

The Clinical Relevance of ^{18}F dUrd in Diagnosing Brain Tumor

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Introduction

In the previous issues of this report¹⁻²⁾, we reported the possible usefulness of ^{18}F -fluoro-2-deoxyuridine (^{18}F Urd) as a brain tumor detecting agent for positron emission computed tomography from the view points of nucleic acid metabolism through the basic experiment using a rat brain tumor model. Then, the preliminary results of the clinical application of this new tracer to the brain tumor patients was also reported³⁾. In this paper, the further clinical investigations of ^{18}F Urd by means of positron emission computed tomography in cerebral glioma patients are presented.

Materials and Methods

13 glioma patients were studied; 8 cases of high grade glioma and 5 cases of low grade glioma. The histological diagnosis were made based on the materials obtained from autopsy, operative specimen or stereotaxic biopsy. 4-8 mCi of ^{18}F Urd was injected intravenously in each patients and a serial scannings were made every five minutes until 40 to 50 minutes using ECAT II. Then the additional one or two separate scannings were made. The two cases were studied using the high resolution, multi-slice positron emission computed tomography-CTI 931, which has recently introduced to our center. The images obtained by positron emission computed tomography and differential absorption ratio (DAR) were investigated.

Results

In all 8 cases of high grade glioma, the clear images of brain tumor were visualized with high contrast on positron emission computed tomography. DAR of the brain tumors were about 3-4 times higher than that of homolateral brain tissue in all 8 cases. In contrast, the positive images of brain tumor were not obtained in 5 cases of benign glioma and DAR in the tumor was similar to that of homolateral brain tissue.

In a case of high grade glioma studied by the new positron emission computed tomography, the interesting result was obtained. Low density area was observed on CT scan, however, the definite tumor location was not certain

even with contrast enhancement (Fig. 1). In contrast, ^{18}F Urd study with the high resolution machine clearly showed the small high uptake lesion at left frontal lobe (Fig. 2). This patient was undertaken operation later, and the histological observation revealed that the specific feature of high grade glioma where ^{18}F Urd was highly accumulated on the positron emission computed tomography.

Discussion

Fluorinated pyrimidines are known to reflect the nucleic acid metabolism⁴⁾, and among the many ^{18}F -radiopharmaceuticals for neoplasms, we paid special attention to ^{18}F Urd, since the tumor uptake of ^{18}F Urd is higher than that of ^{18}F -5-fluorouracil or ^{18}F -fluorouridine⁵⁾. In our previous study, only the brain tumor image was turned up on autoradiography by using ^{18}F Urd, and the tissue sampling analysis revealed that the uptake of ^{18}F Urd in the experimental brain tumor was about ten times higher than that of contralateral normal cortex¹⁾. Also the multiple labeled autoradiographic investigation⁶⁾ showed that the tumor image of ^{18}F Urd was clearly different from that of 2-amino-1- ^{14}C -isobutyric acid which manifests blood brain barrier impairment, but was rather similar to that of 2- ^{14}C -thymidine²⁾. These results suggested that the accumulation of ^{18}F Urd was thought to indicate mainly nucleic acid metabolism of the brain tumor.

On the basis of the above mentioned basic investigations, the clinical application of ^{18}F Urd was carried out to the human glioma patients. As results, the ^{18}F Urd brain tumor images were clearly distinct in all 8 cases of high grade glioma, however, positive image of the tumor was not obtained in all 5 cases of low grade glioma. In addition, DAR pattern showed obvious difference between high and low grade gliomas; the former was 3-4 times higher than the contralateral brain tissue, while the latter remained indistinguishable from the normal brain tissue. These results support our previous report³⁾.

The most interesting finding in this series was obtained in the case studied by the new positron emission computed tomography. Although the recent development of Magnetic Resonance Image has enabled us to detect the small abnormal lesion clearly, it has not yet differentiated the histological grading of glioma. probably it would be the first report to detect the small malignant lesion, which CT scan failed to point out its exact location, from the view points of nucleic acid metabolism.

The combination of high resolution positron emission computed tomography and ^{18}F Urd seems to have a big power in making qualitative diagnosis of glioma patients.

Acknowledgment

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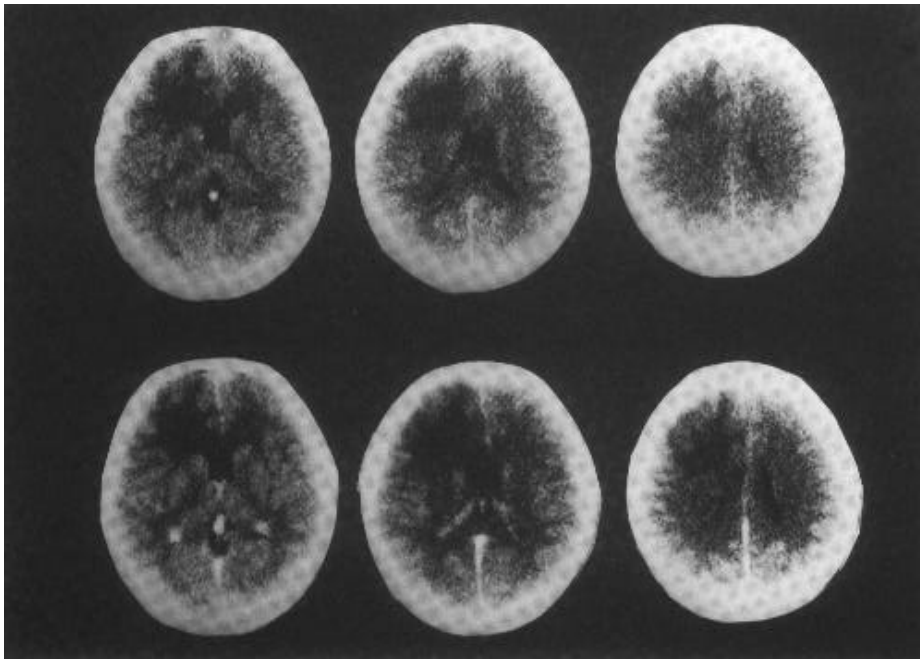


Fig. 1. CT scan of a case of high grade glioma. Low density area was seen at left frontal region, however, definite location of the tumor was not certain even with contrast enhancement (below).

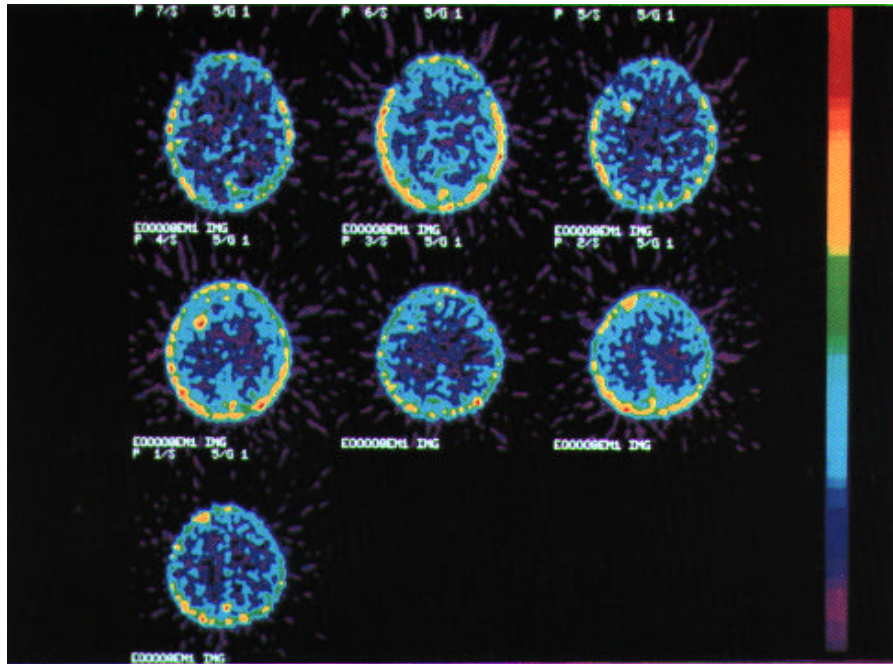


Fig. 2. High resolution positron emission computed tomography image with ^{18}F FDUrd of the same case. The small high uptake lesion was clearly visualized at left frontal region.

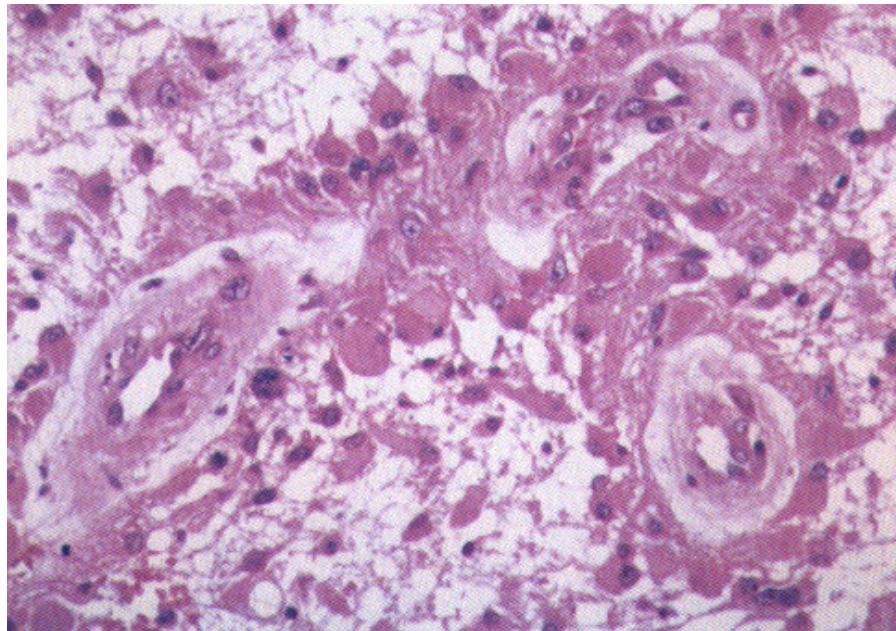


Fig. 3. The histological photograph from the operative specimen of the same case, showing the characteristic feature of high grade glioma.