71

MECHANISM OF TUMOR ACCUMULATION OF Tl-201-CHLORIDE.

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It is said that Tl-201(I) ion shows almost same tumor accumulation and kinetics as K ion. But the mechanism of tumor accumulation of Tl-201 has not been fully understood. The present study was undertaken to explain the mechanism of its tumor accumulation. The following animals and transplanted were used:mice implanted with Ehrlich tumor;rats implanted with Yoshida sarcoma. The localization of Tl-201-chloride in tumor tissue was determined macroautoradiographically at 3, 24 and 48 hours after injection of Tl-201-chloride. Subcellular fractionation of tumor tissues were carried out according to the method of Hogeboom and Schneider at 10 min., 1, 3, 24 and 48 hours after injection of Tl-201-chloride and homogenized. This homogenate was digested with pronase-P and gelfiltered on sephadex G-50. In the both cases of Ehrlich tumor and Yoshida sarcoma, following results were obteined.

Concentration of Tl-201 was predominant in viable tumor tissue rather than in necrotic tumor tissue, regardless of time after the administration. Most of the Tl-201 was localized in the supernatant fraction, and small amount of Tl-201 was accumulated in the other fraction. Tl-201 was fully released from high-molecular substance after digestion with pronase P.

72

METAL BINDING AND DNA ASSOCIATION PARAMETERS OF BLEOMYCIN.

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Bleomycin (BLM) has a suitable bifunctionality for tumor seeking agent. Several radiolabeled BLM have been proposed, but only Co-57 has proved to be stable in vivo and in vitro, and diagnostically useful. However, the considerably long half life of Co-57 causes troubles in handling and preclude its extensive uses. If a certain suitable radionuclide is inserted into BLM, this agent will be geatly useful. We investigated the metal binding properties and DNA association parameters of Co(III)-, Fe(III)- and Ga(III)-BLM, by CD titration and fluorescence quenching technique. Both metal binding constants and apparent DNA association constants of Fe-and Ga-BLM were two or three fold greater than those of Co-BLM. The numbers of nucleotides binding to each metal-BLM were coincident. But the tumor-affinity of Ga-BLM reported as before, showed contrary data to this result. These facts suggests the stability of complex against substitution is more important factor for tumor scanning chelates than the metal binding affinity and tumor affinity of ligand.

73

A COMPARISON OF TUMOR AFFINITY BETWEEN Ga-67-Fe COMPLEX AND Ga-67-TRANSFERRIN.

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With regard to mechanisms of tumor affinity of Ga, a role of transferrin(Tf) is considered to be crucial. However, with the results that Ga-Fe complex was formed and the complex was incorporated into tumor cells, we proposed another mechanism besides the Tf-theory. Here we presented comparative studies in vitro and in vivo on tumor affinity of Ga-Tf and Ga-Fe complex. The results of tissue distribution of Ga-Fe complex with time in tumor bearing rats revealed a low level of blood activity and a high uptake by liver from 1 hour after administration(i.v.). Tumor affinity of Ga-Fe complex was lower than those of Ga only and Ga-Tf. At a lower pH(6.5) where the surrounding of tumor was used to be, a binding of Ga-Tf decreased. On the other hand, the formation of Ga-Fe complex was enhanced and uptake by tumor cells increased. Ga polymer was also noted. When $NaHCO_3$ was not added into the medium, a binding of Ga-Tf decreased to about 50% and uptake by cells was markedly reduced until it reached the same degree as Ga only. Excretion of Ga-Fe complex from tumor cells was enhanced by Deferoxamine and its degree was prominent compared with Ga-Tf. From the above results, we suppose that Ga transported around tumor tissue as Ga-Tf tends to dissociate easily with lowering of pH and a formation of polymer occurs. There might be a possibility of incorporation of Ga polymer into tumor cells.

75

THE EFFECT OF SERUM UIBC ON THE EXCRETION AND DISTRIBUTION OF GA-67.

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In order to confirm clinically the relation between iron and gallium-67 metabolism which has been found to be close with animal models, we studied the effect of serum unsaturated iron binding capacity (UIBC) on the excretion and distribution of injected Ga-67. Fifty cases studied chiefly consisted of hepatoma, lung cancer, and malignant lymphoma. Three consecutive 24 hr urine and feces collections were obtained to determine percentage of the injected Ga-67 dose excreted. Percentage injected dose excreted in the urine in 24, 48, and 72 hr was 11.2 ± 7 %, 15.4 ± 8.4 %, and 17.8 ± 9.5 %, respectively. That excreted in the feces of 6 cases in 72 hr was 3.2 ± 1.3 %. Serum UIBC ranged from 26 to 382 mcg/dl. There was good negative correlation between percentage injected dose excreted in the urine in 72 hr and serum UIBC ($r=-0.59$, $p<0.01$). A case of acute myeloid leukemia whose UIBC was 26 mcg/dl and 72 hr urinary excretion of Ga-67 was 88.6 % of injected dose, showed prominent image of bone and kidney on the scintigram. In other cases, any special feature of the distribution of Ga-67 in relation to serum UIBC could not found.