Case Report

Transient Thyrotoxicosis After Parathyroidectomy in a Hemodialysis Patient with Secondary Hyperparathyroidism

Chieko Hamada, Yuichi Tanaka, Tomoko Sakamoto, Kayo Kaneko, Ichiyu Shou, Mitsumine Fukui, Masaki Fukazawa,[1] Yasuhiko Tomino

A 51-year-old Japanese male had been maintaining hemodialysis for 20 years. He had advanced secondary hyperparathyroidism. He had total parathyroidectomy (PTX) and autotransplantation in 2003. After the operation, clinical and endocrinologic findings showed transient thyrotoxicosis. There was no immunologic finding compatible with Graves' disease and chronic thyroiditis. After PTX, radioisotope accumulation markedly decreased on $^{99m}TcO_4^-$ thyroid gland scintigram and blood flow diminished on thyroid gland ultrasonogram. These findings absolutely recovered with the resolution of thyrotoxicosis within 1 month. It appears that disturbance of the microcirculation in the thyroid gland by manipulation during operation might be a cause of transient thyrotoxicosis after PTX. It is important to consider transient thyrotoxicosis as a complication of PTX in secondary hyperparathyroidism. [*Hong Kong J Nephrol* 2007;9(1):45–9]

Key words: chronic renal failure, parathyroidectomy, secondary hyperparathyroidism, thyrotoxicosis

本個案是一位 51 歲的日藉男性病人，已持續接受血液透析達 20 年。在 2003 年，病人因晚期次發性副甲狀腺亢進而接受了副甲狀腺的全部切除 (PTX) 及自體移植術，並於術後出現與短暫性甲狀腺毒症相關的臨床及內分泌表現，但缺乏與葛瑞夫氏病或慢性甲狀腺炎相符的免疫學變化。術後的 $^{99m}TcO_4^-$ 甲狀腺放射性同位素掃描顯示同位素活動的明顯下降，甲狀腺超音波則發現血流的減少；隨著甲狀腺毒症的消失，這些變化亦完全回復正常。目前相信，病人於 PTX 術後的短暫性甲狀腺毒症，可能歸因於甲狀腺微循環受 PTX 的影響。從本個案可見，對於須接受 PTX 的次發性副甲狀腺亢進症患者，短暫性甲狀腺毒症是術後的可能併發症之一。

Introduction

Advanced secondary hyperparathyroidism (2HPT) is a major complication in patients on dialysis. Management of hyperphosphatemia and hypocalcemia using phosphorous binders and vitamin D preparation is first-line therapy in 2HPT. Patients whose serum phosphorus (Pi) and calcium (Ca) levels are within guideline limits receive vitamin D pulse therapy [1]. As the therapy often presents elevation in serum Pi and Ca levels, it is impossible to maintain parathyroid hormone (PTH) concentration between 150 and 300 pg/mL. Around 2% of dialysis patients in Japan receive parathyroidectomy (PTX) and/or percutaneous ethanol injection of parathyroid (PEIT) [2]. In 1960, PTX was performed in hemodialysis patients with 2HPT [3]. Total PTX with partial subcutaneous transplantation is widely used in patients with 2HPT since many patients with subtotal PTX have recurrent hyperparathyroidism [4–8]. However, it is difficult to identify residual and/or slightly enlarged parathyroid glands before and during PTX. Here, we report a hemodialysis patient with the complication of transient thyrotoxicosis due to intraoperative thyroid gland manipulation after PTX.

Case Report

A 51-year-old Japanese man was admitted to Juntendo University Hospital because of lumbago, irritation and

Division of Nephrology, Department of Internal Medicine, and [1]Department of Surgery, Juntendo University School of Medicine, Tokyo, Japan.
Address correspondence and reprint requests to: Professor Yasuhiko Tomino, Division of Nephrology, Department of Internal Medicine, Juntendo University School of Medicine, 2-1-1 Hongo, Bunkyo-ku, Tokyo 113-8421, Japan.
Fax: (+81) 3-5802-1064; E-mail: yasu@med.juntendo.ac.jp

skin pruritus. He was placed on hemodialysis in 1984 in another hospital due to chronic glomerulonephritis and was diagnosed with 2HPT several years ago. Severe hypercalcemia and hyperphophatemia attributed to resistance to vitamin D_3 treatment had been observed for 2 years. He was transferred to our hospital to evaluate the degree of 2HPT and to determine if PTX was indicated. Laboratory data on admission are shown in Table 1. The levels of intact PTH, Ca and Pi in sera significantly increased although bone alkaline phosphatase (ALP) activity was in the normal range. Three enlarged parathyroid glands were detected by ultrasonography. He had no special family history and no previous autoimmune disease, including thyroid disease.

Three enlarged parathyroid glands (one on the right, two on the left) were detected by ^{99m}Tc-methoxyisobutylisonitrile (MIBI) scintigraphy. No ectopic parathyroid gland was observed on scintigraphy. The three identified hyperplastic parathyroid glands were removed easily by surgery, but the remaining right upper parathyroid gland was not detected during the neck exploration. The histologic diagnosis of all excised parathyroid glands was hyperplasia. A section of a parathyroid gland was implanted in the right forearm. The level of intact PTH rapidly decreased from 90.1 pmol/L to 0.7 pmol/L 7 days after the operation. Three days after PTX, the patient had a high fever (38°C) with tachycardia (heart rate, 199 beats/min from around 65 beats/min). Flomoxef sodium (FMOX) 0.5 g had been administered daily for 3 days postoperatively in order to prevent infection, but after the appearance of the high fever, the antibiotic was changed to imipenem/cilastatin sodium (IPM/CS) 0.5 g/day.

No impairment of physiologic status or evidence of infection was observed. According to thyroid function tests, thyrotoxicosis was confirmed (Table 2). On day 10, the serum levels of free triiodothyronine (FT3), free tyroxine (FT4) and thyroglobulin were elevated. The serum level of thyroid-stimulating hormone (TSH) was markedly decreased. Within 14 days after PTX, the clinical findings attributed to thyrotoxicosis such as fever, sweating and tachycardia subsided without any treatment. The cause of thyrotoxicosis might not be immunologic disorders since antithyroid peroxidase, anti-thyroglobulin and anti-TSH receptor antibodies were not detected. The findings of $^{99m}TcO_4^-$ thyroid gland scintigraphy are shown in Figure 1. The level of radioisotope (RI) uptake after 20 minutes on day 18 after PTX was 0.45%, which is equal to the background levels. The values recovered to the normal range 7 months later. The blood flow in thyroid tissues was shown to be decreased on ultrasonography 17 days after the operation (Figure 2). Blood flow returned to normal 4 months after thyroid function tests showed normal results.

Table 1. Laboratory data on admission

Parameter	Value on admission	Normal range
WBC	4,400/mL	3,900–9,700/mL
RBC	330×10^4/mL	$430 \times 10^4 – 56 \times 10^4$/mL
Hemoglobin	10.9 mg/dL	13.4–17.1 mg/dL
Hematocrit	32.6%	40.4–51.1%
Platelet count	22×10^4/mL	$15.3–34.6 \times 10^4$/mL
Total protein	10.9 μg/L	65–85 μg/L
Albumin	594.5 μmol/L	580–7,540 μmol/L
Urea nitrogen	15 mmol/L	3.2–7.5 mmol/L
Creatinine	1,071.4 mmol/L	53.0–88.4 mmol/L
Uric acid	374.9 mmol/L	208.3–410.6 mmol/L
Sodium	141 mmol/L	58.7–63.1 mmol/L
Potassium	4.9 mmol/L	0.89–1.28 mmol/L
Chloride	104 mmol/L	27.1–30.2 mmol/L
Calcium	2.78 mmol/L	2.20–2.64 mmol/L
Phosphorus	2.03 mmol/L	0.65–1.45 mmol/L
Intact PTH	90.1 pmol/L	
Osteocalcin	92 μg/L	3.1–12.7 μg/L
ALP	208 IU/L	110–348 IU/L
Bone ALP	81 IU/L	< 35.5 IU/L

WBC = white blood cell count; RBC = red blood cell count; PTH = parathyroid hormone; ALP = alkaline phosphatase.

Table 2. Thyroid function test results on day 10 after parathyroidectomy (PTX)

Parameter	Value 10 days post-PTX	Normal range
TSH	< 0.01	0.56–4.4 mU/L
Free triiodothyronine	7.6	3.4–7.2 pmol/L
Free thyroxine	31	9–22 pmol/L
Thyroglobulin	180	≤ 30 μg/L
Anti-TPO antibodies	≤ 300	≤ 300 U/L
Anti-thyroglobulin antibodies	≤ 300	≤ 300 U/L
Anti-TSH receptor antibodies	7.1	≤ 15%

TSH = thyroid stimulating hormone; TPO = thyroid peroxidase.

A significant increase in serum FT3 and FT4 was associated with a marked reduction in serum TSH after PTX (Figure 3). The levels of FT3 and FT4 in sera returned to the normal range within 1 month after the operation. The level of serum TSH was increased at 1 month after PTX and returned to the normal range 3 months later. Antithyroid peroxidase, anti-thyroglobulin and anti-TSH receptor antibodies in sera did not elevate for 12 months after improvement of thyroid function (data not shown).

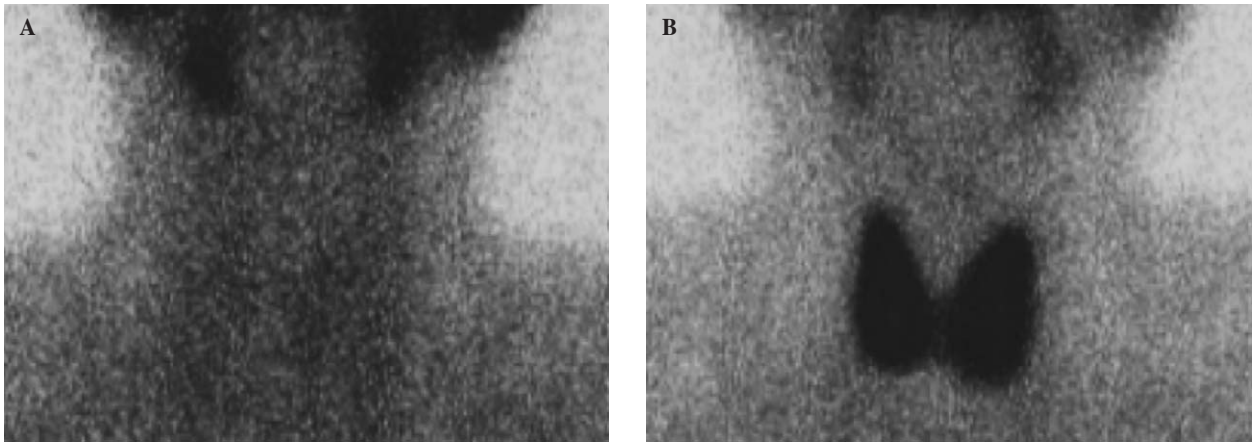

Figure 1. Findings of $^{99m}TcO_4^-$ thyroid gland scintigram. (A) The level of RI uptake 20 minutes after injection was 0.45%, equivalent to the background level on day 18 after parathyroidectomy (PTX). (B) Seven months post-PTX, the level of RI uptake 20 minutes after injection was 2.46%, i.e. it had recovered to the normal range.

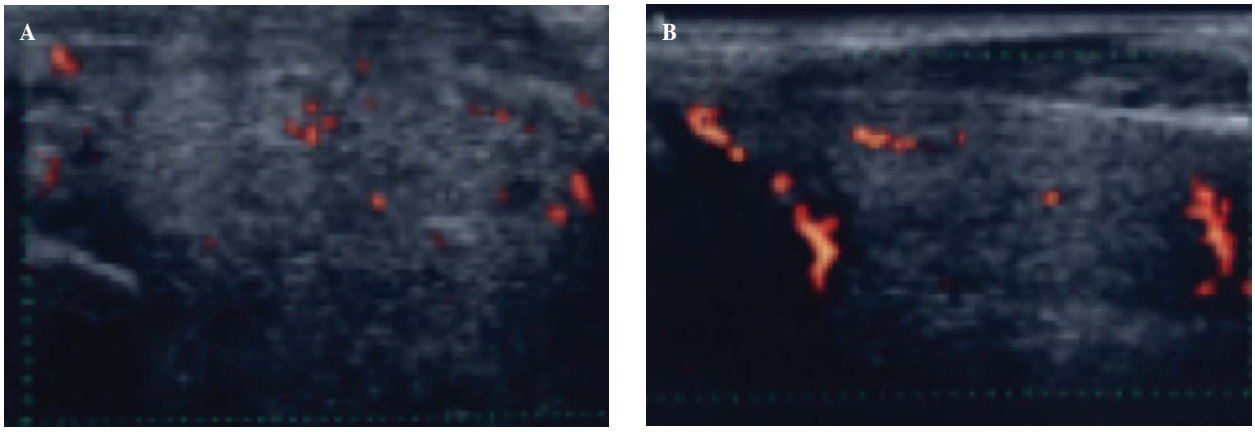

Figure 2. Ultrasonography of the thyroid gland shows: (A) decreased blood flow in thyroid tissues 17 days after parathyroidectomy (PTX); (B) normal blood flow 7 months after PTX, when thyroid function had also recovered to within normal levels.

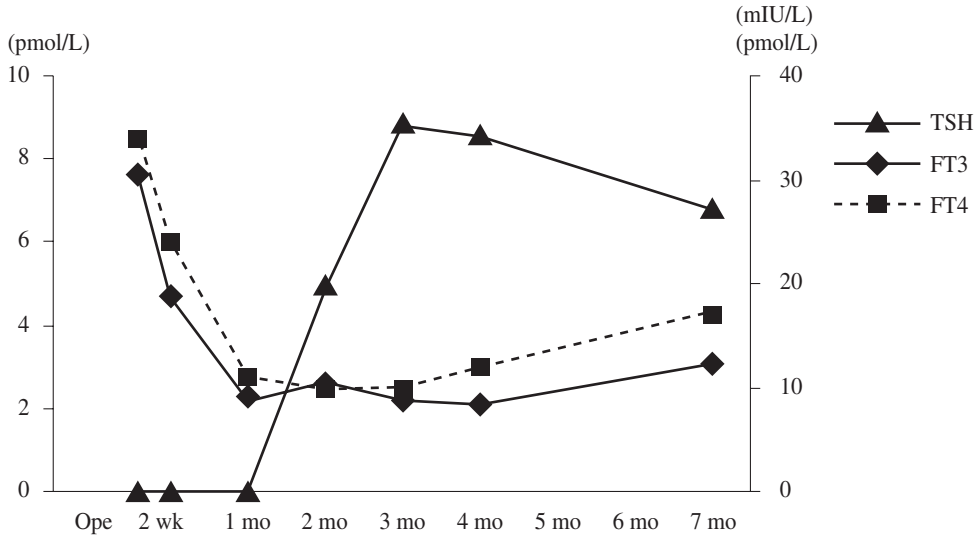

Figure 3. Thyroid function tests before and after parathyroidectomy. Ope = operation.

Discussion

In this report, we have described a hemodialysis patient with advanced 2HPT, with no thyroid function disorder, who had the complication of transient thyrotoxicosis after total PTX. Many dialysis patients have advanced 2HPT in Japan. It is generally recognized that there are various degrees of parathyroid hyperplasia in patients with advanced 2HPT. Vitamin D_3 pulse therapy or vitamin D_3 injection is the first line of treatment in hemodialysis patients with advanced 2HPT [9]. PTX is a well-known treatment for advanced 2HPT in patients with chronic renal failure; 10–30% of hemodialysis patients who have been on hemodialysis for more than 10 years undergo PTX [10]. In advanced 2HPT, multiple enlarged parathyroid glands are present. Post-PTX, some patients continue to have high PTH or experience an increase in intact PTH again, and enlarged residual parathyroid glands have been found in patients with subtotal PTX [4,6,7]. Total PTX and subcutaneous autotransplantation has recently been performed in patients with 2HPT. Since 15–20% of parathyroid glands are present in an ectopic region, about 15% of patients have more than five parathyroid glands [11]. Therefore, it is difficult to identify all the parathyroid glands, including normal parathyroid glands, before and during the operation.

Complications of PTX include injury of recurrent nerves or thyroid arteries, remaining parathyroid glands and hematoma. The most common complication is nerve injury. To remove all parathyroid glands completely, including non-enlarged or ectopic parathyroid glands, looking for the parathyroid glands in extensive cervical region and intraoperative histologic examinations need to be performed. During operation, recurrent nerves and thyroid arteries are marked by ribbons and stretched to place out operation area; these manipulations might induce ischemia, bleeding and adhesion with thyroid destruction. In the present case, three enlarged parathyroid glands were detected before the operation. Since parathyroid glands resemble lymph nodes or fatty tissues, the residual non-hyperplastic parathyroid gland was examined pathologically behind the thyroid gland during the operation.

This patient showed non-infection high fever with tachycardia due to thyrotoxicosis several days after PTX, but these signs improved without any treatment. Since the patient had no thyroid dysfunction before preoperatively, and thyrotoxicosis recovered completely within 1 month prior to recovery of blood flow, the clinical findings were consistent with acute thyroiditis. It appears that palpation of the thyroid gland during neck exploration might produce the clinical and biochemical features of transient thyrotoxicosis. Walfish et al reported that patients with thyrotoxicosis after surgery did not have thyroidal pain and fever [12]. Transient thyroiditis occurred within 2 weeks after operation and recovered completely without treatment within a few months [13]. Lindbolm et al reported that 11 of 26 patients with primary hyperparathyroidism (1HPT) had increase of T4 and T3 concentration, along with elevated TSH level following PTX. They concluded that surgical manipulation of the thyroid gland is not solely responsible, but that a TSH-mediated mechanism may be a contributing factor [14]. Dudczak et at reported TRH-mediated release of TSH in response to decrease in serum Ca concentration, when sodium EDTA was administrated, which was recognized in healthy subjects [15]. As the level of serum TSH was completely suppressed at the peak of thyrotoxicosis, TRH-mediated TSH release is not applicable in this case.

The reason for the postoperative hyperthyroidism in this case is likely to be thyroid manipulation during parathyroid surgery, because thyroid ultrasonography and isotope thyroid scan were consistent with diffuse thyroiditis with remarked suppression of microcirculation. Stang et al examined the risk factors of postoperative hyperthyroidism in 199 consecutive patients who had parathyroid exploration for sporadic 1HPT. They manifested hyperthyroidism independent of age, severity of hyperparathyroidism, anatomic or pathologic features, operation time, and magnification of preoperative Ca concentration, but it was associated with use of lithium and bilateral exploration. They also reported that 15% of patients had symptoms. Of those, five patients (4%) were found to have thyrotoxicosis [1]. It is generally considered that 20% of patients with subtotal PTX have recurrent 2HPT [16,17]. Therefore, total PTX with or without autotransplantation in the forearm is recommended in patients with 2HPT. Lim et al reported that acute thyroiditis as a result of surgical manipulation or trauma following PTX for 2HPT occurred in a peritoneal dialysis patient [18]. He pointed out that the clinical picture resembled sepsis or acute inflammatory thyroiditis. As bilateral exploration is performed during total PTX in patients with 2HPT, it is important to be alert for postoperative thyrotoxicosis when patients have fever, tachycardia and watery diarrhea, which resemble sepsis. It is necessary to evaluate thyroid function before and after PTX in order to diagnose traumatic transient thyroiditis earlier and to avoid unnecessary treatment.

References

1. Young EW, Albert JM, Satayathum S, Goodkin DA, Pisoni RL, Akiba T, et al. Predictors and consequences of altered mineral metabolism: The Dialysis Outcomes and Practice Patterns Study. *Kidney Int* 2005;67:1179–87.

2. Statistical Survey Committee in Japanese Society for Dialysis Therapy 1999. *An Overview of Regular Dialysis Treatment in Japan as of December 31*. 1999 JSDT supply.
3. Stanbury SW, Lumb GA, Nicholson WF. Elective subtotal parathyroidectomy for renal hyperparathyroidism. *Lancet* 1960; 1:793–9.
4. Korzets Z, Magen H, Kraus L, Bernheim J, Bernheim J. Total parathyroidectomy with autotransplantation in hemodialysis patients with secondary hyperparathyroidism—should it be abandoned? *Nephrol Dial Transplant* 1987;2:341–6.
5. Higgins RM, Richardson AJ, Ratcliffe PJ, Woods CG, Oliver DO, Morris PJ. Total parathyroidectomy alone or with autograft for renal hyperparathyroidism? *Q J Med* 1991;79:323–32.
6. Zaraca F, Mazzaferro S, Catarci M, Saputelli A, Alo P, Carboni M. Prospective evaluation of total parathyroidectomy and autotransplantation for the treatment of secondary hyperparathyroidism. *Arch Surg* 1999;134:68–72.
7. Howard RJ, Pfaff WW. Parathyroidectomy in patients with chronic renal failure. *Am J Surg* 1998;175:302–4.
8. Zhong A, Billa V, Rotstein LE, Wong PY, Bargman JM, Vas SI, Oreopoulos DG. Recurrence of hyperparathyroidism after total parathyroidectomy and autotransplantation in peritoneal dialysis patients. *Perit Dial Int* 2000;20:200–8.
9. Packman KS, Demeure MJ. Indications for parathyroidectomy and extent of treatment for patients with secondary hyperparathyroidism. *Surg Clin North Am* 1995;75:465–82.
10. Tominaga Y. Surgical management of secondary hyperparathyroidism in uremia. *Am J Med Sci* 1999;17:90–7.
11. Numano M, Tominaga Y, Uchida K, Orihara A, Tanaka Y, Takagi H. Surgical significance of supernumerary parathyroid glands in renal hyperparathyroidism. *World J Surg* 1998;22:1098–102.
12. Walfish PG, Caplan D, Rosen IB. Postparathyroidectomy transient thyrotoxicosis. *J Clin Endocrinol Metab* 1992;75:224–7.
13. Musi N, Braverman LE, Norris CM Jr. Severe thyrotoxicosis after parathyroid surgery for hyperparathyroidism. *Am J Med* 2000; 108:519–20.
14. Lindblom P, Valdemarsson S, Westerdahl J, Tennvall J, Bergenfelz A. Hyperthyroidism after surgery for primary hyperparathyroidism. *Langenbeck's Arch Surg* 1999;384:575–8.
15. Dudczak R, Waldhausl WK, Bratusch-Marrain P. Effects of sodium EDTA and calcium infusion on prolactin and thyrotropin responses hormone in healthy man. *J Clin Endocrinol Metab* 1983; 56:603–7.
16. Tominaga Y, Tanaka Y, Sato K. Surgical treatment of secondary hyperparathyroidism. *J Bone Miner Metab* 1999;9:294.
17. Olson JA Jr, Leight GS Jr. Surgical management of secondary hyperparathyroidism. *Adv Ren Replace Ther* 2002;9:209–18.
18. Lim W, Luxton G, Hutchison B. Acute thyroiditis following parathyroidectomy for secondary hyperparathyroidism in a chronic renal failure patient. *Int Med J* 2003;33:131–7.