

Clinical Article

The Role of ¹⁸F-Fluorodeoxyglucose Positron Emission Tomography in the Treatment of Brain Abscess

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Objective : The purpose of this study was to evaluate whether ¹⁸F-fluorodeoxyglucose positron emission tomography (FDG-PET) can be used to assess the therapeutic response of brain abscess.

Methods : A study was conducted on 10 consecutive patients with brain abscess. Magnetic resonance imaging (MRI) with diffuse-weighted imaging (DWI) was performed at 3 and 6 weeks after surgical treatment and intravenous antibiotics therapy and FDG-PET at 6 weeks after treatment. The extent of the abscess, signal changes on MRI, and FDG-PET standardized uptake values were analyzed and correlated with the response to therapy.

Results : Aspiration or craniotomy with excision of the abscess followed by intravenous antibiotics for 6-8 weeks resulted in good recovery with no recurrence. In 10 patients, two had low signal intensity on the DWI; one had no uptake on FDG-PET imaging after 6 weeks antibiotics and discontinued intravenous treatment, but the other patient had diffuse, increased uptake on FDG-PET imaging after 6 weeks antibiotics and underwent an additional 2 weeks of intravenous antibiotics. The remaining eight patients had high signals on the DWI. Four had no uptake on FDG-PET imaging and the treatment period varied from 6 to 8 weeks (mean, 6.75 weeks). Among the other four patients, FDG was accumulated in a diffuse or local area corresponding to a high signal area within the DWI and 2 weeks of intravenous antibiotics was added.

Conclusion : MRI plus FDG-PET improved the accuracy of assessing therapeutic responses to antibiotics treatment of brain abscess and aided in optimizing therapy.

Key Words : Brain abscess · ¹⁸F-Fluorodeoxyglucose positron emission tomography · Magnetic resonance imaging · Diffusion-weighted imaging · Antibiotics.

INTRODUCTION

It is well known that evaluating the therapeutic effects of antibiotic therapy on brain abscess includes assessment of clinical symptoms, the results of laboratory tests, and the findings on conventional magnetic resonance imaging (MRI) with diffusion-weighted imaging (DWI). MRI has contributed greatly to the diagnosis of brain abscess. While brain abscess displays a ring-enhancing lesion on contrast-enhanced T1-weighted images, it shows strong high signal on DWI. Treatment response in brain abscess has been monitored by showing the resolution of ring enhancement and the disappearance of the high-signal on DWI. However, discordance between the signal intensity on the DWI and contrast enhancement is often found despite ap-

propriate long-term intravenous antibiotics treatment. It has been reported that contrast enhancement did not disappear completely, although DWI demonstrated low signal on the follow-up²). Recently, several studies have reported that brain abscesses have high uptake of ¹⁸F-Fluorodeoxyglucose (FDG)^{3,8,12,17,19}). Tsuyuguchi et al.¹⁹) suggested that positron emission tomography (PET) studies might more directly reflect the degree of the inflammatory response in a brain abscess than the enhancement pattern of the computed tomography (CT) or MRI; their findings showed decreased PET tracer uptake with treatment. Moreover, postoperative abscess containing bloody lesions may confuse the interpretation of the signal intensity on MRI. However, FDG-PET scan can still be helpful for analyzing an abscess with a small hemorrhage. A method that is capable of reliably evaluating treatment response would be of great benefit both for assessing the therapeutic outcome and for minimizing high cost, long-term antibiotics with all of its known side effects.

The objective of this study was to evaluate the efficacy of FDG-PET for the evaluation of the response to intravenous antibiotic treatment of brain abscesses.

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MATERIALS AND METHODS

Patient population

A study was performed on 10 consecutive patients with brain abscess, who underwent aspiration and drainage or craniotomy with excision, and intravenous antibiotic treatment at one center between 2006 and 2008. Aspiration was recommended for small or deep-seated abscesses as well as those located in eloquent area and multiple abscesses. Craniotomy with excision was performed for larger abscesses with significant mass effect that are superficial and located in non-eloquent regions. The enrolled patients provided written informed consent to participate in the study. Aspirates of purulent material were obtained for culture, immediate Gram stain, and pathological examination. Initial broad-spectrum antibiotic therapy was started until the final results of the culture and sensitivity were available, and then the antibiotic regimen was adjusted as indicated. All patients received intravenous antibiotics with 1) ceftriaxone or cefotaxime+metronidazole, or 2) vancomycin+meropenem. Drainage catheters were left in place for three to six days. Catheter removal was based on the amount of drainage and imaging findings on the follow-up CT scans.

Conventional MRI with DWI was performed at 3 and 6 weeks after surgical treatment and intravenous antibiotics therapy. FDG-PET was performed at 6 weeks following antibiotic treatment to assess the clinical effects of treatment. All MR studies were performed with a 1.5-T or 3.0-T imager capable of echo planar imaging. The signal intensities of the lesions, on the DWI, were interpreted relative to the contralateral brain parenchyma.

FDG-PET acquisition

PET scanning was performed using a Hi-Rez Reveal PET/CT scanner (CTIMI, Knoxville, TN, USA), which was a combined Lutetium Oxyorthosilicate crystal PET scanner with a 6-slice CT scanner. After fasting for at least six hours, the patients received an intravenous injection of 370 MBq (10 mCi) of ^{18}F -FDG and were instructed to rest with their eyes shut in a quiet room. After 40 minutes of resting, transmission CT images were performed for attenuation correction, and then emission PET images were obtained for about 10 minutes with a 336×336 matrix. The transmission corrected images were reconstructed using the ordered-subset expectation maximization algorithm. The PET/CT scanner provides 81 image planes across the 162 mm axial field-of-view with 2.0 mm slice spacing and reconstructed image resolution of 4.5 mm full width at half maximum at center. Any area with increased FDG uptake above the intensity of the adjacent gray/whiter matter was interpreted as a positive lesion by visual inspection.

RESULTS

The clinical characteristics of the patients are summarized in

Table 1. The patients ranged in age from 44 to 67 (average 53.1 years). There were seven men and three women. The initial symptoms were headache in five patients, seizures in three patients, and confusion in two patients. Four patients with a brain abscess underwent burr hole surgery with aspiration, and craniotomy with excision was performed in 6 patients. The removal of the abscess by aspiration or craniotomy with excision, and intravenous antibiotic treatment resulted in good recovery and no recurrence. The mean volume of the abscess on contrast-enhanced T1-weighted MRI was 21.8 cm³ (range 3.8-53.8 cm³) before the aspiration. On the 3-week MRI, the mean volume was reduced to 6.6 cm³ (range 1.6-22.4 cm³). On the 6-week MRI, the mean volume was 1.9 cm³ (range 0.2-3.6 cm³). No follow-up contrast-enhanced T1-weighted MRI showed the complete resolution of rim enhancement.

Fig. 1 shows the summary of the 6-week MRI with DWI and FDG-PET imaging results and the therapeutic response data. Among the 10 patients, two had low signal intensity on the DWI; one had no uptake on FDG-PET imaging after 6 weeks antibiotics and discontinued intravenous treatment at 6 weeks (Fig. 2), however, the other had diffuse, high uptake on FDG-PET imaging at 6 weeks antibiotic treatment and had 8 weeks of treatment with additional 2 weeks of intravenous antibiotics (Fig. 3). The remaining eight patients had high signal intensity on the DWI. Four patients had no uptake on FDG-PET imaging at 6 weeks and treatment period varied from six to eight weeks (mean 6.75 weeks) (Fig. 4). Among the other four patients, FDG at 6 weeks PET imaging was accumulated in a diffuse or local area corresponding to a high signal area within DWI and two weeks of intravenous antibiotics was added (Fig. 5). In two patients, subacute intraleisonal hemorrhages in the abscess cavity were found on the MRI; these lesions showed high signal intensity on the DWI and no FDG uptake.

Among the 10 patients, nine had predisposing factors that included: a contiguous infection that spread from the middle ear (1 patient) and teeth (1 patient); one patient had a basal skull fracture; meningitis coexisted with the brain abscess in three patients and a subdural empyema was also present in one patient. The co-morbid conditions were systemic lupus erythematosus, a liver abscess, pneumonia, diabetes mellitus, liver cirrhosis, and congenital heart disease. One patient had both diabetes mellitus and liver cirrhosis.

The brain abscess was caused by many different organisms that were isolated from cultured specimens: *Coagulase negative staphylococcus* in 1 specimen, *Streptococcus pneumoniae* in 1 specimen, *Providencia stuartii* in 1 specimen, *Fusobacterium nucleatum* in 1 specimen, *Actinomyces* in 1 specimen, and *Micrococcus species* in 1 specimen were isolated from the abscess. AFB 3+ staining was noted on microscopy in 1 specimen, but there was no growth on culture. In one patient, *Klebsiella pneumoniae* was isolated from the sputum; however, it was not identified in the abscess fluid. Among the 10 patients, there were 2 patients with no organism identified.

Table 1. Summary of 10 patients with brain abscess

Case	Sex/Age	Site	Predisposing factor	Postcontrast T1 image	MRI Volume (cc)		Organism
					Initial	6 weeks	
1	M/60	Cerebellum	Dental infection	Rim enhancement	10.9	1.2	Actinomycosis
2	M/51	Frontal, subdural	Basal skull fracture	Subdural empyema	32.4	3.6	No growth
3	F/47	Frontal	Meningitis, SLE	Rim enhancement	6.5	1.2	Micrococcus species
4	M/48	Parietal	Unknown	Rim enhancement	19.2	2.6	Coagulase negative staphylococcus
5	F/67	Multiple	Liver abscess	Rim enhancement	3.8	0.6	No growth
6	M/68	Cerebellum	Pneumonia	Rim enhancement	16.2	0.2	Klebsiella pneumonia (sputum)
7	F/54	Multiple	Meningitis	Rim enhancement	17.4	2.3	AFB stain 3+
8	M/47	Parietal	Diabetes mellitus, liver cirrhosis	Rim enhancement	10.3	1.3	Streptococcus pneumoniae
9	M/44	Temporal	Otitis media	Rim enhancement	47.5	3.2	Providencia stuartii
10	M/45	Frontal	Meningitis, congenital heart disease	Rim enhancement	53.8	3.2	Fusobacterium nucleatum

Case	Surgical method	DWI signal; 6 weeks	FDG-PET SUVmax; 6 weeks	IV antibiotics (duration)	Antimicrobial therapy
1	Excision	Low	(-)	6 weeks	Ceftriaxone, metronidazole
2	Excision	Low	Diffuse hypermetabolism	8 weeks	Ceftriaxone, metronidazole
3	Aspiration	High (lesion)	(-)	6 weeks	Vancomycin, meropenem
4	Aspiration	High (lesion)	(-)	6 weeks	Cefotaxime, metronidazole
5	Aspiration	High (rim)	(-)	8 weeks	Ceftriaxone, metronidazole
6	Excision	High (surrounding)	(-)	7 weeks	Ceftriaxone, metronidazole
7	Excision	High (lesion)	Diffuse uptake on soft tissue	8 weeks	Ceftriaxone, metronidazole, anti-tbc drug
8	Aspiration	High (surrounding)	Diffuse uptake on soft tissue	8 weeks	Ceftriaxone, metronidazole
9	Excision	High (partial)	5.2	8 weeks	Cefotaxime, metronidazole
10	Excision	High (partial)	6.4	8 weeks	Cefotaxime, metronidazole

DWI : diffusion-weighted imaging, FDG-PET : fluorodeoxyglucose positron emission tomography, SUV : standard uptake value, tbc : tuberculosis

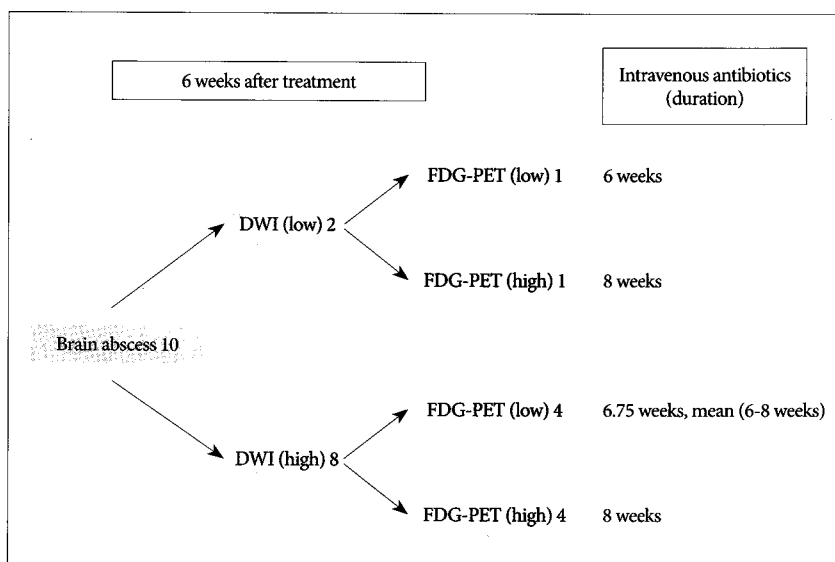


Fig. 1. Flow chart illustrating the results following the treatment of brain abscesses. DWI : diffusion-weighted imaging, FDG-PET : fluorodeoxyglucose positron emission tomography.

DISCUSSION

The advent of CT scanning has resulted in a dramatic decrease in the mortality rate from brain abscesses because of early and improved diagnosis with exact localization of the lesion¹⁴. Recently, the additional use of conventional MRI with DWI has played an important role in the diagnosis and follow-up of brain abscesses^{7,10,18}. Restricted diffusion within the abscess cavity on DWI is characteristic of an abscess, which might reflect the high viscosity of protein filled fluid and the high concentration of inflammatory cells. The interpretation of imaging of brain abscesses following antibiotic treatment is important factor for the determination of treatment duration

and the therapeutic response. The appropriate duration of antibiotic therapy remains unclear. A six to eight week course of intravenous antibiotics has been generally recommended, provided that the causative organisms are susceptible to the medication and that adequate surgical drainage can be performed^{5,7,10}. Mamelak et al.¹¹ proposed that intravenous antibiotics should be continued for at least 6 weeks. Long-term intravenous antibiotics increase the cost, the hospital stay, and drug induced complications, such as bone marrow suppression, peripheral neuropathy, and future drug resistance. Therefore, Sjölin et al.¹⁶ suggested that in certain situations, a shorter course of treatment should be considered.

Traditional radiographic methods used to assess the therapeutic response to antibiotic therapy, such as conventional MRI with DWI, can provide clinically useful information on the abscess volume and extent. The disappearance of rim enhancement and the decrease of DWI signal density within brain abscess after appropriate intravenous antibiotic treatment has been demonstrated in the literature^{2,5,10}. DWI is based on the microscopic motion of water molecules and depends mostly on the water located in the extracellular space⁹. Restricted water motion in brain abscess has increased signal intensity on DWI. Contrast enhancement usually correlates with the disruption of the blood-brain barrier (BBB). The reasons for discordance between the signal intensity on the DWI and contrast enhancement contrast-enhanced T1-weighted images remain uncertain. Several recent studies have shown that DWI was superior to conventional contrast-enhanced T1-weighted imaging in evaluating the success or failure of abscess therapy^{2,5}. Cartes-Zumelzu et al.³ reported that rim enhancement in follow-up MRI decreased slightly but did not change substantially in some cases compared with the respective features on pretreatment studies, whereas DWI demonstrated low signal intensity.

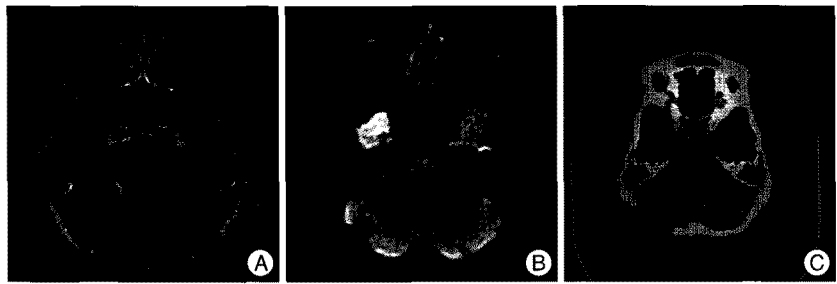


Fig. 2. Case 1 : Brain abscess in the right cerebellar hemisphere. Preoperative contrast-enhanced T1-weighted image (A) shows ring enhancement with central necrosis. After 6 weeks of antibiotics, diffusion weighted image MRI (B) reveals low signal intensity and FDG-PET (C) shows no uptake. The treatment period with intravenous antibiotics was 6 weeks. MRI : magnetic resonance imaging, FDG-PET : fluorodeoxyglucose positron emission tomography.

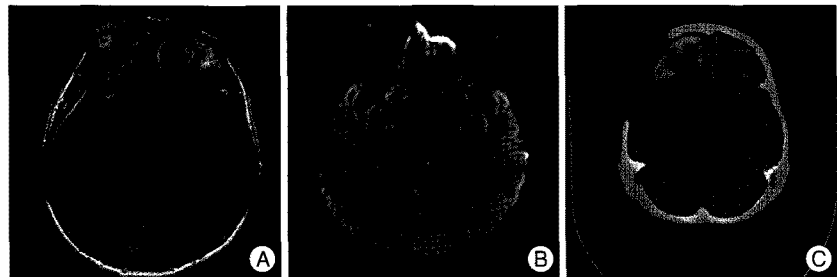


Fig. 3. Case 2 : Brain abscess in the right frontal lobe. Preoperative contrast-enhanced T1-weighted image (A) shows an enhanced lesion with subdural empyema. After 6 weeks of antibiotics, diffusion weighted image MRI (B) reveals low signal intensity and FDG-PET (C) shows diffuse and high uptake. The treatment period with intravenous antibiotics was 8 weeks. MRI : magnetic resonance imaging, FDG-PET : fluorodeoxyglucose positron emission tomography.

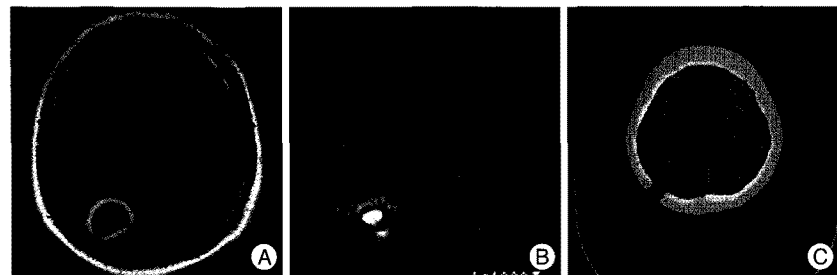


Fig. 4. Case 4 : Brain abscess in the right parietal lobe. Preoperative contrast-enhanced T1-weighted image (A) shows ring enhancement with central necrosis. After 6 weeks of antibiotics, diffusion weighted image MRI (B) reveals persistent high signal intensity in the abscess cavity, which was related to postoperative bleeding into the abscess cavity and FDG-PET (C) shows no uptake. The treatment period with intravenous antibiotics was 6 weeks. MRI : magnetic resonance imaging, FDG-PET : fluorodeoxyglucose positron emission tomography.

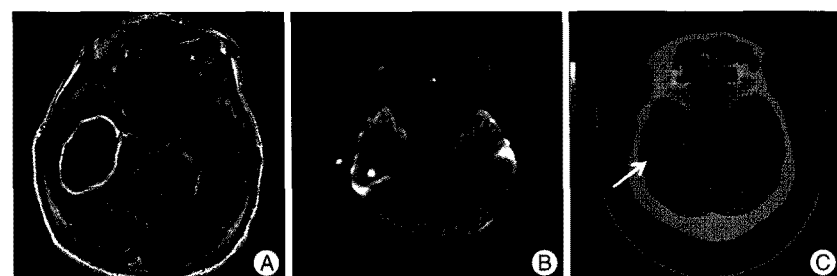


Fig. 5. Case 9 : Brain abscess in the right temporal lobe. Preoperative contrast-enhanced T1-weighted image (A) shows ring enhancement with central necrosis. After 6 weeks of antibiotics, diffusion weighted image MRI (B) reveals persistent high signal intensity, like a spot, in the abscess cavity and FDG-PET (C) shows high uptake (arrow, SUV_{max} : 5.2). The treatment period with intravenous antibiotics was 8 weeks. MRI : magnetic resonance imaging, FDG-PET : fluorodeoxyglucose positron emission tomography, SUV : standardized uptake value.

FDG-PET is a useful method for the study of glucose metabolism in intracranial disease, particularly brain tumors⁴). Functional imaging using PET is expected to be more sensitive than anatomical imaging such as CT and MRI in detecting abnormalities of the brain; therefore, PET imaging might have a high clinical value in some cases¹³). Several studies have shown high FDG uptake in an abscess^{3,4,8,12,15,19,20}. Yamada et al.²⁰ showed that FDG uptake increased in turpentine-induced inflammatory tissue. This inflammation is characterized by fibroblast proliferation and neovascularization with mononuclear cell infiltration. It was suggested that macrophages and neurotrophils in inflammatory tissue utilize glucose as an energy source for chemotaxis and phagocytosis. Although the mechanism of FDG uptake in abscesses remains unclear, it may be related to increased glucose metabolism associated with the inflammatory process and increased cellularity, rather than disruption of the BBB in the brain abscess¹⁹). Ichiya et al.⁶ reported that FDG-PET can be successfully used for the detection of infectious lesions as well as in the evaluation of lesion activity. The disappearance of hot uptake on the FDG-PET indicates a treatment of brain abscess. Tsuyuguchi et al.¹⁹ reported that PET studies more directly reflect the degrees of inflammatory response in brain abscess than enhancement on MRI—thus suggesting that PET is useful in detecting inflammatory lesions and in assessing the clinical effects of antibiotics treatment. FDG uptake corresponds closely to the area of contrast enhancement on MRI. However, FDG-PET showed increased uptake of FDG in a smaller area, corresponding to an enhanced area, which indicated the BBB disruption within MRI.

To our knowledge, there are no reports with large number of patients, which described assessment of therapeutic response in patients with brain abscess using follow-up DWI and FDG-PET. In the present study, 50% of the patients had discrepancies between the FDG-PET and DWI. Among 2 patients with low signal intensity on the DWI, one case with hot FDG uptake had eight weeks of treatment with an additional two weeks of intravenous antibiotics. In another case with low FDG uptake, one discontinued the intravenous antibiotics at 6 weeks. In 4 patients with high signal intensity on the DWI with high FDG uptake, intravenous antibiotics were provided for eight weeks. Four patients with high signal intensity on the DWI and no uptake on the FDG-PET, treatment period was determined by clinical findings and imaging, and varied from six to eight weeks. The FDG-PET imaging could be used to determine whether treatment at six weeks is sufficient following intravenous antibiotics therapy for a brain abscess, adding information on the abscess to that obtained from the DWI. The results of this study suggest that FDG-PET plus DWI might be decisive for the assessment of the clinical outcome of antibiotic treatment of brain abscesses.

Abscesses with hemorrhage on conventional MRI cause confusion in the interpretation of the signal intensity on the DWI¹). The subacute blood products appear as high signal intensity on the DWI in the abscess cavity. From diffusion measurements of

intracranial hematomas, intracellular hemoglobin states (oxy-, deoxy-, and methemoglobin) have been reported to cause restricted diffusion (high signal) in hyperacute, acute, and early subacute hematomas despite their marked differences on conventional MRI¹). Although an abscess can be fully treated with complete recovery, high signal intensity can persist on the DWI. In two patients (cases 3 and 4), the lesions showed no uptake on the FDG-PET and intravenous antibiotics were discontinued at six weeks.

Conventional MRI with DWI is not always accurate in assessing the outcome of treatment of a brain abscess; discrepancies between FDG-PET and DWI are found in some cases. Therefore, conventional MRI with DWI plus FDG-PET can improve the accuracy of evaluating treatment effects. Little is known concerning FDG-PET finding associated with follow-up MRI in the assessment of brain abscess therapy. The number of patients included in this study was small. Therefore, this study should be interpreted as a preliminary study on the improvement of evaluation of therapeutic response in patients with brain abscess.

CONCLUSION

Our results suggest that imaging findings of the FDG-PET as well as the MRI improve the accuracy of assessing therapeutic response to antibiotics in patients with brain abscesses and aid in optimizing therapy. Further studies are needed to investigate FDG-PET and MRI findings both prior to and following antibiotic treatment.

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