Lung Uptake of Technetium-99m Microaggregated Albumin in the Rats After Immunization with Macroaggregated Albumin

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During the study of liver uptake of Tc-99m human serum albumin (Tc-HSA) in the sensitized dogs, one of authors recognized and reported the occasional occurrence of lung uptake of the Tc-HSA. As a possible cause of lung visualization, pulmonary microembolization of intravascular aggregated albumin was proposed. The purpose of the present study is to verify this hypothesis and to investigate the exact mechanism involved in this phenomenon by using Tc-99m microaggregated albumin (Tc-MIAA).

Wister strain male rats were immunized by two subcutaneous injections of 5 mg of HSA or human macroaggregated albumin (MAA) in incomplete adjuvant at two weeks interval. Two weeks after the second injection of antigen, lung and liver scannings were performed using Tc-MIAA, Tc-HSA and Tc-sulfur colloid. MIAA was prepared by the sonication of MAA. The particle size was assessed microscopically and by organ distribution studies in the control rats.

As the results, in all rats immunized with MAA, MIAA were markedly accumulated in the lungs with similar or greater activity than in the liver. However, no lung was visualized in the same group when rats were injected Tc-sulfur colloid or Tc-HSA. On the other hand, in the group which was immunized with HSA, there was no visualization of the lung by Tc-HSA, Tc-MIAA or Tc-sulfur colloid.

Increased deposition of Tc-MIAA in the lung of the rats after immunization with MAA strongly suggested that the mechanism for lung visualization in the present study was due to microembolization of clumping particle (antigen-antibody complex). In clinical condition, immune mechanism may be an unlikely cause for intravascular aggregation of liver particles. However, some other unknown mechanism, particularly abnormality in the plasma protein may cause intravascular aggregation of liver particles.

The absence of liver accumulation of HSA in the rats sensitized with HSA were unexpected from the previous experience with dogs. This appears to suggest some difference in immune responce between two species. However, exact mechanism for this difference remain for the further study.

A Basic Study for Clinical Application of ^{111}In-chloride Bone Marrow Agent

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It is assumed that trace amounts of ionic Indium-111 is specifically bound to serum transferrin and then in part distributed to the erythroid line in active bone marrow when injected intravenously in the form of $^{111}In\text{-}Cl_3$ at acid pH.

However, the exact distribution and metabolism has not as yet solved, so that there are practically several difficulties in the evaluation of scan images.

8 cases with various hematological disorders (aplastic anemia, myeloid leucemia, malignant lymphoma, multiple myeloma, iron-deficiency anemia) were evaluated with scan images and organ distribution of Indium compared with ^{59}Fe-citrate metabolism. Indium-binding affinity to serum protein was also studied with single radial immuno-diffusion method combined with autoradiography.

It was made clear that Indium was bound to transferrin specifically in all cases, and accumulates

in the active bone marrow in proportion to erythroid cell counts and according to distribution of hemopoietic tissue. It was characteristic that in the cases of severe hypoplastic erythropoisis, the bone marrow activity was markedly decreased, and renal activity was remarkably increased. Localized hypoplasia due to tumour cell replacement was also detected. But in the slightly hypoplastic cases the evaluation of scan images was frequently difficult.

As a consequence, further investigation of metabolsim are needed for clinical application.

In-Chloride; As Bone Marrow Imaging and Tumor—Localizing Agents

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Indium-111-chloride ($^{111}InCl_3$) was used as bone marrow and tumorlocalizing agents in 38 patients 46 scintigrams), who were suspected or diagnosed having malignant disease clinically, and who were irradiated to malignant disease.

The regions, where clinically suspected malignant disease, where abnormally accumulated on scintigrams, and where irradiated, were excluded to estimate the normal distribution of $^{111}InCl_3$.

The scintigrams were taken 24–72 hrs after injection of $^{111}InCl_3$ 1–3 mCi.

The percentage and score distribution of $^{111}InCl_3$ were appreciated on scintigram 48 hrs after injection in 23 regions.

As the liver showed the highest accumulation of ^{111}In on all scintigrams, the liver appreciated as 2+. Comparing with the radioactivity in the liver, other regions showed similar (2+), moderately decreased (+), severely decreased (−) accumulation on scintigrams.

The score is given one for 2+, 0.5 for +, 0 for −.

The score and percentage distribution are followings; liver 100 (100%), lumbar vertebra 58.5 (100%), mediastinum 55 (100%), nasopharynx 50 (100%), testis 47.5 (95%), heart 44.5 (89%), pelvis 43.5 (78%).

High accumulation in the lumbar vertebra and the pelvis show that $^{111}InCl_3$ would be effective as bone marrow imaging agent.

Irradiated bone marrow showed markedly decreased accumulation of ^{111}In. In a patient of seminoma with irradiation of 3200 rads to the pelvic area and 4800 rads to the para-aortic area 4.5 years ago, there is no evidence of accumulation of ^{111}In in these areas. This suggest that there would be no recovery of bone marrow activity after irradiation over 3200 rads.

Malignant disease in mediastinum, hilar region, and esophagus, is well visualized, when these areas are irradiated about 2000 rads or when malignant disease is recurrenced after irradiation, due to vertebral marrow suppression by irradiation and due to high tumor concentration of ^{111}In.

We conclude that $^{111}InCl_3$ would be effective as bone marrow imaging and tumor-localizing agents.

The Bone Marrow Uptak of ^{111}In-Chloride and Erythropoietic Activity

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Indium-111 chloride was introduced as a bone marrow imaging agent in expectation of reflecting the hematopoietic, especially, ertythropoietic activity. But there have been reported some counter data in the animal experiments. The purpose of this report is to clarify to what extent the marrow