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Positron emission computed tomography (PECT) has enabled us to demonstrate various in vivo physiological information with the aid of positron emitting radiopharmaceuticals, which could not be obtained by current diagnostic tools. In this study, we investigated the relationship between glucose and amino acid metabolism in human and experimental brain tumors.

Materials and Methods

1) Regional glucose metabolism and amino acid metabolism were examined by ECAT II using 18F-fluorodeoxyglucose (FDG) and 11C-methionine respectively in six brain tumor patients, three were high grade and three were low grade astrocytoma. In all cases, the PECT examination started from intravenous bolus injection of the tracer, then a serial scan was performed. The examination time was 50-70 minutes, and arterial blood samples were withdrawn at given times for evaluating radioactivity. Histological diagnosis were made by stereotaxic biopsy or operative specimen.

2) The two types of experimental rat brain tumors; implanted KEG-1 glioma and ethylnitrosourea (ENU) induced brain tumor models, were used for assessing glucose and amino acid metabolism simultaneously by the multiple labeled autoradiographic technique we have developed.[3] 18F-FDG (2-3mCi) and 14C-methionine (100μCi/kg) were given intravenously to anesthetized tumor bearing rats. Animals were sacrificed 45 minutes after injection and the frozen brains were cut 20 μm thickness in a cryostat. Sections were then exposed to X-ray films twice; for the first six hours to obtain the 18F image and two days later, the second exposure was done to get 14C image. The sections used for autoradiography were subsequently stained by hematoxylin-eosin and compared with autoradiographic images.

Results

High grade astrocytoma patients showed high uptake of both 18FDG and 11C-methionine in their tumors comparing with the contralateral brains (Fig.

1). On the other hand, low accumulation of 18FDG was observed in three cases of low grade astrocytoma while the 11C-methionine uptake remained elevated in the tumors (Fig. 2). In the KEG-1 glioma which grew rapidly the accumulation of both 18FDG and 14C-methionine were higher than the contralateral brains (Fig. 3). However, dissociation of glucose and amino acid metabolism was observed in the slowly growing ENU induced brain tumors; low uptake of FDG and high uptake of methionine (Fig. 4). We also observed that the accumulating patterns of FDG and methionine were contrary to each other in some tumors; methionine seemed to accumulate in the surface area and FDG gathered mainly in deep area of the tumors (Fig. 3).

Discussion and Conclusion

It has been already reported about the correlation between glucose metabolism and histological grading in cerebral gliomas[2], and our results seemed to support the previous reports both in clinical and experimental tumors. Methionine is an essential amino acid and is rapidly incorporated into brain proteins.[5] No recycled tracer occurs and its side-metabolism towards S-adenosylmethionine and transmethylation pathway is considered to be negligible in the brain during the PECT examination period.[4] Therefore, PECT study using 11C-methionine made it possible to demonstrate local protein synthesis in the brain.[1] In this study the correction of cerebral blood volume by 11CO PECT study was performed in three cases, but the activity in the blood was reduced to negligible level at the end of the study in the all six cases examined.

Both energy and protein synthesis are necessary for tumor growing, and it seemed natural that amino acid metabolism might be closely related with histological grading of tumors. In this point of view, it is of great interest why amino acid metabolism remains high while glucose utilization is low in low grade astrocytoma and slow growing experimental tumors, and why the accumulating patterns of FDG and methionine were contrary to each other in some experimental tumors. These results will provide us an important clue for understanding the management of brain tumor.

Acknowledgement

Collaborations of all the members of Cyclotron and Radioisotope Center, Tohoku University were greatly appreciated. This work was supported in part by Grant-in-Aid for Cancer Research No. 59015008 from the Ministry of Education, Science and Culture of Japan.

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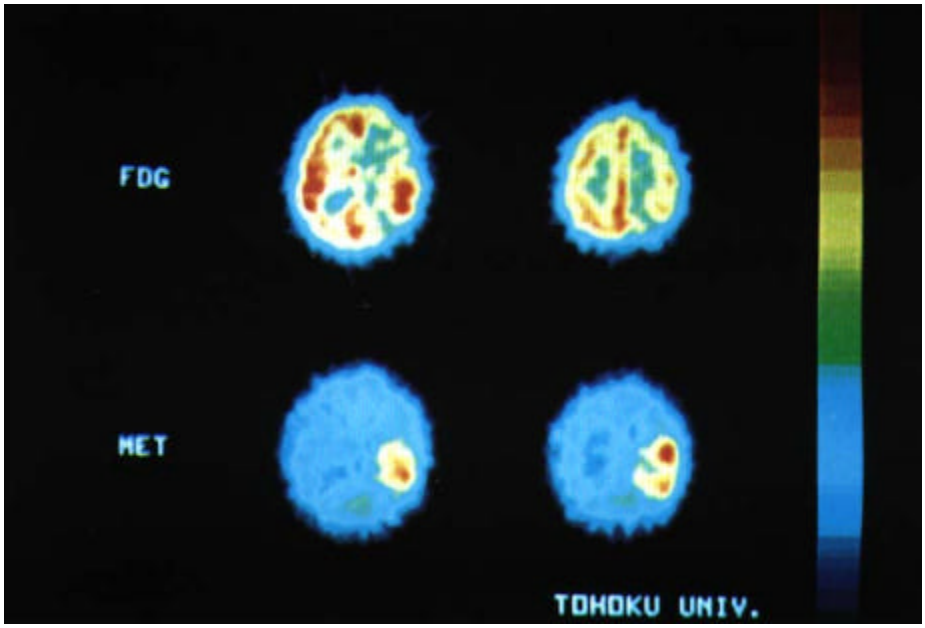

Fig. 1. Positron CT findings of high grade astrocytoma. CMRgl and methionine uptake in the tumor were increased.

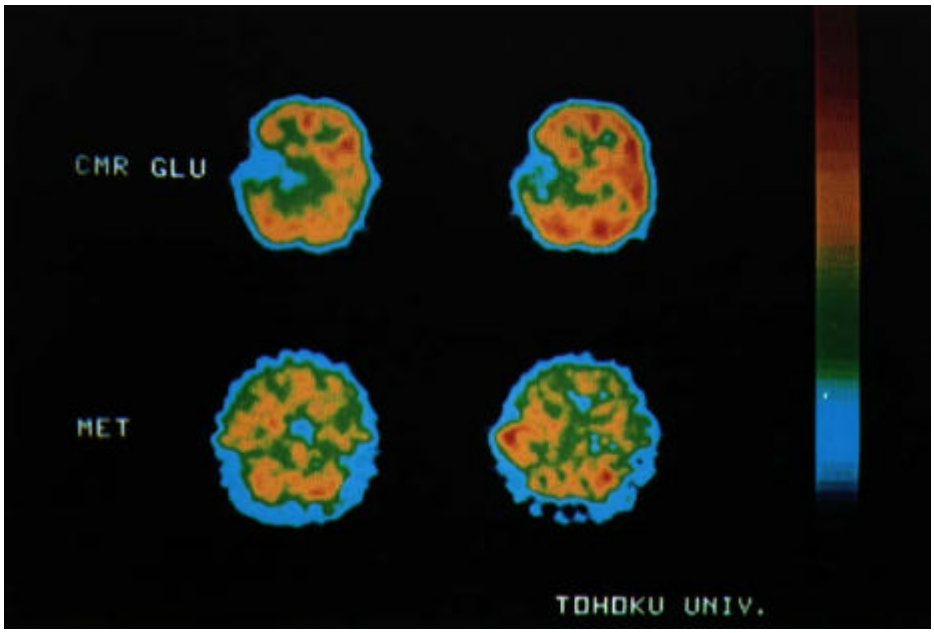

Fig. 2. Positron CT findings of low grade astrocytoma. CMRgl in the tumor was decreased, however, the high uptake of methionine.

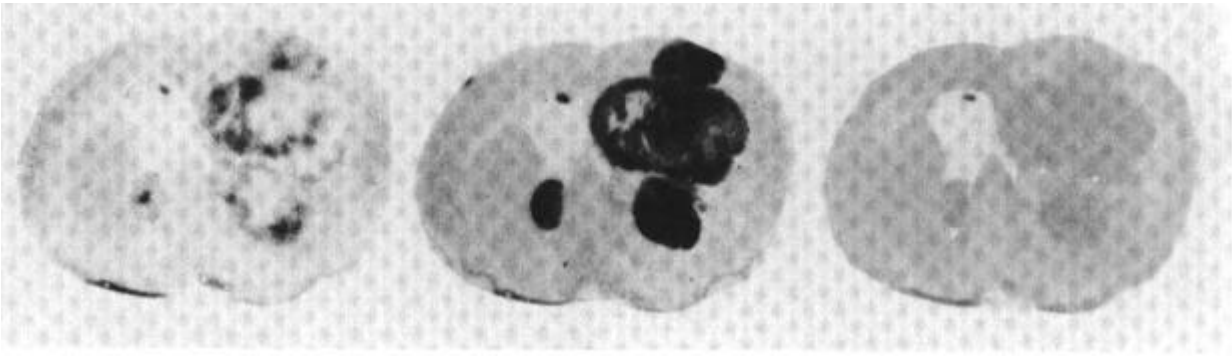

Fig. 3. Three different images obtained from the same section of KEG-1 implanted brain tumor bearing rat – 18F-FDG autoradiography (left), 14C-methionine autoradiography (center) and hematoxylin and eosin stainning (right). Both FDG and methionine uptake were increased, however, their accumulating patterns were contrary to each other.

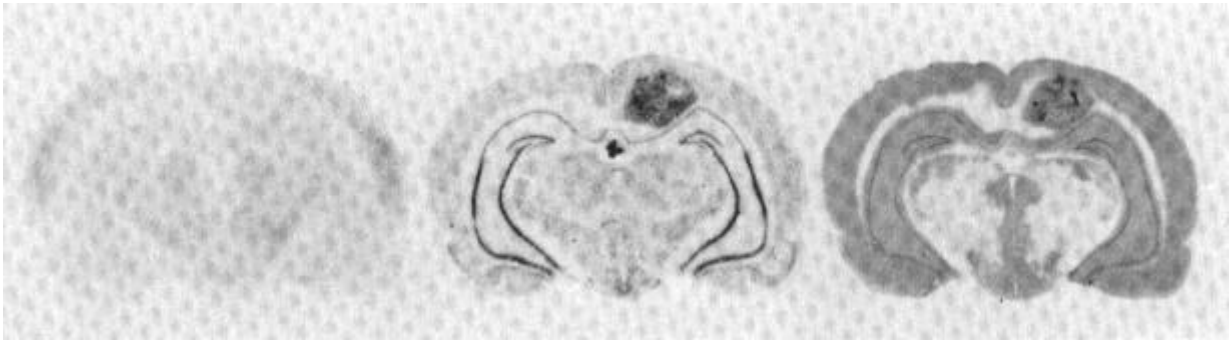

Fig. 4. Three different images of ENU induced tumor bearing rat – FDG (left), methionine (center) and hematoxylin and eosin stained section (right). The dissociation between CMRgl and methionine uptake was evident.