

CASE REPORT

Mediastinal spread of medullary thyroid carcinoma imaged by locally formulated ^{99m}Tc- DMSA (V)

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Abstract

Medullary thyroid carcinoma (MTC) is a distinct C-cell tumour of the thyroid gland that produces calcitonin in high quantities. Various imaging techniques are available in nuclear medicine to image MTC which include ^{131}I-MIBG and somatostatin receptor imaging agent ^{111}In-Octreotide. Due to the nonavailability of these agents in Pakistan, we tried using locally prepared ^{99m}Tc-labelled pentavalent dimercaptosuccinic acid (^{99m}Tc (V)-DMSA) in a patient suspected of advanced MTC. CT with contrast could not be performed in this patient due to raised serum urea and creatinine levels indicating renal impairment. ^{99m}Tc(V)-DMSA was prepared by modification of a locally formulated kit of renal DMSA. Significant accumulation of the tracer was seen in the gross disease present in the neck and mediastinum. The resolution and good physical characteristics of ^{99m}Tc(V)-DMSA make it a useful agent for MTC imaging, where other modalities are not available.

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Introduction

Medullary thyroid carcinoma (MTC) is an uncommon tumour accounting for 3-10% of all thyroid malignancies [1]. According to the radiotherapy record of Institute of Radiotherapy and Nuclear Medicine (IRNUM), there are only 65 cases of MTC from 1994 to 2011, which comprises about 12% of all neuroendocrine tumours and 0.08% of all malignant cases registered in the hospital.

MTC arises from thyroid C-cells which produce calcitonin. Hence, an elevated serum calcitonin level is a reliable marker of a well-differentiated MTC [2, 3]. This tumour is mostly resistant to external beam radiation therapy (EBRT) and chemotherapy in most of the cases [4]. The treatment of gross primary and recurrent disease is surgery [5]. But for a successful surgical attempt, a knowledge of the extent of disease is very important. Efforts to delineate the disease has been made in the past using various imaging techniques like conventional x-rays, computed tomography (CT), magnetic resonance imaging (MRI), abdominal and neck ultrasound. However,

these modalities pose some difficulties in the detection of recurrent and metastatic MTC due to the distortion of normal anatomy after the surgery [6]. Bone scan is used to look for skeletal involvement in the disease process. The functional imaging tools commonly employed for the evaluation and visualization of MTC are radioiodinated (^{123}I) or (^{131}I) metaiodobenzylguanidine (MIBG), thallium chloride (^{201}TI), pentavalent ^{99m}Tc-dimer captosuccinic acid (^{99m}Tc(V)-DMSA), and ^{111}In- and ^{99m}Tc-labelled octreotides [6, 7]. Out of these ^{111}In- and ^{99m}Tc-labelled octreotides have proved more useful but their high cost and nonavailability at most of the nuclear medicine institutes in our country are the major hindrances in the way of their routine use [8, 9]. Alternatively, ^{18}F-FDG PET and monoclonal anti-CEA labelled antibodies also have proved to be advantageous, but their use in the routine workup of MTC patients is also limited because of the abovementioned reasons [10-12].

Where conventional imaging techniques (US, CT and MRI) fail to localize the tumour or the metastatic lesion, radionuclide techniques are the next diagnostic step in the evaluation of a MTC patient depending upon the availability of the method and experience of the professionals in a nuclear medicine facility. Several authors believe that imaging with ^{99m}Tc(V)-DMSA is the most cost-effective and time-efficient technique for MTC evaluation [11, 13].

Previously published work from this institute reports successful visualisation of MTC using ^{99m}Tc(V)-DMSA and ^{131}I MIBG [14, 15]. The present case is yet another example of successful diagnosis of MTC using locally formulated ^{99m}Tc(V)-DMSA where the scan yielded good quality images and provided important clinical information helpful in subsequent patient care.

Case Report

A 38-year-old male was diagnosed four years ago as a case of MTC after excision biopsies from a neck mass. He was given EBRT (50 Gy) to the neck and superior mediastinum at this institute but was subsequently lost to follow-up until 3 years ago when he reported with dyspnoea and chest tightness. At the time of his second presentation, his serum calcitonin was very high at >2000pg/ml (normal range 0-8.4). He had palpable lymph nodes in the neck but due to his severe chest tightness and breathlessness, there was a clinical suspicion of advanced disease in the mediastinal lymph nodes. On routine check-up, his renal profile was found to be deranged with high serum urea and creatinine values.

The case was discussed in the institutional tumour board and then referred to nuclear medicine department for somatostatin receptor Imaging (SSR). However, due to nonavailability of this radiopharmaceutical, it was decided to perform ^{99m}Tc(V)-DMSA scintigraphy using locally formulated radiopharmaceutical. In some institutes, DMSA(V) is available in the form of a freeze-dried kit, which is then reconstituted. We however prepared the radiopharmaceutical using renal DMSA vial which labels with ^{99m}Tc in +3 oxidation state (trivalent) at pH 3-4; this was converted to DMSA(V) with pH 8.5 (determined by pH indicator strips) under aseptic conditions. The renal DMSA kit (supplied by IPD, PINSTECH Islamabad, Pakistan) contained dimercaptosuccinic acid (1.0 mg), $SnCl_2.2H_2O$ (0.35 mg), ascorbic acid (0.5 mg), and mannitol (20 mg). 1 ml of 0.167N solution of $NaHCO_3$ (which can be prepared by dissolving 280 mg of analytical grade $NaHCO_3$ in 20 ml of distilled water) was added to the vial to make the medium alkaline. The pH of this DMSA vial lies in the range of 8.4 to 8.5. 20 mCi (740 MBq) of fresh elute of sodium pertechnetate obtained Mo/Tc Generator (PAKGEN provided by IPD, PINSTECH Islamabad, Pakistan) was added to this vial. The vial was incubated for 15 minutes to complete the reaction. Quality control tests were performed by thin-layer chromatography (TLC); the radiochemical purity (RCP) was found to be more than 95%.

The preparation was then injected intra venously into the patient's antecubital vein through an indwelling intravenous cannula.

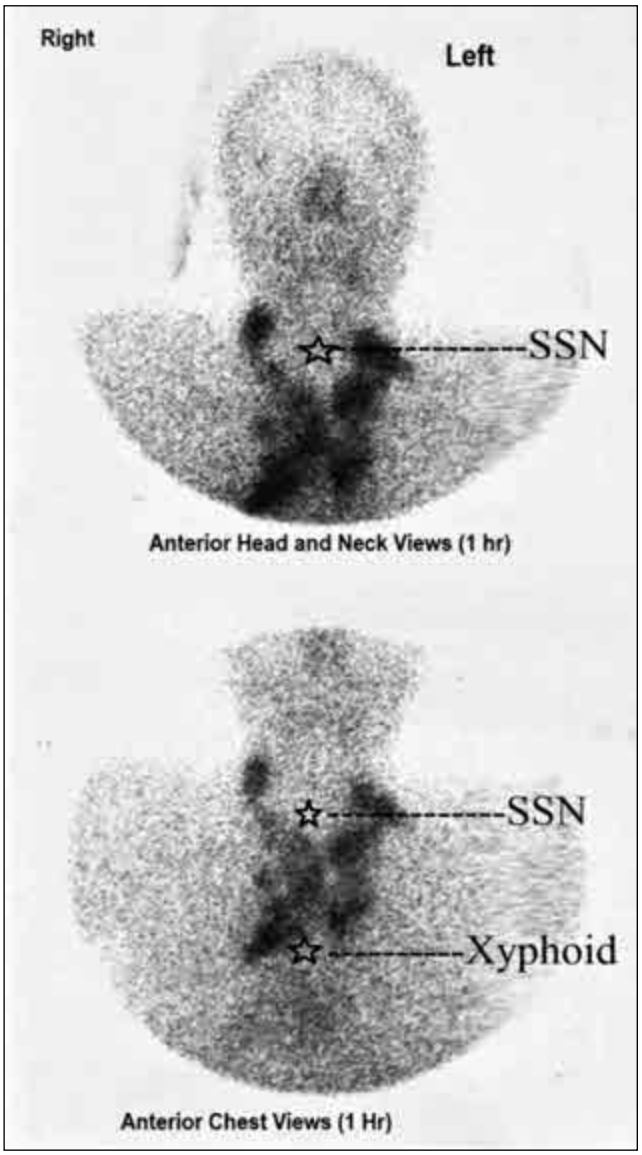

Figure 1 *^{99m}Tc(V) DMSA scan 1-hour images in the anterior projection*

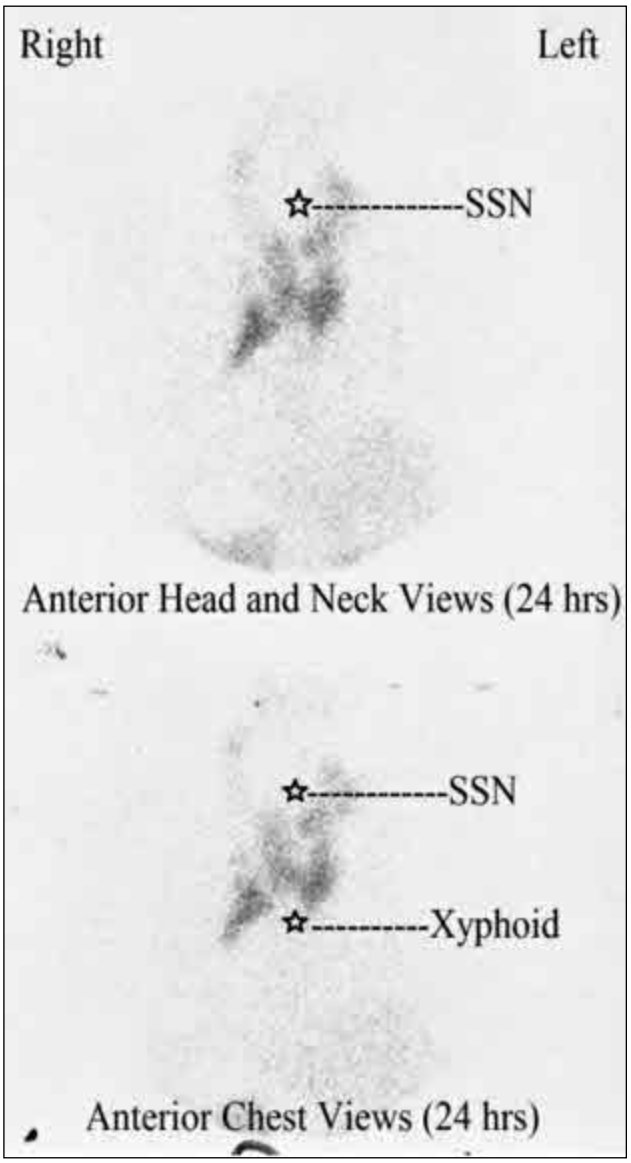

Figure 2 *^{99m}Tc(V) DMSA scan 24-hour images in the anterior projection*

Early (1-hour) and delayed (24-hour) anterior spot images of the head, neck, chest and abdomen were acquired using Siemens Orbitor gamma camera with low-energy all-purpose (LEAP) collimator and energy window of 15% centered at 140 KeV photopeak.

The 1-hour images were very sharp with excellent resolution and showed good radiopharmaceutical avidity by the tumour and seemed potentially useful determining and evaluating sites of metastases in the head, neck and chest region (Figure 1). The 24-hour post tracer injection images were additionally acquired to see the tracer residence over a prolonged period of time and to look for any redistribution (Figure 2).

Discussion

MTC is a rare and slow-growing tumour but poses challenges in the management. It originates from parafollicular C-cells and secretes copious calcitonin; hence high cacitonin levels are used as a marker of disease

recurrence or residual disease. These tumours do not concentrate radioiodine and show poor response to chemotherapy and radiation therapy. Surgery is therefore the only strategy for potential cure; but for successful surgical management, early detection of recurrence is very important. Conventional radiographic imaging modalities are often employed for detecting the recurrence or the residue of the tumour. But the results of these techniques are sometimes negative in presence of elevated calcitonin levels because of the lower sensitivity of morphological imaging modalities in scarred or previously violated tissues or organs. Therefore, functional nuclear medicine imaging studies such as radioiodinated (^{123}I or ^{131}I) meta-iodobenzylguanidine (MIBG), thallium chloride (^{201}TI), pentavalent ^{99m}Tc-dimer captosuccinic acid (^{99m}Tc(V)DMSA), ^{111}In- and ^{99m}Tc-labelled octreotides, ^{18}F-FDG PET and monoclonal anti-CEA labelled antibodies, are explored as a second-line options to detect MTC recurrence. But all of these techniques have associated merits and demerits. Amongst them ^{99m}Tc(V)DMSA has superior characteristics, such as better physical properties, lower cost, wide availability and less time delay between radiotracer injection and imaging, which makes it a better imaging agent for detection of recurrence and metastatic MTC.

In this particular case, where CT scan with contrast was deemed unsuitable due to renal impairment, we tried using ^{99m}Tc(V)DMSA functional imaging as the primary diagnostic test, and the technique provided excellent quality images with the uptake persisting in the tumour for many hours as indicated by the 24-hr images. We have previously imaged MTC imaged with ^{99m}Tc(V)DMSA and we think that this agent can also be used in future for targetting these tumours with ^{188}Re-labelled pentavalent DMSA (^{188}Re(V)DMSA) [14].

^{99m}Tc(V)-DMSA is a radiopharmaceutical which is used to evaluate, image and manage a large number of tumours, but the exact mechanism of ^{99m}Tc-(V)DMSA uptake in tumours is still unknown. One suggested mechanism is the pH-sensitive character of ^{99m}Tc-(V)DMSA which is reported as a factor influencing its accumulation in cancer cells [16]. Several reports from Papantoniou and colleagues suggested that ^{99m}Tc(V)-DMSA uptake by breast tumours is related to proliferative activity, which is either directly related to tumour grade or to the mitotic activity [17]. It is also thought that the mechanism of uptake of ^{99m}Tc-(V)DMSA be due to the structural similarity between ^{99m}Tc-(V)DMSA core (phosphate-like ion TcO_4^{-3}) and PO_4^{-3}), which is avidly taken up by some cancer cells, but some other studies suggest a more cell specific ^{99m}Tc-(V)DMSA uptake than the phosphate localization. Our experience of avid and persistent ^{99m}Tc-(V)DMSA uptake in all the tumour deposits in the neck and mediastinum have encouraged us to explore its potentials and various clinical settings.

Conclusion

^{99m}Tc (V) DMSA is an economical and readily available imaging agent for the detection of MTC in the clinical setting of recurrence detection especially in the head, neck and mediastinal regions.

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