



# Parathyromatosis type 2 detected by $^{99m}\text{Tc}$ -MIBI SPECT/CT

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**Abstract:** Parathyromatosis, which is defined as multiple foci of benign hyperfunctioning parathyroid tissue in neck or mediastinum, is a rare but severe cause of persistent/recurrent renal hyperparathyroidism (rHPT) after parathyroidectomy (PTX). It is hard to detect and remove all the foci. We present a case of parathyromatosis in a haemodialysed patient, who had three PTXs for persistent/recurrent rHPT and was free of recurrence during 31-month follow-up after the third PTX.  $^{99m}\text{Tc}$ -MIBI SPECT/CT scan prior to the third PTX located all the lesions. The presented case suggests that preoperative  $^{99m}\text{Tc}$ -MIBI SPECT/CT is useful for successful surgical removal of parathyromatosis.

**Keywords:** Parathyromatosis;  $^{99m}\text{Tc}$ -MIBI SPECT/CT; renal hyperparathyroidism (rHPT); parathyroidectomy (PTX)

Submitted Jun 26, 2019. Accepted for publication Nov 04, 2019.

doi: 10.21037/gs.2019.11.13

View this article at: <http://dx.doi.org/10.21037/gs.2019.11.13>

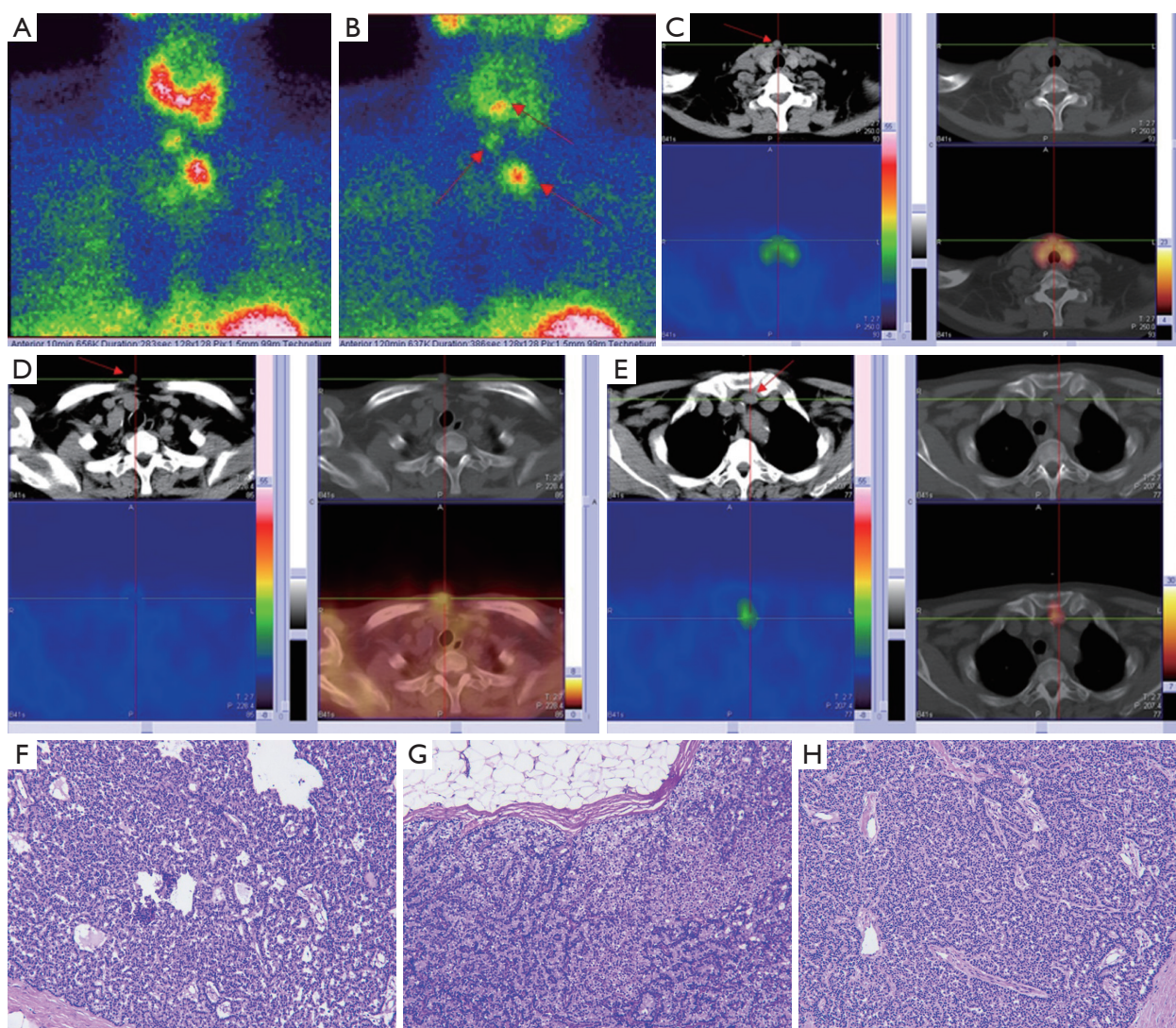
## Introduction

Renal hyperparathyroidism (rHPT) is an intractable disease of patients with chronic kidney disease (CKD), leading to substantial morbidity or mortality (1,2). Although diet regulation, sufficient hemodialysis, medical treatment such as vitamin D and calcimimetics, and parathyroidectomy (PTX) are effective in most cases (2), there are still several patients having persistent or recurrence of rHPT (1). Parathyromatosis, which is defined as multiple foci of benign hyperfunctioning parathyroid tissue in neck or mediastinum (3), is a rare but severe cause of persistent/recurrent rHPT. It is difficult to detect and remove all the foci.  $^{99m}\text{Tc}$ -methoxyisobutylisonitrile (MIBI) SPECT/CT has been used to detect hyperfunctioning parathyroid glands for its high sensitivity and specificity in patients with rHPT (2,4). We report a case of rHPT who achieved long-term recurrent-free after the third surgery guided by the preoperative  $^{99m}\text{Tc}$ -MIBI SPECT/CT localization of the hyper-functioning parathyroid tissues.

## Case presentation

A 61-year-old woman with renal failure due to microscopic

polyarteritis on maintenance hemodialysis regularly since 2004 developed rHPT. Refractory to medical treatment, she received parathyroidectomy (PTX) and transplantation of parathyroid tissue into the muscle of right forearm in December 2012. During the operation, 3 enlarged parathyroid glands (PTGs) were found and removed. The 3 PTGs located relatively at the superior left, superior and inferior right of the thyroid bed, measuring 2.4 cm × 1.6 cm, 1.0 cm × 1.2 cm and 0.6 cm × 0.8 cm, weighed 6.1, 1.2 and 0.5 g respectively, and were all revealed hyperplastic nodular parathyroid tissue histopathologically. Thymectomy was not performed. After the first operation, her serum calcium and parathyroid hormone (PTH) levels decreased to 7.3 mg/dL and 211 pg/mL, respectively. In July 2013, due to elevated PTH (>3,480.0 pg/mL) and serum calcium levels (3.17 mmol/L), she received a second operation to remove implanted parathyroid tissue. And then, her serum calcium (2.24 mmol/L) and PTH (62.8 pg/mL) dropped. However, her PTH raised progressively up to 1,253.1 pg/mL until she had a percutaneous ethanol injection therapy (PEIT) of the auto-transplantation site in April 2015. Unfortunately, her PTH (3,342.0 pg/mL),



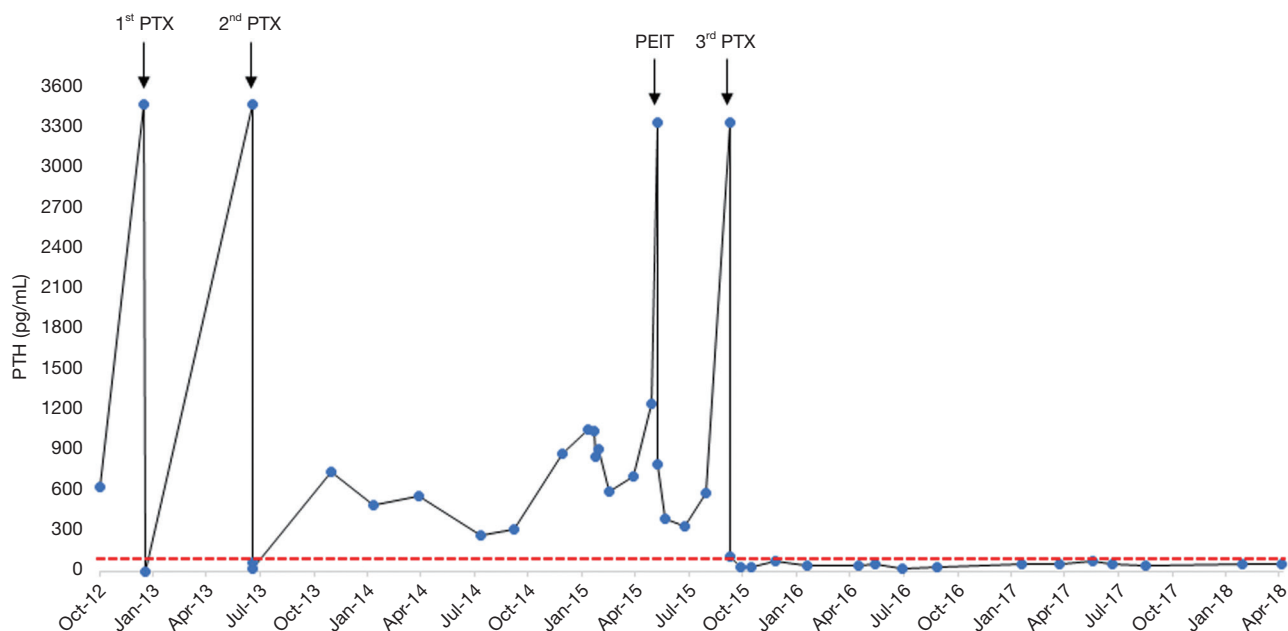
**Figure 1**  $^{99m}\text{Tc}$ -MIBI imaging before 3<sup>rd</sup> PTX.  $^{99m}\text{Tc}$ -MIBI dual-phase planar imaging showed three foci (red arrows) of elevated uptake on early phase (A) and slow washout on delayed phase (B) of the tracer, which were identified by SPECT/CT: (C,D,E). Histopathology (H&E,  $\times 100$ ) showed two benign parathyroid nodules beneath the platysma muscle (F,G) and another one above left to sternum (H).

serum calcium (3.52 mmol/L) both raised up again 5 months later. In September 2015,  $^{99m}\text{Tc}$ -MIBI imaging performed. Dual-phase planar imaging showed three foci of elevated uptake on early phase (Figure 1A) and slow washout on delayed phase (Figure 1B) of the tracer, which were identified by cross section images of early phase SPECT/CT (Figure 1C,D,E). In October 2015, the patient received a third surgery. During the operation, guided by the result of  $^{99m}\text{Tc}$ -MIBI, 3 nodules were identified and then removed (2 nodules beneath the platysma muscle measuring 1 cm  $\times$  1 cm each, the other

one above left to sternum measuring 2 cm  $\times$  2 cm). It was proved pathologically that all the 3 were hyperplastic parathyroid tissues (Figure 1F,G,H). Postoperative (at 24 hours) serum calcium and PTH were 2.77 mmol/L and 109 pg/mL respectively. The patient's PTH remained stable in the range 15.0–80.0 pg/mL during the 31 months follow-up until the last visit (Figure 2).

## Discussion

Several factors have been associated with persistent or



**Figure 2** PTH response to therapeutic interventions during the last 6 years. Dashed line, upper normal limit for PTH (100 pg/mL) in hemodialysis patients. PTH, parathyroid hormone; PTX, parathyroidectomy; PEIT, percutaneous ethanol injection therapy.

recurrence of rHPT, including surgical inexperience, ectopic or supernumerary glands, parathyroid carcinoma, and, rarely, parathyromatosis (5). Parathyromatosis was first described by Palmer *et al.* in 1975 (6), defined as multiple foci of benign hyperfunctioning parathyroid tissue in the neck or mediastinum (3). By Reddick *et al.* in 1977 (3), parathyromatosis was classified into 2 types (3,7): Type 1, defined as parathyroid rests left behind during ontogenesis that develop under the physiologic stimuli; Type 2, defined as a consequence of spillage and seeding of parathyroid tissue within the operative field as the result of improper handling of the glands during surgical extirpation (8). The autograft of parathyroid tissue which cause recurrence of disease is considered as type 2 parathyromatosis (9). The first cause of recurrence/persistence of rHPT of this case is type 2 parathyromatosis, including intended autograft in arm and non-intended seeding in subcutaneous tissue during operation. We speculated that rupture of capsule happened during the first surgical exploration. The second cause is the gland above and left to the sternum, which should be the left inferior parathyroid gland left *in situ* after the first operation. All of them were localized by  $^{99m}\text{Tc}$ -MIBI imaging. Without proper preoperative localization, re-operation may fail to find all of the lesions for recurrent/persistent rPTH patients. Although occasionally successful

medical management of a patient with parathyromatosis was reported (10), complete surgical extirpation of all parathyroid tissue is the best option for treatment. But identification of all the hyperplastic foci such as ectopic, supernumerary glands and parathyromatosis is difficult. Currently, ultrasound (US) and  $^{99m}\text{Tc}$ -MIBI imaging are first-line choices for preoperative localization of hyperfunctioning parathyroid glands (11-13). However, US is operator-dependent and findings of parathyromatosis including multiple hypoechoic or hypervascular nodules appear atypical and non-specific.  $^{99m}\text{Tc}$ -MIBI SPECT/CT can get over the difficulty in pointing out the location of the lesion than  $^{99m}\text{Tc}$ -MIBI planar imaging and is helpful to reduce failure rate of surgery (14). Similar to previous studies (2), when  $^{99m}\text{Tc}$ -MIBI imaging performed in our hospital, patient without special preparation was injected intravenously with 740 MBq of  $^{99m}\text{Tc}$ -MIBI. Planar imaging of neck and mediastinum was acquired at 10 min (early phase) and 120 min (delayed phase) after injection, while SPECT/CT imaging of the neck and mediastinum was obtained immediately after 10 minutes planar imaging. Interpretation of  $^{99m}\text{Tc}$ -MIBI images was performed in consensus by 2 experienced nuclear medicine physicians. A positive result was recognized if there was a definite focus of increased or separate tracer uptake relative to the uptake

in the thyroid tissue of neck or mediastinum on images (15). Precise location of each focus by cross section images of SPECT/CT was also reported (15).

In conclusion, the present case suggests that  $^{99m}\text{Tc}$ -MIBI SPECT/CT is valuable for preoperative localization of hyperfunctional glands, especially parathyromatosis, of recurrent/persistent rHPT patients.

### Acknowledgments

None.

### Footnote

*Conflicts of Interest:* The authors have no conflicts of interest to declare.

*Ethical Statement:* The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. Written informed consent was obtained from the patient for publication of this manuscript and any accompanying images.

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**Cite this article as:** Cao H, Zeng M, Fang H, Tang L, Liu W. Parathyromatosis type 2 detected by  $^{99m}\text{Tc}$ -MIBI SPECT/CT. *Gland Surg* 2019;8(6):806-809. doi: 10.21037/gs.2019.11.13