Surgical Management of Secondary Hyperparathyroidism

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Abstract

To summarize the effect and experience of parathyroidectomy in patients with renal secondary hyperparathyroidism. A retrospective analysis was made about the clinical and pathological data of 23 patients with renal secondary hyperparathyroidism who underwent parathyroidectomy in the Department of Otolaryngology-Head and Neck Surgery of the Sixth Affiliated Hospital of Sun Yat-sen University from March 2013 to May 2015. The anatomical variation of parathyroid glands and the therapeutical effects of parathyroidectomy were also analyzed. The serum parathyroid hormone (PTH) level dropped to normal level after surgery in 22 cases underwent total parathyroidectomy and auto transplantation in the forearm. The serum calcium level turned normal or slightly lower than normal level in 22 of the 23 cases (22/23). The serum PTH level was higher than normal but 1 time lower than the original level in 1 patient who underwent subtotal parathyroidectomy. Postoperative clinical symptoms such as ostealgia and itch of skin have been gradually relieved in all cases. Skin ectopic calcification was excised in 1 case without recurrence, and ectopic calcification in another case reduced significantly after operation. Parathyroidectomy is an effective therapeuetic strategy in management of patients with renal secondary hyperparathyroidism.

Keywords Secondary hyperparathyroidism; Parathyroid hormones; Parathyroidectomy; Chronic renal failure
1. Introduction

Secondary hyperparathyroidism is a common complication in patients with chronic renal failure, and about 40% of such patients with dialysis have secondary hyperparathyroidism, the complications of secondary hyperparathyroidism directly decrease the quality of life [1,2]. Drug therapy and ultrasound-guided ablation therapy of hyperparathyroidism are ineffective; however, parathyroidectomy is an effective treatment technique [3-6].

During March 2013-May 2015, 23 cases of secondary hyperparathyroidism underwent parathyroid surgery in Department of Otolaryngology-Head and Neck Surgery in the Sixth Affiliated Hospital of Sun Yat-sen University.

2. Materials and Methods

2.1 Clinical data

During March 2013 to May 2015, 23 patients with secondary hyperparathyroidism underwent parathyroid surgery in Department of Otolaryngology - Head and Neck Surgery, the Sixth Affiliated Hospital of Sun Yat-sen University, and the clinical and pathological data are summarized as below. There were 9 males and 14 females, and the male to female ratio was 1:1.6; the age ranged from 33 to 60 years old, with a median age of 50 years. The hemodialysis time ranged from 1.5 to 13 years, with a median time of 5 years; time of ostealgia: 14 days to 3 years; 1 case with rib fractures, 3 cases associated with urinary tract stones, and 5 cases with ectopic calcification.

The main clinical manifestations include: body itching in 2 cases, malaise in 1 case, and palpable thyroid mass in 4 cases. All the 23 patients had no hoarseness, dyspnea or dysphagia. Preoperative levels of parathyroid hormone (PTH) were above 300 pg / ml in all the patients. Preoperative serum calcium concentration ranged from 2.18 to 2.93 mmol / L, with the median value of 2.51 mmol / L, and the average value of 2.39 mmol / L; preoperative alkaline phosphatase (AKP) was 85-1014U / L, with the median value of 327U / L and the average value of 443 U / L; preoperative serum phosphorus concentration was 0.78-3.52 mmol / L, with the median value of 2.21 mmol / L and the average value of 2.23 mmol / L.

2.2 Preoperative imaging findings

Twenty-one patients underwent neck ultrasonography, and the results showed that 7 patients had 4 parathyroid glands; 6 patients had 3 parathyroid glands; 5 patients had 2 parathyroid glands, 2 patients had only 1 parathyroid gland and 1 patient without parathyroid gland. Twenty cases underwent enhanced CT of the neck, and the reports showed: 7 patients had 4 parathyroid glands; 3 cases have 3 parathyroid glands; 6 patients had 2 parathyroid glands; 3 patients had only 1 parathyroid gland and 1 patient without parathyroid gland. Two patients underwent enhanced MRI of the neck, suggesting that the patients have two parathyroid glands. Eighteen cases underwent scintigraphy Technetium 99 examination, and the reports showed that 4 cases had positive radionuclide in the thyroid area, 6 cases were weakly positive and 8 cases were negative.

2.3 Treatment

2.3.1 Surgical procedure

Twenty-two patients received bilateral parathyroidectomy and parathyroid gland transplantation in forearm under general anesthesia. Intraoperative frozen section examination was performed routinely, and serum PTH level was checked about 10 minutes after parathyroidectomy. Pathologically confirmed relatively normal parathyroid gland tissues were cut into small pieces with the size of 1mm × 1mm × 1mm, then 30 pieces were implanted into the musculi brachioradialis of the forearm without arteriovenous fistula, and the
transplantation site was labeled with non-absorbable silk knot. Two patients had tumor-like calcification and 1 patient received resection of soft-tissue of calcification in the hip.

2.3.2 Postoperative management
(1) The changes of clinical symptoms and signs.
(2) Hemodialysis was performed at least 4 hours after operation, and treatment of hypertension, anemia, and symptomatic and supportive treatment were given simultaneously.
(3) Observe the changes of the volume of the wound drainage, prevent postoperative hypocalcemia, and monitor serum calcium and serum magnesium. Calcium supplement rate does not exceed 1g / hour. Oral application calcium and active vitamin D; monitor of the amount of fluid and adjustment of electrolyte disturbances; use of antibiotics to prevent infection; use of proton pump inhibitors to protect the stomach mucosa, and prevention of osteoporosis-related complications.

2.4 Follow-up
Follow-up information was obtained by the telephone and outpatient review. Follow-up time started from the date of the first treatment and ended until August 25, 2016.

3. Results

3.1 Improvement of clinical symptoms
The ostealgia and skin itching disappeared, the roughness of skin began to reduce and the appetite improved on the first postoperative day. Three patients had transient numbness in the face and upper limb because of hypocalcemia, and the symptom disappeared after intravenous use of calcium. Five patients had transient fatigue, and the symptom disappeared about 2-3 weeks after operation. One patient with multi soft-tissue mass of ectopic calcification in the hip and shoulder, the size of the masses began to decrease about 2 days after operation and the average size was reduced by 40% within a week. Hoarseness or cough caused by recurrent laryngeal nerve injury or other operation related complications had not been found in any of the patients.

3.2 Surgical exploration
During the surgical exploration, we found that 22 patients had four parathyroid glands, and 1 patient had 5 parathyroid glands. The sizes of parathyroid glands ranged from 0.8 cm x 1.0 cm to 3.2 cm x 2.5 cm. Pathologic results demonstrated hyperplasia of the parathyroid tissue. Nine patients had ectopic parathyroid, including 1 in the left lobe of the thyroid gland and 1 in the right, 5 in the gap between the posterior esophageal wall and the prevertebral fascia, and 1 behind the annular cartilage, and 1 in the thymus (Figure 1, 2 and 3). Most of the parathyroid glands (68/89, 76.4%) were in close proximity with the adjacent recurrent laryngeal nerve. Papillary thyroid carcinoma was found in 1 patient, and both parathyroidectomy and thyroidectomy were performed at one procedure.

Figure 1. Surgical exploration of the right parathyroid glands
3.3 Postoperative recovery

Hemodialysis was performed in 23 cases about 4 to 24 hours after the operation. The average volume of wound drainage was 24 ml, with the range from 10 ml to 40 ml on the first postoperative day. The drainage tube was removed 3-4 days after operation and the stitches in were removed about 7 days after operation for the neck area, and 12 days for the forearm wound, and the wound healed well in all patients.

3.4 Postoperative levels of PTH

Postoperative levels of PTH were detected 10 minutes after removal of the parathyroid, and the results showed that the levels of PTH were normal in the patients (22/23). After about one week, the mean calcium decreased to the normal range with the mean value of 1.99 mmol / L; the mean level of serum phosphorus was 1.15 mmol / L and the mean value of serum alkaline phosphatase was 1044 U / L.

3.5 Results of follow-up

Postoperative routine examination of PTH was performed every four months for all patients during follow-up. By the latest follow-up on August 25, 2016, hyperparathyroidism was found in two patients; however, the PTH returned to the normal levels after ablation of the transplant parathyroid in the right forearm. All patients had no clinical symptoms such as pain or itchy skin during follow-up.

4. Discussion

4.1 Surgical indications

Secondary hyperparathyroidism is one of the most common complications of chronic renal failure, and the incidence of hyperparathyroidism in such patients with dialysis is about 40% [1, 2]. For patients with chronic renal failure and hyperparathyroidism in the early stage, the symptoms can be controlled by the limit of phosphorus intake or/and use of phosphate binders and oral vitamin D, while for patients in the intermediate stage, the symptoms can be improved by application of 1, 25 (OH) 2D3, Ca2+-sensing receptor (CaR) agonists, and new active vitamin D or /and ultrasound-guided parathyroid ablation. With further deterioration of the disease, surgical intervention such as parathyroidectomy is required [1, 3, 6-10]. The accepted surgical indications include: (1) sustained hypocalcemia with blood calcium> 11.5mg / dl; (2) seriously high levels of PTH (PTH> 300pg / ml) and high levels of AKP; (3) Ca x P > 70, with evidence of ectopic calcification; (4) refractory pruritus; (5) progressive ostealgia, bone fracture or bone deformity; (6) parathyroid gland was swollen, probably compression of the trachea or esophagus or other vital organs; (7) resistance of medical treatment [1, 3, 6-10]. The
conditions of the 23 patients meet the above operative indications, and symptoms improved significantly after surgical treatment.

4.2 Techniques of intraoperative identification of parathyroid glands and the results of surgical treatment

Intraoperative identification of parathyroid glands is not so difficult according to abnormal parathyroid glands, such as hyperplasia or adenoma. The weight of normal parathyroid glands ranges from 35 mg to 40 mg, with the average size of 5 mm × 3 mm × 2 mm, and the intraoperative manifestations of parathyroid glands include soft texture, color brown, available compression; however, the size of abnormal gland ranges from 5 mm to 80 mm, and the weight ranges from 4 g to 120 g, with round shape, dark-yellow color and slightly hard and incompressible texture. Experienced doctors can identify most of the parathyroid glands; however, some of the parathyroid glands cannot be identified easily, and intraoperative frozen section pathological examination should be done to confirm the identification. According to the experience from our study and some other studies, all the suspected parathyroid glands should be confirmed by pathologic frozen section [9]. In order to determine whether the parathyroidectomy is completed on purpose, we strongly recommend the intraoperative use of rapid examination of serum PTH to confirm the adequacy of the range of exploration and resection [9, 11, 12]. Irvin, etc. also recommended the use of rapid intraoperative examination of serum PTH such as immunohistochemical chemiluminescence PTH assay (Immunochemiluminescent assay, ICMA) [13]. About 10 minutes after complete resection of parathyroid glands, the value of PTH reduced 82% compared with the preoperative value. In this study, intraoperative radionuclide examination of PTH was performed immediately after resection of parathyroid, and the levels of PTH returned to normal level in time, and the follow-up results also verified the outcome of surgical treatment.

Persistent and refractory hyperparathyroidism after surgery may cause by the following conditions, such as ectopic parathyroid glands, uncommon number of parathyroid glands (more than 5) or autologous transplantation of parathyroid adenomas [9, 14, 15]. Ectopic parathyroid glands include parathyroid glands embodied in the thyroid, or located in esophagus, carotid sheath, thymus or mediastinum. If the parathyroid glands cannot be found after a comprehensive exploration, one of the most possible reasons is that the glands may be located within the thyroid gland, and the suspected ipsilateral swollen thyroid gland should be detected. The number of parathyroid glands is equal to or more than 5 in 8% of the patients, if intraoperative hyperparathyroidism persists after conventional resection of four glands, further exploration should be performed in the thyroid gland and the common area of the ectopic region. In this study, 1 patient underwent common resection of 4 parathyroid glands, and intraoperative examination showed that the levels of PTH decreased but still higher than normal; therefore, further exploration was performed and ectopic parathyroid glands were found in the paraesophageal area. In addition, the suspected relatively normal parathyroid gland tissue used for autologous transplantation should be verified by frozen section examination to exclude parathyroid adenoma, which may have high function of PTH secretion and leads to postoperative refractory hyperparathyroidism.

4.3 Treatment of postoperative hypocalcemia

Serum calcium levels begin to decrease about 6-12 h after parathyroidectomy and will drop below normal levels in 1 to 3 days. Severe hypocalcemia may occur particularly in patients underwent total parathyroidectomy [16]. If hypocalcemia-related symptoms appeared, such as numbness of the lips or limbs, and convulsions, intravenous use of calcium is effective. For patients with severe hypocalcemia, short-term use of vitamin D may also be considered, such as calcitriol, in order to maintain the levels of serum calcium in the normal range. In addition to PTH insufficiency and hungry bone syndrome, hypocalcemia may also be caused by lack of serum magnesium;
so routine determination of serum magnesium is necessary. When the levels of serum magnesium decreased lower than 0.615 mmol/L, supply of serum magnesium is needed. Meanwhile, laryngospasm caused by hypocalcemia should be observed seriously. In this study, hypocalcemia has been corrected in time without hypocalcemia associated symptoms. Given the limited scale of cases in this study, further studies with expanded samples and long-term observations should be conducted to further clarify the role of parathyroidectomy in renal hyperparathyroidism.

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Competing Financial Interests

The authors declare no competing financial interests.

References