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Biological distribution of ^{131}I-labeled anti-nucleus antigen monoclonal antibody chTNT in patients with pulmonary metastases from differentiated thyroid carcinoma

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Abstract This work is to study the *in vivo* biological distribution of ^{131}I-labeled mouse/human chimeric monoclonal antibody (^{131}I-chTNT) in patients with pulmonary metastases from differentiated thyroid carcinoma. Ten patients with differentiated thyroid carcinoma were injected intravenously with a single dose of ^{131}I-chTNT (5 MBq·kg^{-1} body weight). Radioactivity of blood and urine samples was measured at different time points. The *in vivo* stability and the metabolic status of ^{131}I-chTNT were detected with supersaturated trichloroacetic acid. Continuous imaging was performed to outline the region of interest (ROI) and estimate the intake level on the whole body, major organs and tumor lesions at different time points. The serum time-radioactivity curve of ^{131}I-chTNT accorded with the two-compartment model after a single intravenous injection: $T_{1/2}$(h)=65.28±14.83, $AUC_{0\text{-}t}$(MBq·h·mL^{-1})=8.93±1.32, $AUC_{0\text{-}\infty}$(MBq·h·mL^{-1})=10.58±2.19, and CL(mL·min^{-1}·kg^{-1})=1635±359. The time-radioactivity percentage curve of ^{131}I-chTNT urine excretion accorded with the one-compartment model after a single intravenous injection: $T_{1/2}$(h)=99±10, and accumulative (31±9) % radioactivity of the injected dose was excreted in urine in one week. The percentages of serum ^{131}I-chTNT in radioactive components at 24, 48 and 72 h were over 95% and it was still (88±7) % at 168 h. As for chemical composition of radioactive substances in urine, radioactivity in urine samples originated from free ^{131}I by 100%. Radioactivity of ^{131}I-chTNT after intravenous administration was mainly concentrated in the lung and liver, least in the brain. Radioactivity of tumor tissues reached the maximum at 24 h and the tumor/normal tissue (*T/N*) ratio reached the maximum (1.28~3.83) during 3~7 d. The characteristics of *in vivo* biological distribution of ^{131}I-chTNT in patients with pulmonary metastases from differentiated thyroid carcinoma are favorable for its therapeutic application for the metastasis tumors.

Key words Radionuclide, chTNT, Biological distribution, Pulmonary metastasis

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1 Introduction

Currently, lung metastases from differentiated thyroid carcinoma are mainly treated with large dose ^{131}I internal irradiation in clinical medicine. However, pulmonary metastatic foci in some patients do not ingest ^{131}I, causing failure of the treatment[1]. In this article, we study the *in vivo* biological distribution of ^{131}I-labeled mouse/human chimeric monoclonal antibody (^{131}I-chTNT) in patients with pulmonary metastases from differentiated thyroid carcinoma, in hopes of providing scientific evidence for further exploring its value of clinical application in treating lung metastases from thyroid carcinoma.

2 Materials and methods

2.1 Subjects

Ten patients (6 males and 4 females) with differentiated thyroid carcinoma were included in the

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study. They had a mean age of 41.3 years (16~78 years) and mean weight of 59±11.5 kg. Six of them had papillary carcinoma, and the others had follicular carcinoma. General conditions of the patients were moderate, with their expected survival time over three months. Having not been treated in at least one month before the study with radiotherapy, chemotherapy, radionuclide imaging or other treatments, they had thier hemogram, hepatic and renal functions within the normal range. Results of their tests for human anti-mouse antibody (HAMA) responses and iodine allergy testing were negative. The whole body ^{131}I imaging, ultrasonic and CT scan were employed to determine that there were no residual thyroid tissues, recurrent or distal metastasis foci in other sites apart from the existence of pulmonary metastasis foci that did not incept ^{131}I.

2.2 Major apparatuses and drugs

The apparatuses include SkyLight SPECT (single photon emission computerized tomograph, Philips), RM-905a radioactivity counter (China Metrology Development Corp. Group), GC-2016 radioimmunoassay (RIA) γ counter (Xi'an Zhongjia Co) and TDL-5Z centrifuge (Toshiba). ^{131}I-chTNT was purchased from the Shanghai Meien Biotechnology Corp., Ltd. It was clear primrose liquid with radioactivity of 370 MBq·mL^{-1}, radiochemical purity of ≥ 95%, specific antibody binding activity of ≥ 50%, bacterial endotoxin of <10 EU·mL^{-1}, and pH of 6.5~7.5.

2.3 Methods

2.3.1 Standard ^{131}I-chTNT curve and the detection limit

Radioactive activity of 1 mL ^{131}I-chTNT solution (diluted already) was 7.15 MBq, as determined by the RM-905a counter. A share of 20 μL solution, which was diluted in ratios of 1:2, 1:4, 1:8, 1:16, 1:32 and 1:64, was measured at each concentration. GC-2016 RIA γ counter was used to determine the counts per minute (cpm), then the linear regression equation for specific radioactivity of solution (kBq) vs. the cpm data as derived and the standard curve was plotted.

2.3.2 The administration dose

The intravenous infusion of ^{131}I-chTNT was performed at 5 MBq·kg^{-1} and 5 mL volume. RM-905a counter was applied to determine the radioactivity of the ^{131}I-chTNT injector before (full injector) and after (empty injector) the injection and the difference of the two measurements was the administration dose of ^{131}I-chTNT.

2.3.3 Collecting and processing the serum samples

One milliliter of the intravenous blood was collected at 0.5, 4, 24, 48, 60, 72, 144 and 168 h after ^{131}I-chTNT administration, respectively. The serum (~500 μL) was isolated by centrifugation. From each sample, 20 μL serum was measured (in cpm) using the RIA γ counter. After correction, time-radioactivity curve of the serum samples was plotted and the pharmacokinetic parameters were calculated. Protein was all precipitated from 400 μL of each serum sample by 1.2 mL supersaturated trichloroacetic acid (TCA). The radioactivity (in cpm) in the precipitate was measured by the RIA γ counter to determine the *in vivo* stability of ^{131}I-chTNT.

2.3.4 Collecting and processing of urine samples

Daily urine output (24 h urine) of all the patients was collected for one week after ^{131}I-chTNT administration. The radioactivity was measured, analyzed against the standard curve and the percentage of daily urine radioactivity among the total injected doses was calculated to plot time-radioactivity curve of the urine. Urinary metabolite of ^{131}I-chTNT was analyzed by TCA precipitation and radioactivity measurements of 400 μL urine sample.

2.3.5 *In vivo* imaging

The SPECT equipped with a high-energy collimator was used to collect the anterior and posterior images of the whole body at 0.5, 24, 48, 72, 120 and 168 h, at the 364 keV peak with a 25% window width, 1024×256 matrix and 10 cm·min^{-1} velocity.

2.3.6 Image analyzing

Three experienced physicians specialized in nuclear medicine were recruited to read the films collectively, to observe if there were abnormal foci of radioactive concentration in the lung or not. The ROI