Technetium-99m-Tetrofosmin Imaging of Differentiated Mixed Thyroid Cancer

Michele Klain, Simone Maurea, Secondo Lastoria, Alberto Cuocolo, Annamaria Colao and Marco Salvatore

Departments of Nuclear Medicine and Endocrinology, CNR Center for Nuclear Medicine, University Federico II; and Department of Nuclear Medicine, National Cancer Institute, Napoli, Italy

This report describes the accurate localization of metastatic lesions in a patient with differentiated mixed thyroid cancer using 99mTc-tetrofosmin imaging. A 66-yr-old woman with a cytological diagnosis of follicular thyroid cancer associated with a large amount of goiter changes was studied by 99mTc-tetrofosmin total-body scintigraphy. No significant tetrofosmin uptake was observed in the thyroid nodules, which mainly showed goiter abnormalities. Abnormal increased tetrofosmin uptake, however, was found in metastatic tumor lesions located in the cervical and dorsal spine as well as in the left lower chest wall and lungs. In conclusion, 99mTc-tetrofosmin, a new radiopharmaceutical proposed for myocardial perfusion imaging, may be useful in patients with thyroid cancer.

Key Words: technetium-99m-tetrofosmin; total-body imaging; thyroid cancer; metastasis


Technetium-99m-1,2-bis (2-ethoxyethyl) phosphino] ethane (tetrofosmin) is a new lipophilic technetium-phosphine dioxo-cation proposed for myocardial perfusion imaging (1,2). Human biodistribution studies demonstrated thyroid uptake of tetrofosmin (1). In particular, thyroid glands show significant early uptake with successive tracer washout so that it is almost undetectable 4 hr after injection (1). Previous experimental studies demonstrated that thyroid tetrofosmin uptake is not blocked by perchlorate, therefore thyroid tracer accumulation is not due to free pertechnetate but represents uptake of the 99mTc complex itself, as described for 201Tl and 99mTc methoxy isobutyl isonitrile (sestamibi) (3,4). In this report, we describe the results of tetrofosmin imaging in a patient with metastatic differentiated mixed thyroid cancer.

CASE REPORT

A 66-yr-old woman with back pain was admitted to our department for diagnostic evaluation. The patient underwent dorsal spine x-ray tomography using antero-posterior and lateral views demonstrating osteolysis of the 12th vertebra. To further evaluate this abnormality, spinal CT and fine-needle aspiration biopsy (FNAB) were also performed. An osteolytic lesion of the 12th dorsal vertebra was detected and FNAB findings documented a metastatic abnormality by well-differentiated follicular thyroid adenocarcinoma.

Successively, the patient underwent diagnostic evaluation of the thyroid gland. Thyroid physical examination showed two solid nodules, one for each lobe. No abnormal lymph nodes were detected in the neck. Laboratory measurements of thyroid function were normal. Serum thyroglobulin was 114 ng/ml (normal value < 50), while carcinoembryonic antigen and tissue peptide antigen levels were in the normal range. The patient underwent US and FNAB of the thyroid, which showed the presence of multiple nodules in an enlarged gland. The two largest nodules were located in the middle of right lobe and in the inferior region of left lobe. FNAB findings of these lesions documented a prevalence of goiter abnormalities associated to the presence of a small amount of atypical cells suggesting well-differentiated follicular thyroid adenocarcinoma. Thyroid scintigraphy with 99mTc pertechnetate showed no significant uptake in the right lobe and inhomogeneous activity in the left lobe (Fig. 1). No extra-thyroid lesions with increased 99mTc pertechnetate uptake were found. Total-body scintigraphy with 99mTc-tetrofosmin (740 MBq i.v.; images obtained 30–120 min postinjection) was performed after the patient gave informed consent.

Faint tetrofosmin thyroid uptake was observed in the left lobe, while inhomogeneous activity was found in the right lobe (Fig. 2A). The two nodules clinically detected and described on US images had no significant tracer uptake. Extra-thyroid images detected five lesions with significant accumulation of tetrofosmin. A bilobate area of intense uptake was located in the cervical spine (Fig. 2B). Irregular increased uptake was also found in the dorsal spine where radiographs and CT showed abnormalities (Fig. 2B). Finally, three other lesions were detected in the chest (Fig. 2A, B). Early (30–60 min) and delayed (120 min) tetrofosmin images were comparable. Thyroid uptake of tetrofosmin in a normal health subject is shown in Figure 3A. Normal chest and abdominal tetrofosmin distribution are illustrated in Figure 3B.

The patient also underwent 99mTc-sestamibi (740 MBq i.v.; images obtained 15–120 min postinjection) total-body imaging as part of an ongoing research protocol in our laboratory. Sestamibi images were comparable to those of tetrofosmin. Radionuclide bone scanning, cervical CT associated with FNAB, chest radiography and CT were performed to further characterize the lesions observed on the tetrofosmin images. Technetium-99m-methylene diphosphonate (MDP) bone scanning demonstrated reduced uptake in the upper portion of the cervical spine (Fig. 4A). Increased but inhomogeneous uptake in the lower region of the dorsal spine was observed (Fig. 4B). The cervical CT study without contrast en-

Received Oct. 28, 1994; revision accepted Apr. 12, 1995.

For correspondence or reprints contact: Simone Maurea, MD, Via Raffaele de Cesare n. 7, 80132 Napoli, Italy.
enhancement showed a large (6 cm) inhomogeneous bilobate lesion in the upper portion of the cervical spine (Fig. 5). FNAB findings

documented a metastatic lesion by well-differentiated follicular thy-
roid adenocarcinoma. This lesion involved regional soft tissues with

only adjacent bone erosion. The chest radiograph demonstrated a
clear abnormality in the left lower hemithorax (Fig. 6), but the two
foci of faint uptake, depicted in the lungs on the tetrofosmin images,
were not identified. Chest CT confirmed the lesion in the left lower
hemithorax and showed two nodules in the lungs, one for each. Similarly, the lesion of the left lower chest wall consisted of regional
soft-tissue abnormalities without bone involvement.

The patient underwent total thyroidectomy and a follicular-

apillary (mixed) thyroid adenocarcinoma was histologically doc-
umented. In particular, the left lobe lesion was characterized by

the presence of calcification and blood. The right lobe lesion was
cystic with associated calcification. The tumor was invasive and not
capsulated with vascular tumor emboli. One month after surgery,
the patient underwent serum thyroglobulin assay, which measured
153 ng/ml, and 131I total-body scanning, which showed intense

radionuclide abnormal uptake in all extra-thyroidal tumor lesions
previously described. Therefore, 131I therapy (100 mCi) was per-
formed to treat tumor metastases.

**DISCUSSION**

Different tracers are used in the evaluation of patients

with thyroid cancer (5–7). Thallium-201 has been used in

the evaluation of clinically suspicious primary nodules or
during postsurgical follow-up, particularly in those patients

with tumor lesions not iodine-avid (8–11). Thallium, is not

ideal, however, for radionuclide imaging, and 99mTc-labeled

compounds have been proposed to circumvent this limitation.

Our preliminary results demonstrated that 99mTc-V-

DMSA may be concentrated in primary and metastatic sites

differentiated thyroid carcinomas (12). These findings

suggest that DMSA allows better characterization of

primary malignant thyroid nodules compared to [99mTc]per-

technetate scintigraphy and it is more sensitive than 131I in

the evaluation of metastases (12). We recently described

99mTc-V-DMSA uptake in a patient with thyroid involve-

ment by histiocytosis X (13). Septamibi, a lipophilic radiophar-
maceutical, has been proposed for evaluation of thy-
roid abnormalities such as functional and neoplastic

disorders (14–19).

Tetrofosmin is a new lipophilic technetium-phosphine
agent proposed initially for myocardial perfusion imaging

(2). The precise mechanism of tetrofosmin uptake into

myocardial cells is not well known, but it is likely to be

similar to that of septamibi (2). Preliminary experimental

data demonstrated that tetrofosmin accumulates in the mi-

tochondria, phenomenon dependent on the amount of pro-
teins and energetic substrate (20). In this report, we used
tetrofosmin with our patient since we hypothesized that its

biological features and intracellular uptake mechanisms

could justify its clinical applications in neoplastic diseases.

![FIGURE 1. Technetium-99m-pertechnetate scintigraphy (anterior view) depicts no significant uptake in the right lobe; there is faint visualization of the upper pole of this lobe (arrow). Reduced activity in the nodule located in the inferior pole of the left lobe (arrow). A radioactive marker is located in the jugular region (small arrow).](image)

![FIGURE 2. Technetium-99m - tetrofosmin scintigraphy. (A) Anterior view shows no significant uptake in the thyroid nodules (arrows), but there is a focus of abnormal uptake in the upper right hemithorax (arrow). (B) Chest and abdomen posterior view shows abnormal uptake in cervical and dorsal spine and in the left hemithorax (arrows). There is normal tracer distribution in the myocardium, superior pole of the kidneys.](image)
In particular, the physiological characteristics of this tracer, which rapidly clears from normal thyroid tissue, suggest that it may be retained longer in malignant tumor lesions.

In our patient, tetrofosmin imaging clearly detected multiple metastatic lesions in the spine and chest as well as increased abnormal uptake in tumor sites. Sestamibi imaging showed comparable results. These tumor lesions were then confirmed using morphologic imaging modalities and/or FNAB. No increased tetrofosmin and sestamibi uptake were observed in the thyroid nodules. This latter finding may be explained by the fact that goiter changes mainly occur in such lesions (18). The association of thyroid cancer and goiter abnormalities observed in this study has been widely described and is not surprising (21). We compared tetrofosmin and 201Tl images in this study. The labeling of this tracer with 99mTc, however, represents a significant advantage for scintigraphic imaging compared to 201Tl. Thus, 99mTc-tetrofosmin total-body scintigraphy accurately staged thyroid tumors.

In patients with differentiated thyroid tumors, the most frequent sites of metastases are lymph nodes, lungs and bones (22). In our patient, unusual metastatic lesions occurred in the soft tissues of the chest wall and cervical spine. These findings were documented by integrated, but discordant imaging results. CT images showed soft-tissue abnormalities in these anatomic regions, but corresponding increased 99mTc MDP was not observed. Conversely, abnormal tetrofosmin uptake was found.

CONCLUSION

In a patient with well-differentiated mixed thyroid carcinoma, tetrofosmin total-body scintigraphy detected unusual metastatic lesions. Therefore, this radionuclide technique may be useful in patients with thyroid cancer. Further in vitro and clinical studies are needed to assess tetrofosmin's role in the evaluation of thyroid tumors.

ACKNOWLEDGMENTS

The authors thank Vincenzo De Rosa, MD for his valuable help in performing cervical computed tomography.

FIGURE 3. Technetium-99m-tetrofosmin imaging in a normal subject. (A) Neck anterior view shows normal tracer distribution in the thyroid, with physiological uptake in the salivary glands. (B) Chest and abdomen posterior view shows physiological tracer distribution in the myocardium (M), liver (L) and gallbladder (G). Inhomogeneous activity in the bowel (B). Diffuse and mild activity in the lungs, with photon attenuation in the spine.

FIGURE 4. Technetium-99m-MDP bone scan. (A) Right lateral view of the cervical spine and skull shows reduced activity in the cervical spine (arrow). (B) Posterior view of the spine shows increased but inhomogeneous uptake in the dorsal spine (arrow).