Reoperation for Renal Hyperparathyroidism

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Abstract. Reoperation for secondary hyperparathyroidism (HPT) due to uremia (2HPT) may be required among patients with persistent renal failure if not all parathyroid glands are removed at the initial operation. Between March 1981 and July 2001, altogether 1110 patients underwent total parathyroidectomy with forearm autograft for advanced 2HPT in our department. In this study, we evaluated the clinical features of patients who required reoperation and classified them into persistent HPT [the lowest intact parathyroid (PTH) level after initial operation remained higher than 60 pg/ml] and recurrent HPT (the lowest intact PTH level was normalized after surgery but reelevated became high enough to require reoperation). Removal of residual glands was indicated in 30 (2.7%) cases for persistent or recurrent HPT. All remaining glands were detected by preoperative imaging diagnoses. In 44 (4.0%) patients persistent HPT was recognized and in 15 of them (1.4% of all cases) reoperation was required. In 11 cases, the responsible glands were supernumerary ones removed from the mediastinum. In 4 cases, the glands were resected from the neck. In 15 cases (1.4%), reoperation was performed for recurrent HPT when residual glands were left either in the neck or in the thymic tongue. In all but one case, the missed glands were supernumerary. This study reveals that it is often difficult to avoid persistent HPT induced by mediastinal supernumerary glands and recurrent HPT caused by small glands left in the neck. Our findings indicate that patients with uremia should be closely followed considering the possibility that persistent or recurrent HPT may occur after parathyroidectomy.

In the surgical treatment of hyperparathyroidism (HPT), neck reexploration should be avoided, particularly because of the risk of recurrent nerve injury [1, 2]. In secondary HPT due to uremia (2HPT), the risk of recurrent HPT is not negligible [3]. In Japan most patients with chronic renal failure require continuous maintenance hemodialysis (HD) for a long period because opportunities for renal transplantation are rare. Then, residual glands left in situ, although microscopic, can be enlarged by the ongoing stimulation of renal failure [4]. In this situation we have regarded total parathyroidectomy with autotransplantation (PTx + ATx) as the appropriate surgical procedure [2] and have performed this operation in more than 1000 cases of 2HPT. In spite of careful neck exploration at the time of operation, a few patients develop persistent or recurrent HPT necessitating reoperation for remaining ectopic and/or small parathyroid glands in the neck that were overlooked. The aim of this study was to evaluate retrospectively the clinical features of cases requiring reoperation due to persistent or recurrent HPT.

Materials and Methods

Definition of Recurrent and Persistent HPT

As the serum calcium level of parathyroid hormone (PTH) is influenced by the postoperative treatment in patients with 2HPT, we have defined persistent and recurrent HPT by the postoperative measurement of the serum intact PTH level (Allegro kit; normal range: 3–60 pg/ml; Nichols Institute Diagnostics, San Diego, CA, USA). In patients with persistent HPT the lowest intact PTH level remains higher than the upper normal limit (>60 pg/ml) and in patients with recurrent HPT the level is normalized (≤60 pg/ml) within 2 weeks after operation and becomes elevated again more than 6 months postoperatively.

Patients

Between March 1981 and September 2001, 1110 patients underwent total PTx + ATx for advanced 2HPT in the Nagoya Second Red Cross Hospital. The operative strategy for total PTx + ATx
has been previously reported [4]. In the present series we routinely resected the thymic tongues and opened the carotid sheaths bilaterally to avoid leaving any parathyroid glands behind, especially supernumerary ones. Out of 1110 patients, 30 (2.7%) underwent reoperation with removal of residual parathyroid glands. There were 16 men and 14 women with a mean age of 47.3 ± 10.1 years (range: 28–66 years). All patients were treated by hemodialysis and none had undergone transplantation at the time of reoperation. Eighty-one patients who underwent only graftectomy for graft-dependent recurrent HPT were eliminated from this study.

Surgical Indication for Reoperation

Accepted indications for reoperation in our department were a high level of intact PTH (≥500 pg/ml), detection of residual parathyroid glands by two or more kinds of imaging diagnosis, findings of ostitis fibrosa cystica or high bone turnover, and at least one factor refractory to medical treatment.

Modified Casanova’s Test

In cases with recurrent HPT, modified Casanova’s test [5] was performed when it was difficult to evaluate whether the origin was a residual gland or grafted tissue. The test involved total ischemic blockade of the graft-bearing arm with a tourniquet at the pressure of maximum blood pressure plus 100 mmHg and measurements of the circulated intact PTH levels. Blood for intact PTH levels were sampled from the antecubital vein in the non-grafted arm before and 10 and 20 minutes after blockade. After releasing the blockade, samples were also obtained to observe the recovery of the serum intact PTH level. When the ratio of the minimum intact PTH level during and before blockade was more than 60%, we suggested existence of residual glandular tissue.

Imaging Diagnosis

In persistent 2HPT, all patients who required reoperation underwent scintigraphic scanning with either thallous chloride 201 (201Tl) or technetium 99m sestamibi (99mTc-MIBI). When missed glands were identified by the examination, computed tomography (CT) was done, focusing on the scintigraphy uptake area. Ultrasonography (US) was also performed with the aim to facilitate exploration of the neck area. Patients with recurrent HPT underwent initially only US examination, and CT and scintigraphic scanning were performed only after positive detection by US. Magnetic resonance imaging (MRI) was performed complementarily in both persistent and recurrent HPT.

Operative Procedure

Reoperation was performed under general anesthesia. When missed glands were suspected in the neck, a lateral cervical approach was chosen. When the glands were thought to be located in the middle or posterior mediastinum, sternotomy was routinely performed. In patients with recurrent HPT, where the origins of PTH hypersecretion indicated both autograft tissue and residual gland in the neck or mediastinum, a graftectomy was initially performed. Because in every case an autograft in the forearm had been performed at the initial PTx, a new autotransplantation was not performed at reoperation.

Results

Persistent HPT

The incidence of persistent HPT was 44/1110 cases (4.4%). In 15 (34.1%) of them, reoperation was required; the remaining 29 patients (65.9%) could be followed by medical treatment. Fourteen patients underwent reoperation once, and the remaining patient required reexploration twice. The mean period between the initial operation and reoperation was 38.5 ± 37.8 months (range: 5–136 months) and the mean preoperative intact PTH level was 846.4 ± 250.3 pg/ml (range: 316–1300 pg/ml). In three patients, persistent HPT had developed because only three glands were removed at the initial operation, whereas, in three other patients persistent HPT occurred although only one or two supernumerary glands remained to be removed (Table 1). The results of preoperative imaging studies are shown in Table 2. The scintigram, CT, US, and MRI could identify 16 of 16 residual glands (100%), 14 of 16 (87.5%), 3 of 13 (23.1%), and 6 of 9 (66.7%), respectively (Table 2).

The location of the residual glands is described in Figures 1A and 1B. In 11 (73.3%) of 15 patients the residual glands were located in the mediastinum and all were supernumerary. The aortico-pulmonary window (A-P window) was the most common location (5/11, 45.5% of the mediastinal parathyroid glands). Three glands left in the anterior mediastinum could be removed through the neck incision. Sternotomy was required to extirpate the mediastinal glands in seven cases. In one case, the gland was removed from the aortic arch by an endoscopic procedure. In four patients the missed glands were located in the neck, and one of those was an undescended gland found at the level of the bifurcation of the right carotid artery. The mean weight of resected glands was 2693.3 ± 2208.8 mg (range: 300–8165 mg; Table 1).

The clinical course of patients who required reoperations is described in Table 3. None of the patients underwent graftectomy before reoperation. In three cases a subsequent graftectomy was required because of reelevation of intact PTH level after the reoperation. In another case, a graftectomy was done immediately after the reoperation because the serum calcium level was not decreased by removal of the residual gland alone.

Recurrent HPT

In 15 of the 1110 cases (1.4%), reoperation was carried out for recurrent HPT and a total of 19 missed glands were removed. The mean period between the initial operation and reoperation was 107.2 ± 46.2 months (range 37–183 months), and the mean preoperative intact PTH level was 834.7 ± 235.1 pg/ml (range: 410–1300 pg/ml). In 14 of 15 cases, four or more glands were resected at the initial PTx, whereas in one case only two glands were removed at the initial PTx (Table 4). In preoperative imaging studies, scintigraphy, CT, US, and MRI could identify 15 of 19 glands (78.9%), 17 of 19 (89.5%), 17 of 19 (89.5%), and 5 of 5 (100%), respectively (Table 2). In 4 cases two missed glands could be detected by one or more of the imaging tests used.

Figure 2 shows the location of the residual glands. All missed glands were located in the cervical area or in the thymic tongue.