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^{99m}Tc (V) dimercaptosuccinic acid (DMSA) is a new tumor imaging agent that has been successfully used to image patients with medullary thyroid carcinoma (MTC). Since 1986, studies have been performed in 32 patients with histologically proven MTC at Guy's Hospital, London, England. Five patients with primary tumor were studied prior to surgery, four patients were studied after successful removal of the primary tumor, and 26 patients with biochemical evidence of recurrence were studied. Eight patients were studied serially to assess progression of disease, and four patients were studied before and after surgery. Twenty-one of the 26 patients with disease had positive scans with four false-negative scans and three true negative scans. One patient had a false-positive scan (sensitivity 80%, specificity 75%). Two of the false-negative scans were obtained in patients with moderate but stable elevations of calcitonin but no other evidence of recurrence. One false-negative scan was obtained in a patient who was discovered on screening to have an abnormal pentagastrin response, and a small 1 cm tumor was subsequently removed. Uptake in local neck recurrence was frequently intense, but uptake at sites of bone metastases was less marked. ^{99m}Tc (V) DMSA is an inexpensive radiopharmaceutical which produces good quality images and has been shown to have an acceptable sensitivity and specificity in the follow-up of patients with MTC and thereby contributes significantly to the management of these patients. (Henry Ford Hosp Med J 1989;37:167-8)

In 1984 Ohta et al (1) reported their experience of imaging patients with known malignancy using a newly developed technetium 99m-labeled radiopharmaceutical, pentavalent dimercaptosuccinic acid ([V] DMSA). Of the patients imaged, five had medullary thyroid carcinoma (MTC) and all showed uptake of ^{99m}Tc (V) DMSA in their tumors. Other groups have also reported success in imaging patients with MTC. In 1988 Patel et al (2) reported 15 MTC patients and showed positive localization in 80% of those studied. In 1989 Guerra et al (3) studied 26 patients with MTC using ^{99m}Tc (V) DMSA and showed a sensitivity of 84.2% for the technique. Following the 1987 report of our experience using ^{99m}Tc (V) DMSA to image ten patients with MTC when a sensitivity of 80% was achieved (4), we now report our four-year experience of using ^{99m}Tc (V) DMSA in routine management of patients with histologically proven MTC.

Patients and Methods

The 32 patients studied included ten males and 22 females ranging in age from 14 to 86 years. Of these patients, 26 had sporadic MTC, four had multiple endocrine neoplasia type 2A (MEN 2A), and two had MEN 2B. Five patients with primary tumors were studied prior to surgery, four patients were studied after successful removal of the primary tumor, and 26 patients with biochemical evidence of residual or recurrent tumor were studied. Eight patients were studied serially to assess the progression of disease, and four were studied before and after surgery. A total of 56 scans were performed. All patients were evaluated by ^{99m}Tc medronate methylene diphosphonate (MDP) bone scans, chest roentgenograms, and computed tomography to define accurately the extent of their disease.

^{99m}Tc (V) DMSA was prepared using the previously reported method (4) and labeled with 370 MBq (10 mCi) of ^{99m}Tc. Following intravenous administration, whole body images were acquired at 3 hours using a large field of view gamma camera and a general all-purpose collimator. No image enhancement was used, although single photon emission computed tomography (SPECT) was performed in two patients to define accurately the extent of their neck recurrence before surgery.

Results

Uptake of ^{99m}Tc (V) DMSA varied from intense to slight. Uptake in small lesions less than 1 cm and in bone metastases was usually less than the uptake in soft tissue disease. Of the five patients with primary tumors, one patient showed no significant uptake in the thyroid. This 17-year-old girl, the sibling of a known case of MEN 2A, had an abnormal calcitonin (CT) response to pentagastrin. At surgery a small focus of MTC, about 1 cm in diameter, was discovered. The other four patients with primary tumors showed positive uptake on imaging, and in two patients involved local lymph nodes were also imaged.

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In the patients studied postoperatively, the four patients with successful removal of tumors had negative scans. In two other patients studied postoperatively, involvement of mediastinal nodes necessitated sternal splitting to approach the mediastinum. Postoperative scans showed uptake in both patients in unresectable tumor and also in the sternum at the site of surgery.

Two patients were studied following radiotherapy to the neck, and both showed low grade diffuse uptake in the neck within the radiotherapy field.

Of the 26 patients studied with biochemical evidence of recurrence, four patients had false-negative studies with no abnormal uptake of ^{99m}Tc (V) DMSA visualized. Three of the four patients had stable CT levels, and no disease could be imaged despite extensive investigation with computed tomography and ^{99m}Tc MDP bone imaging. In one patient with diffuse lung metastases, uptake was initially negative but subsequently became positive as the metastases increased in size. The remaining 22 patients had uptake on imaging. The degree of ^{99m}Tc (V) DMSA accumulation varied with site of uptake, and uptake in sites of neck recurrence was frequently intense whereas uptake in bone metastases was less marked and frequently identified only when the ^{99m}Tc (V) DMSA study was reviewed with a ^{99m}Tc diphosphonate bone scan.

Discussion

No successful treatment currently exists for the management of some MTC patients. Surgery of the primary tumor, if performed early before local lymph nodes become involved, may be followed by a long disease-free interval. Primary surgery when local lymph nodes are involved, however, remains only palliative despite attempts at extensive neck and mediastinal resections. The slow-growing nature of tumor has encouraged many surgeons to attempt extensive dissections to debulk the tumor, reduce symptoms caused by vasoactive peptides, and give the patient several years of relative symptom-free existence. Other therapeutic options tried in recent years but with little success include external beam radiotherapy, chemotherapy, and ^{131}I meta-iodo-benzylguanidine therapy (5,6). One of the main problems in the assessment of new therapies for this disease is the inability to define accurately the extent and activity of the disease and therefore to assess its response to therapy. Radionuclide techniques such as ^{99m}Tc diphosphonate bone scanning, ^{99m}Tc colloid, and ^{99m}Tc pertechnetate glucoheptonate have been shown to be sensitive techniques for identifying metastatic disease in the bone, liver, and brain, respectively, but do not accurately define the extent of the primary disease or local recurrence. ^{201}thallous chloride has been used to image MTC (7,8), but although uptake in the primary tumor or local recurrence is marked, the normal biodistribution of ^{201}thallous chloride in the myocardium, lungs, and liver significantly diminishes the usefulness of this agent to image metastases in these sites.

Both ultrasound and computed tomography may be used to assess the neck for recurrence, but their specificity is low when assessing the involvement of lymph nodes, which are frequently enlarged secondary to inflammatory change rather than metastatic involvement. Surgery with major neck and mediastinal dissection also produces gross distortion of the normal anatomy and may make interpretation of both computed tomography and ultrasound images difficult. Therefore, there is a need for an imaging technique that will accurately define the extent and activity of primary and metastatic disease so that as new therapeutic agents are developed their efficacy may be readily assessed. ^{99m}Tc (V) DMSA is inexpensive and can be easily prepared in most nuclear medicine departments. Because there is little nonspecific uptake of the agent, it produces excellent images which require no processing. It is also an ideal agent for SPECT studies, although SPECT is usually unnecessary because of the high uptake visualized on most planar studies.

False-positive images do occur following radiotherapy and surgery involving bones, but awareness of this usually resolves the problem when interpreting a posttherapy image. False-negative images occur when tumor volume is small, which in our opinion is also the cause of false-negative studies in the well recognized group of patients whose CT levels fail to fall to the normal range in the postoperative period and remain elevated but do not increase. This phenomenon may partly explain the negative results reported by Hilditch et al (9).

^{99m}Tc (V) DMSA has been demonstrated in an increasing number of patients to be the imaging method of choice in the follow-up of patients with MTC to define accurately the presence and extent of disease.

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