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Diagnosis of Bone Metastasis due to Medullary Thyroid Cancer With ^{99m}Tc- (V) DMSA SPECT Imaging

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ABSTRACT

Given the limited availability of PET/CT scans, ^{99m}Tc-(V) DMSA scintigraphy can be used to investigate possible metastases, especially in bone, in individuals with medullary thyroid cancer, even if there are no noticeable signs or symptoms of pain.

1 | Introduction

Both developing and developed countries are affected by thyroid cancer, which is one of the most prevalent types of cancer worldwide [1]. The disease is estimated to cause 600,000 new cases each year [2]. Only about 1%–2% of thyroid cancers develop in the medulla, making it a relatively rare disease [3]. It is believed that medullary thyroid cancer (MTC) causes a high rate of mortality, with 8.6% of thyroid cancer-related deaths being caused by MTC [1]. A lack of high-quality evidence hinders the development of a consensus regarding MTC diagnosis and treatment, contrary to differentiated thyroid cancers [4]. MTC is associated with an autosomal dominant hereditary condition (multiple endocrine neoplasia [MEN]) in around 20% of cases and manifests as a random tumor in the remainder [5]. The MEN syndromes encompass MEN1, MEN2, and MEN4. MEN2 is classified into three distinct subtypes based on different phenotypes: MEN2A, MEN2B, and family medullary thyroid carcinoma (FMTC). The primary tumors associated with MEN1 are mostly parathyroid, gastroenteropancreatic neuroendocrine tumors, and pituitary tumors. Individuals diagnosed with MEN type 2A (MEN2A) frequently experience the development of MTC and pheochromocytoma. MEN type 2B (MEN2B) primarily encompasses MTC and pheochromocytoma [6]. Patients with MEN2B may exhibit distinctive clinical features, including a "Marfanoid" body habitus and numerous mucosal neuromas on the lips and tongue [7]. The FMTC is mainly limited to MTC. The clinical symptoms of MEN4 closely resemble those of MEN1, however, the associated mutant genes are distinct [6]. The first-line and curative treatment for thyroid cancer is a total thyroidectomy and neck dissection [8]. Surgical intervention and imaging-guided local treatments, such as tyrosine kinase inhibitors, can be combined to treat progressive MTC [9].

MTC can be diagnosed using different anatomical and functional imaging procedures. Before primary surgery, ultrasounds, computed tomography (CT), magnetic resonance imaging (MRI), and nuclear medicine are all possible ways to diagnose. Furthermore, Serial serum calcitonin assays and radionuclide imaging are typically used to monitor residual

Abbreviations: ^{18}F-DOPA, ^{18}F-fluorodihydroxyphenylalanine; ^{18}F-FDG, ^{18}F-fluorodeoxyglucose; ^{68}Ga DOTA-TATE, Gallium-68 dotatate; ^{99m}Tc-(V) DMSA, [^{99m}Tc]-pentavalent dimercaptosuccinic acid; CT, Computed Tomography; FMTC, Family Medullary Thyroid Carcinoma; FNA, Fine needle aspiration; LEHR, Low Energy High-Resolution; MEN, Multiple Endocrine Neoplasia; MEN2A, Multiple Endocrine Neoplasia type 2A; MEN2B, Multiple Endocrine Neoplasia type 2B; MIBG, Metaiodobenzylguanidine; MRI, Magnetic Resonance Imaging; MTC, Medullary Thyroid Cancer; PET, Positron Emission Tomography; SPECT, Single-Photon Emission Computed Tomography; SUV_{max}, Maximum standardized uptake value.

or recurrent disease following surgery [10]. In the diagnosis of MTC, ^{99m}Tc (V)-DMSA (Penta-valent dimercaptosuccinic acid) is one of the most effective tumor-seeking imaging agents [11]. This radiopharmaceutical is formulated as a coordination complex between ^{99m}Tc and DMSA at oxidation state "+5", which is formed by adding 7% sodium bicarbonate to the radiopharmaceutical DMSA [12]. It is believed that ^{99m}Tc (V)-DMSA is localized in malignant cells due to the production of lactic acid in these cells, which alters the pH of the tumor to an acidic state. It is caused by this acidification that succinic acid precursor ^{99m}Tc (V)-DMSA is accumulated [13]. The thyroid is shown to be significantly reduced in uptake on ^{99m}Tc (V)-DMSA imaging in patients with MTC. The liver and spleen scans indicate that metastases are more likely to be detected with reduced tracer uptake. In contrast, bone metastases can be detected as areas with increased tracer uptake on bone scans [14]. A selective uptake of ^{99m}Tc (V)-DMSA occurs at sites of primary, recurrent, and metastatic medullary carcinomas of the thyroid. Because it has a low and nonspecific uptake in liver and bone marrow, it is ideal for identifying liver and bone metastases. In suspected primary, recurrent, and metastatic thyroid cancers, this increases the specificity of diagnosis [15].

2 | Case Description

The patient was a 40-year-old woman with a history of left lobe thyroid nodule who underwent FNA (fine needle aspiration) and finally total thyroidectomy in 2008. A pathology result showed modularly thyroid carcinoma (MTC). The tumor size measured 1.5 × 2 × 3 cm in report. After surgery, the patient received 25 courses of regional radiotherapy. After being diagnosed with pheochromocytoma in subsequent examinations, the patient underwent left adrenalectomy surgery due to his severe and uncontrollable hypertension. In addition, the patient's sister had pheochromocytoma as well. It was observed that the patient's serum calcitonin levels had increased gradually and then suddenly over the past 2 years, exceeding 2000 pg/mL. Here are some other laboratory results for the patient: Ur = 25, Cr = 0.75, Ca = 10.1, TSH = 3, FT4 = 1.05, PTH = 51.8.

3 | Methods

Magnetic resonance imaging (MRI) of the pelvis and lower spine was performed after she complained of ambiguous pain in the lower pelvis and revealed a focal fusiform region of signal change with size of 24 × 13 mm on the right side of the sacrum vertebra (S1) near the spinal canal. Since the lesion wasn't emphasized in the MRI as metastasis, the patient was under periodic control due to the absence of much pain or motion limitation. Despite, her calcitonin level remained at 2000 pg/mL on serial controls. Consequently, the attending physician ordered a whole-body scintigraphy with ^{99m}Tc (V)-DMSA radiopharmaceutical. Anterior and posterior whole-body scans as well as pelvic SPECT imaging were performed 2 h after intravenously injecting 20 mCi of radiopharmaceutical, using a Siemens dual-headed gamma camera with Low Energy High-Resolution (LEHR) collimators.

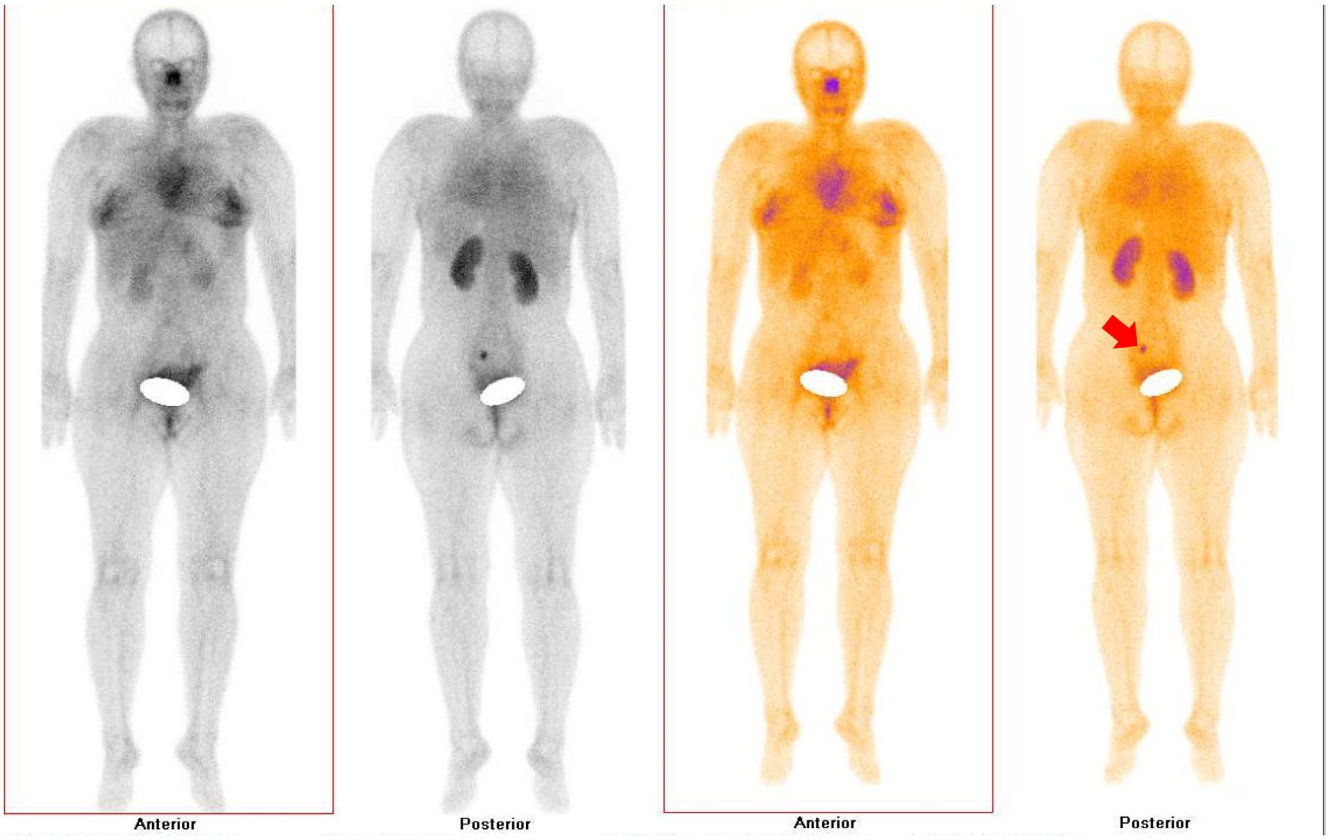

FIGURE 1 | Anterior and posterior views of whole-body scans with ^{99m}Tc (V)-DMSA showed a focal lesion with increased uptake of radiotracer on the right side of the S1 vertebra (Red arrow).

4 | Conclusion and Results

There was a focal lesion with radiopharmaceutical increased uptake on the right side of the S1 vertebra in whole body scan (Figure 1), which is more evident in the posterior views and SPECT images (Figure 2). This outcome was consistent with the results of the MRI. Other parts of the patient's body showed normal physiologic distribution of ^{99m}Tc (V)-DMSA radiopharmaceutical.

Subsequently, as the patient did not consent to a bone sample at the lesion site, a PET/CT scan was ordered with the ^{68}Ga-Dotatate radiopharmaceutical. The scan revealed a focal area with a significant and abnormal increase in radiopharmaceutical ($SUV_{max} = 14.12$), indicating osteometastasis on the left side of the sacrum between the ala and vertebral body (Figure 3). This finding aligns perfectly with the ^{99m}Tc (V)-DMSA scan report. There was also a relative increase in the right adrenal region after being diagnosed with hyperplasia following a left adrenalectomy.

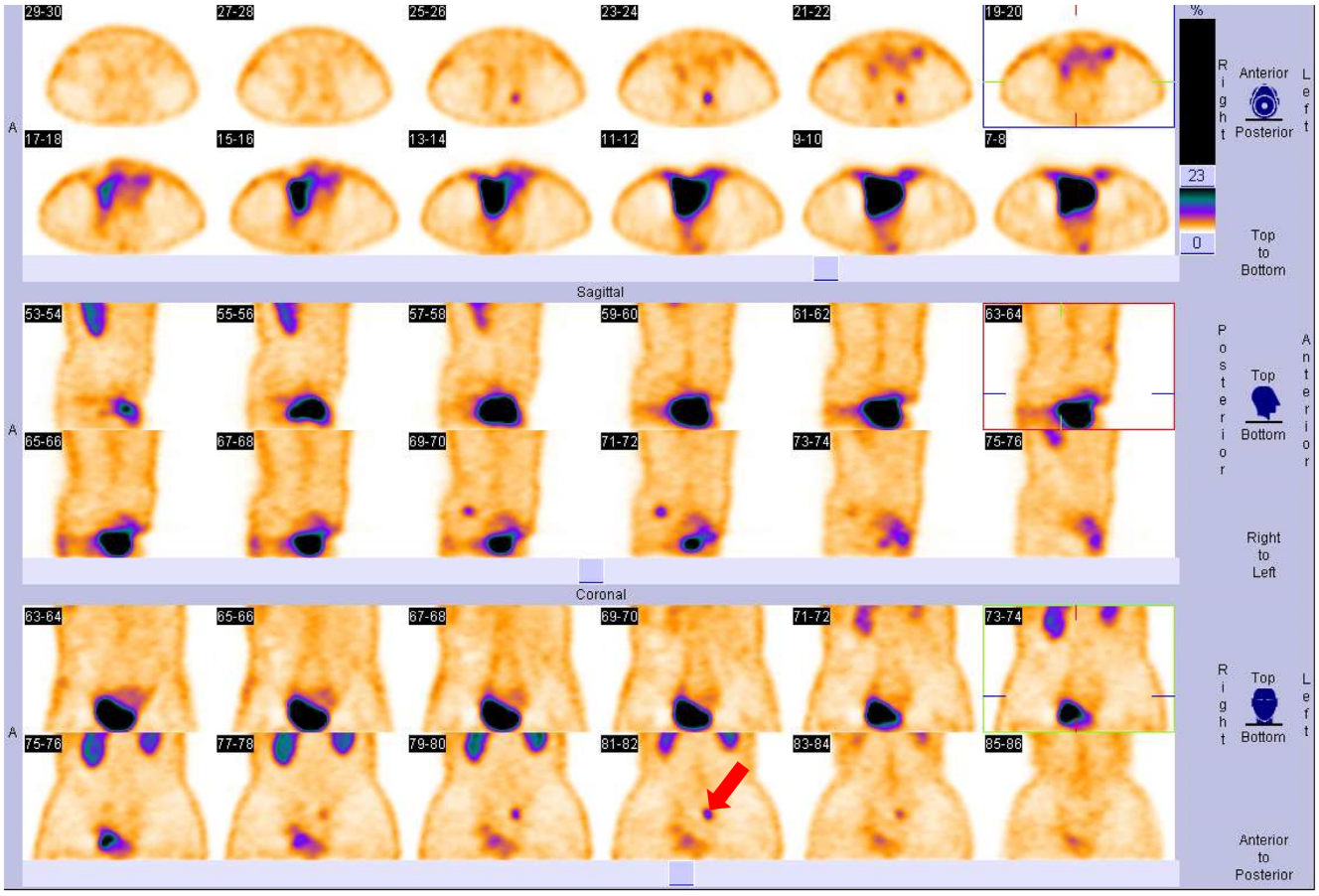

FIGURE 2 | SPECT projections of the pelvic revealed an increased ^{99m}Tc (V)-DMSA avid lesion on the right aspect of S1 with better resolution and accuracy (Red arrow).

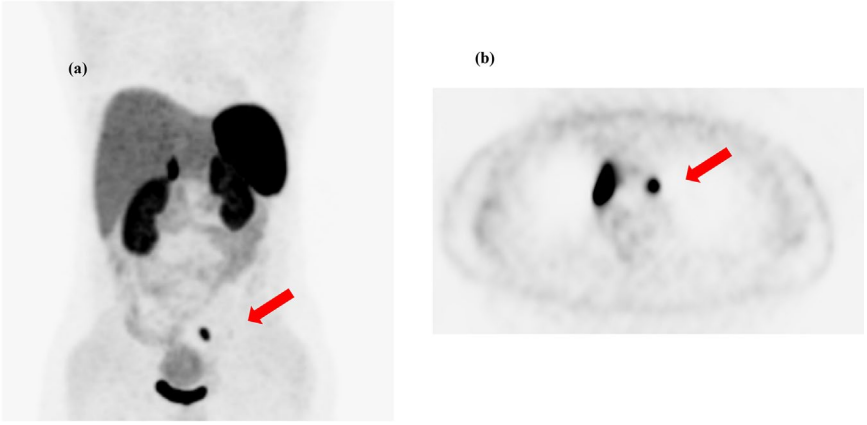

FIGURE 3 | Coronal (a) and transverse (b) sections of ^{68}Ga-Dotatate PET/CT scan confirmed an abnormal focal tracer avid bony metastases in the left side of the sacrum between the ala and vertebral body (Red arrows).

Currently, the patient is under medical supervision regularly, however, no specific action has been implemented concerning the lesion. Furthermore, the patient does not report any localized pain or limitations in movement.

5 | Discussion

Medullary thyroid carcinoma is a rare cancer that originates from the parafollicular C cells, which are part of the neuroendocrine system. Due to its unique characteristics and its typical relationship with other endocrine tumors, this disease, though rare, attracts more attention than it does cases [16]. Whereas most MTCs are sporadic, hereditary variants of MTCs can manifest either alone or in conjunction with other endocrine neoplasias, particularly type 2 syndrome (MEN 2) [17]. Currently, the primary treatment strategy is total surgical excision of the tumor and nodal metastases with a curative aim [18].

MTC can be diagnosed using a variety of anatomical and functional imaging methods. Prior to the main surgery, the illness is staged using ultrasound, computed tomography (CT), and magnetic resonance imaging (MRI). Nuclear medicine procedures are used specifically to detect and locate recurring illnesses in cases where serum tumor marker levels are high and the results of morphologic imaging approaches are ambiguous [19]. The commonly employed radiopharmaceuticals for diagnosing and monitoring MTC, which have labels with γ emitting radionuclides, include metaiodobenzylguanidine (MIBG) labeled with either ^{131}I or ^{123}I, ^{99m}Tc-pentavalent dimercaptosuccinic acid (^{99m}Tc(V)-DMSA), ^{111}In-pentetreotide (Octreoscan), and ^{99m}Tc-EDDA/HYNIC-Tyr3-octreotide (Tektrotyd) [20, 21]. Radiopharmaceuticals labeled with positron-emitting radionuclides suitable for positron emission tomography with computed tomography (PET/CT) include ^{18}F-fluorodeoxyglucose (^{18}F-FDG), ^{18}F-fluorodihydroxyphenylalanine (^{18}F-DOPA), and ^{68}Ga-labeled somatostatin analogues (^{68}Ga-DOTATATE or DOTATOC) [22, 23].

Various levels of sensitivity have been reported for the diagnosis of metastatic or recurrent illness in MTC with ^{99m}Tc (V)-DMSA, ranging from 44.4% to 95% [24]. Based on the literature, traditional nuclear medicine procedures using γ emitting radionuclides have poorer overall sensitivity compared to positron emission tomography/computed tomography (PET/CT) [25]. Nevertheless, the considerable quantity of individuals who test negative or positive for the condition indicates that ^{99m}Tc(V)-DMSA scintigraphy could be employed in conjunction with ^{18}F-FDG PET/CT to exclude the presence of any remaining or spreading disease [10].

However, still, applicability of PET/CT in nuclear medicine worldwide is still limited. The current study demonstrated that ^{99m}Tc (V)-DMSA scintigraphy is an appropriate technique for evaluating and monitoring patients with MTC following thyroidectomy and subsequent therapies. It exhibits satisfactory accuracy when compared to the ^{68}Ga-Dotatate scan, and may even outperform it in certain instances. Given the constraints and limited availability of PET/CT scan, this approach can be employed to examine potential metastases in patients, even in the absence of discernible indications and symptoms of discomfort.

Recently, personalized medicine has developed into a significant approach in healthcare, facilitating customized treatments according to individual patient profiles. Incorporating AI-driven detection tools is essential in this advancement, especially within the domain of otolaryngology. As Taciuc et al. [26] pointed out, neural networks are increasingly used to improve diagnosis accuracy and treatment techniques in this field. These AI systems can scan massive volumes of data, including patient histories, images, and genetic information, resulting in more precise and personalized care recommendations.

6 | Conclusion

In conclusion, while PET/CT scans remain the gold standard for detecting metastases, ^{99m}Tc-(V) DMSA scintigraphy offers a valuable alternative in assessing MTC. Its ability to identify potential bone metastases, even in asymptomatic patients, underscores its significance in early detection and management. Clinicians may improve patient outcomes and treatment options by using this strategy, which ensures holistic care for people with this challenging illness.

Author Contributions

Esmaeil Gharepapagh: conceptualization, methodology, project administration, supervision, writing – review and editing. **Jalil Houshyar:** conceptualization, methodology, validation, visualization. **Farzad Farajbakhsh Mamaghani:** methodology. **Mahsa Karbasi:** writing – original draft. **Sahar Rezaei:** conceptualization, supervision, writing – review and editing.

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Consent

Written informed consent was obtained from the patient to publish this report following the journal's patient consent policy.

Conflicts of Interest

The authors declare no conflicts of interest.

Data Availability Statement

Detailed information is included in this article and if further explanation is required, please contact the corresponding author.

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