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Thoracoscopic Removal of Hypertrophic Mediastinal Parathyroid Glands in Recurrent Secondary Hyperparathyroidism

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Abstract

Background Hypertrophic mediastinal parathyroid glands (HMPGs) play a role in recurrent secondary hyperparathyroidism (SHPT). Thoracoscopic retrieval of HMPGs has been proposed.

Methods Twelve patients with recurrent SHPT owing to HMPGs were enrolled. We divided the locations of HMPGs below the innominate vein and right to the ascending aorta as Zone I, those below the innominate vein and left to the ascending aorta as Zone II, and those between the aortic arch and pulmonary artery as Zone III. Sestamibi scans combined with computed tomography (CT) scans were arranged to identify the location of HMPGs. Three trocars of the right or left thoracoscopic approach were applied for Zone I or Zone II; four trocars of the left thoracoscopic approach were applied for Zone III.

Results Sestamibi and CT scans could positively find the 15 parathyroid glands of the 12 patients. Thirteen HMPGs were retrieved successfully with a thoracoscopic approach. The mean operation time was 155 min (range 80–292) and the mean hospital stay was 5.9 days (4–8). After a mean follow-up of 29.6 months (3–61), calcium and intact parathyroid hormone levels returned to normal ranges in all patients except for one who preferred two-stage surgery. Neither perioperative mortality, nor major complications occurred.

Conclusions HMPGs in recurrent SHPT may be multiple. Sestamibi scans combined with CT scans can guide optimal approaches. The thoracoscopic approach provides a safe and feasible technique in retrieving HMPGs in Zones I or II using 3 trocars. For HMPGs in Zone III, they should be handled with care using 4 trocars.

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Introduction

In uraemic patients, persistent or recurrent secondary hyperparathyroidism (SHPT) after parathyroidectomy plus autotransplantation remains a challenging problem for clinical physicians. The incidence of recurrent SHPT ranges from 0 to 80 % using different surgical approaches [1–4]. It generally results from hyperplasia of the grafted parathyroid, inadequate initial dissection or supernumerary or ectopic glands [2, 4, 5]. After initial successful surgery and exclusion of graft hyperplasia, the recurrence occurs mainly because of hypertrophy of supernumerary or ectopic parathyroid glands in the neck or mediastinum [4, 5]. Primary and SHPT due to hypertrophic mediastinal parathyroid glands (HMPGs) is rare with a prevalence of 1 %

in patients undergoing surgery [6, 7]. The prevalence is higher in patients with persistent or recurrent hyperparathyroidism [8, 9]. HMPGs in uraemic patients resulting in persistent or recurrent SHPT are not common and there is a lack of discussion on the optimal management in literature. Traditionally, it requires adequate preoperative localization by multimodality images [10, 11]. Previously, a major thoracic incision was usually advised in order to remove the HMPG, when the mediastinal location was confirmed [7, 12, 13]. Since the advent of using a thoracoscope in mediastinal procedures, more patients have received thoracoscopic mediastinal parathyroidectomies [14–16]. Owing to the rarity of ectopic mediastinal parathyroids in uraemic patients, the majority of articles on the subjects involved only a few case reports [15, 16]. Herein, we report the results of thoracoscopic mediastinal parathyroidectomy in 12 uraemic patients with recurrent SHPT. The algorithm of the management of HMPGs in uraemic patients with persistent or recurrent SHPT is also presented.

Patients and methods

From Jan. 2008 to Dec. 2013, 421 patients (including studied patients) with SHPT were operated on with total parathyroidectomy with or without autotransplantation were reviewed. Routinely, when four or more glands were found during surgery, we performed total parathyroidectomy, thymectomy and an autotransplantation of 140 mg of the parathyroid tissue to the subcutaneous tissue of the right forearm. If less than four glands were found during surgery, we did not do an autotransplantation. The procedure of partial parathyroidectomy was abandoned in this department because the recurrence was a big problem in SHPT without a further kidney transplantation [17, 18]. This retrospective study followed the standard operation procedure of parathyroid surgery of the hospital. Fifty-four (12.8 %) of them had recurrent (No = 36) or persistent (No = 18) SHPT. Among 421 patients, 12 patients (2.9 %) were confirmed to have HMPGs and underwent surgical retrieval of HMPGs. Generally, in most dialysis centers, laboratory data such as serum levels of calcium, phosphorus, and intact-parathyroid hormone (i-PTH) were checked regularly after cervical parathyroidectomy. If i-PTH levels increased to higher than 500 pg/ml postoperatively within 6 months and patients had symptoms such as bone pain, skin itching, insomnia and general weakness, it was defined as persistent SHPT, while if such symptoms occurred after 6 months, it was defined as recurrent SHPT. Patients with persistent or recurrent SHPT were initially treated by nephrologists using medications such as cinacalcet, calcitriol. or biphosphonate. In this hospital, uraemic patients must wait at least 7 years to get a cadaver kidney transplantation and only 25 % of them can get one in 10 years.

Re-operation was indicated when prolonged high parathyroid hormone levels (>500 pg/ml), persistent symptoms or failures of medical treatment were present. A Technetium 99m-sestamibi (Sestamibi) scan of the neck, mediastinum and forearm was arranged first to detect the location of hypertrophic parathyroid glands. Besides, the ratio of i-PTH in the graft-bearing arm versus the contralateral arm was less than 2 in all patients to confirm that no graft hyperplasia was present in the arm. Once the HMPG was detected using Sestamibi scans plus single photon emission computed tomography, computed tomography (CT) scans of chest were subsequently performed to precisely localize the anatomic position of the HMPG and to correlate with parathyroid scans. If the Sestamibi scan could not identify ectopic glands, we would repeat the examination 6–12 months later when they could be more easily identified. A HMPG is defined a gland that is located below the innominate vein and disseminates beside ascending aorta, aortic arch, aorto-pulmonary window or trachea. We classified the usual locations of HMPGs that needed thoracoscopic removal to three Zones: HMPGs below the innominate vein and right to the medial aspect of ascending aorta as Zone I, those below the innominate vein and left to the medial aspect of ascending aorta as Zone II, and those between the aortic arch and pulmonary artery as Zone III (Table 1; Fig. 1). This classification was a new invention and was based on an earlier report from Dr. Rondone et al. [16]. However, they did not mention any classification. The surgical approach was decided after consultations between general and thoracic surgeons. Right (Zone I) or left (Zone II and Zone III) thoracoscopic approaches depended on the relative location with the sternum, aortic arch and pulmonary artery. Video-assisted thoracoscopic surgery (VATS) was performed under general anesthesia using a double-lumen endotracheal tube. Patients were placed in 30° lateral decubitus (right in 2 patients and left in 10). Three trocars were used, and all patients were operated on using a standard 10-mm rigid thoracoscope (Karl Storz) with a 30° angle at the 7th intercostal space of the mid-axillary line. A 10-mm trocar was inserted at the 5th intercostal space of the anterior axillary line and a 5-mm trocar was inserted at the 5th intercostal space of the posterior axillary line. If the HMPG was located in Zone III, a fourth 5-mm trocar was inserted at the 6th intercostal space of the left anterior axillary line, to retract the left pulmonary artery. The dissection was carried out using an endoscopic harmonic scalpel (Ethicon Endo-Surgery, ACE 36E). We removed surrounding fat in association with a parathyroid gland to avoid the rupture of the capsule. All HMPGs were confirmed by intra-operative frozen sections. A single chest tube was placed and

Table 1 Boundaries of Zone I, Zone II, and Zone III locations of HMPGs in 12 patients

Zone	Boundaries	HMPGs
Zone I	Innominate vein, aortic arch, right to medial aspect of ascending aorta, sternum	2
Zone II	Innominate vein, aortic arch, left to medial aspect of ascending aorta, sternum	8
Zone III	Aortic arch, left pulmonary artery, trachea, sternum	3

removed during the following days. Serum levels of calcium, phosphorus, and i-PTH were checked in all patients, postoperatively at 1 week and 3 months to confirm the biological results.

Results

Totally, 12 uremic patients with recurrent SHPT were diagnosed as having HMPGs. The characteristics of patients are shown on Table 2. There were 5 men and 7 women. The ages of these patients ranged from 21 to 65 years (45.5 ± 13.3) (mean ± SD). The duration of hemodialysis ranged from 7 to 20 years with an average of 13.4 ± 4.5 years. The duration from initial cervical exploration to recurrent hyperparathyroidism ranged from 10 to 94 months (49.1 ± 27.3). Before this surgery, two patients had been operated on twice in their necks and two patients had five glands removed in previous operations. The clinical presentation included bone pain in 10 patients, skin itching in 2, general weakness in 2 and hypercalcemia in 1. The locations of HMPGs were mapped and classified to three zones according to the relative position to the normal mediastinal anatomy (Fig. 1). Two glands were located in Zone I, 8 in Zone II, and 3 in Zone III as shown on Tables 1 and 2. Preoperative Sestamibi scans, CT scans, locations of HMPGs and serum levels of calcium, phosphorus and i-PTH are shown in Table 3. The mean of preoperative calcium, phosphorus and i-PTH levels were 10.3 ± 0.9 mg/dl (8.8–11.8), 5.5 ± 1.3 mg/dl (3.4–7.3), and 1531 ± 864 pg/ml (530–3,560) respectively. The size of the 13 removed HMPGs ranged from 0.9 to 2.5 cm. VATS to retrieve HMPGs below the innominate vein using 3 trocars was carried out in 10 patients to remove 2 glands in Zone I and 8 glands in Zone II. VATS to retrieve HMPGs using 4 trocars was carried out to remove 3 glands in zone III as shown on Tables 1 and 4. The mean operating time was 152 ± 60 min (80–292) and the mean operating time in Zone III (234 ± 58 min, No = 3) was longer than that of the other locations (124 ± 27 min, No = 9) ($p = 0.001$). The mean hospital stay was 5.9 ± 1.3 days (4–8). Except for patient No. 11 who preferred two-stage surgery for the parathyroid gland at the left lower neck, all other patients undergoing thoracoscopic retrieval of HMPGs were biologically normal at the mean

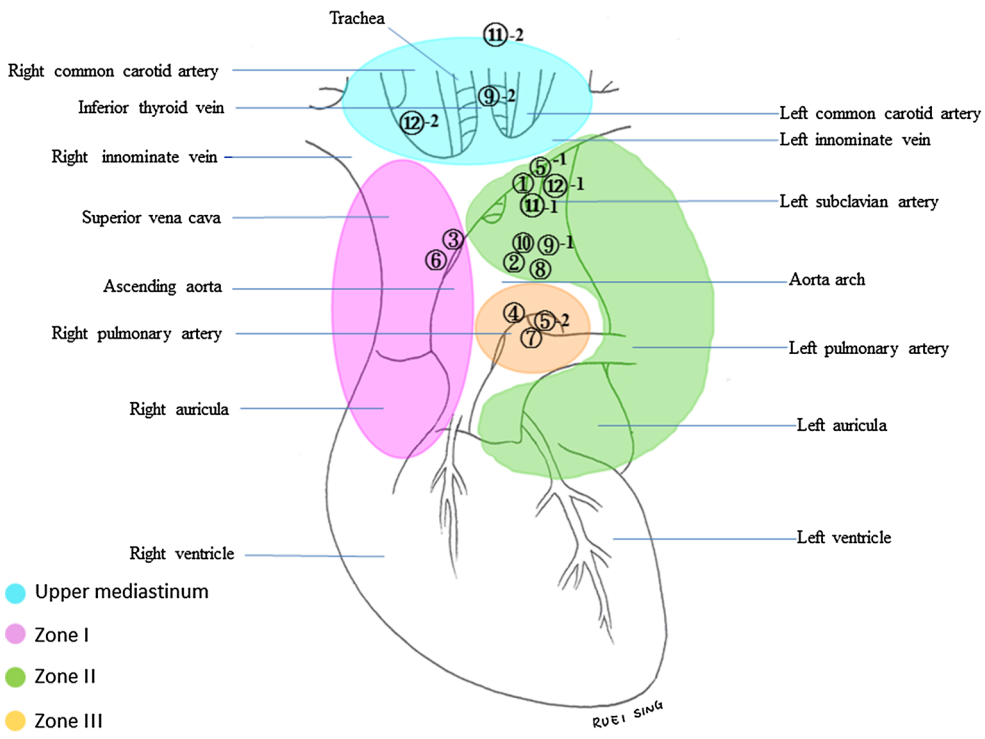


Fig. 1 The locations of 13 HMPGs, a gland at *left lower neck*, a gland in *left upper* mediastinum and a gland in *right upper* mediastinum in 12 patients with recurrent hyperparathyroidism

Table 2 Characteristics of the patients

Patients	Age	Sex	Recurrent or persistent	Duration of dialysis (years)	Months after last total parathyroidectomy	Times of neck surgery (No of glands removed)	Clinical presentation
1	57	F	R	13	48	1 (4)	Bone pain
2	65	F	R	12	70	1 (4)	Insomnia, general weakness
3	52	F	R	11	46	1 (4)	Hypercalcemia
4	43	F	R	20	14	2 (4)	Bone pain
5	38	M	R	7	58	1 (4)	Bone pain, skin itching
6	21	M	R	10	10	1 (5)	Bone pain
7	62	F	R	16	60	1 (4)	Bone pain
8	58	F	R	14	84	1 (4)	Bone pain
9	35	M	R	20	21	1 (4)	Bone pain
10	40	M	R	19	24	1 (4)	Bone pain
11	34	F	R	8	60	1 (4)	Bone pain, general weakness
12	41	M	R	11	94	2 (5)	Bone pain, skin itching
Mean ± SD	45.5 ± 13.3			13.4 ± 4.5	49.1 ± 27.3		
Range	(21–78)			(7–20)	(10–94)		

Table 3 Preoperative work-ups and locations of hypertrophic mediastinal hyperparathyroid glands in recurrent and persistent SHPT

Patients	Sestamibi scans	CT scans	Locations of HMPGs	Calcium (mg/dl)	Phosphorus (mg/dl)	i-PTH (pg/ml)
1	Yes	Yes	Left retro-innominate vein (Zone II)	10	5.8	1089
2	Yes	Yes	Left peri-aortic (Zone II)	11.3	4.2	1170
3	Yes	Yes	Right retro-innominate vein (Zone I)	11.7	5.5	769
4	Yes	Yes	Aorto-pulmonary window (Zone III)	10.5	5.7	1513
5	Yes	Yes	Aorto-pulmonary window (Zone III), left retro-innominate vein (Zone II)	10.6	6.5	530
6	Yes	Yes	Right retro-innominate vein (Zone I)	9.9	3.9	1516
7	Yes	Yes	Aorto-pulmonary window (Zone III)	11.8	4.2	2205
8	Yes	Yes	Left peri-aortic (Zone II)	9.8	5.9	1026
9	Yes	Yes	Left peri-aortic (Zone II), left upper mediastium	8.8	7	3560
10	Yes	Yes	Left peri-aortic (Zone II)	9.7	7.3	2500
11	Yes	Yes	Left retro-innominate vein (Zone II), left lower neck	10.5	6.5	1681
12	Yes	Yes	Left retro-innominate vein (Zone II), right upper mediastium	9.5	3.4	815
Mean ± SD				10.3 ± 0.9	5.5 ± 1.3	1531 ± 864
Range				(8.8–11.8)	(3.4–7.3)	(530–3560)

i-PTH intact parathyroid hormone

follow-up of 30 ± 22 months (range 3–61 months). Three months after surgery the mean of calcium, phosphorus and i-PTH levels were 8.1 ± 0.9 mg/dl (6.5–9.5), 4.4 ± 1.5 mg/dl (1.9–6.9), and 53 ± 106 pg/ml (8.2–388), respectively, as shown on Table 4.

Patient No. 5 had two parathyroid glands (one in Zone II and the other in Zone III) in the Sestamibi scan preoperatively. Both glands were also seen in the preoperative chest CT scan and were removed with left VATS at the same time using 3 trocars for one in Zone II and 4 trocars for the other in Zone III. Patient No. 11 who had one positive location with the Sestamibi scan in the lower neck 1 year after surgery (Fig. 2a), yet had i-PTH levels around 400 pg/ml and normal calcium levels without clinical symptoms. She then had symptoms of bone pain and general weakness 6 years after surgery and her calcium, phosphorus, and i-PTH levels were 10.5 mg/ml, 6.5 mg/ml, and 1,681 pg/ml, respectively. Her Sestamibi and CT scans showed two parathyroid glands (Fig. 2b), one at the left lower neck and the other in Zone II of the mediastinum

Table 4 Surgical approaches, number of trocars, size of removed parathyroid gland and results of surgery

Patients	Surgical approaches	Trocars (no.)	Size of parathyroid glands (cm)	Operating time (min)	Hospital days	3 months post-operation			Follow-up months	Complications
						Ca (mg/dl)	P (mg/dl)	i-PTH (pg/ml)		
1	Left VATS	3	2	80	6	9.5	5.8	22	61	Af with RVR
2	Left VATS	3	2.5	150	8	8.7	5.3	10	51	Pleural effusion
3	Right VATS	3	0.9	98	4	6.5	6.9	8.2	51	Hypocalcemia
4	Left VATS	4	3.4	292	5	6.8	2.6	33.2	47	Hypocalcemia
5	Left VATS	4	1, 1.8	232	7	8	4	17.6	47	
6	Right VATS	3	1.5	120	5	8.7	1.9	17.7	35	
7	Left VATS	4	2	177	6	9	4.6	44.1	26	Hoarseness
8	Left VATS	3	1.8	171	5	8.4	3.2	14	15	
9	Left VATS and cervical	3	2, 1.2	124	7	7.3	4	16	8	Hypocalcemia
10	Left VATS	3	2.5	124	5	7.5	4.7	16	8	
11	Left VATS (staged surgery)	3	2.5	112	5	7.6	6.3	388	3	
12	Left VATS and mediastinol scope	3	1, 1.8	180	8	8.9	3.6	48	3	
Mean ± SD				152 ± 60	5.9 ± 1.3	8.1 ± 0.9	4.4 ± 1.5	53 ± 106	30 ± 22	
Range			(0.9–2.5)	(80–292)	(4–8)	(6.5–9.5)	(1.–6.9)	(8.2–388)	(3–61)	

VATS video-assisted thoracoscopic surgery, *Ca* calcium, *P* phosphorus, *iPTH* intact parathyroid hormone, *Af with RVR* atrial fibrillation with rapid ventricular response

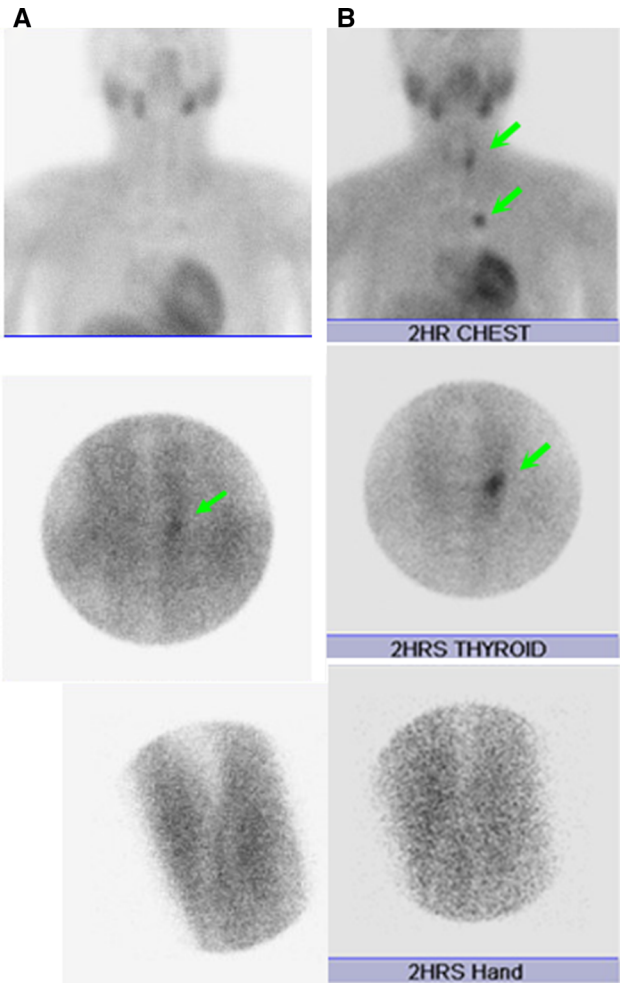


Fig. 2 **a** 1 year after first surgery, patient No. 11 had one positive location at the *left lower neck* in the Sestamibi scan. *Upper* no evidence of positive location at the mediastinum. *Middle* one positive location at the *left lower neck*. Lower no positive location at the forearm. **b** 6 years after first surgery, patient No. 11 had two positive locations of hypertrophic parathyroid gland in the Sestamibi scan, one at *left lower neck* and the other in Zone II of the mediastinum. *Upper* one positive location at the *left lower neck* and the other one in Zone II of the mediastinum. *Middle* one positive location at the *left lower neck*. *Lower* no positive location at the forearm

(Fig. 3a, b). She preferred two-stage surgery and her HMPG in Zone II was removed under left VATS first. Patient No. 12 had one positive location with the Sestamibi scan at the left upper neck (Fig. 4a) and had cervical retrieval 1 year after the first surgery. Seven years after the second surgery, the patient had two positive locations of HMPGs in Sestamibi and CT scans, one in the right superior mediastinum and the other in Zone II (Figs. 4b, 5a, b). We performed the mediastinoscopic approach for the gland in the right upper mediastinum and left VATS for the gland in Zone II at the same time.

One patient had atelectasis with pleural effusion and was hospitalized for 8 days with complete recovery. One patient with a HMPG at the aorto-pulmonary window (Zone IV) experienced temporary vocal cord palsy. Six patients had transient hypocalcemia (<7.5 mg/dl) and recovered after intravenous replacement and medication within 3 months. Neither mortality nor major complications were found as shown in Table 4.

Discussions

Twelve patients (2.9 %) with HMPGs participated in this study and during the same period we operated on 421 patients with symptomatic SHPT. Recurrent or persistent hyperparathyroidism remained around 5–80 % after subtotal parathyroidectomy or total parathyroidectomy with autotransplantation in SHPT [1, 2, 19]. Findings at re-operation mainly included graft hyperplasia (49 %), supernumerary glands (20 %), remnant hyperplasia (17 %), a missed in situ gland (7 %), and a negative exploration (5 %) [20]. It was difficult to localize the source of hormone excess and to determine whether it was in the neck, mediastinum or at the forearm. It was still useful that our previous study reported a valuable method in differentiating the location of the hypertrophic parathyroids at the grafted site using the i-PTH gradient of the graft-bearing arm versus the contra-lateral arm was being less than 2 [4]. All patients with HMPGs in this study had gradients less than 2. After exclusion of graft hyperplasia or a missed initial exploration in the neck, the mediastinal location of hypertrophic glands plays an important role in persistent or recurrent hyperparathyroidism. The incidence and mechanism of the mediastinal location of parathyroids in uraemic patients after total parathyroidectomy remains unclear. It may result from initial supernumerary glands or ectopic locations of small glands with secondary nodular hyperplasia after total parathyroidectomy and long-term hemodialysis [19, 21]. Residual or ectopic small glands have the potential to be transformed to nodular hyperplasia during hemodialysis after total parathyroidectomy. Some authors have advised to routinely survey supernumerary glands before the first parathyroidectomy. But it is difficult to detect with a preoperative image study before the first parathyroidectomy if the supernumerary gland is less than 500 mg [19]. Routine preoperative imagines are not recommended before primary surgery for SHPT. Mediastinal locations of hypertrophic parathyroids have been more frequently discussed in patients with primary hyperparathyroidism. Nilubol et al. have reported 3.5 % (32 in 922) mediastinal parathyroid glands in patients with hyperparathyroidism receiving parathyroidectomy [22]. In uraemic patients with recurrent or persistent SHPT after total parathyroidectomy, the incidence of HMPGs was estimated at about 5–37 % of patients [19, 23]. Fifty-four

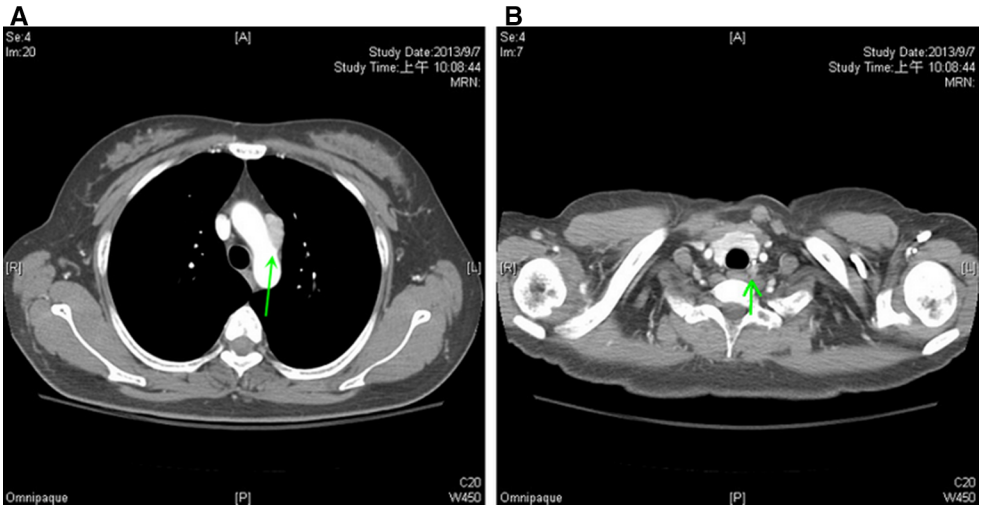


Fig. 3 6 years after the first surgery, the CT scan showed patient No. 11 had one positive location in zone II and the other one at the left lower neck. **a** one positive location in Zone II. **b** the other positive location at *left lower neck*

patients (12.8 %) among the 421 operated on for symptomatic SHPT were recurrent or persistent hyperparathyroidism and 12 patients (2.9 %) due to HMPGs. These 12 patients did not show the true incidence of the disease and all belonged to recurrent hyperparathyroidism.

Most patients with recurrent or persistent SHPT with HMPGs need re-operation if they have little chance to get a kidney transplantation or have symptoms of bone pain, skin itching, general weakness, and insomnia despite medical treatments. The success of surgery depends on the definite preoperative localization of HMPGs. Our previous study demonstrated that the Sestamibi scan successfully identified the parathyroid remnants in 85 % of patients with persistent or recurrent SHPT [4]. The Sestamibi scan would be arranged to detect overlooking the supernumerary glands or ectopic locations of the parathyroid if no graft hyperplasia was found in the forearm. The detecting rate of Sestamibi scans for ectopic parathyroid glands ranged from 90 to 95 % in literature [10, 11]. To avoid negative exploration, combined Sestamibi with CT scans of chest or neck to identify the location of HMPGs is necessary to reveal the anatomical position of ectopic glands, even when the smallest diameter is 0.5 cm in size [24]. No other image studies such as those using magnetic resonance imagining or ultrasonography were necessary for preoperative localization in this study. Twelve patients were found to have 13 HMPGs using Sestamibi and CT scans. Concomitantly, one had a parathyroid at left lower neck, another had a gland in left upper mediastium, and the other had a parathyroid at right upper mediastinum. Multi foci of the recurrent site were a quite unique finding compared to reported results in literature. Peri-operative frozen sections of surgical specimens confirmed the parathyroid tissue in all patients and the sensitivity of frozen sections to prove the parathyroid gland was 100 % in this series. We did not use a gamma probe or rapid parathyroid hormone determinations as previously reported [21, 22], because the results of PTH levels would not change our surgical procedure. However, our successful rate was almost 100 % in this study. For those supernumerary glands weighing less than 500 mg or too small to be detected by the Sestamibi scan still pose a great challenge for clinical physicians to find them [25]. Serial periodic examinations from 6 to 12 months are helpful in these kinds of patients as it was clear from the cases of patient No. 11 and No. 12 in this study.

The vast majority of ectopic parathyroid gland could be removed via a cervical incision [15, 16, 26]. Approximately 2 % of HMPGs required a thoracic approach to retrieve parathyroid glands. Traditionally, HMPGs were treated through a mediastinotomy or thoracotomy procedure that could be associated significant morbidity reported as high as 29 % [7, 13, 15, 27, 28]. The complications included pneumonia, pleural effusion, pneumothorax, atrial fibrillation, innominte vein thromobis, and injuries to phernic and brachial nerves. There were also reports of sternal wound infection, dehiscence, and non-union (8 %), recurrent laryngeal nerve palsies, chilous fistula (6.2 %), mediastinitis and death from the procedure [7, 13, 15, 27, 29].

Because uraemic patients with SHPT usually have poor general conditions, mediastinotomy or thoracotomy can cause even more risk.

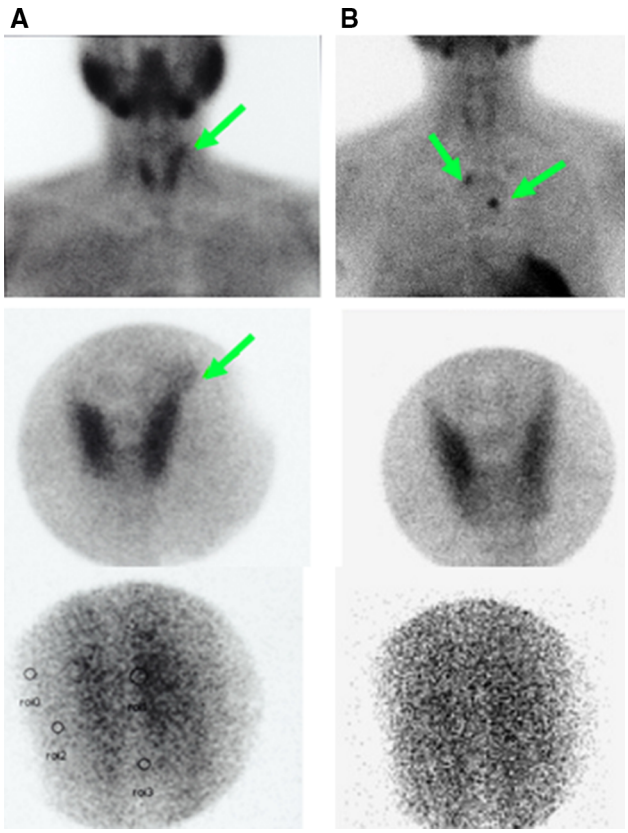


Fig. 4 **a** Patient No. 12 had one positive location in the Sestamibi at the left upper neck and had cervical retrieval 1 year after the first surgery. *Upper* one positive location of the Sestamibi scan at the *left upper neck*, but none in the mediastinum. *Middle* one positive location of the Sestamibi scan at the *left upper neck*. *Lower* no positive location at the forearm. **b** 7 years after the second surgery, patient No. 12 had two positive locations in the Sestamibi scan, one in the *right upper mediastinum*, and the other one in Zone II

Minimal invasive or video-assisted mediastinal parathyroidectomy has been clearly associated to less duration of surgery, lower morbidity, and shorter length of hospital stay [15, 16, 26]. The literature series reporting hospital stay from 2.7 to 4.5 days for thoracoscopic parathyroidecotmy have been confirmed in this study. Compared with hospital stay from 9 to 14 days for open sterno-thoracotomic approaches, VATS is a much better procedure [15, 16, 26, 27]. We have also found that HMPGs in the aorto-pulmonary window can be removed via 4 trocars to avoid a conversion.

To reduce the invasiveness of sternotomy, previously, we proposed the "inverted T" partial sternotomy to explore the aorta-pulmonary window [30]. However, with the advance of thoracoscopic instruments and techniques, most deep mediastinal glands can be removed successfully via the thoracoscopic approach [14–16]. The rarity of deep mediastinal parathyroids in SHPT explains the low number of reported series in literature. These reports have shown that the thoracoscopic approach is a feasible and safe alternative technique in the management of HMPGs. We have started VATS for recurrent or persistent HMPGs since 2008 and found it is a less invasive method. The mean hospital stay was 5.9 days, which was 1 to 2 days longer than that reported previously [15, 16]. This might be due to a regular dialysis before and after surgery in this kind of patients and postoperative hypocalcemia that required intravenous replacement. According to our experience in VATS, we think that patients can be performed with the minimal invasive approach, even after they have undergone previous cardiac or thoracic surgery. However, in this study we do not experience any case of re-do surgery.

The limitation of our study is that we do not have comparison with open surgery. It seems unethical to patients, using open surgery as a control group for comparison.

In the algorithm as shown on Table 5 that we have proposed, patients with recurrent and persistent hyperparathyroidism should have the i-PTH gradient of the grafted versus contra-lateral arm being less than 2 at first. A Sestamibi scan to identify locations and numbers of HMPGs and then a CT scan to confirm the anatomic location should be performed before the surgical procedure. If a correct mediastinal location cannot be achieved using a Sestamibi scan, repeat the examination 6–12 months later, but do not do thoracoscopic explorations [16]. We classify the locations of HMPGs to three zones according to the related anatomy to the innominate vein, aorta and pulmonary artery. For parathyroid glands in upper mediastium, it is easy to expose them by direct transcervical (less than 5 cm below sternal notch) or mediastinoscopic (more than 5 cm below sternal notch) approaches. For HMPGS in Zone I or Zone II, right or left thoracoscopic approaches through 3 trocars can easily remove the glands. However, for HMPGS in Zone III, it is necessary to have a fourth trocar to retract the left pulmonary artery, to get an adequate exposure, to avoid injury to the recurrent laryngeal nerve or phrenic nerve, and to preserve the intact parathyroid gland, which is easy to rupture in a poor surgical field. A previous report mentioned that the thoracoscopic approach was converted owing to technique difficulties in retrieving the HMPG in Zone III [16]. It was also proved in this study that the operating time in Zone III was twice as long as that in the other Zones. We suggest inserting a fourth trocar at the beginning of the procedure.

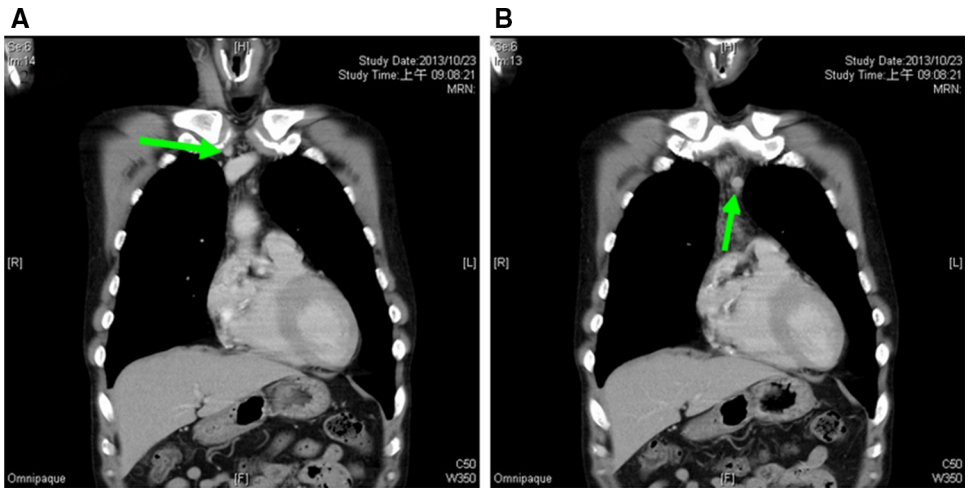
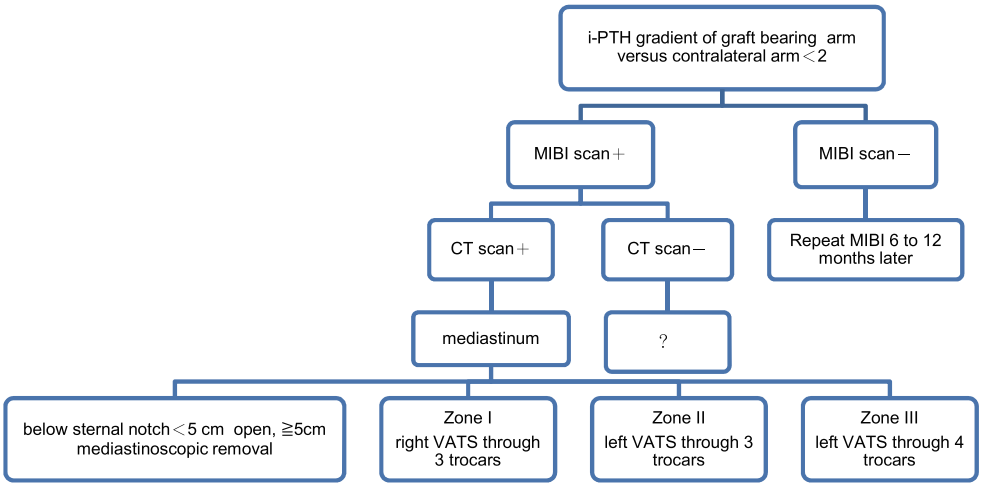


Fig. 5 7 years after second surgery, patients No. 12 had two positive locations in the CT scan. **a** One positive location in *right upper mediastium*. **b** The other positive location in Zone II

Table 5 Algorithm: persistent or recurrent secondary hyperparathyroidism due to hypertrophic mediastinal parathyroid glands



Indications for surgery: bone pain, skin itching, general weakness, insomnia, Ca > 10.1 mg/dl, P > 4.5 mg/dl, i-PTH > 500 pg/ml

MIBI Sestamibi, *VATS* video-assisted thoracoscopic surgery, *Ca* calcium, *P* phosphorus, *i-PTH* intact parathyroid hormone

? Never happen in this study

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