

# Hepatic metastasis of differentiated thyroid carcinoma

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## Abstract

**BACKGROUND:** Differentiated thyroid cancers (DTC) often form metastases in neck lymph nodes, lungs and bones. Other metastases — to the brain, kidneys, skin and liver are rare. Liver metastases of DTC occur in the terminal phase of the disease and predominantly do not accumulate radioiodine. Functional (accumulating radioiodine) metastases are very rare.

**MATERIAL AND METHODS:** In an 85 year old patient with DTC of the follicular type after removal of the thyroid and lymph nodes metastases on the neck and after the elimination of thyroid remnants by radioiodine, a functional metastasis in the liver was detected by combination of whole-body scintigraphy following administration of  $^{131}\text{I}$  and liver scintigraphy by using  $^{99\text{m}}\text{Tc}$ -colloid, supplemented by bone scintigraphy after administration of  $^{99\text{m}}\text{Tc}$ -MDP. At first, the high thyroglobulin serum level was falsely negative after repeated radioiodine treatment. The patient was treated for this hepatic accumulating metastasis eight times by 59.2 GBq total dose of radioiodine. Radioiodine treatments were repeated for 7 years, the patient died at the age of 92 years.

**CONCLUSIONS:** It is necessary to distinguish between diffuse and focal radioiodine accumulation in a liver. Only a focal accumulation is characteristic for functional liver metastasis in which thyroxin synthesis is preserved. The correspondence of focal accumulation of radioiodine on whole-body scintigraphy with “cold” area on liver scintigraphy is specific for diagnosis of this metastasis. At the same time, it confirms the fact that radioio-

dine therapy can be both promising and successful, as we can see in the case of our patient.

**Key words:** differentiated thyroid carcinoma, functionally active hepatic metastasis, radioiodine treatment,  $^{131}\text{I}$  whole body scintigraphy, liver scintigraphy

## Introduction

Thyroid carcinomas account for approximately 1% of all human cancers. Most often, there are differentiated cancers (DTC), which are divided according to histopathological classification into follicular and papillary carcinomas. These tumours are mostly restricted to the thyroid gland or they overgrow to the thyroid capsule or surrounding structures. DTC often forms metastases in lymph nodes on the neck, lungs and bones. Other metastases — to the brain, kidneys, skin and liver are rare. The author describes the case of a patient with follicular DTC, in whom a functional liver metastasis has been detected. The author also presents a review of literature on patients who have suffered from this rare type of metastases.

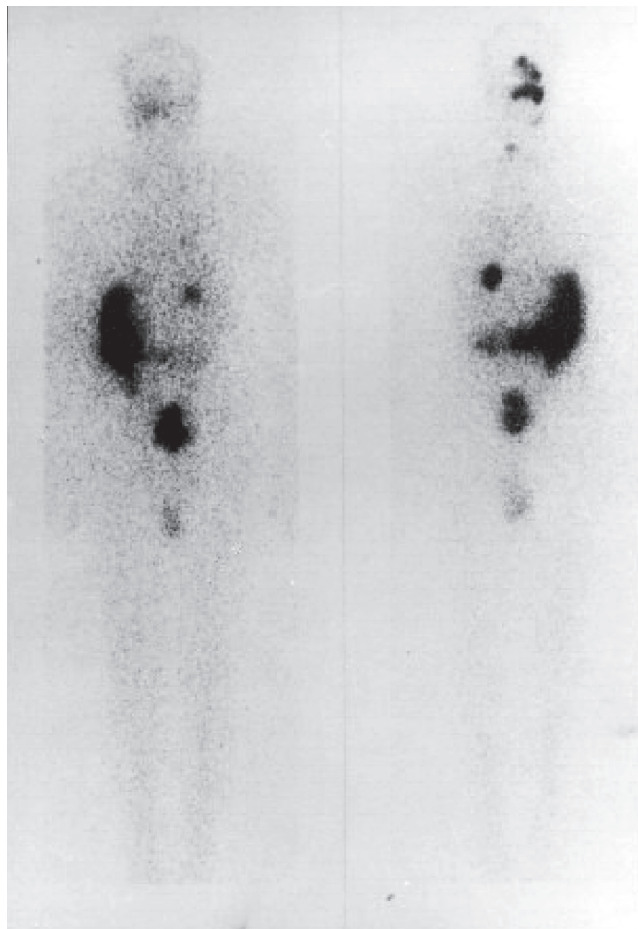
## Material, methods and results

In 1986, a 78 year old patient was diagnosed with a nodular goitre with normal function, which progressively increased to the size  $6 \times 8$  cm. In 1993, swelling developed on the left side of his neck. FNB from the swollen side led to the suspicion of DTC metastasis. A near total thyroidectomy and lymph nodes dissection on the left side of the neck were performed. During pathological examination, follicular DTC and its metastasis in lymph nodes were found. In 1993, we eliminated thyroid remnants using 3.7 GBq  $^{131}\text{I}$  therapy (Iodine-131 Sodium Iodide, Nuclear Research Institute, Řež, Czech Republic) and a hypothyroidism developed. The serum level of TSH was 71 mU/l (normal upper limit 5 mU/l). The serum level of thyroglobulin was also high — 160  $\mu\text{g/l}$  (normal upper limit 10  $\mu\text{g/l}$ ). A lung X-ray did not find any pathological changes.

All following scintigraphic examinations were done using a single head gamma camera DIACAM (Siemens, Erlangen, Germany).

Using whole body  $^{131}\text{I}$  scintigraphy after therapeutic dose 7.4 GBq of radioiodine, we could see a thyroid remnant and focal radioiodine accumulation in the costophrenic angle (Figure 1). After radioiodine treatment, external radiotherapy with  $^{60}\text{Co}$  was

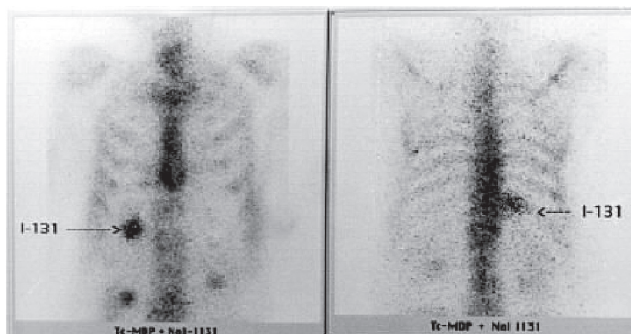
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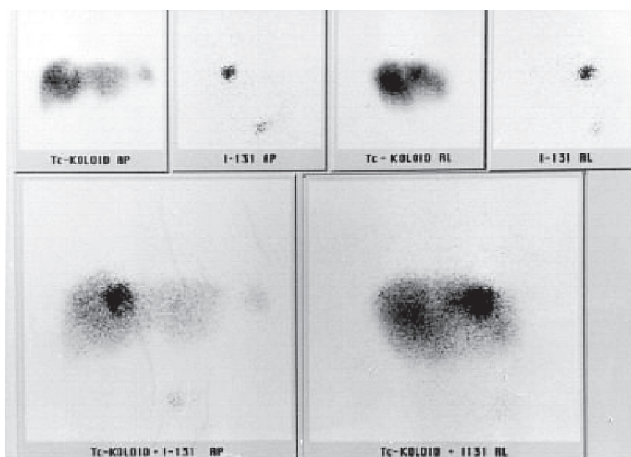
**Figure 1.** Whole body scintigraphy ( $^{131}\text{I}$ ). Posterior (on the left) and anterior (on the right) projection.

performed to the neck and mediastinum. Then we put our patient on a course of substitute and suppressive treatment with levothyroxinum natrium (Euthyrox, Merck) 100  $\mu\text{g}$  daily. In 1994, after withdrawal of thyroid hormones, the patient was treated with radioiodine again. During this time, the level of thyroglobulin was 70.6  $\mu\text{g}/\text{l}$  and antibodies against thyroglobulin were negative.

By means of simultaneous scintigrams after i.v. injection of 700 MBq of  $^{99\text{m}}\text{Tc}$ -methylene diphosphonate (Acidum medronicum) (MDP Kit, Nuclear Research Institute, Řež, the Czech Republic) and p.o. application of therapeutic 7.4 GBq of radioiodine, we found focal accumulation of radioiodine (Figure 2). It was not localized in the bone, but in the liver, because on the following similar simultaneous scintigraphy after therapeutic radioiodine and i.v. injection of 100 MBq of  $^{99\text{m}}\text{Tc}$  — tin colloid (Amerscan Hepatate II Agent, Amersham plc, Little Chalfont, Buckinghamshire, United Kingdom), we confirmed the focal defect in the same localization because it was the area of highest accumulation of radioiodine during whole body scintigraphy (Figure 3). This defect was in the upper part of the right liver lobe. After putting the patient on Euthyrox therapy, the serum level of TSH was 0.1 mU/l and serum level of thyroglobulin was also normal — 8  $\mu\text{g}/\text{l}$ . The antibodies against thyroglobulin were negative.



**Figure 2.** Simultaneous static bone scintigraphy ( $^{99\text{m}}\text{Tc}$  MDP) and static scintigraphy ( $^{131}\text{I}$ ). Anterior and posterior projection.



**Figure 3.** Simultaneous static scintigraphy ( $^{131}\text{I}$ ) and static liver scintigraphy ( $^{99\text{m}}\text{Tc}$  tin colloid). Anterior and right lateral projection.

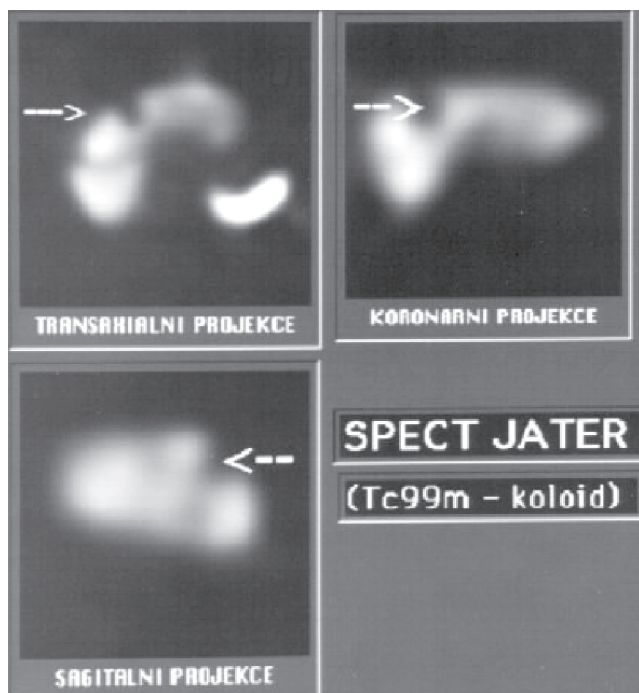
We performed SPECT of the liver after i.v. injection of 500 MBq of  $^{99\text{m}}\text{Tc}$ - tin colloid. We again validated the focal defect in the ventrocranial part of the right liver lobe (Figure 4).

The patient was treated for this hepatic accumulating metastasis eight times by 59.2 GBq total dose of radioiodine. Radioiodine treatments were carried altogether for 7 years, the patient died at the age of 92 years old in 2000.

## Discussion

For follow-up of patients with DTC, after the elimination of thyroid gland, the regular determination of the serum level of thyroglobulin is important; this is a sensitive and specific tumour marker. In a small number of cases it can be false negative. Thyroglobulin assessment is periodically supplemented by whole body scintigraphy following a diagnostic dose of radioiodine after withdrawal of thyroid hormone treatment. The functional metastases, which are possibly present, are stimulated by the subsequently increased level of TSH. Whole body scintigraphy is false negative in non-functional metastases. The determination of serum thyroglobulin [6] helps in this situation.

In our patient, the initially pathologic thyroglobulin level normalized (false negative finding) with positive scintigraphic detec-



**Figure 4.** SPECT of liver with  $^{99m}\text{Tc}$  tin colloid. Images of single transverse, coronal and sagittal slices.

tion (true positive finding). Liver metastases of DTC are usually found in the terminal phase of the disease. They are often accompanied by metastases to the other organs. Mostly, they do not accumulate radioiodine, probably as a result of their dedifferentiation. Finding liver metastases of DTC in autopsies is not rare [8]. They are found more often in follicular than papillary DTC [4, 5]. We had several such cases among our patients.

A different situation is shown in our case of functional liver metastasis (in which some level of radioiodine organification was preserved), which are rare. Prof. Nimec, who has the largest set of patients with DTC in the Czech Republic, proved the functional liver metastases in just two patients out of 3600 patients with DTC [4]. Brown et al [2] described finding solitary functionally active liver metastases in one patient (out of 235), who was in good condition twelve years after radioiodine treatment, and died after the development of hepatomegaly. Atmaran et al. [1] found bone, lung and functional liver metastasis in two patients (from 349) with DTC, which had such high hormonal production that even after the thyroid hormone withdrawal, the euthyroid state was maintained. Woolfenden et al [9] found two patients with functionally active metastases out of 31 patients with DTC (one of these two patients also had bone metastasis, the second patient also had lung and mediastinal metastases).

It is necessary to distinguish between diffuse and focal radioiodine accumulation in the liver. Diffuse accumulation is found quite often and it is a physiological accumulation of endogenous thyroxine or albumin labelled by radioiodine [3, 7, 10]. Focal accumulation is characteristic for functional liver metastasis in which thyroxine synthesis is preserved. Correspondence of focal accumulation of radioiodine on whole-body scintigraphy with "cold" areas on liver scintigraphy is specific for diagnosis of this metastasis [1]. At the same time, it confirms the fact that radioiodine therapy can be promising and successful as we can see in the case of our patient, described above.

## Conclusions

In an 85 year old patient, the combination of radioiodine whole body scintigraphy, bone scintigraphy, liver scintigraphy and serum thyroglobulin disclosed the very rare functional hepatic metastasis of DTC. The specific sign for diagnosis of this metastasis is the correspondence of focal accumulation of radioiodine on whole-body scintigraphy with "cold" area on liver scintigraphy. At the same time, it affirms the fact that radioiodine therapy can be promising and successful, as we can see in the case of our patient. The patient was successfully treated for this hepatic accumulating metastasis eight times by 59.2 GBq total dose of radioiodine. Radioiodine treatment has lasted for 7 years, the patient died at the age of 92.

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