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Evaluation of treatment effects in brain abscess with positron emission tomography: Comparison of fluorine-18-fluorodeoxyglucose and carbon-11-methionine

Naohiro TSUYUGUCHI,* Ichiro SUNADA,**** Kenji OHATA,* Toshihiro TAKAMI,* Akimasa NISHIO,* Mitsuhiro HARA,* Joji KAWABE,*** Terue OKAMURA** and Hironobu OCHI***

*Department of Neurosurgery, **Department of Radiology and ***Department of Nuclear Medicine, Osaka City University Medical School
****Department of Neurosurgery, Saiseikai Ibaraki Hospital

Positron emission tomography (PET) imaging is in common use preoperatively to clinically evaluate patients who present with central nervous system mass lesions. The usefulness of PET is also recognized as a method to detect intracranial tumorous lesions. A number of papers report that some inflammatory processes also showed the uptake of Fluorine-18-Fluorodeoxyglucose (FDG) and Carbon-11-Methionine (Met) tracers. We performed two PET studies before and after treatment in 4 patients with brain abscess. PET showed the uptake of both tracers to the brain abscess before treatment. The area showing an increased uptake of Met corresponded closely to the enhanced area on both CT and MR images. FDG-PET visually showed an uptake of FDG in a small area corresponding to an enhanced lesion within the CT and MR images. After treatment the area of lesions became small on enhancement CT or MRI and both PET studies showed reduced lesion and decreased uptake. The mechanism of Met uptake in the inflammatory area may be related to the higher metabolic rate and the active transport of amino acids as well as disruption of the blood brain barrier. Furthermore, it appears that the mechanism of FDG uptake is also related to a higher metabolic rate and, in addition, is related to the increased density of inflammatory cells. PET studies, more directly, reflect the degree of inflammatory response in brain abscess than enhancement CT or MRI. Therefore, PET is useful in detecting the inflammatory lesion and assessing the clinical effects of antibiotics treatment on brain abscesses.

Key words: positron emission tomography, methionine, FDG, abscess, brain

INTRODUCTION

POSITRON EMISSION TOMOGRAPHY (PET) with Fluorine-18-Fluorodeoxyglucose (FDG) is an excellent diagnostic method for studying brain tumors.[1,2] High FDG uptake is usually associated with malignant tumors and low uptake with the benign type. On the other hand, Carbon-11-Methionine (Met) PET is clinically useful for evaluating the extent of cerebral gliomas rather than the grade of malignancy.

A number of papers report that some inflammatory processes also showed uptake of FDG and Met tracers.[3–11] We performed PET studies with Methionine or FDG before and after treatment in patient with brain abscess to evaluate the effect of antibiotics.

CASES AND METHODS

We examined FDG and Met PET studies in 4 patients with brain abscesses. All patients showed no sign of any other systemic disease, and all underwent PET studies before aspiration and drainage of the abscess and antibiotic treatment, and each case also received a histological diagnosis. Some patients had a second PET study as part of a follow-up examination that was conducted during the

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For reprint contact: Naohiro Tsuyuguchi, M.D., Department of Neurosurgery, Osaka City University Medical School, 1–4–3, Asahimachi, Abeno, Osaka 545–8586, JAPAN.
E-mail: nao@med.osaka-cu.ac.jp

Table 1 Case summary and the results of the first PET

Case	Age	Sex	Site	FDG		Met		Bacteria
				SUV	LN	SUV	LN	
1	59	M	L-f	2.6	0.72	/	/	/
2	66	M	L-o	3.88	0.64	1.93	1.76	α-streptococcus
3	43	M	R-f	/	/	2.63	1.63	peputococcus
4	68	M	L-f	/	/	1.69	1.64	α-streptococcus

M: male, F: female, L: left, R: right, f: frontal, o: occipital, SUV: standard uptake value, TN: tumor versus normal ratio

This presents the summary of our studies (cases 1–4)

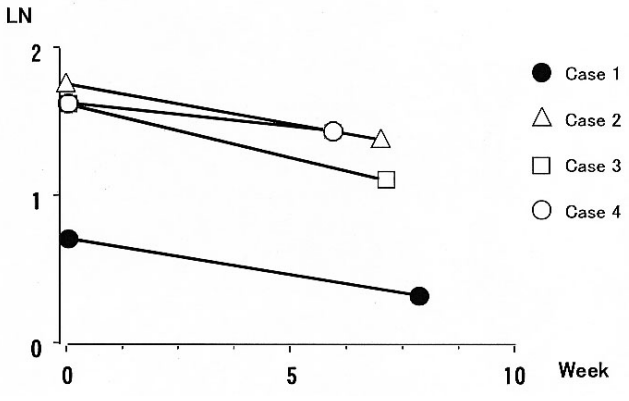


Fig. 1 The vertical axis: LN (tumor versus normal ratio), The horizontal axis: time (in weeks) between first and second PET studies. The open symbols show Met and the closed symbols show FDG. This figure indicates by graphs the changes in tracer uptake prior to and after treatment. In each case, the degree of uptake decreased.

clinical recovery period.

One patient underwent two FDG-PET studies that consisted of a pre- and post-treatment examination. Two patients underwent two Met-PET studies. One patient underwent one FDG-PET and two Met-PET studies. All patients received contrast CT imaging (Toshiba, X vigor) or Gd enhanced MR imaging (Siemens 1.0 T, Magnetom Impact) at pre-treatment and post-treatment within 3 days of PET being performed.

PET was performed with both FDG and Met. The PET scanner (Shimadzu, HEADTOM IV) had a spatial resolution of 4.5 mm full width at half maximum and a slice thickness of 7 mm. The PET images were reconstructed by measured attenuation correction. The images, compromising 10-minute scans, were obtained 50 minutes after intravenous administration of 185 MBq FDG for the FDG-PET studies after a 5-hour fasting period and 20 minutes after administration of 370 MBq Met injection for the Met-PET studies after a 5-hour fasting period. Throughout the study, the patient's eyes and ears were patched, and the patient's head was immobilized by a head holder. The portion of the lesion with the highest uptake of tracer was selected as the region of interest (ROI). If no abnormality could be detected in PET images, a region of interest of the same size was placed over an area corresponding to the CT or MR abnormality. Lesion versus normal ratio (LN) was defined as the ratio of average radioisotope counts per pixel in the lesion (L) ROI divided by average counts per pixel in several normal gray matter (N) ROIs, and the standardized uptake value (SUV) was calculated over the same lesion ROI as follows: SUV = [(pixel count/pixel volume)/(injected radioisotope activity/body weight)] × calibration factor. To evaluate the differences between FDG and Met uptake pre- and post-treatment, we produced a graph plotting the LN of the first and second PET studies against time (in weeks) during antibiotic treatment.

RESULTS

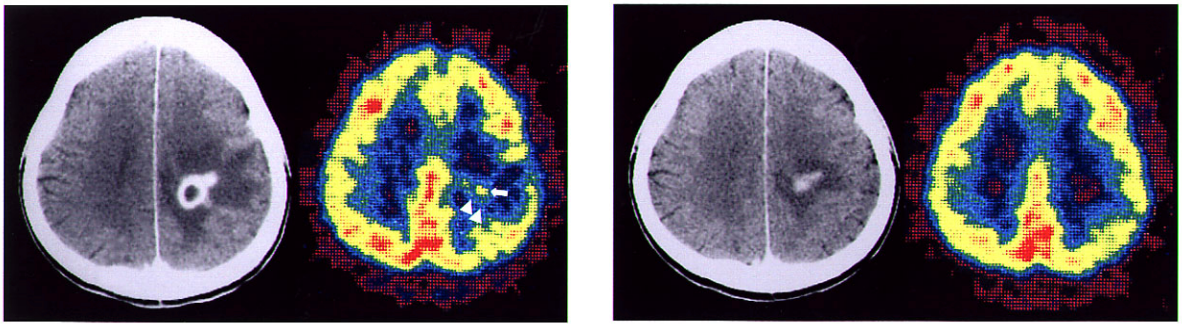
Table 1 shows the results of tracer uptake before treatment in all four cases. All abscess lesions showed higher Met uptake than contralateral gray matter (LN > 1.0). In our study (cases 2, 3 and 4), the area of increased Met uptake corresponded closely to a portion of the enhanced areas on the CT and MR images. On the other hand, FDG uptake in the abscess lesions in our cases was lower than that which occurred in contra lateral gray matter (LN < 1.0) and FDG was accumulated in a smaller area corresponding to an enhanced area within the CT and MR images (cases 1 and 2). The bacteria that caused the brain abscesses were of various types. The degree of tracer uptake in PET was not associated with a specific type kind of bacteria.

Figure 1 indicates by means of graphs the differences between tracer uptake pre- and post-treatment. In this figure, the vertical axis shows LN and the horizontal axis shows the time (in weeks) between the first and second PET studies. The open symbols show Met and the closed symbols show FDG. The first PET study was performed prior to pre treatment and the second PET study was performed after treatment had been completed. In all cases, the rate of uptake decreased, but Met uptake remained slightly high after treatment (LN > 1.0).

Two typical cases are presented.

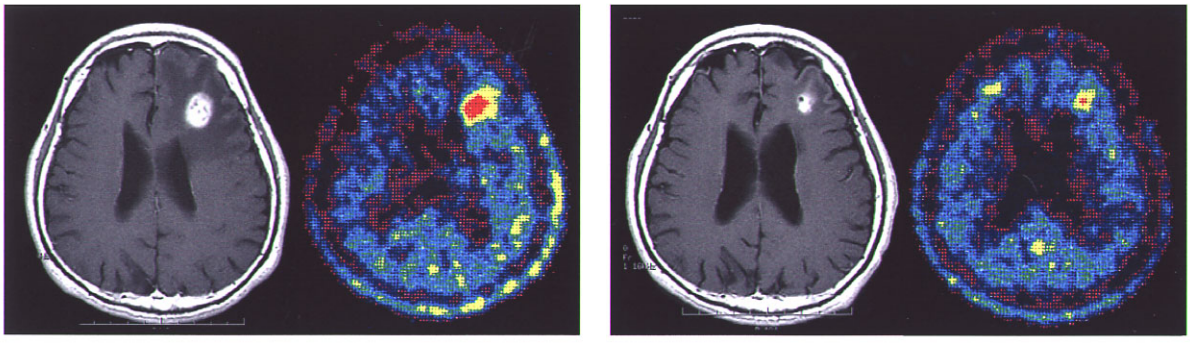
Case 1

A 59-year-old man had had headache and fever for over



a b c d

Fig. 2 Case 1: Brain abscess in left frontal lobe. Before antibiotic treatment, a contrast CT scan (a) shows a ring-like enhanced lesion with brain edema. FDG-PET (b) shows faint accumulation (*arrow*) and low accumulation (*arrowheads*) in a portion of ring-like lesion (*arrow*) and decreased uptake in the lesion around it. After two months administration of antibiotics, contrast CT (c) shows a small enhanced lesion and decreased edema. FDG-PET (d) shows no uptake.



a b c d

Fig. 3 Case 2: Brain abscess in left frontal lobe. Before antibiotic treatment, Gd enhanced MR image (a) shows an enhanced lesion with brain edema. Met-PET (b) shows high uptake in the lesion. After administration of antibiotics for seven weeks, Gd enhanced MR (c) shows a small enhanced lesion. Met-PET (d) shows a small accumulated lesion.

10 days before admission, and right hemiparesis occurred 2 days prior to admission. No other disease was evident. Contrast CT showed a ring-like enhanced lesion with brain edema in the left frontal region (Fig. 2a). An FDG-PET examination was performed, and the image revealed a faint frontal uptake (LN: 0.72, SUV: 2.60) of FDG and decreased uptake around the lesion. The uptake was between the gray and white matter (Fig. 2b). A brain abscess was suspected and stereotactic aspiration guided by CT was performed. Pathological examination of the biopsy sample showed the presence of a brain abscess, and a bacteriological study revealed the presence of streptococcus. After administration of antibiotics over for two months, the symptoms disappeared. At that time, contrast CT showed a small enhanced lesion and decreased edema (Fig. 2c). FDG-PET showed no obvious uptake in the lesion (LN: 0.33, SUV: 2.22) (Fig. 2d).

Case 2

A 68-year-old man had had headache and fever for 14 days or so before admission, and general convulsion occurred one day prior to admission. He had no history of previous occurrence. A Gd enhanced MR imaging showed a round enhanced lesion with brain edema in the left frontal region (Fig. 3a). A Met-PET examination was performed, and the image revealed high uptake of Met in the lesion (LN: 1.64, SUV: 1.69) but no uptake in the edema (Fig. 3b). The area of Met uptake corresponded closely to the areas of enhancement in MRI. A brain abscess was suspected and stereotactic aspiration guided by CT was performed. Pathological examination of the biopsy sample showed the presence of a brain abscess, and a bacteriological study revealed streptococcus. After administration of antibiotics for seven weeks, symptoms disappeared and the inflammatory response was negative. At that time, Gd enhanced MR showed a small enhanced lesion with no edema (Fig. 3c). Met-PET showed slight

uptake of Met in the lesion (LN: 1.45, SUV: 1.54) (Fig. 3d).

DISCUSSION

The PET examinations conducted in our study demonstrated a high uptake of Met and moderate uptake of FDG in the abnormal enhancement area on CT or MR before treatment. These data confirmed several recent reports of high uptake of Met and FDG related to brain abscesses.

Met-PET is a powerful tool to help differentiate tumorous lesions from non-tumorous tissue.[1,2] The Met-PET images can identify the existence of tumor cells as a hot lesion, even in a small tumor lesion. On the findings of an experimental study, Kubota et al. have reported that Met PET was able to differentiate inflammation from tumor[12] but increased uptake of Met has occasionally been seen in brain hematoma and in necrotic areas secondary to radiation therapy performed to treat brain tumors.[13,14] Ishii et al. presented results showing high Methionine uptake in a brain abscess caused by a gram positive bacterium, where the LN value was 1.76, and the area of increased Met uptake was larger than the area of the Gd enhanced lesion detected by MRI.[10] Dethy et al. showed increased uptake of Met in different zones at the periphery of the abscess and an LN value of 1.7.[11]

Other experimental data suggest that Met uptake is related to the protein synthesis rate and the activity of the amino acid transport system.[15] Ishii et al. speculated that the mechanism of Met uptake in brain abscess was due to increased metabolism and active amino acid transport as a result of the increased density of inflammatory cells as well as disruption of the blood brain barrier (BBB) arising from the discrepancy between the area of Met uptake and the Gd enhanced lesion as shown on MRI.[10] In the present study, the area of increased uptake of Met corresponded closely to a portion of the enhanced areas on the CT and MR images. On the other hand, decreasing isotope counts for Met after treatment were indicated in the second PET. Therefore, the mechanism of Met uptake in brain abscess may be related not only to disruption of the BBB but also to increased metabolism or active amino acid transport and increased density of inflammatory cells, as was reported by Ishii.[10]

FDG-PET is a useful way to study glucose metabolism in intracranial disease, particularly brain tumors.[2] High FDG uptake has been observed in malignant brain tumors and low uptake in differentiated gliomas. In the post-treatment follow-up period, FDG-PET can be used to assess whether residual tumors are present and can also detect tumor recurrence.[16] Som et al. reported no increase in FDG uptake in experimental inflammatory lesions and suggested that FDG could be useful in the differential diagnosis of tumors versus inflammatory lesions,[17] but some studies have reported high FDG uptake in humans with inflammation.[3–5] Tahara et al. reviewed two cases of abdominal abscess both of which displayed high FDG uptake.[6] Dethy et al. reported ring-like accumulation of FDG in a brain abscess with an uptake LN ratio of 1.0.[11] Mineura et al. reported high uptake of FDG in enhanced lesions on enhanced CT.[7] Sasaki et al. showed an accumulation of FDG at the periphery of the abscess.[8] Meyer et al. showed that the FDG uptake appeared to occur within the irregular boundary of the contrast-enhanced walls of the abscess.[9] All the above studies showed the visual accumulation of FDG in the abscess. The uptake of FDG in the abscess was the same as that in contralateral gray matter but higher than in contralateral white matter. Our two FDG-PET studies showed LN values of less than 1.0, but we detected accumulation of FDG upon visual evaluation. An autoradiographic study in brain tumors has indeed emphasized the possible contribution of macrophages and young granulation tissue to increased FDG uptake.[18] Furthermore, Yamada et al. showed that FDG uptake increased in turpentine-induced inflammatory tissue.[19] This inflammation is characterized by fibroblast proliferation and neovascularization with mononuclear cell infiltration (macrophages, lymphocytes and plasma cells). It was suggested that macrophages and neutrophils in inflammatory tissue utilize glucose as an energy source for chemotaxis and phagocytosis, whereas fibroblasts utilize the same substance for proliferation. In our study, FDG-PET showed increased uptake of FDG in a smaller area, corresponding to an enhanced area, which indicated the BBB disruption, within the CT and MR images. Therefore, although the mechanism of FDG uptake in abscesses remains unclear, it may be related to increased glucose metabolism in the inflammatory process and increased cellularity rather than disruption of the BBB in the brain abscess.

We suggest that PET studies more directly reflect the degree of inflammatory response in brain abscess than enhancement CT or MRI, as our finding showed decreased PET tracer uptake on treatment. Both PET studies could be useful in evaluating the clinical effects of treatment on brain abscesses. Met-PET is more sensitive in detecting lesions, but may be more affected by the BBB distruption than FDG-PET. From the standpoint of visual diagnosis the degree of FDG uptake may correlate with the clinical course.

CONCLUSION

Our results show that both FDG and Met tracers accumulate in brain abscesses as well as in brain tumors, and we suggest that PET could be useful in detecting inflammatory lesions and recognizing the clinical effects of antibiotics on brain abscess.

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