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THE SIGNIFICANCE OF RADIOIMMUNOIMAGING IN THE MANAGEMENT OF CANCER PATIENTS

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In this article, the significance of radioimmunoimaging (RII) as a mornitoring means for gastric colorectal and lung cancer patients was reported. By using I - 131 or Tc - 99m labeled C50 (antiCEA) and 3H11 (anti human gastric cancer), 86 positive lesions were identified in 50 cancer patiens. 77 out of the 86 lesions (89.5%) were true positive, 4 false positive by post - surgecal pathology, biopsy or CT scan. The other 5 remained to be unexplained and needed further follow - up.

In our clinical practice, RII with antitumor McAbs suggested its unique value in the management of cancer patients. Totally, 14 occult lesions in 9 cancer patients missed by the other examination were identified by this technique. And owing to the RII findings, all of these patients got proper treatment in time.

Key words: Radioimmunoimaging, Monoclonal antibody, CEA, Tc - 99m, I - 131.

The targets of used in radioimmunoimaging (RII) radiolabeled monoclonal antibodies (McAbs) are tumor associated antigens or tumor markers which reflect the functional feature of malignant cells.[1] Therefor, it might be a good idear to employ RII with radiolabeled McAbs as a monitoring means for the management of cancer patients in order to disclose the recurrence and metastasis at early stage. The aim of this study was just designed for this purpose.

MATERIALS AND METHODS

Antibodies, Reagents and Instruments

McAb 3H11 (anti human gastric cancer, BICR*) and McAb C50 (anti CEA, BIBP**); Tc - 99m generator (CIAE***); Iodogen, 2 - mercaptoethhanol, stannous chioride (Sigma Co., USA); SPECT system (Sopha Medical Co., France).

Radiolabeling of McAbs:

I - 131 - C50, Tc - 99m - 3H11 and Tc - 99m - C50 were prepared by Iodogen and Schwartz

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methods, respectively. The labeled McAbs were purified by a Sephadex G - 50 column and filtrated through a 0.22 μ microfilter before administration. The specific activities were 3.7—7.4 MBq/mg for I - 131 - McAbs and 92.5—111 MBqs/mg for Tc - 99m - McAbs, respectively.

Preparation for Patients

For all of patients to be examined (colorectal carcinoma 33; lung cancer 20; gastric cancer 7 breast cancer), a skin test of 100 μg of relevant unlabeled McAbs for each case before the admini - stration of radiolabeled McAb. In addition, patients recieved I-131-McAb were orally given Lugol's solution to bolck thyroid in advance. Then, 3.7—7.4 MBq of I - 131 - McAbs (1—2 mg) or 92.5—111 MBq of Tc - 99m - McAbs(0.8—2 mg) mixed with 100 ml (10 g) HSA and 5 mg dexamethason was infused intravenuously. The imaging protocals are shown in Table 1.

Data Proccessing

Tomographic data were prefiltrated with Butterworth 4/16 filter and reconstructed into sections in 3 demensions with a thickness of 6.67 mm. The plana data were proceeded by a program for double nuclide imaging substraction which was developed by ourselvies.

Table 1. Imaging protocals for Tc - 99m and I - 131 labeled McAbs

Hours after injection	For the imaging of Tc - 99m - McAbs	For the imaging of I - 131 - McAbs
1 - 2	Whole body scan	-
5 - 7 & 20 - 24	Tomographic aquisition	-
71 - 95	-	1.8 - 3.7 MBq Tc - 99m - RBC was injected i.v.
72 - 96	-	Double nuclid planar aquisition

Interpretation of the Results and follow up of Patients

RII images were viewed by 2 or more qualified nuclear physisians. In combinati on with reviewing patient history and all available clinical information, the diagnosis was made up. Then, a surgery was followed for the preoperative case. For the postoperative cases, the means to follow up was CT scan, B - US and biopsy if posible and neccessary. The course of follow - up covered 6 months or longer.

RESULTS

Between July 1993 and December 1994, 48 patients with suspected occult cancer underwent RII with 131 - I labeled C50 (anti CEA)/3H11 (anti - gastric cancer). 37 of the 48 cases were assessable after a follow - up course covering 6 months at least. Totally, 62 RII positive lesions were found in the 36 cases by double nuclide imaging substraction of I - 131 - McAb/Tc - 99m - RBC and 59 of them were in agreement with the findings of CT, MRI, B - US and bone scan or confirmed by biopsy

and surgery during the course of follow - up. The other 3 positive lesions found by RII were false positive accoding to the follow - up data. Besides, 8 out of the 59 (13.6%) RII positive lesions were confirmed to be malignant lesions (metastasis or recurrence) during the course of follow - up. One breast cancer patient with lymphatic metastasis at right axilla showed a false negative scan.

For the tomographic imaging of Tc - 99m - McAbs, 24 CEA (+) lesions in 13 cases were identified by RII; 18 of them were confirmed to be malignant by surgery, biopsy or MRI. 1 lesion at the stoma of a postoperative patient (colorectal carcinoma) was confirmed to be false positive by surgery. The other 5 positive lesions found by RII remained to be unassessable and needed further follow - up. Of the 18 true positive lesions, 6 (33.3%) positive by RII but negative or equivocal by the other examinations were laterly confirmed to be malignant by pathology.

Table 2 listed the lesions missed by the other examinations but identified by RII. It should be pointed out that it was 1—6 months later even though some lesions in Table 2 were also disclosed by CT scan or B - US during the course of follow-up.

Table 2. Occult cancer lesions identified by RII

Cancer of	Lesions		Confirmed by
	Site	No.	
Colorectum	pel. scar	4	biopsy, CT
	liver	2	biopsy
	lung	1	CT
Lung	liver	3	B - US
	brain	1	CT
Stomach	abdominal L.N.	2	surgery
	abdominal wall	1	surgery

DISSCUSION

Because of the biological behavior of malignant cells, cancer metastasis is often disseminated and distant from the oregional lesions. Therefore, the effective monitoring method used for the management of cancer patients should be tumor specific and whole body covering. Our clinical practice proved that RII of radiolabeled antitumor McAbs was such a means. Malignant lesions in all parts of the body could be disclosed with one injection of radiolabeled antitumor McAbs (Figure 1.) and, in the most of cases the characteristic of a mass could be identified at the same time when its anatomical site was located.[2] The accuracy of RII elevated dramatically as the development of labeling techniques and the extensive use of SPECT. The minimum lesion detected by RII was as small as 0.5 cm so far.[3] Thus, the value of RII in the early detection of occult cancer lesions is becoming more and more significant.

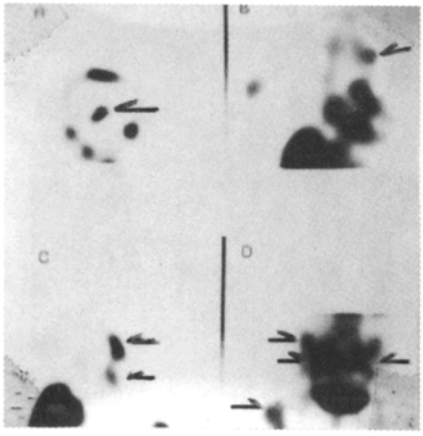

Fig. 1. Tomographic image of a lung cancer patient (A: metastasis in occipital lobe, B: metastatic L.N. of left subclavian artery, C: origional lesions in the left lung and D: metastases at bilateral sacroiliac joints and left femur)

Clinically, it is important to disclose cancer recurrence and metastasis at early stage so that

correct and proper procedures for therapy might be arranged. Routine means to monitoring recurrence and metastasis are CT and B - US but, unfortunately, they are diseffective on some occasion, especialy when used to identify the tumor recurrence in the pelvis scar tissue of postoperative colorectal cancer patients.[4] In contrast, RII suggested its unique value in this respect (Figure 2,3,4,5).

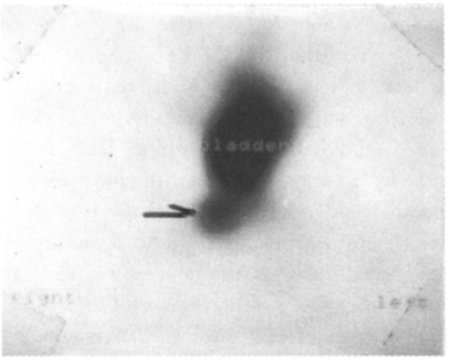

Fig. 2. A postoperative patient of rectal carcinomar with an elevated serum CEA leval; CT scan found nothing abnormal but a slight thickening of the scar tissue, while RII disclosed a tumor reccurence at the site of scar tissue.

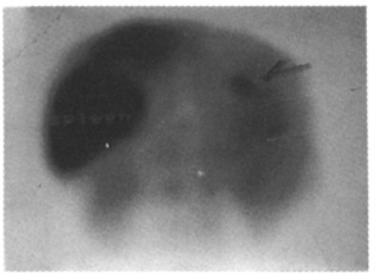

Fig. 4. In a postoperative patient with a prior history of rectal carcinoma, RII found a CEA (+) lesion at the right lobe of liver which was missed by B - US 3 weeks before RII.

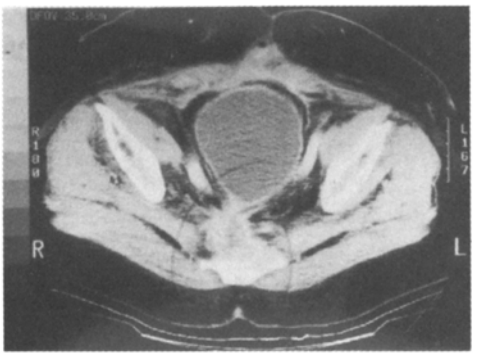

Fig. 3. 6 mon. later, the RII finding was proved by CT scan during the course of follow - up.

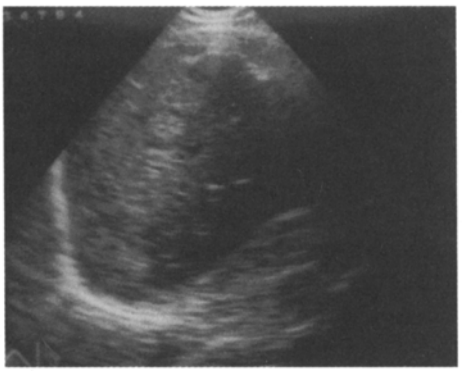

Fig. 5. During the course of follow - up a mass was found by B - US in the same site as indicated by RII, wich was proved to be a metastatic lesion by biopsy.

The significance of RII in the management of postoperative cancer patients were stated above but it was not limited to such a extent. For the preoperative cases, RII could also offer valuable information to the clinical doctors so that a proper surgical field could be determined (Figure 6).

There are some points that should be taken into account in order to make full use of the advantage of RII in the management of cancer patients and to give a correct inerpretation about the scan. Firstly, the scan should be, at least, cover the trunk of patients in case some lesions were missed (Figure 7, 8). Secondly, patient's serum CEA level was used by some auther as a indication of the RII with anti - CEA McAbs.[4,5] Whereas, in our study, some recurrent lesions were also identified in some postoperative cases with prior history of colorectal carcinoma and normal levels of serum CEA. Thus, it was also reasonable to employ this technique on the suspected recurrent cases of colorectal carcinoma whether his (or her) serum CEA level is abnormal or not. Thirdly, some nonspecific activity was found within the colon and gall bladder but it didn't interfere the image interpretation. The nonspecific accumulated activity could be idetified by its clearence and, at least, by the change of its position over time. Therefore, multiple phase scan is preferred on this occasion. And lastly, some false positive scan were found when the planar double nuclide imaging substraction technique was emploied. This might be partialy caused by the difference in energies of the two kinds of γ photons. One should be cautious to the scan interpretation when this technique is emploied. For the tomographic imaging of 99m - Tc - McAb, a false positive scan was also encountered (Figure 9). The early accumulation of radioactivity (4 hours postinjection) at this site suggested that this false positive scan might be due to the hyperemia of the inflammatory lesion.

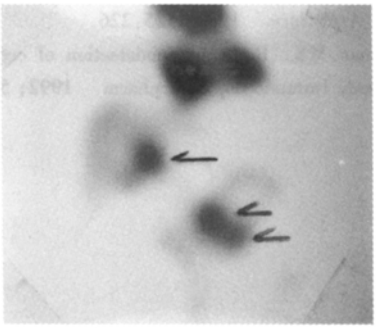

Fig. 6. Besides the origioanl lesion in the stomach, a metastasis at the port of liver was also identified by RII and proved by surgery.

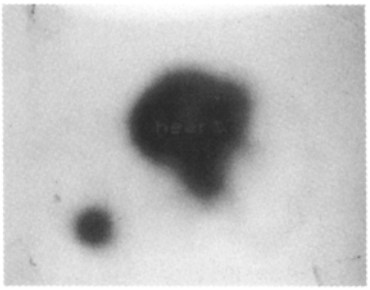

Fig. 7. A CEA(+) lesion in the right lung was detected by preoperative RII in a patient with right colon carcinoma.

Fig. 8. CT scan confirmed the findings of RII.

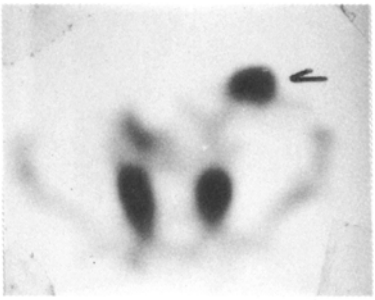

Fig. 9. Early accumulation of radioactivity (4 h) was found at the site of inflammatory mass at the stoma, which remained to be a "hot spot" untill 23 h after the administration of 99m - Tc - C50 and resulted in a false positive result.

From all stated above, one may arrive some conclusions as following:

RII was effective and efficient for the detection of occult cancer.

As a tumor specific functional imaging me - thod, RII is an effective complement ot those ana - tomy - based imaging method and has a unique cli - nical value in the detection of occult cancer lesions, especialy in the identification of tumor recurrence in the pelvis scar tissue of postoperative petients.

Lesions found by RII were the distribution of tumor marker in and/or around the lesions. The extent of tumor marker might spread extensively enough before the formation of malignant lesions which can be disclosed by routine examinations, for example, CT scan. Therefore, RII could identified tumor recurrence and metastasis earlier.

In the mangement of both pre - and post - operative cancer patients, RII was helpful if it was performed on a right case in a right way at right time.

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