.

Methods

Imaging modalities

FDG-PET

Data acquisition was performed with a PET/CT system. The system could produce transverse, coronal, and sagittal reconstructions of CT, PET, and fusion PET/CT data for interpretation.

Patients fasted for at least 4 hours before FDG administration, and 185 MBq of FDG was intravenously administered to each patient. Images were acquired 1 hour after FDG administration.

MRI

Excluding one patient with an implanted pacemaker, MRI was performed for 21 patients before the PET scan. MRI images including diffusion-weighted images (DWI), T2 weighted images, or contrast enhanced T1 weighted images were acquired using 1.5-T superconducting system.

Image analysis of PET

We assumed that the local uptake of PCNSL would show more intense than that of other tumors, and that whole body PET would detect valuable extracranial lesions suggesting lymphoma or unexpected primary cancer. According to the PET evaluations described in the following paragraph, we examined the PET scans if they were specific findings
for PCNSL. We evaluated the diagnostic accuracy of PET for PCNSL and, in addition, compared it with that of MRI.

PET images were interpreted by at least two board-certified nuclear medicine physicians.

Brain tumor

Maximum Standardized Uptake Value (SUV max) was used to assess the metabolism of tumor quantitatively. After the region of interest was manually placed surrounding the entire lesions, SUV was calculated using the following equation: $\text{SUV} = \frac{\text{activity within the lesion (MBq/kg)}}{\text{activity injected (MBq)}} / \text{weight (kg)}$.

For qualitative assessment, the degrees and patterns of uptakes were evaluated. The degrees of uptakes were classified into 3 categories: "Intense", "Equivocal" or "Negative" compared to normal gray matter. Regarding the patterns of uptakes, we divided them into two visual groups: homogeneous or heterogeneous.

Extracranial lesions

Primary CNS lymphoma (PCNSL) is, by definition, an NHL restricted to the CNS, but it has been reported that PET revealed extracranial lesions in patients of PCNSL at a certain rate [6].

We interpreted increased extracranial FDG uptakes as pathological lesions when they visually exceeded physiological uptake in the organs. When available, findings of diagnostic CT or MRI were reviewed during the interpretation of PET images.

Results

The final diagnosis of brain tumors is listed in Fig. 2 on page 6. Of 22 patients, there were 9 with PCNSL, 6 with high grade glioma, 2 with brain metastasis, one with hemangioblastoma, and 4 with non-neoplastic lesion.

The representative cases with PCNSL, high grade glioma, or metastasis are shown in Fig. 3 on page 7, Fig. 4 on page 8, and Fig. 5 on page 9.

Quantitative assessment

FDG tumor uptakes of all cases were quantitatively assessed except for one case with intracranial hematoma showing a poor contrast with the physiological uptake. SUV max of PCNSL (ranging from 3.8 to 24.5, median 10.3) was significantly higher than that of other diseases (ranging from 3.7 to 13.1, median 5.5) ($P<0.05$; Mann-Whitney test). There was
no significant difference, however, of SUV max between patients with PCNSL and those with high grade glioma (ranging from 4.4 to 13.1, median 5.8) (P=0.08; Mann-Whitney test), which may be caused by the small number of patients (Fig. 6 on page 10).

**Qualitative assessment**

In the qualitative assessment, there were 8 cases with "Intense" uptakes including 7 with PCNSL and one with high grade glioma, and 14 cases with "Equivocal" or "Negative" uptakes including 2 with PCNSL, 5 with high grade glioma, and 7 with disorders other than lymphoma or high grade glioma. In all cases with PCNSL, the uptakes were evaluated as homogenous, while there were four cases showing heterogeneous uptakes among patients with other diseases (two with high grade glioma and two with brain metastasis).

**Diagnostic accuracy**

With an SUV max cut off value of 8.0, the sensitivity, specificity, and diagnostic accuracy for PCNSL was 78%, 83%, and 81% respectively. In a qualitative assessment, the sensitivity, specificity, and diagnostic accuracy was 78%, 92%, and 86 % respectively, if an "Intense" uptake is interpreted as a positive finding for PCNSL.

The sensitivity, specificity, and accuracy of MRI for PCNSL was 67% (6/9), 67% (8/12), and 67% (14/21), respectively. All the 14 cases with accurate MRI diagnosis were also evaluated correctly by FDG-PET. PET yielded true positive and true negative results for one of three cases with MRI false negative results and three of four cases with MRI false positive results, respectively. For remaining two with MRI false negative result and one with MRI false positive result, however, the PET results were concodantly false negative and false positive (Fig. 7 on page 11, Fig. 8 on page 12).

**Extracranial lesions**

Extracranial abnormal uptakes were found in four cases (18%), all of which helped the characterization of brain tumors by suggesting primary cancers in two cases with brain metastases (including lung cancer and gallbladder carcinoma), and bone involvement in two cases with lymphoma (Fig. 5 on page 9, Fig. 9 on page 13).

**Images for this section:**
<table>
<thead>
<tr>
<th>Final diagnosis</th>
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<tbody>
<tr>
<td></td>
<td>Resection</td>
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<td>Lymphoma</td>
<td>9</td>
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<tr>
<td>Glioma/ grade 3 or 4</td>
<td>6</td>
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<tr>
<td>Metastatic brain tumor</td>
<td>2</td>
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<tr>
<td>Hematoma</td>
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<td>Hemangioblastoma</td>
<td>1</td>
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<tr>
<td>PML*</td>
<td>1</td>
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<tr>
<td>Non-neoplasm</td>
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</table>

*Progressive multifocal leucoencephalopathy

Fig. 2: Here shows final diagnosis of this patient population. Note the difference of diagnostic procedures between patients with lymphoma and high grade glioma.
Fig. 3: In this 57 year old female patient, multiple cerebral lesions were detected by MRI, showing high intensity area in T2 weighted images (T2WI) and diffusion weighted images (DWI). Abnormal FDG-PET showed homogenous "positive" uptakes in the areas corresponding to the lesions detected by MRI. The lesions were finally diagnosed as PCNSL by biopsy.
Fig. 4: In this 68 year old female patient, the left temporal lobe lesion with high intensity in T2WI and contrast enhanced T1 weighted images (CE-T1WI) had a "negative" FDG uptake lower than cerebral cortex. Whole body FDG-PET scan showed no abnormal extracranial uptake. Surgery revealed the tumor as glioblastoma multiforme.
Fig. 5: In this 62 year old female with right parietal lobe tumor, an "equivocal" FDG accumulation was peripherally observed corresponding to the ring-shaped enhancement in MRI. Whole body FDG-PET detected an abnormal uptake in the right upper abdomen. Unexpected gallbladder carcinoma with brain metastasis was suspected, which was histopathologically confirmed by surgery.
Fig. 6

- SUV max
- PCNSL
- Glioma
- Other than PSNSL

P < 0.05

P = 0.08
Fig. 7

9 with PCNSL

“PCNSL” 6

“Others” 3

12 with disorders other than PCNSL

“PCNSL” 4

“Others” 8

“PCNSL” 1

“Others” 3

“PCNSL” 0

“Others” 8
Fig. 8: In this patient with a "negative" uptake in the brain tumor, no abnormal findings were seen in the extracranial organs at the time of first PET scan. Nine months later, diffuse uptake increase emerged in multiple organs including the bone marrow, lung, spleen, liver, and kidney. Bone marrow biopsy revealed that he had intravascular lymphomatosis.
Primary CNS lymphoma (PCNSL) is, by definition, an NHL restricted to the CNS, but it has been reported that PET revealed extracranial lesions in patients with PCNSL at a certain rate. In this 70 year old female patient with left frontal lobe tumor, extracranial abnormal uptakes were found in multiple bones, which helped the characterization of the brain tumor as lymphoma.
Conclusion

The whole body FDG-PET could be reasonably useful for the diagnosis of PCNSL. An avid FDG uptake was thought to be a pathognomonic sign of PCNSL, and the detection of extracranial lesions could be of some help for characterization of brain tumors. It should be noted that, however, there could be exceptional cases.

For the evaluation of brain tumors, MRI should be preferentially performed, but FDG-PET could play an additional role.

References


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