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著者	Kubota K., Matsuzawa T., Fujiwara T., Abe Y., Ito M., Hatazawa J., Sato T., Kawabe H., Miyazawa H., Ido T., Ishiwata K.
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Kubota K., Matsuzawa T., Fujiwara T., Abe Y., Ito M., Hatazawa J., Sato T., Kawabe H., Miyazawa H., Ido T.* and Ishiwata K.*
Department of Nuclear Medicine and Radiology, Research Institute for Tuberculosis and Cancer, Tohoku University
Cyclotron and Radioisotope Center, Tohoku University*

We have reported that ^{11}C-L-methionine(C11-LMet) was a useful radiopharmaceuticals among various labelled amino acids for the diagnosis of cancer using positron emission computed tomography.[1] C11-LMet is a essential amino acid and the uptake is high in organs such as the liver, pancreas, as well as in tumors, but low in the heart, lung and brain. Accordingly, tumor imaging with C11-LMet formed a high contrast to the surrounding brain[2], lung and mediastinum.[3] The extent to which C11-LMet accumulate in a lung tumor was closely correlated to the tumors viability such as benigh or malignant, viable or necrotic.[4] After a series of tumor detection studies, differential diagnosis of tumor from inflammation is a necessary step for the assessment of C11-LMet imaging. In this report, we studied experimentally whether C11-LMet accumulated into inflammatory tissues or not.

Materials and Methods

C11-LMet used in this study was synthesized from $^{11}CH_3I$ and homocystein following the modified methods of Comar et al.[5] $^{11}CO_2$ was produced by the proton irradiation of a nitrogen gas target system. $^{11}CH_3I$ was synthesized from $^{11}CO_2$ using an on-line automated system.[6] 38 male and 7 female Donryu rats weighing from 140 to 180 g were used for the experiment. Transplantable ascitic hepatoma AH109A cells were inoculated s.c. on the back of rats. When the tumor grew to about 1 g, the animals were used. Aseptic inflammations on the rats were produced by s.c. injections of 0.1 ml croton oil(Nakarai Kagaku, Kyoto) and by 0.2 ml of 1.5 % carrageenan(NW3.0×10^5, Tokyo Kasei Kogyo). They were used 4 days and 24 hrs after injection respectively. The animals were fasted for 24 hrs and 100 μCi of C11-LMet was injected i.v. through the tail vein. The animals were killed by cervical dislocation at 5, 10, 20 and 40 min after injection. Organs and tissue samples were excised, blotted to remove adhering blood, weighed, and counted in a well-type NaI(Tl) auto-gamma counter. Data were expressed as the differential absorption ratio(DAR)[7].

$$DAR = \frac{\text{Tissue counts(cpm) / Tissue weight(g)}}{\text{Injected RI counts(cpm) / Animal body weight(g)}}$$

Ratios for tumor to each tissues were calculated. From 6 to 10 rats were used for each data point. Tissue samples of AH109A tumor, croton oil and carrageenan inflammations were fixed, sectioned and stained with hematoxylin and eosine for histological examination.

Results

Figure 1 showed the time-activity curves of C11-LMet tissue distribution. Both inflammation induced by croton oil and carrageenan showed lower uptakes than those of pancreas, liver, kidney, tumor and muscle, also showed gradual excretion pattern of time-activity curves. The activities of pancreas and liver increased until 20 min after injection then decreased. But tumor activity was rising even at 40 min. Table 1 showed the DAR values of each tissues and tumor/tissue ratios at 20 min. Tumor/blood ratio was 7.6, tumor/muscle was 4.3. These values were a bit lower than the previous experiment by us. DARs of both inflammations were significantly lower than the muscle but higher than the blood. Adrenal gland and ovary showed more than double activities of muscle. Fig. 2-a,b,c, showed photomicrographs of AH109A tumor(×400), carrageenan inflammation(×200) and croton oil inflammation(×200) respectively.

An experimental hepatoma AH109A contained many mitotic cells and its growth rate was very fast. It had abundant of blood capillaries as the matrix of tumor and very little necrotic tissue. Carrageenan inflammation induced 24 hrs after injection, formed edematous acute exudative inflammation characterized by migrating cells such as macrophages and neutrophils surrounding the abscess of injection site. Croton oil inflammation induced 4 days after injection, formed granulation tissue of the healing stage of inflammation characterized by fibroblasts and lymphocytes surrounding the injection site.

Conclusion

In this study, we demonstrated that two different types of inflammation, acute exudative inflammation by carrageenan and granulative healing inflammation by croton oil showed a low level accumulation of C11-LMet as was in the muscle or blood. And hepatoma AH109A exhibited high uptake was clearly differentiated from the inflammations. It is suggested that we can differentiate cancer from inflammation with positron emission tomography by using C11-LMet.

Acknowledgement

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Table 1. Tissue distribution of ^{11}C-L-methionine in Donryu rats 20 min after injection. n=7-10

Tissue	DAR(means±S.D.)	Tumor/Tissue Ratio
AH109A tumor	2.58 ± 0.48	1
Croton oil inflammation	0.40 ± 0.13	6.5
Carrageenan inflammation	0.51 ± 0.06	5.1
Blood	0.34 ± 0.05	7.6
Muscle	0.60 ± 0.05	4.3
Lung	1.40 ± 0.27	1.8
Myocardium	0.72 ± 0.11	3.6
Liver	5.22 ± 0.88	0.49
Pancreas	10.56 ± 2.20	0.24
Kidney	2.11 ± 0.21	1.2
Adrenal gland	2.13 ± 0.25	1.2
Uterus	0.79 ± 0.06	3.3
Ovary	1.81 ± 0.48	1.4

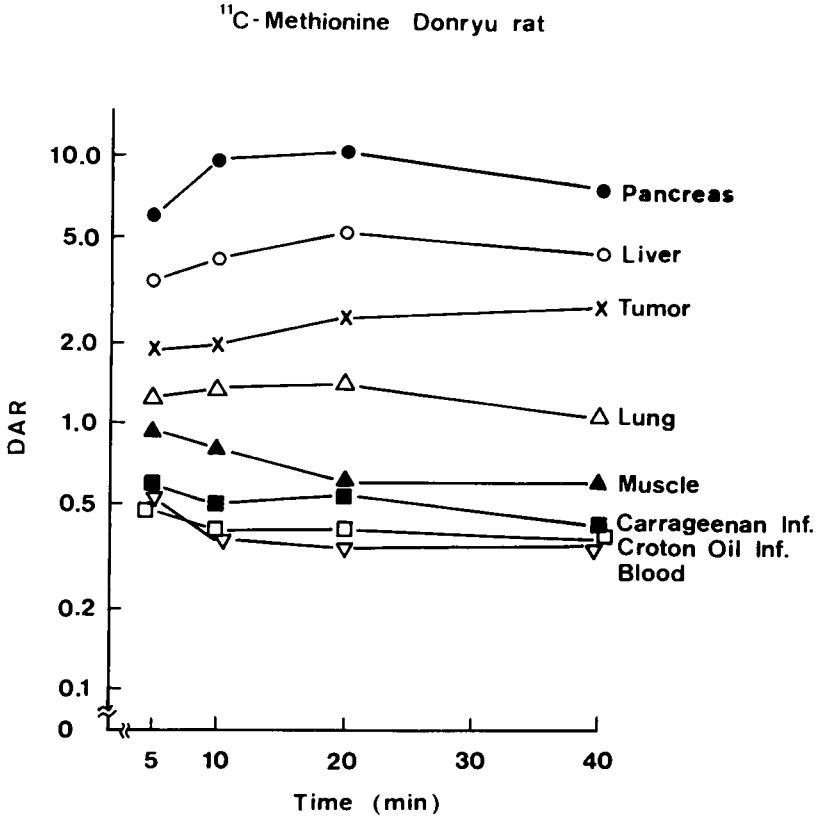

Fig. 1. Time activity curves of C11-L-Methionine in Donryu rats with AH109A tumor, aseptic inflammations by s.c. injection of croton oil and 1.5 % carrageenan.

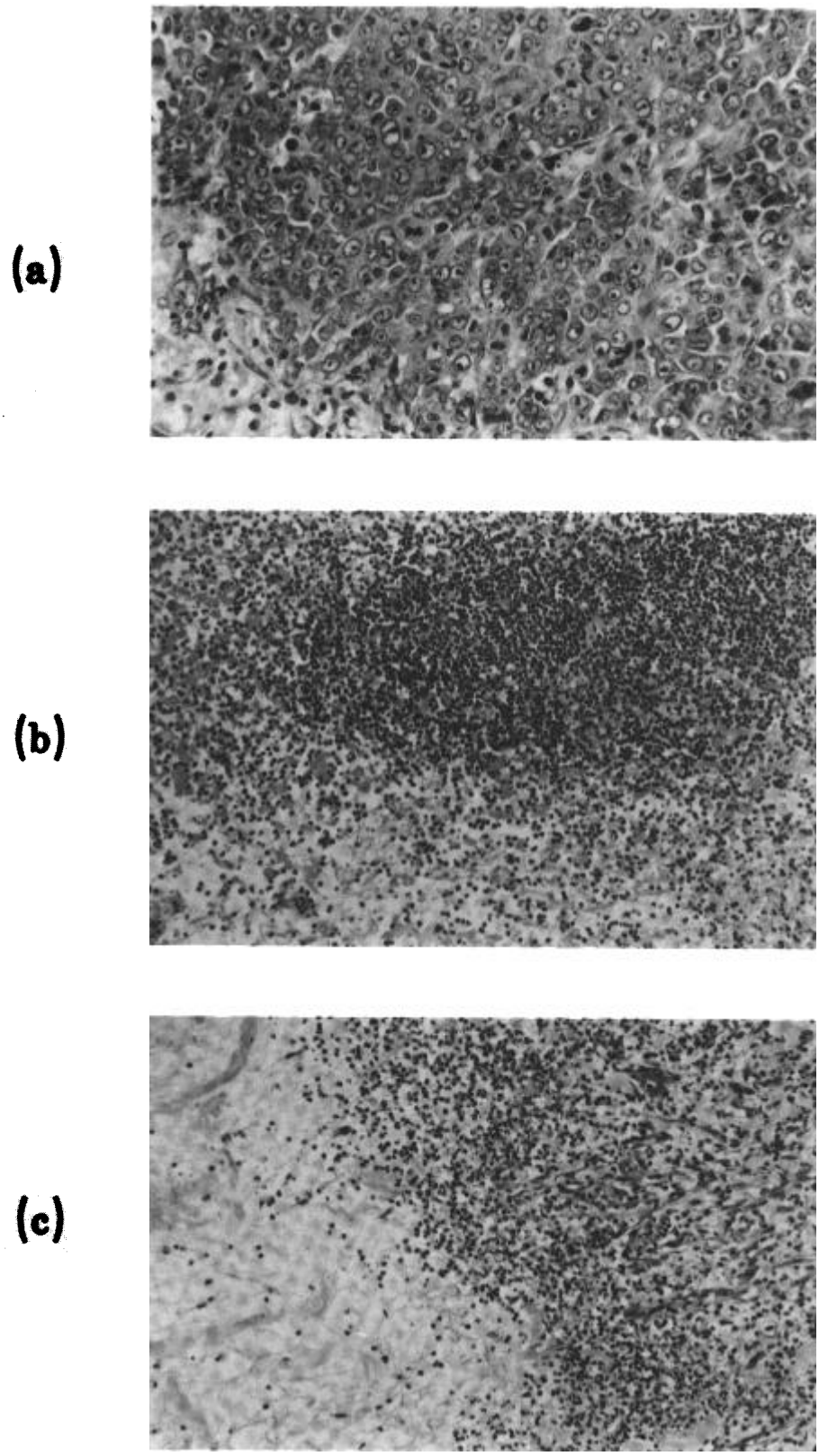

Fig. 2. Photo-micrographs of AH109A tumor (a)×400, carrageenan inflammation (b)×200, croton oil inflammation (c)×200.