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# Surgical Treatment for Renal Hyperparathyroidism - Report of 23 Cases

Seiji MARUBAYASHI[1], Yasuhiko FUKUDA[1], Hiroshi WATANABE[1], Chiko MATSUSAKA[1], Yoshio OHSHIRO[1], Kohsaku NITTA[1], Hiroshi YAHATA[1], Toshimasa ASAHARA[1], Kiyohiko DOHI[1], Satoru HARADA[2], Yorimitsu TATSUKAWA[3], Hiroyuki KAMIKAWA[4], Takashi OOKUBO[5], Hiroshi SASAKI[5], Tatsuhiro YAMASHITA[6], Katsuki YASUDA[7], Hirofumi NAKAYAMA[8] and Hisao ITO[8]

1) *Second Department of Surgery, Hiroshima University School of Medicine, 1-2-3, Kasumi, Minami-ku, Hiroshima 734, Japan*
2) *Harada Hospital, 1-8, Hirose, Naka-ku, Hiroshima 730, Japan*
3) *Sanyoh Clinic, 2-8-2, Nogami, Fukuyama 720, Japan*
4) *Kamikawa Clinic, 1165-1, Tohkaichi, Miyoshi 728, Japan*
5) *Fukuma Hospital, 1-11-3, Kannonhonmachi, Nishi-ku, Hiroshima 733, Japan*
6) *Yamashita Clinic, 15-10, Kuchida, Asakita-ku, Hiroshima 739-17, Japan*
7) *Yasuda Surgical Hospital, 3365, Shimono, Takehara 725, Japan*
8) *First Department of Pathology, Hiroshima University School of Medicine, 1-2-3, Kasumi, Minami-ku, Hiroshima 734, Japan*

## ABSTRACT

The present study describes surgical resection in 23 patients under maintenance hemodialysis with hyperparathyroidism. Twenty-three patients under maintenance hemodialysis had subtotal parathyroidectomy (s-PTx, n=12) or parathyroid gland transplantation combined with total parathyroidectomy (Tx, n=11) performed from January 1979 to January 1991. Their ages ranged from 8 to 63 years.

The PTH levels were elevated in all patients preoperatively from 2.5 to 120 times over the upper limit of normal. After s-PTx, PTH levels sharply declined in all but one patient. Clinical symptoms improved in 11 cases with PTH decrease. After Tx, an abrupt decline in PTH was observed after surgery in 10 patients. One patient was reoperated because of persistent hyperparathyroidism. Another patient showed a PTH increase 13 months after surgery. The transplanted parathyroid gland was subtotally resected. Five months after reoperation, the condition recurred and the patient underwent total resection of the transplanted parathyroid gland and its re-autografting into the forearm.

In the patients with renal hyperparathyroidism, s-PTx or Tx improved clinical symptoms; this indicates the high reliability of both procedures in treating the disease. A long-term follow-up study must be conducted to check the possible postoperative recurrence of hyperparathyroidism from residual and/or autograft parathyroid gland.

***Key words:*** *Secondary hyperparathyroidism, Chronic renal failure, Parathyroidectomy, Renal osteodystrophy*

The occurrence of hyperparathyroidism associated with chronic renal failure has long been recognized. In 1960, Stanbury et al[12] performed elective subtotal parathyroidectomy (s-PTx) in patients with hyperparathyroidism and observed mitigation or elimination of clinical manifestations. They suggested that s-PTx could normalize the metabolism of phosphorus and calcium by reducing the functional parathyroid gland volume. In 1967, Ogg et al[6] described the effectiveness of total parathyroidectomy (PTx). However, Radke and coworkers[9] reported in 1976 that multiple fracture developed in dialysis patients after PTx, resulting in death, and argued against the validity of this procedure. With recent increases in the number of patients undergoing prolonged dialysis, recurrence of secondary hyperparathyroidism after s-PTx has been a focus of surgeons' concern[13]. In 1975, Wells et al[14] reported successful results of parathyroid gland transplantation combined with total parathyroidectomy (Tx) in patients with renal hyperparathyroidism. Since then, Tx or s-PTx has been popularly carried out as a surgical treatment for renal hyperparathyroidism[2]. The present paper describes the findings on 23 patients with renal hyperparathyroidism, and their postoperative follow-up during 6 months to 10 years.

**Table 1.** Surgical treatment for renal hyperparathyroidism

| | Male | Female | No. of cases |
|---|---|---|---|
| Subtotal parathyroidectomy | 5 | 7 | 12 |
| Parathyroid gland transplantation combined with total parathyroidectomy | 7 | 4 | 11 |
| Total No. | 12 | 11 | 23 |

## MATERIALS AND METHODS

The indications for surgical treatment were evident clinical features of hyperparathyroidism (bone decalcification, subperiosteal resorption, pathologic fracture etc.), biochemical abnormalities that progressed despite aggressive medical management, and promise of symptomatic improvement or prevention of complications due to parathyroidectomy. According to our criteria, 23 dialysis patients with chronic renal failure between January 1979 and January 1991 were treated surgically. The cases were divided into two groups: 12 undergoing s-PTx and 11, Tx (Table 1). Tx was performed, as a rule, for patients treated after July 1986.

The subjects consisted of 12 men and 11 women, aged 8 to 63, who had been under dialysis for 2 to 10 years until operation.

Our usual surgical procedure was to use a transverse collar skin incision with subplatysmal flap dissection and midline splitting of the cervical strap muscles. The thyroid gland was mobilized anteromedially. Recurrent laryngeal nerves were identified and protected. A systemic research for parathyroid tissue was then begun.

The resected parathyroid gland weighed 0.47 to 14.25 g. As s-PTx, the remaining parathyroid gland was 20 to 180 mg. As autografts, 30 to 50 mg of the resected parathyroid gland tissues, 1 $mm^3$ in size, were transplanted into the muscle of the forearm (or the sternocleidomastoid muscle in two cases).

The tissue removed was verified by frozen section. Some tissue was routinely cryopreserved for the potential of hypoparathyroidism.

Ionized calcium in the blood was monitored after the operation; if it decreased, calcium gluconate was administered. When oral intake became possible, oral calcium drugs or activated vitamin $D_3$ was given.

## RESULTS

1) Clinical manifestations of renal hyperparathyroidism

Preoperative clinical findings included bone pain and/or fracture in all patients. Ectopic calcification was observed in two patients; severe pruritus, in one.

2) PTH levels after s-PTx

Preoperative PTH values were elevated from 2.7 to 35.4 times over the upper limit of normal value (Fig. 1). However, postoperative PTH levels sharply declined in all but one patient; there have been no increases in PTH in three patients followed up for 10 years. It is interesting that clinical symptoms improved in 11 cases of PTH decrease, while neither PTH decrease nor symptomatic improvement was noted after surgery in one case. No significant correlation was found between preoperative PTH values and parathyroid gland weights.

3) PTH level after Tx

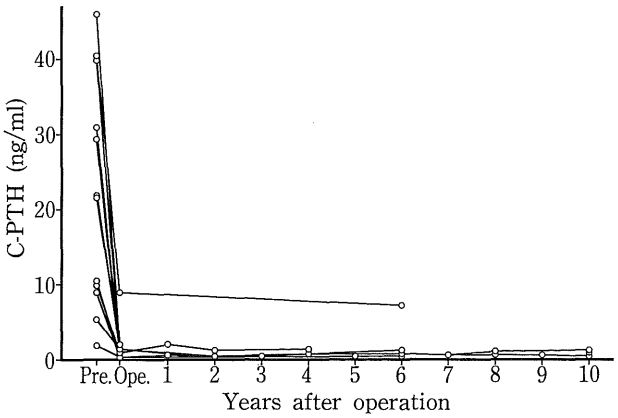


**Fig. 1.** The changes in the levels of serum PTH after subtotal parathyroidectomy in 12 patients with renal hyperparathyroidism.

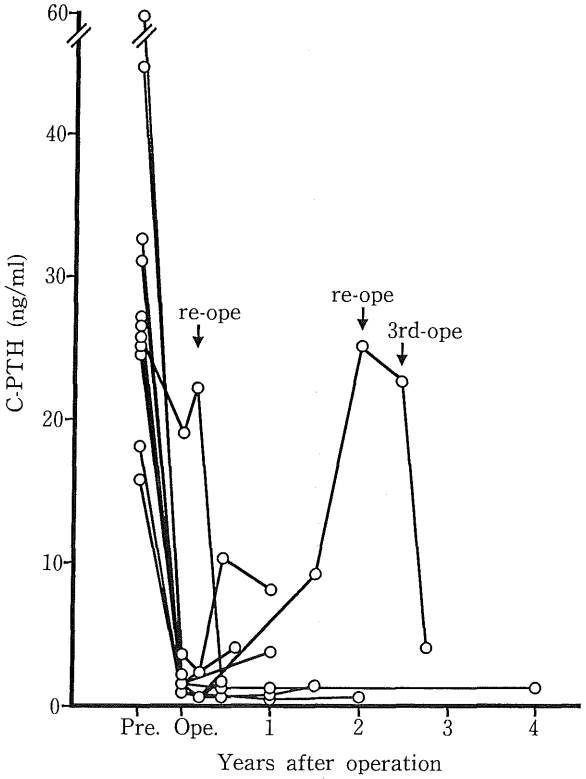


**Fig. 2.** The changes in the levels of serum PTH after parathyroid gland transplantation combined with total parathyroidectomy.

**Table 2.** Recurrent or persistent renal hyperparathyroidism

| | The first operation | | | The second operation | | | The third operation | | |
|---|---|---|---|---|---|---|---|---|---|
| | Operative method | Wt. of extirpated glands (g) | Histology | Duration after the first ope. | Histology | Operative method | Duration after the 2nd ope. | Histology | Operative method |
| O.O. (39y.o. Male) | Total PTx 3 gland; parathyroid 1 gland; thyroid 50mg was transplanted | 3.9 | Chief cell hyperplasia | 3 months | Chief cell hyperplasia | Parathyroid tumor located below the thyroid was removed | | | |
| K.K. (43y.o. Male) | Total PTx 40mg was transplanted | 4.9 | Chief cell hyperplasia | 13 months | Chief cell hyperplasia | Subtotal resection of transplanted glands | 5 months | Adenoma | Total resection of transplanted glands (7g). 25 mg was transplanted. |

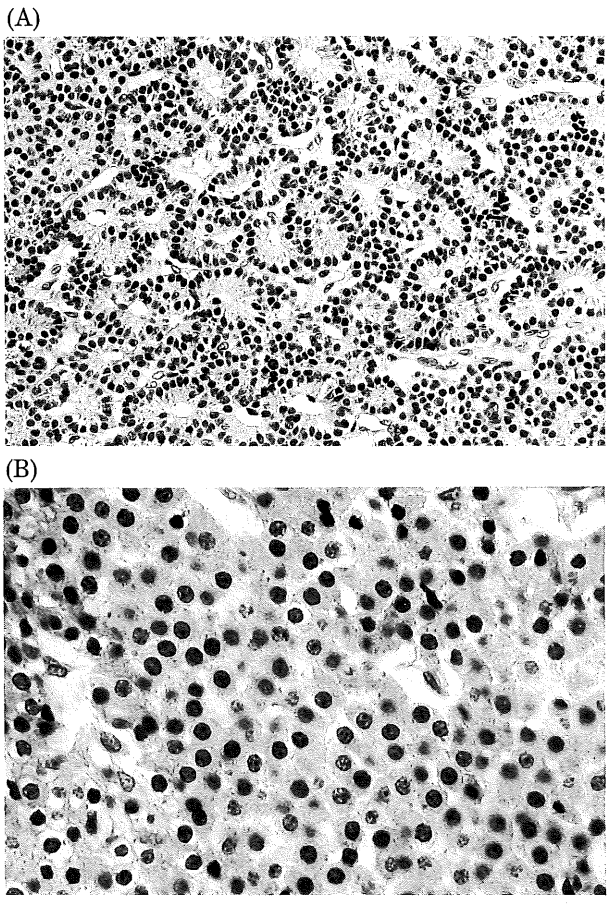

**Fig. 3.** Hyperplasia of the parathyroid gland
A: Chief cell hyperplasia. Chief cells are arranged in acini. The cytoplasm are clear and the nuclei are basally oriented (×140, HE stain).
B: Oxyphil cell hyperplasia. The Oxyphilic cell shows a sheet like pattern without cellular atypia (×550, HE stain).

Tx was performed in 11 patients treated, as a rule, after July 1986. Preoperative PTH values were elevated from 32 to 120 times over the upper limit of normal value. As shown in Fig. 2, an abrupt decline in PTH was observed after surgery in 10 patients. In one patient, neither PTH decline nor symptomatic improvement was seen after surgery; the patient was then treated by resection of four parathyroid glands (Table 2), one of which was found by postoperative histologic examination to be part of the thyroid gland, and not a parathyroid gland. Three months after surgery, the patient was reoperated, and has had an uneventful postoperative course with relieved arthralgia and mitigation of other clinical symptoms.

Patient KK showed a PTH decrease sooner after surgery. Postoperative histologic examination showed chief cell hyperplasia (Fig. 3). However, 13 months after operation the level of PTH increased. Swelling of the graft in the forearm was clinically observed. The PTH level in the venous blood of the forearm was three times higher than that in the contralateral forearm; integration of $^{201}$TlCl - $^{99m}$Tc subtraction was also evident only in the parathyroid autotransplanted forearm. Thus autotransplantation-induced hyperparathyroidism was diagnosed. The transplanted parathyroid gland was subtotally resected. The histologic diagnosis was chief cell hyperplasia. Five months after reoperation, the condition recurred and the patient underwent total resection of the transplanted parathyroid gland and its re-autografting into the forearm. Microscopically, the lesion was not encapsulated but well circumscribed. It consisted predominantly of cells with slightly granular, occasionally vacuolated cystoplasm (Fig. 4). The nuclear size was relatively uniform but huge clustered hyperchromatic nuclei were noted. Mitoses were extremely rare. The cells showed a wide variety of mixed patterns: solid sheets of cell nests, trabeculae or tubular structures. Nodular appearance was absent. The vascular stroma showed no amyloid deposition. The lesion was considered to be a chief-cell adenoma showing tertiary hyperparathyroidism. No malignant findings were observed.

Table 3 summarizes the therapeutic effect of

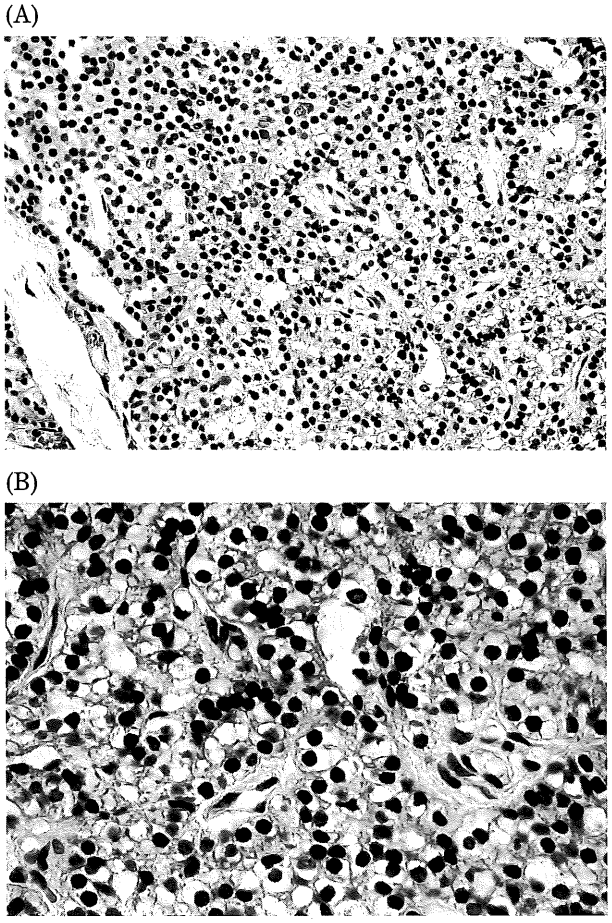

**Fig. 4.** Adenoma of the parathyroid gland
A: The tumor cells show a glandular structure with compact arrangement. The stroma of the tumor is vascular rich without apparent fibrous tissue. (×140, HE stain).
B: The tumor cells show a slightly pleomorphic appearance with a perinuclear clear cytoplasmic area. (×550, HE stain).

s-PTx or Tx. Tx gave rise to recurrence in one of the 11 cases. Improvements in symptoms were observed in 11 of the 12 s-PTx cases and in 9 of the 11 Tx cases. As a conclusion, both operations were highly reliable.

## DISCUSSION

In chronic renal failure, several regulatory and metabolic mechanisms are operative in the maintenance of intracorporeal homeostasis. Renal hyperparathyroidism seems to be a condition produced by excessive functioning of those mechanisms.

With recent advances in molecular biology, PTH biosynthesis and secretory regulations in the parathyroid glands have been gradually elucidated[3,8,11]. It has been reported that 1,25 $(OH)_2D_3$ inhibits PTH biosynthesis at the receptor level in parathyroid cells. In human chronic renal failure, a decrease in 1,25 $(OH)_2D_3$ receptors in the parathyroid glands has been observed[3]. It has also been obvious at the m-RNA level that 1,25 $(OH)_2D_3$ receptors are under down-regulation by PTH while being under up-regulation by 1,25 $(OH)_2D_3$[10]. These experimental data imply the importance of 1,25 $(OH)_2D_3$ in the treatment of renal hyperparathyroidism.

There has been controversy over whether s-PTx or Tx is recommendable as an operative procedure. While s-PTx has the great advantage of one operative field and the sizable drawback of operative difficulty at recurrence, Tx poses the risk of cancerization of the transplanted gland, which is apt to swell, presumably because of excess residual parathyroid gland[1].

Ohara et al[7] reported that the incidence of recurrent or persistent hyperparathyroidism was 5 to 12.5% (mean, 8.1%) for s-PTx, and 3 to 25% (mean, 4.8%) for Tx. Saxe and associates[10] reported figures of 12% and 6.4%, respectively. Niederle and co-workers[5] observed post-Tx recurrence of hyperparathyroidism in 4.6% of their relevant patients. In our experience, recurrent or persistent hyperparathyroidism developed in 1 of 12 s-PTx cases (8.3%) and in 2 of 11 Tx cases (18.2%), slightly higher than the figures reported by others. Evidence from other reports, however, shows that Tx is currently preferable since it allows excision under local anesthesia, as compared with s-PTx which requires extensive surgical invasion and difficult cervical manipulations at reoperation[5,7,10,13].

In the present study there was recurrence in one of the 11 Tx cases; histologic examination revealed that it was due to parathyroid gland adenoma, which show evidence of acquired proliferative character by the autograft (Fig. 4). Possible factors involved in postoperative recurrence seem to be stimulants such as hypocalcemia, changes in PTH secretory kinetics of hyperplastic parathyroid remainders, and acquisition of tumorous character by autografts[1,13]. Long-term follow-up study is therefore needed to check the postoperative recurrence of hyperparathyroidism.

**Table 3.** Results of surgical treatment for renal hyperparathyroidism

| | No. of cases | No. of recurrence | No. of improvement of clinical observation |
|---|---|---|---|
| Subtotal parathyroidectomy | 12 | 0 | 11/12 |
| Parathyroid transplantation combined with total parathyroidectomy | 11 | 1 | 9/11 |

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