Establishment of Radioimmunoassay for γ-oncofetal Antigen (Basic Fetoprotein) and Study on Serological Diagnosis of Malignant Neoplasia by Use of the Radioimmunoassay

Masaru, ISHII
Clinical Laboratory, Saitama Cancer Center

A new fetoprotein electrophoresed in gamma region has been found in human fetal serum and human fetal gut and brain extracts as well as in several types of carcinomas by Ouchterlony tests using anti-γ-globulin fraction of human fetal gut extracts rabbit antiserum absorbed with both normal human plasma and normal human adult gut extracts. This fetoprotein was immunologically different from alpha fetoprotein, carcinoembryonic antigen, alpha 2-H immunologically identical to ferritin and other known serum proteins. Moreover, this fetoprotein was also seemed to be distinct from γ-fetoprotein already described by Edynak et al. because of discrepancy of those distributions in human fetal organs.

The fetoprotein was isolated from ascites of a patient with hepatoma by the techniques of ion-exchange chromatography, affinity chromatography, electrofocussing and gel filtration. The isolated fetoprotein was demonstrated to be highly pure by immunoelectrophoretic and electrophoretic methods. The fetoprotein was shown to have an isoelectric point of 9.3. Because of its property, it was named basic fetoprotein (BFP).

For the establishment of BFP radioimmunoassay anti-BFP antiserum and isotope-labeled BFP were prepared as follows. Monospecific anti-BFP antiserum was produced by immunizing the purified BFP to a rabbit. Preparation of 125-I labeled BFP was performed by the method of Hunter and Greenwood and 125-BFP had a radiospecific activity of 10 mCi/mg of BFP. A radioimmunoassay of BFP was developed based on a coprecipitation-inhibition technique using two antibody method. The sensitivity could allow reproducible detection of 5ng of BFP/m*l* of serum.

By this radioimmunoassay sera of 101 normal subjects, 214 patients with malignant neoplasia, 169 patients with non-malignant disease and 12 umbilical cord were tested for BFP. BFP could be detected in all out of 101 normal subjects and the BFP level was less than 100 ng/m*l* with the exception of a case. Sera of 157 out of 169 patients with non-malignant neoplasia were BFP level less than 200 ng/m*l*. Twelve cases that BFP level was more than 200 ng/ml were composed of 5 hepatitis, a cirrhosis of liver, 3 aplastic anemia, 2 pneumonia and a systemic lupus erythematosus. On the other hand, sera of 82 out of 214 patients with malignant neoplasia resulted in BFP level more than 200 ng/m*l* and those 82 cases were composed of various types of malignant neoplasia.

From above-described results, quantitative determination of BFP in serum by the radioimmunoassay was concluded to be useful for diagnosis of various types of malignant neoplasia.

Diagnosis of Intracranial Tumor by Brain Scanning with Combined Use of Different Radionuclides and Clinical Comparison with Computed Tomography

Hideo HIRATSUKA*, Kodai OKADA*, Reiki YOSHIDA*, Yasuo SUGANUMA*, Masahiro OHATA*, Kiyohide KOMATSU*, Yutaka INABA* and Takeo OKAYAMA**
**Department of Neurosurgery, School of Medicine, Tokyo Medical and Dental University*
***Department of Radiology, School of Medicine, Tokyo Medical and Dental University*

The purpose of this paper is to compare the diagnostic value of radionuclide brain scanning and X-ray computed tomography (CT) in the evaluation of patients with brain tumor. Our study is based on 179 radionuclide scans and 133 CT scans on patients with brain tumor.

In radionuclide imaging, overall positive rate was 87.7%, while CT missed only one case with posi-

tiveness of 99.1%. In radionuclide imaging with ^{99m}Tc-pertechnetate, high positiveness was obtained in meningiomas, acoustic neurinomas and metastatic tumors and those poorly localized were midline tumors, tumors located at the base of the skull. However, improved brain scan images and specificity were obtained with combined use of different radioisotopes (^{99m}Tc-pertechnetate, ^{99m}Tc-diphosphonate and ^{67}Ga-citrate) in 39 cases. Scans with ^{99m}Tc-diphosphonate are useful for detecting lesions of the skull. In cases with meningiomas, scans with ^{99m}Tc-diphosphonate showed contiguous bone damage by tumor infiltration. They are also useful for differentiating tumor from infarction, when CT scans show low density areas. In cerebral infarction, most lesions are better demonstrated with ^{99m}Tc-diphosphonate than with ^{99m}Tc-pertechnetate, while tumors are usually visualized better with ^{99m}Tc-pertechnetate than with ^{99m}Tc-diphosphonate. Brain scanning with ^{67}Ga-citrate was occasionally more useful for delineating tumors than those with ^{99m}Tc-pertechnetate, especially tumors located at the skull base. In addition, dynamic study by bolus injection of radionuclide and delayed scanning are essential for "nature" diagnosis of brain tumors. We emphasized usefullness of different informations from different isotopes.

CT was very sensitive in detecting mass lesions with detailed morphological changes. CT detects glioma of low grade malignancy missed by radionuclide scanning. Basically, CT displays the morphological pattern of the tumor and the brain more precisely, while radionuclide scanning defines tissue function or dynamic aspect. Future emphasis in nuclear medicine must be placed on the study of tumor specificity and dynamic aspect of the lesion rather than its structure, prospecting the development of more specific radiopharmaceuticals. Radionuclide imaging and CT are two noninvasive procedures that have a high rate of detection of intracranial tumors. From this comparative study, we conclude these two procedures are to be complementary in the investigation of intracranial tumors.

Production and Tumor Affinity of Thulium-167

Atsushi ANDO*, Tatsunosuke HIRAKI*, Shigeru SANADA*, Kinichi HISADA**, Itsuko ANDO**, Yoshiaki SHIROTA**, Koh SAKAMOTO***, Kenji DOISHITA****

**School of Paramedicine, Kanazawa University, **School of Medicine, Kanazawa University ***Faculty of Science, Kanazawa University, ****Fukui Prefectural College*

Recent studies have shown that rare earth radionuclides of high atomic numbers concentrate favorably in tumor tissues and bone, Among these nuclides ^{167}Tm is reported to be one of acceptable tumor localizing agents in view of its decay characteristics, the half-life of 9.24 d and the EC dacay followed by a 208 keV gamma-ray. The present study concerns a new method of production of a high activity ^{167}Tm, via a reaction ^{169}Yb (γ, n) ^{167}Yb $\xrightarrow[17.7m]{EC}$ ^{167}Tm. In a photo-reaction on ytterbium at moderate energies the 93.1d ^{168}Tm is not produced and other longlived nuclides ^{170}Tm (T 1/2=130d) and ^{171}Tm (T 1/2=1.91y) are produced in negligible amounts due to small cross sections of the (γ, p) reaction. ^{167}Tm-citrate was injected intravenously to the rats subcutaneously transplanted Yoshida sarcoma and was injected intraperitoneally to the mice subcutaneously transplanted Ehrlich tumor. These animals were sacrificed and distributions of ^{167}Tm in the organs and tumor were determined. On the other hand, the tumor tissues and liver were excised and subcellular fractionation of these organs were carried out according to be method of Hogeboom and schneider. ^{167}Tm of each fraction was counted by a well type scintillation counter. In Yoshida sarcoma and Ehrlich tumor, most of the radioactivity was localized in the supernatant fraction, and small amount of radioactivity was accumulated in the mitochondrial fraction (lysosome contains in this fraction). But in the liver, most of the radioactivity was concentrated in the mitochondrial