Annals of Nuclear Medicine Vol. 18, No. 5, 443–446, 2004

Metastatic insular thyroid carcinoma: Visualized on Tc-99m pertechnetate, Tc-99m MDP and iodine-131 scintigraphy; a review of the literature for other radionuclide agents

Pınar Özgen KIRATLI,* P. Pelin Özcan KARA,* Eser Lay ERGÜN* and Gökhan GEDİKOĞLU**

*Departments of *Nuclear Medicine and **Pathology, Hacettepe University Medical Center, Ankara, Turkey*

Poorly differentiated insular thyroid carcinoma is classified as a separate entity among other tumors of the thyroid gland. Its histological pattern and clinical course are regarded as intermediate between well-differentiated and anaplastic thyroid cancer. The authors report Tc-99m pertechnetate, Tc-99m MDP and radioiodine imaging features in a 33-year-old male patient with metastatic insular carcinoma of the thyroid. The extent of involvement was almost identical in all three studies. Insular carcinoma of the thyroid was shown by biopsy, and the patient received a cumulative dose of 14,800 MBq (400 mCi) radioactive I-131. Other radionuclide imaging agents are also reviewed.

Key words: insular thyroid carcinoma, Tc-99m pertechnetate, Tc-99m MDP and I-131 scintigraphy

INTRODUCTION

INSULAR THYROID CARCINOMA is a poorly differentiated thyroid cancer histologically defined as the formation of solid clusters (insulae) of tumor cells containing a variable number of small follicles, small size and uniformity of tumor cells, consistently present mitotic activity, capsular and blood vessel invasion and frequent necrotic foci of the thyroid.[1] It is believed to be of follicular origin and has a characteristic histopathologic appearance consisting of nests or insulae of medium sized tumor cells.[1,2] Despite poorly differentiated histological findings, immunohistochemistry is positive for thyroglobulin (Tg), and radioiodine (I-131) uptake has been found in some, but not all insular carcinomas.[2] Patient follow-up provided evidence that this tumor type is an aggressive and often lethal form of differentiated thyroid cancer (DTC). In the study of Carcangiu et al.,[1] 80% of the patients developed metastases and progression of the disease which led to death in most.

In DTC whole body I-131 scintigraphy is the method of choice for the detection of metastatic lesions with a positive rate of approximately 75%,[1] while only 1% of the DTC patients concentrate Tc-99m pertechnetate.[3] There have been limited reports regarding accumulation of Tc-99m pertechnetate and I-131 in DTC and in their metastatic lesions.[4–6]

The authors present a case with insular type follicular thyroid carcinoma demonstrating a pathologic appearance unusually matched on Tc-99m pertechnetate, Tc-99m MDP and I-131 scintigraphy. A review of the literature regarding other radionuclide imaging modalities in insular thyroid carcinoma is presented as well.

CASE REPORT

A 33-year-old male patient presented in June 2002 with a pathologic fracture on the 1/3 proximal portion of his right humerus from where biopsy was taken and revealed malignant epithelial tumor metastases of the thyroid gland (Fig. 1 a and b). He had a history of partial thyroidectomy for multinodular goiter 4 years previously and was diagnosed with nonspecific thyroiditis with nodular colloidal goiter at another center. The original specimens were re-examined and a diagnosis of insular type follicular

Received February 25, 2004, revision accepted February 25, 2004.

For reprint contact: Pınar Özgen Kıratlı, M.D., Department of Nuclear Medicine, Hacettepe University Medical Centcr, 06100 Sıhhıye, Ankara, TURKEY.

E-mail: pkiratli@hacettepe.edu.tr

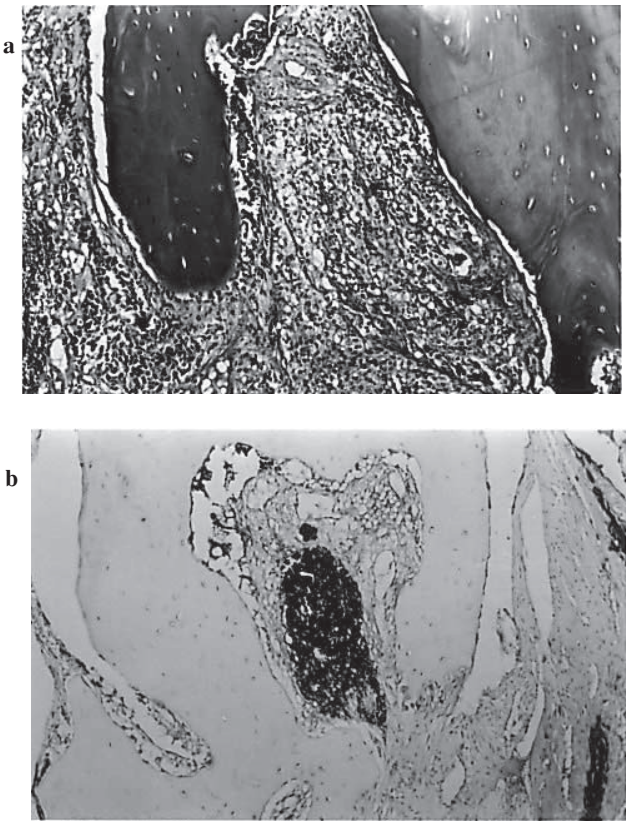

Fig. 1 a: Tumoral nests were found between the bone trabeculae (HE, × 230). b: Immunohistochemically strong positivity of the thyroglobulin in the tumoral area, strepavidin biotin (× 15).

carcinoma of thyroid was established. A neck ultrasonography revealed nodules in the right thyroid lobe and lymphadenopathy around the right carotid artery suggesting recurrence of the disease. Subsequently he was referred to our Nuclear Medicine Department for a thyroid scintigraphy with Tc-99m pertechnetate that showed residual functioning thyroid tissue. Uptake of the radioactivity was not limited to the thyroid gland, but multiple areas showing pathologic accumulation of Tc-99m pertechnetate were observed on his spot view and whole body imaging (Figs. 2 and 3). A consecutive bone scan with Tc-99m MDP displayed multiple sites of osteoblastic activity which were most compatible with metastasis and were almost identical to the pertechnetate scan (Fig. 3 a and b). These findings were correlated with his chest x-ray and thoraco-abdominal computed tomography studies (Fig. 4 a and b). His TSH level was 1.63 mIU/*l* (n: 0.465–4.68) and Tg > 300 ng/m*l* (n: 0–40). Radioiodine treatment was decided, but in order to decrease the tumor burden he initially underwent right thyroidectomy. Almost a month after the surgery, when his TSH level was 3.37 mIU/*l*, Tg was 223.17 ng/m*l* and anti Tg-ab was >2,000 U/m*l* (0–70), an I-131 therapy dose of 7,400 MBq (200 mCi) was administered. The postradiotherapy scan on day 7 with I-131 showed almost exactly the same

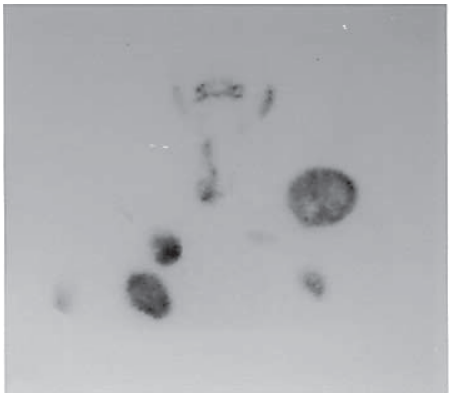

Fig. 2 Anterior neck image of the patient with Tc-99m pertechnetate was obtained using LEAP collimator. Accumulation of radioactivity was seen in multiple sites in the neck and at various sites.

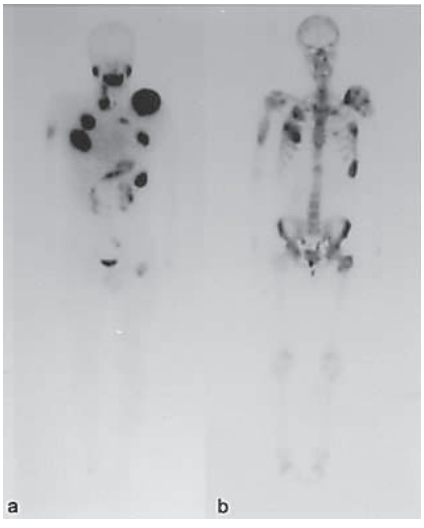

Fig. 3 Anterior whole body imaging of the patient with Tc-99m pertechnetate (a) showed multiple areas of radioactivity accumulation which are concordant with the Tc-99m MDP scintigram (b) showing osteoblastic activity in the thoracic 11 vertebra, left shoulder, right humerus, ribs and greater throcanter of left femur suggestive of disseminated metastatic disease.

metastatic lesions as the previous scans (Fig. 5). Six months later he was hospitalized for a painful mass lesion in his left arm. A bone scan showed a prominent uptake in the left proximal humerus as well as new pathological sites in the pelvic bones with no significant change in other metastatic lesions (Fig. 6a). So he received another dose of 7,400 MBq (200 mCi) RAI (Fig. 6b) for the progression of his disease. His TSH Ievel was >75 mIU/*l*, Tg level 107 ng/m*l* and anti Tg-ab <20 U/m*l*.

Seven months later the control radioiodine scan showed minimally decreased intensity in the metastatic lesions. Due to the extensive metastases causing severe pain, we decided to administer palliative radiotherapy to him.

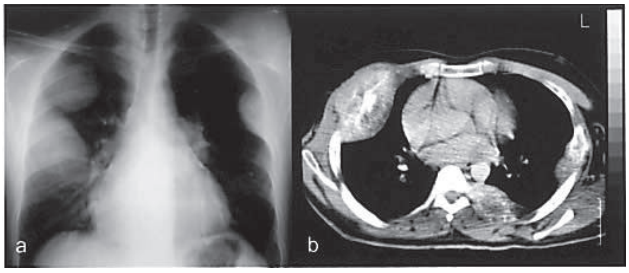

Fig. 4 Chest roentgenogram (a) and thoracic computed tomographic images (b) show expansion of the ribs due to metastases.

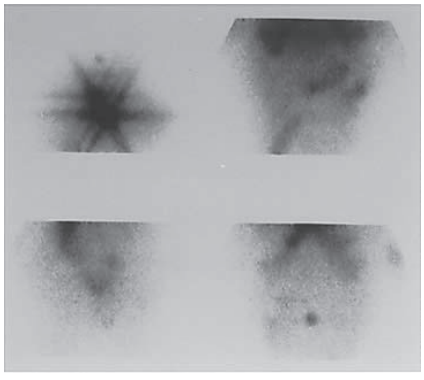

Fig. 5 Post-radioiodine therapy scan on day 7, showed avid concentration of the tracer in the thyroid bed and abdomen (*upper row*) and rest of the body—the pelvis and thorax (*lower row*).

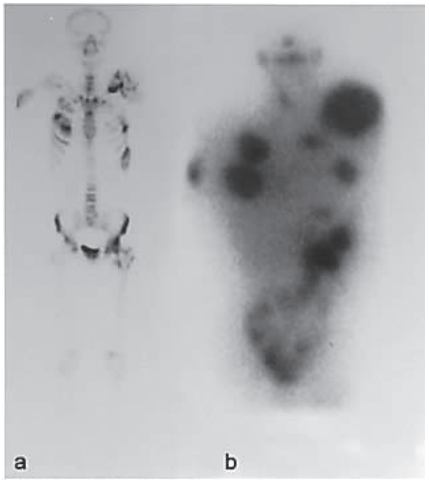

Fig. 6 Bone scan obtained 6 months later showing abnormal uptake in the left shoulder as well as new sites in the pelvis with not much change in the rest of the skeleton (a). These findings led the patient to receive another dose of RAI therapy where the post therapy scan showed minimal concentration of the tracer in the thyroid bed representing residual functioning thyroid tissue as well as other multiple metastatic areas on whole body imaging (b).

DISCUSSION

Insular thyroid carcinoma was first defined by Carcangiu et al. in 1984.[1] Capsular and blood vessel invasion is seen frequently, and metastases to regional lymph nodes, lungs and bones are common.[1] Progression of the disease leads to death in most patients with a mean survival time of 3.9 years.[1] Despite its poorly differentiated histological findings, insular carcinoma accumulates radioiodine.[2]

Thyroid carcinoma does not usually concentrate a significant amount of either Tc-99m pertechnetate or I-131 compared to normal tissue. The small percentage of cancers that demonstrate Tc-99m pertechnetate uptake without appreciable radioiodine accumulation may do so on the basis of the carcinoma retaining its anion trapping mechanism with a defective organification mechanism.[7] Both Tc-99m and I-123 have been shown to accumulate in extrathyroidal metastatic sites prior to thyroid surgery.[8] These extrathyroidal concentrations of the radiotracers can be almost equal to the intensity of the thyroid gland, but this is a rare occurrence. There have been only a few reported cases of confirmed and clearly defined thyroid carcinomas concentrating both Tc-99m and I-131 at the primary site.[4,5,9] In the presence of native thyroid tissue, detection of thyroid cancer metastases has been quite uncommon.[6]

We present the findings on Tc-99m pertechnetate, Tc-99m MDP and whole-body I-131 scintigraphies in an insular thyroid carcinoma case. Although the patient had undergone subtotal thyroidectomy previously, there was still a significant amount of residual thyroid tissue mainly in the right lobe and both Tc-99m pertechnetate and I-131 showed accumulation of activity in the primary site as well as the metastatic sites more extensively than in the case described by Verma et al.[10] Besides, increased Tc-99m MDP uptake clearly matching the metastases was also seen.

This type of thyroid carcinoma should be considered aggresive and classified between well-differentiated and poorly-differentiated thyroid carcinomas. This patient might have had a better prognosis if he had been initially diagnosed as having insular thyroid carcinoma and treated appropriately.

Radioiodine whole body scintigraphy is considered as a first line study in patients with DTC, but the need for cessation of thyroid hormone replacement before imaging and failure to calculate radioiodine uptake in 30% of the patients[11] led the researchers to evaluate other radionuclide imaging agents.

Tc-99m MIBI, Tl-201 and Tc-99m tetrofosmin do not require withholding of thyroid hormone suppression. However, despite this advantage they have limited use in diagnosing metastatic lesions in the lower thoracic and lumbar spine and pelvic bones due to their excretion through gut. Additionally, sometimes nonvisualization of the residual thyroid gland as seen in the images from the

study of Degirmenci et al.[12] should be considered an important problem. Yen et al. propose Tc-99m V-DMSA whole body imaging immediately postoperatively after total thyroidectomy as a screening procedure for all patients with insular thyroid carcinoma.[13] Tc-99m V-DMSA is a tumor seeking agent previously reported as useful in the detection of soft tissue tumors, such as those of the head and neck, medullary thyroid carcinoma and aggressive fibromatosis. The mechanism of Tc-99m V-DMSA accumulation has yet to be elucidated but is currently believed to be associated with the volume of blood flow in the lesions and phosphate metabolism or pH of the tumors.[14] So the amount of Tc-99m V-DMSA accumulation may be correlated with the metabolic turnover rate of the tumor cell.

In recent studies it has been shown that somatostatin inhibits basal and TSH stimulated adenylate cyclase activity in normal and neoplastic human thyroid tissues[15] and that octreotide inhibits cell growth and protease activity in DTC.[16] Radiopharmaceutical accumulation is observed in the normal thyroid gland but initial *in vitro* studies did not demonstrate somatostatin receptor uptake in epithelial thyroid cells, and so the uptake mechanism is not known yet. Tenebaum et al. have suggested that somatostatin scintigraphy could be helpful in patients with negative I-131 scan with high Tg levels so these patients could potentially benefit from octreotide therapy.[17]

There are conflicting results in FDG-PET imaging. Recently Zettinig et al. reported a case with insular thyroid carcinoma imaged with FDG-PET.[18] Despite poorly differentiated histological findings, glucose metabolism was not increased in this patient, and the PET study was negative in their study. On the other hand, Scott et al. mentioned its importance in the preoperative thyroid cancer patient for its ability to show cervical node metastases.[19]

In conclusion, this article describes a case of metastatic insular thyroid carcinoma along with a description of this extremely rare thyroid tumor and a review of the other radionuclide imaging modalities in this type of tumor. In this insular thyroid carcinoma case, pathologic radioactivity accumulations in metastatic lesions were observed not only on Tc-99m MDP and radioiodine scintigraphies but also Tc-pertechnetate scintigraphy. In our opinion, insular thyroid carcinoma should be accepted and treated as an aggressive type of thyroid carcinoma.

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