^{18}F-Choline PET/CT Sheds Light on a Parathyroid Adenoma – A First in the Philippines: A Case Report

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ABSTRACT

The parathyroid glands play a crucial role in calcium regulation through parathyroid hormone (PTH) production. Indicators for those with hyperparathyroidism would be elevated serum calcium and PTH levels with further evaluation followed by imaging with neck ultrasonography and parathyroid scintigraphy. Limitations in the initial imaging modalities include operator-dependent sensitivity in neck ultrasonography, and poor spatial resolution, and poor sensitivity for smaller-sized adenomas in parathyroid scintigraphy.

This case report describes a 24-year-old female with elevated parathyroid hormone, and borderline elevated calcium levels with an initial diagnosis of primary hyperparathyroidism secondary to a suspected parathyroid adenoma. The dual tracer dual-phase scintigraphy accompanied by SPECT/CT and subtraction method was negative for a parathyroid adenoma, however, ultrasonography of the neck showed a suspicious nodular structure. Due to the high clinical suspicion, a subsequent ^{18}F-Choline PET/CT was done and identified an ^{18}F-Choline-avid lesion, highly suggestive of a parathyroid adenoma. This prompted parathyroidectomy in which histopathology as well as intra-operative reduction in parathyroid hormone levels, confirmed the presence of a parathyroid adenoma.

This is the first recorded ^{18}F-Choline PET/CT usage for a parathyroid adenoma in the country and highlights the potential of its usage as a sensitive and specific imaging modality in cases where conventional imaging is inconclusive.

Keywords: parathyroid adenoma, hyperparathyroidism, ^{18}F-Choline PET/CT, parathyroid scintigraphy

INTRODUCTION

The parathyroid glands are small glands seen in the posterior aspect of the thyroid with the main function of calcium homeostasis through the production of parathyroid hormone (PTH).[1-3] A single parathyroid adenoma has been seen to be responsible for 80 to 85% of hyperparathyroidism cases with parathyroid carcinomas in 1% of all cases.[4] Laboratories such as serum calcium levels and PTH serve as the indicators of hyperparathyroidism however, these may remain mild and sporadic.[1,5]

Neck ultrasonography and parathyroid nuclear medicine scans are the most common imaging modalities for the localization of hyperfunctioning parathyroid glands.[1] On neck ultrasonography, adequate visualization of the parathyroid gland and hypervascularity on Doppler raise suspicion for a pathologic process. Some limitations of ultrasonography may be that it is operator-dependent with limited sensitivity dependent on the size and anatomic location.[6]

Dual tracer, ^{99m}Technetium-Pertechnetate (^{99m}Tc-O_4^-) and ^{99m}Technetium-Sestamibi (^{99m}Tc-MIBI), and dual-

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phased, early and delayed imaging, scintigraphy with or without Single-Photon Emission Computed Tomography and Computed Tomography (SPECT/CT), via imaging with the use of a gamma camera, is the standard of care in many centers due to its wide availability and accessibility, and expertise in Nuclear Medicine.[5,7,8]

Other modalities such as thin-section Computed Tomography (CT), and Magnetic Resonance imaging (MRI) may be considered for pre-operative surgical planning, however, the lack of sensitivity and high radiation exposure of these image modalities should be considered.[6]

Positron emitter radiotracers images using Positron Emission Tomography/Computed Tomography (PET/CT) scanners allow for non-invasive high-resolution functional and anatomic imaging. ^{18}F-Fluoromethylcholine (^{18}F-Choline), a marker of cellular proliferation, has been established as a valuable radiotracer for imaging of hyperfunctioning parathyroid glands or adenomas.[9]

This study aims to describe the findings of the ^{18}F-Choline PET/CT scan in a 24-year-old female in a case of primary hyperparathyroidism secondary to a suspected parathyroid adenoma.

This is the first recorded use of ^{18}F-Choline for a suspected parathyroid adenoma in the Philippines and is the highlight of the study.

CASE PRESENTATION AND CLINICAL COURSE

This is a case of a 24-year-old female, initially presenting with laboratories of elevated Intact Parathyroid Hormone (PTH) of 233.50 pg/mL (Reference range: 18.5 - 88.0), borderline elevated calcium levels of 1.28 mmol/L (Reference range: 1.0-1.3), and low Total Vitamin D (25-OH) of 22.29 ng/mL (Reference range: 30 - 100). The initial diagnosis was primary hyperparathyroidism secondary to a suspected parathyroid adenoma thus the parathyroid glands were further evaluated using the dual-tracer dual-phase parathyroid scintigraphy with SPECT/CT and neck ultrasound.

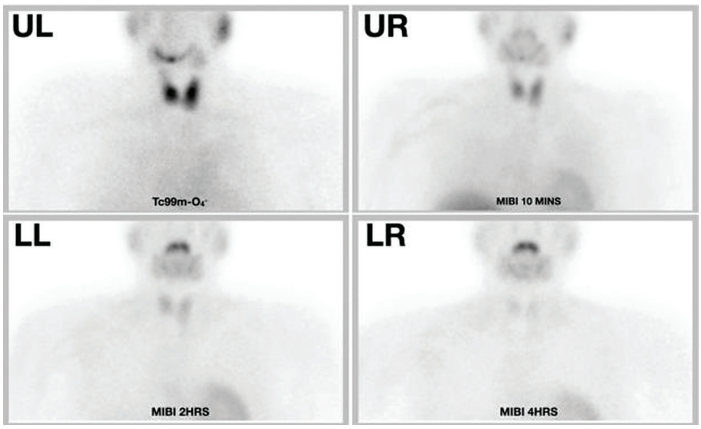
Dual Tracer Dual Phase Parathyroid Scintigraphy Protocol

No special preparation was done for the scan. Imaging of the head to chest was obtained after IV administration of 74 - 150 MBq (2-4mCi) ^{99m}Tc-O_4^-. Static images were obtained. Subsequent imaging was done with delayed static images at the 2nd and 4th hour after injection of 400 - 900 MBq (10-25mCi) of ^{99m}Tc-MIBI. SPECT/CT images were obtained at 10 minutes and 4 hours post-injection of ^{99m}Tc-MIBI. The dosage given is detailed by the EANM practice guidelines.[10]

The initial images after injection of ^{99m}Tc-O_4^- show increased tracer uptake in the bilateral thyroid lobes, likely relating to thickened thyroid tissue. Subsequent imaging after injection of ^{99m}Tc-MIBI showed similar tracer activity as the initial pertechnetate images. No focal sestamibi-avid lesion is seen throughout the study. The SPECT/CT images and subtraction method images showed no sestamibi-avid lesion to suggest the presence of a parathyroid adenoma (Figure 1). The rest of the findings were unremarkable with no adverse events occurring at the time of the scan.

A neck ultrasound was done, which showed a normal-sized thyroid gland with a heterogeneous hypoechoic solid nodule, below the right thyroid lobe, measuring 1.5 x 1.7 x 0.9 cm and appearing hypervascular on color interrogation. This potentially indicates the presence of a parathyroid adenoma. However, with the incohesive findings between the imaging, the patient opted for monitoring with no further management done.

Approximately six months after the initial laboratory tests and imaging modalities, the Intact Parathyroid Hormone (PTH) remained persistently elevated at 101.80 pg/mL. An ^{18}F-Choline PET/CT was done for further evaluation.



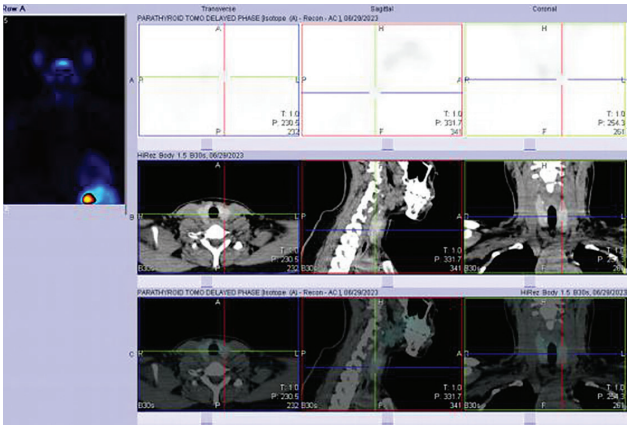


Figure 1. ***Dual Tracer Scintigraphy.*** ^{99m}Tc-O4- **(UL)**, ^{99m}Tc-MIBI **(UR)**. Delayed 2-hour **(LL)** and 4-hour **(LR)** ^{99m}Tc-MIBI images. **(Right)** 4th-Hour SPECT-CT better visualizes no sestamibi-avid lesion.

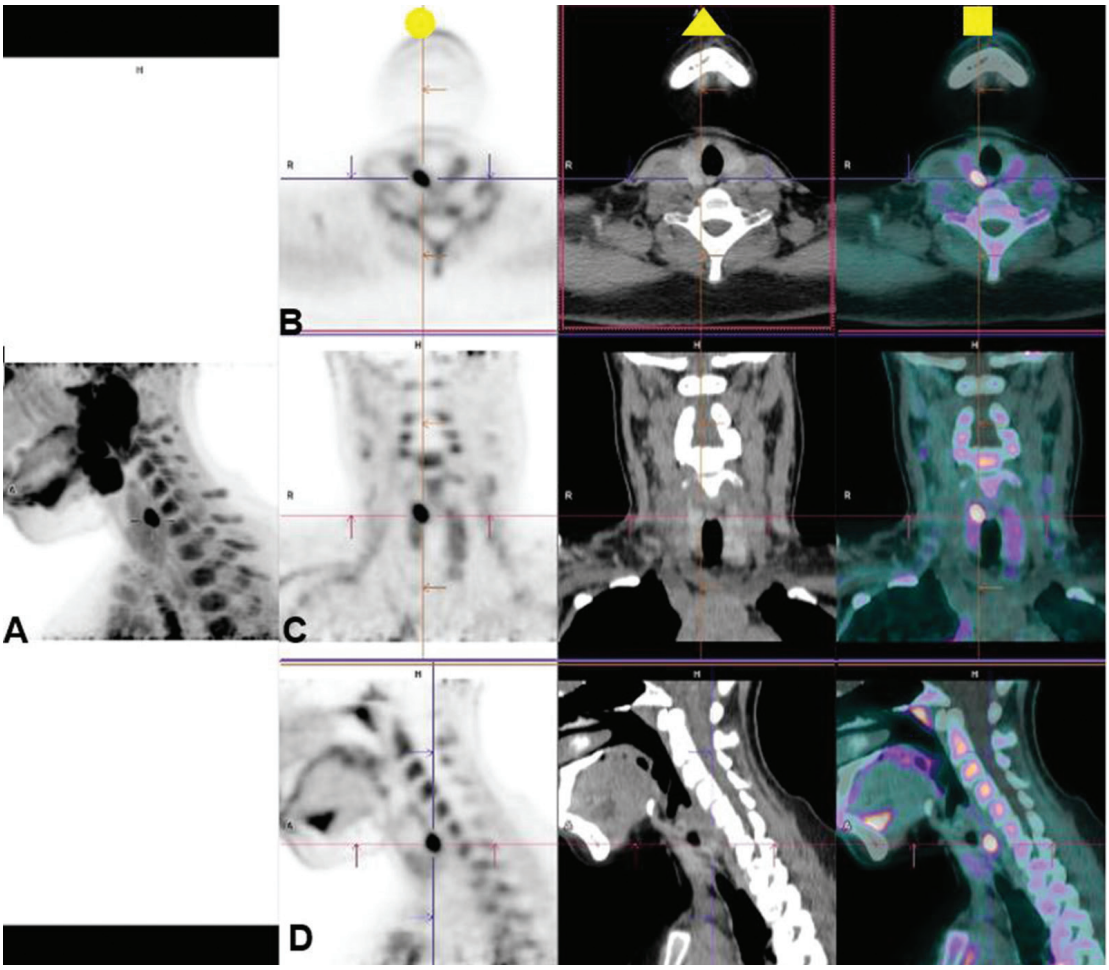


Figure 2. ***^{18}F-Choline PET/CT.*** **(A)** Lateral Maximum Intensity Projection (MIP), **(B)** Axial View, **(C)** Coronal View, **(D)** Sagittal View. ^{18}F Choline-positive nodular structure (Crosshair).

● *Attenuation Correction (AC) PET,* ▲ *Low dose CT,* ■ *Fused CT-based Attenuation Correction,*

PET/CT ^{18}F-Fluoromethylcholine (^{18}F-Choline) Protocol

No special preparations are needed for the scan. Emission images were obtained after 1 hour of intravenous injection of 100 - 300 MBq (2.7 - 8.1mCi). Delayed emission images are optional. Low-dose plain CT of the neck may be obtained. Contrast CT of the neck was done. The dosage given and protocol are detailed by the EANM practice guidelines.[10]

The images showed increased ^{18}F-Choline uptake in an enhancing nodular focus measuring 0.8 x 0.9 x 1.2 cm (AP x T x CC), inferior to an enlarged right thyroid lobe (Figure 2). This is suggestive of a parathyroid adenoma. There were no other ^{18}F-Choline-avid lesions noted elsewhere in the visualized structures. No adverse events occurred during the scan.

A month after the ^{18}F-Choline PET/CT scan, the patient underwent surgical excision of the nodular structure, which revealed on frozen section examination an enlarged, hypercellular parathyroid gland. The intraoperative reduction in parathyroid hormone levels from 162.60 pg/mL to 9.30 pg/mL (Table 1) following gland removal also supported the diagnosis.

Table 1. Trend of Parathyroid Hormone Levels

Timing	PTH (pg/mL)	Reference Range (pg/mL)
Initial Work-up (6 months prior ^{18}F-Choline)	233.50	18.5 – 88.0
Before ^{18}F-Choline	101.80	15.0 – 65.0
Pre-incision surgical removal of parathyroid adenoma (One month after ^{18}F-Choline)	162.60	18.5 – 88.0
10 minutes post-excision of parathyroid adenoma	19.80	18.5 – 88.0
20 minutes post-excision of parathyroid adenoma	9.30	18.5 – 88.0

DISCUSSION

Molecular parathyroid imaging is the gold standard for the localization of parathyroid adenomas.[1] ^{99m}Tc-O_4^- enters the thyroid via the Sodium/Iodide$^-$ symporters (NIS) and allows for the visualization of the thyroid gland. ^{99m}Tc-MIBI is lipophilic and a cation that binds to the negative charge of the mitochondria in the oxyphil cells of the parathyroid gland. Once inside the thyroid and oxyphil cells, ^{99m}Tc decays to ^{99}Tc releasing a low-energy photon that is detected by a gamma camera and is visualized on imaging. The prototypical features of a parathyroid adenoma are early washout of ^{99m}Tc-O_4^- with retention of ^{99m}Tc-MIBI in the delayed images due to the dense number of mitochondria in the oxyphil cells.[7,8]

This dual tracer dual-phase technique accurately detects parathyroid adenomas with sensitivity and specificity of up to 92.9% and 90.3%, respectively.[11] However, some studies have shown false negative rates of up to 22 to 30% due to factors including the low-to-moderate mitochondrial cellularity and small-sized parathyroid adenomas, and the limited spatial resolution of the gamma camera of 5 to 7 mm.[12-15] False positives may be seen in cases with functioning thyroid nodules or malignancies, that cause the persistent retention or delayed washout of ^{99m}Tc-O_4^-.[7]

^{18}F-Choline serves as a marker of cellular proliferation and is used in the evaluation of parathyroid adenomas or hyperplasia, as increased choline uptake is required for the synthesis of phosphatidylcholine, a major membrane phospholipid.^{18}F-Choline, once localized in the parathyroid cells, emits positrons that release high-energy photons.[9] Imaging using the PET/CT scanner then provides high-quality images, better spatial resolution with a detection rate of up to 0.4 mm, and a reduced scanning time of 30 minutes compared to 4 hours in the dual tracer scintigraphy.[16]

Multiple studies have shown ^{18}F-Choline PET/CT to have a high sensitivity and specificity in patients with negative or discordant conventional imaging ranging from 88.6% to 92% and 99.6% to 100%, respectively.[17,18] A study by Michaud et al. showed a detection rate of 92% for ^{18}F-Choline PET/CT and more significantly solved discrepant results between scintigraphy and US findings.[19]

The use of the ^{18}F-Choline radiotracer in the Philippines faces several limitations. These include the limited availability of PET/CT scanners, limited production of the radiotracer, and the cost of the procedure, which is 2 to 3 times more expensive than conventional parathyroid scintigraphy. At present, ^{18}F-Choline is produced and available as an imaging modality at only one institution in the Philippines.

In the patient, an ^{18}F-Choline PET/CT was used as a confirmatory test due to the incohesive findings of a suspicious ultrasound finding and negative parathyroid scintigraphy study. An ^{18}F-Choline-avid enhancing nodular structure on PET/CT prompted parathyroidectomy and led to a diagnosis of a parathyroid adenoma. Taking into consideration the prolonged time difference as well as the different mechanisms of localization between the dual tracer and ^{18}F-Choline scans, a false negative parathyroid scintigraphy cannot truly be concluded, however, a poor mitochondrial-containing parathyroid adenoma can be considered.

At the time of writing, this is the first recorded ^{18}F-Choline PET-CT scan used for the evaluation of a parathyroid adenoma in the Philippines.

CONCLUSION

^{18}F-Fluoromethylcholine PET/CT is a highly sensitive and specific imaging test that may be used in negative parathyroid scintigraphy scans for patients with high clinical suspicion of a parathyroid adenoma. Further studies on cost-effectiveness should be conducted before ^{18}F-Choline can be accepted as the imaging modality of choice for parathyroid adenomas.

Declaration of Patient Consent

The authors attest to having secured all necessary patient consent documentation. In the form, the patient has given her consent for her images and other clinical information to be reported in the journal. The patient understands that no patient identifiers will be disclosed in this journal and due efforts will be made to conceal her identity, but anonymity cannot be guaranteed.

Statement of Authorship

All authors certified fulfillment of ICMJE authorship criteria.

Author Disclosure

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