NOTE

Diagnostic Significance of $^{197}\text{HgCl}_2$ -scintigraphy in Thyroid Carcinoma[†]

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1. Introduction

Radioisotopes have become extensively utilized as a useful means for the diagnosis of malignant tumors. Above all, devoted studies aimed at development of radioisotopes with satisfactory tumor affinity are being pursued by many investigators, and there are reports of laboratory and clinical investigations of such tumor affinity radioisotopes as ^{67}Ga -citrate¹⁾, ^{57}Co -bleomycin²⁾, $^{99\text{m}}\text{Tc}$ -bleomycin³⁾, ^{111}In -bleomycin⁴⁾ and so forth. Our previous clinical trials of ^{75}Se -selenomethionine, ^{57}Co -bleomycin and $^{99\text{m}}\text{Tc}$ -bleomycin in a series of cases of thyroid carcinomas had failed to yield gratifying results.

However, as a result of our scanning study on the thyroid carcinoma and its lung metastasis using $^{197}\text{HgCl}_2$, a considerable accumulation of the radioisotope was very useful in these cases.

2. Method

$^{197}\text{HgCl}_2$ was mixed with glutathione to make $^{197}\text{HgCl}_2$ -glutathione, which was intravenously administered at a dose of 1.0 to 1.5 mCi. About 24 hours later, the scanning was performed by the use of whole-body-scanner (Table 1). In the cases of the lung

Table 1 Method

$^{197}\text{HgCl}_2(\text{mCi})$ was mixed glutathione (4ml with 200mg)
↓
$^{197}\text{HgCl}_2$ -glutathione
↓ intravenous injection (1.0~1.5mCi)
↓ about 24 hours later
Scintiscanning by whole-body-scanner

metastasis and mediastinal metastasis of the thyroid carcinoma, the contrast of accumulation figure of radioisotope was not clear by the only use of $^{197}\text{HgCl}_2$. It was presumable because the radioisotope was evenly distributed in the blood. When a subtraction scanning method⁵⁾ was made using $^{197}\text{HgCl}_2$ plus ^{131}I -RISA, a clear accumulation figure was observed.

3. Results and Discussion

The scintigram by $^{197}\text{HgCl}_2$ -glutathione shows an image accumulated by the radioisotope on the nodule of the thyroid carcinoma (Fig. 1). In the same case, the scin-

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tigram by ^{99m}Tc , on the contrary, shows an image being deficient with the radioisotope on the nodule (Fig. 2). Through the study on the thyroid carcinoma by means of $^{197}\text{HgCl}_2$ -scintigraphy plus ^{99m}Tc -scintigraphy, both positive and deficient images are observed in the same nodule. Hence, the study is considered to be very useful for diagnosis of malignant tumor of the thyroid.

Fig. 1

Fig. 2

The scintigrams by $^{197}\text{HgCl}_2$ on various thyroid diseases, are as shown in Table 2. Of 36 cases of thyroid carcinomas, 31 cases were positive (86.1%) and 5 were negative (13.9%). Of 40 cases of benign thyroid adenomas, 6 cases were positive (15%) and 34 negative (85%). Of 13 cases of chronic thyroiditis, 12 cases were positive (92.3%) against 1 negative (7.7%). Eight cases of hyperthyroidism were all negative. From these data, the accumulation in chronic thyroiditis is highly positive, and the thyroid is obviously felt a diffuse goiter by palpation, and an accumulation of radioisotope in the thyroid is seen by means of $^{197}\text{HgCl}_2$ scan as well as ^{99m}Tc scan. But, in the case of thyroid carcinoma, on the contrary, a figure of the scan is positive by

Table 2 ^{197}Hg -Scintigram of thyroid diseases

	No. of cases	positive	negative
malignant tumor	36	31(86.1%)	5(13.9%)
adenoma	40	6(15%)	34(85%)
chronic thyroiditis	13	12(92.3%)	1(7.7%)
subacute thyroiditis	1	1(100%)	0(0%)
hyperthyroidism	10	0(0%)	10(100%)

$^{197}\text{HgCl}_2$, while it is a deficient by ^{99m}Tc scan. Hence, the two cases can be discriminated.

In the thyroid carcinoma, 5 cases were observed negative, which involved carcinoma tissues with a size of as small as 2 cm or under in diameter and a tumor which has caused a cystic degeneration. Therefore, it is noted that in the case of the carcinoma of smaller than 2 cm, there are some cases where an accumulation figure is not observed by scintigraphy.

When the thyroid carcinoma is examined by $^{197}\text{HgCl}_2$ on the histological types (Table 3), anaplastic carcinoma showed 100% positive, while a well-differentiated papillary adenocarcinoma was 83% and follicular adenocarcinoma was 75% positive. Then it is clear that more accumulation of $^{197}\text{HgCl}_2$ is observed in an anaplastic carcinoma which has strong cellular fission.

Table 3 ^{197}Hg -Scintigram of thyroid cancer

Histology	No. of cases	positive	negative
papillary adenocarcinoma	24	20(83.3%)	4(16.7%)
follicular adenocarcinoma	4	3(75%)	1(25%)
anaplastic carcinoma	7	7(100%)	0(0%)
reticulum cell sarcoma	1	1(100%)	0(0%)

Of 40 cases of thyroid adenomas, positive were 6 cases, where the tissue were undifferentiated, that is, 1 trabecular adenoma, 1 papillary adenoma, 2 tubular adenomas and 2 Hürthle cell adenomas were positive. In the well-differentiated adenomas, that is simple adenoma, colloid adenoma and adenomatous goiter, each having a large follicle, no accumulation of $^{197}\text{HgCl}_2$ was seen.

Referring to above results, it is noted

that an accumulation is observed in the thyroid carcinoma but there is some limit in scintiscan for indication of images.

Then about 24 hours after intravenous injection of $^{197}\text{HgCl}_2$ at a dose of 1.0 to 1.5 mCi, the operation was performed. Resecting small tissue pieces each of thyroid tumor, normal thyroid tissue, the lymph node and the cervical muscle, and also taking some of the blood at the same time, these radioactivity were determined by the use of a well-type-scintillation counter to see the cpm per gram of wet weight.

As to the uptake ratio of $^{197}\text{HgCl}_2$ into each tissue of the thyroid carcinoma, it was observed that the carcinoma tissue was 2.36 times as much as the blood, the normal thyroid tissue 1.02 times, the muscle 0.65 times and metastatic lymph node of the carcinoma 6.4 times respectively (Fig. 3).

Fig. 3 The uptake of $^{197}\text{HgCl}_2$ (tissue/blood ratio) thyroid carcinoma.

Further, the carcinoma tissue stood at 2.7 times as much as normal thyroid tissue, the blood 1.08 times, the muscle 0.79 times and the lymph node 7.83 times respectively. The uptake of $^{197}\text{HgCl}_2$ into the carcinoma tissue and the lymph node, indicated a statistically significant value, compared with those of the normal thyroid tissue, the muscle and the blood ($p < 0.02$).

Fig. 4 The uptake of $^{197}\text{HgCl}_2$ (tissue/normal thyroid tissue ratio) thyroid carcinoma.

In the case of adenoma, however, the uptake of $^{197}\text{HgCl}_2$ was indicated to be 1.49 times as much as the normal thyroid tissue (Fig. 4).

When the normal tissue is compared with other tissue, the carcinoma is noted to show a higher value statistically than those of adenoma and blood. From the above, the figure of $^{197}\text{HgCl}_2$ scintigram is supported by determination of $^{197}\text{HgCl}_2$ intake in thyroid tumor, also proving that such determination is useful for diagnosis of a tumor which is small that a scintigram may not indicate, or a tumor which has caused a cystic degeneration.

In order to see what part of the carcinoma tissue takes up or accumulates the $^{197}\text{HgCl}_2$, we examined, using TCA, the radioactivity ratio of protein fraction and non-protein fraction out of the carcinoma tissue in which $^{197}\text{HgCl}_2$ has been taken up. It was observed that as much as 85.7% was existent in combination with protein fraction. It is suggested, therefore, what the

$^{197}\text{HgCl}_2$ would be existent in a combined condition with protein.

To determine systematically which tissue accumulates the $^{197}\text{HgCl}_2$, a microautoradiography was taken by a freeze-drying method⁶⁾, and it was found that the $^{197}\text{HgCl}_2$ were taken up into carcinoma cells.

4. Conclusion

1) It was noted that $^{197}\text{HgCl}_2$ was very important as a tumor affinity radioisotope in thyroid cancer. Of 36 cases of thyroid carcinoma, 31 cases showed an accumulation of the radioisotope. The remaining 5 cases which showed negative accumulation, involved either a small tumor or a tumor which has caused cystic degeneration.

2) In the case where a tumor is so small that an accumulation cannot be observed by scintiscan, $^{197}\text{HgCl}_2$ is administered prior to operation, and the tumor tissue taken out is measured by a well-type scintillation counter. Then a significant uptake into the carcinoma tissue of the radioisotope is observed.

3) It is ascertained that mechanically, the $^{197}\text{HgCl}_2$ is taken into carcinoma tissue combining with protein, and morphologically, it is taken into carcinoma cells.

References

- 1) Edward, C.L. and Hayes, R.L.: Tumor Scanning with ^{67}Ga -citrate, *J. Nucl. Med.*, **10**, 103 (1966)
- 2) Maeda, T., Kono, A. and Kojima, M.: Tumor Scanning with ^{57}Co -Bleomycin, *Radioisotopes*, **21**, 436 (1972)
- 3) Mori, T., and Torizuka, K.: Clinical evaluation of $^{99\text{m}}\text{Tc}$ -bleomycin scintigraphy for diagnosis of thyroid cancer, *J. Nucl. Med.*, **15**, 518 (1974)
- 4) Thakur, M.L., Merrick, M.V. and Gunasekera, S.W.: Some pharmacological aspects of a new radiopharmaceutical, indium-111-bleomycin: Symposium on New Developments in Radiopharmaceuticals and Labelled Compounds (Copenhagen March 1973)
- 5) Fujii, T., Kusama, S. and Takizawa, M.: Subtraction scintigram for tumor scanning clinical application to lung cancer using $^{197}\text{HgCl}_2$ and ^{131}I -RISA, *Radioisotopes*, **22**, 579 (1973)
- 6) Nagata, T.: Autoradiography of soluble compounds: Its technique and application, *Shinshu Med. J.*, **18**, 1033 (1970)