

COMPARISON OF $^{99m}\text{Tc(V)}$ -DMSA WITH ^{99m}Tc -EDDA/HYNIC-TYR³-OCTREOTIDE SCINTIGRAPHY IN THE DETECTION OF MEDULLARY THYROID TUMOR FOCI IN A PATIENT WITH ELEVATED LEVEL OF CALCITONIN AFTER SURGERY: A CASE REPORT

Hameedullah,¹ Aakif Ullah Khan,² Muhammad Rauf Khattak,¹ Shakil Ahmad¹
Shaheen Iqbal¹

¹ Institute of Radiotherapy and Nuclear Medicine (IRNUM), Peshawar, Pakistan;

² Swat Institute of Nuclear Medicine, Oncology and Radiotherapy (SINOR), Swat, Pakistan.

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ABSTRACT

Technetium-99m Pentavalent Dimecaptosuccinic acid ($^{99m}\text{Tc(V)}$ -DMSA) scintigraphy was performed in a patient with histopathologically proven medullary thyroid carcinoma having high level of calcitonin using a locally formulated kit. Marked uptake of the radiotracer was observed by the locally metastatic foci. The same patient was then subjected to somatostatin receptor scintigraphy (OctreoScan) and the results were found comparable. Both the scanning was completed within 24 hrs with good quality images. In house preparation from renal DMSA kit, better resolution, good stability and easy procedure with minimum cost make $^{99m}\text{Tc(V)}$ -DMSA, a good imaging agent for visualization of medullary thyroid carcinoma in centre's where ^{99m}Tc -EDDA/HYNIC-Tyr³-Octreotide is not available.

Key words: Octreotide, MTC, Calcitonin, ^{99m}Tc (V)-DMSA, Radiochemical purity

Introduction

Medullary Thyroid Carcinoma (MTC) is an uncommon but challenging malignant tumor that arises from the parafollicular calcitonin secreting cells of the thyroid.^{1,2} Hence elevated serum calcitonin level is a reliable marker for differentiate recurrent MTC.³ MTC accounts for 3% - 10% of all thyroid cancers and 13.4% of all thyroid-related deaths.⁴ According to the oncology registry record of the Institute of Radiotherapy and Nuclear Medicine (IRNUM), there are 59 cases of MTC in the last 10 years which comprises about 0.09% of all malignant cases registered in the hospital. In time diagnosis, staging and assessment of recurrence in medullary thyroid carcinoma (MTC) is of utmost importance for the proper management of the disease.⁵ This tumor is resistant to external beam radiotherapy (EBRT) and show poor response to

chemotherapy. Hence, surgery is the only strategy for potential treatment.^{2,6-8} However for successful surgical attempt, one should be familiar with site and extent of disease.⁹ The conventional imaging techniques sometimes show negative results or have some limitations to be applied.¹⁰ Therefore nuclear medicine techniques are sought to image, detect or visualize MTC.

The various functional imaging tools commonly used for this purpose are: iodinated (^{123}I) or (^{131}I) metaiodobenzylguanidine (MIBG), Thallium chloride, (^{201}Tl), pentavalent ^{99m}Tc dimecaptosuccinic acid ($^{99m}\text{Tc(V)}$ -DMSA), ^{111}In and ^{99m}Tc labeled octreotide, ^{18}F -FDG PET, monoclonal anti-CEA labeled antibodies, and other PET tracers, such as ^{18}F -DOPA and ^{68}Ga -DOTATOC or ^{68}Ga -DOTATATE, have shown encouraging results.¹¹⁻¹³

Correspondence : Mr. Hameedullah
Institute of Radiotherapy and
Nuclear Medicine (IRNUM),
Peshawar, Pakistan
Tel: +92-91-9216114-17 Ext: 150
Email: hameedullahirnum@gmail.com

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The selection of radiopharmaceuticals depends upon the availability, financial implications and ultimately the comfort of the treating clinician.¹⁴ Out of them ^{99m}Tc labeled octreotide (^{99m}Tc-EDDA/HYNIC-Tyr³-Octreotide scintigraphy is now considered as the most appropriate method for the diagnosis, staging and assessment of treatment response in MTC especially in lesions that express with somatostatin receptors.¹⁵ It has many advantages including fast clearance, easy labeling, rapid tissue penetration and lesser time to scan the patient. In our clinical set up where patients flow is limited and clinical indications are few, the tracer is not always readily available at many institutes and its price also makes it unaffordable by many patients which might delay the imaging procedures. Alternatively ^{99m}Tc(V)-DMSA has a crucial role in the preoperative evaluation, assessment of residual disease or recurrence of MTC and other related soft tissue tumors.^{14,16-18} But now the use of this agent is going to be abandoned in most countries due to the introduction of newer alternatives like ⁶⁸Ga-DOTATOC or ⁶⁸Ga-DOTATATE.¹⁹ However several authors still believe that ^{99m}Tc(V)-DMSA is the most cost effective and time efficient tool for imaging MTC.²⁰ Previously published work from our institute also suggest ^{99m}Tc(V)-DMSA, a good tumor seeking agent for visualization of MTC and its involved lymph nodes in the mediastinum.^{9,21} As ^{99m}Tc(V)-DMSA can be easily formulated from the renal DMSA kit and has comparable results with ^{99m}Tc-EDDA/HYNIC-Tyr³-Octreotide (Tektrotyd), we successfully imaged a patient of MTC with locally formulated ^{99m}Tc(V)-DMSA and then made its comparison with the results of ^{99m}Tc-EDDA/HYNIC-Tyr³-Octreotide (Tektrotyd) scintigraphy for lesion detection sensitivities.

Case Report

A 35 years old male was diagnosed one year ago as a case of MTC after excision biopsy from neck swelling, was referred to nuclear medicine department from oncology section for somatostatin receptor scintigraphy. At the time of presentation, his serum calcitonin level was 6324pg/ml (normal range is <8.4). However due to nonavailability of this radiopharmaceutical, it was decided to perform ^{99m}Tc(V)-DMSA scan for this patient. Owing to our previous experience, the radio-

pharmaceutical was locally prepared using renal DMSA kit.⁹ The commercial DMSA kit supplied by Isotope Production Division (IPD), PINSTECH, Islamabad, Pakistan that contains 1mg DMSA, 0.35 mg of SnCl₂·2H₂O, 0.35 mg of Ascorbic acid and 20 mg of mannitol was taken and were mixed with 1ml of 0.167M sodium bicarbonate solution to make the medium alkaline. The pH of the reaction mixture was (8.4-8.5) determined by pH indicator strips. Then 20mCi (740MBq) of freshly eluted Sodium Pertechnetate (Na ^{99m}TcO₄) from Mo⁹⁹/Tc^{99m} Generator was added to the vial. The vial was incubated for 15 minutes at room temperature for reaction to complete. Quality control tests were carried out by thin-layer chromatography (TLC) and the radiochemical purity (RCP) was found to be 95.6 ± 0.5%. The whole process was carried out under aseptic condition. The radiopharmaceutical was then injected into the median cubital vein of the patient through an indwelling IV cannula. Early 2-3 hrs (Fig. 1a & 1b) and delayed 24 hrs (Fig. 1c) anterior spot images of the cervico-thoracic region and abdomen were acquired using Siemens Orbitor Gamma camera with low energy all purpose (LEAP) collimator and energy window of 15% centered at 141KeV photopeak.

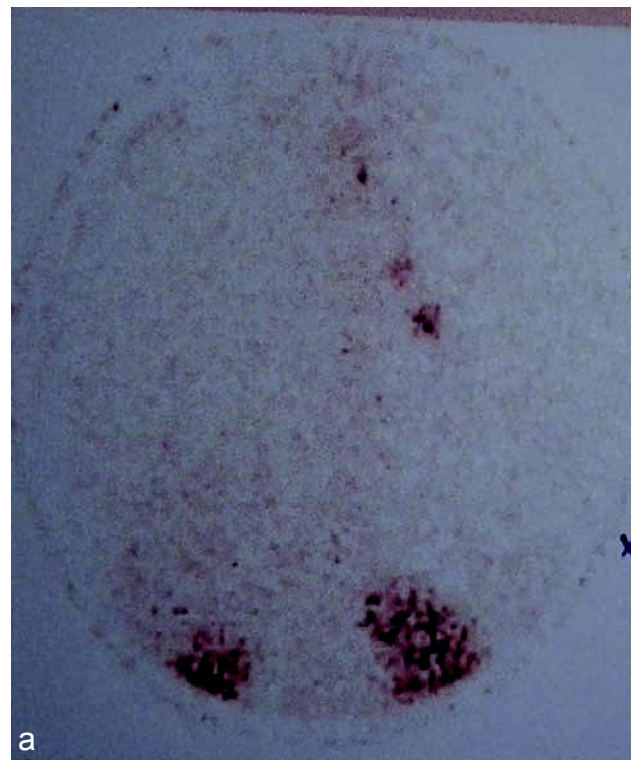


Figure 1(a): ^{99m}Tc(V)-DMSA scan 1-hour.



Figure 1(b): $^{99m}\text{Tc(V)}$ -DMSA scan 1-hour images of the anterior head and neck region images of the anterior thoracic region.



Figure 1(c): $^{99m}\text{Tc(V)}$ -DMSA scan 24 hours images of the anterior chest region.

After one month of the $^{99m}\text{Tc(V)}$ -DMSA scan, the same patient underwent with ^{99m}Tc -EDDA/HYNIC-Tyr³-Octreotide scintigraphy. The cold kit with brand name, Tektrotyd, was obtained from PARS, Isotope Company, Iran. The kit was reconstituted with 30 mCi (1110 MBq) of ^{99m}Tc and the labeling yield was found $98.2 \pm 0.2\%$. Then 20 mCi (740 MBq) of the radiopharmaceutical was also slowly injected into the median cubital vein, having a close look at the vital signs. After 2-3 hrs (Fig. 2a) and 4hrs (Fig. 2b) post injection, whole body imaging was performed on the same institutional protocols.

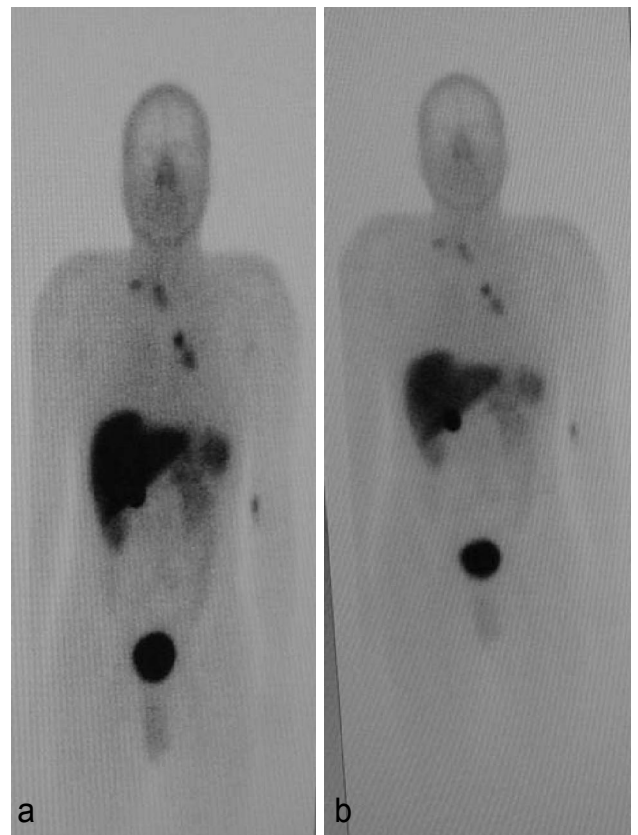


Figure: 2-hours **2(a)** and 4 hours **2(b)** whole body imaging of ^{99m}Tc -EDDA/HYNIC-Tyr³-Octreotide scan

All the images were compared and interpreted by the nuclear physician in view of the clinical presentation of the patient. The images were very sharp with excellent resolution and the lesion detection potentials were common in both the cases. Marked uptake of both the radiotracer was seen in four foci of the neck thoracic region and showed good radiotracers avidity by the lesions. The number of lesions detected by the $^{99m}\text{Tc(V)}$ -DMSA on the initial scan in the neck

and thorax region were found to be the same as detected later by ^{99m}Tc-EDDA/HYNIC-Tyr³-Octreotide scintigraphy. No additional focus was detected by the Octreoscan. The 24 hrs post injections images were additionally acquired to see the redistribution of the tracers over a long period of time.

Discussion

MTC is a rare neuroendocrine tumor and octreotide scan is considered as a specific imaging agent for detection of primary and metastatic MTC with higher sensitivity.²² Somatostatin receptor scintigraphy is used to detect the primary tumor focus for staging, decision of therapy protocol, and evaluation of therapy response in neuroendocrine tumors and other related cancers.²³ It has proved to be better than other diagnostic tools in the detection of cervical and mediastinal lymph node metastases in MTC or other somatostatin receptor-positive tumors.²⁴ Several study support that the sensitivity and specificity of Octreoscan is higher than that of ^{99m}Tc (V)-DMSA in the work up of MTC.²⁵ However limitations are associated with this radiotracer like availability and high prices. In most developing and under developed countries, it is imported from other developed countries and patients have to wait for a prolong duration. Patient's affordability is another major hurdle in its routine use. In such conditions ^{99m}Tc DMSA (V) scanning is an affordable and a reasonably sensitive imaging agent for localization of recurrent or metastatic disease.

^{99m}TcDMSA(V) is a non specific multifunctional imaging agent that commonly accumulates in MTC.²⁶ Its role in the evaluation of MTC has already been compared with other functional imaging tools like ¹³¹I MIBG, ^{99m}Tc tetrofosmin and ²⁰¹Tl scintigraphy etc.^{21,27} ^{99m}TcDMSA (V) plays a crucial role in the assessment of residual tumor or metastatic disease in patients with medullary thyroid cancer especially with high postoperative calcitonin levels.¹⁴ The ease of preparation of ^{99m}TcDMSA(V) and good imaging characteristics of the radiopharmaceutical make it an alternative imaging tool in patients having proven MTC.²⁰ MTC is an uncommon NET and patients are neither readily available nor always compliant for the tedious procedures of research.²¹ Hence further studies are needed to better define the role of ^{99m}Tc DMSA(V)

in MTC patients. Our experience of avid and persistent ^{99m}TcDMSA(V) uptake in all the tumor deposits in the thoracic region have encouraged us to explore its potentials where EDDA/HYNIC-Tyr³-Octreotide and ⁶⁸Ga-DOTATOC or ⁶⁸Ga-DOTATATE is not available. Moreover, ^{99m}Tc DMSA (V) show low uptake in the liver and spleen as compared to Octreotide scan, hence the uptake in these region will be clearly appreciated where it will be overshadowed with octreotide. The prolong residence of the of ^{99m}Tc DMSA (V) can also be utilized for an alternate therapeutic option when tagged with β emitting radionuclides like ¹⁸⁸Re, ¹⁸⁶Re and others.

Conclusion

Locally formulated ^{99m}TcDMSA (V) scintigraphy is an easy, economical and promising imaging modality in MTC patients with high levels of calcitonin. In comparison with ^{99m}Tc-EDDA/HYNIC-Tyr³- octreotide scintigraphy, its availability and application is easier. It can be used as an alternative imaging method when ^{99m}Tc-EDDA/HYNIC-Tyr³-octreotide and ⁶⁸Ga-DOTATOC or ⁶⁸Ga-DOTATATE is not available.

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