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The Management of Well-Differentiated Thyroid Cancer with End-Stage Renal Disease

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The occurrence of thyroid cancer in patients with end-stage renal disease is rare. We have had the experience of treating two such patients. The problems, encountered in these patients, were the enlarged parathyroid glands at the time of total thyroidectomy and the treatment of these patients with ^{131}I when the biologic half-life of radioiodine increases after hemodialysis. Both patients were treated by total thyroidectomy and postoperative administration of ^{131}I, either empirically or dosimetrically, and are living and well, 9 yr and 7 yr after operations, respectively.

Key Words: Well-differentiated thyroid cancer; end-stage renal disease.

Introduction

The combination of thyroid cancers in patients with end-stage renal disease (ESRD) is rare. Problems encountered in dealing with these patients included the enlarged parathyroid glands during a total thyroidectomy and the administration of ^{131}I for postoperative adjuvant treatment when the biologic half-life of radioiodine increases after hemodialysis. It is our purpose in this study to report our two experiences in the intraoperative management of parathyroids and the postoperative administration of radioiodine, either dosimetrically or empirically.

Case Report

Case A

A 48-yr-old male was noted to have hypertension and impaired renal function after an accident in 1988. Chronic glomerulonephritis was documented after a series of laboratory and other studies. Hemodialysis was begun in January 1993, when the patient began to show the signs and symptoms of uremia. In October 1993, the patient was admitted to the hospital because of a nodular lesion in the neck, noted for 8 mo. He also complained of myalgia, present for 1 yr, and coughing, choking, and hoarseness of several months' duration. A fine needle aspirate of the nodular lesion in the neck showed a papillary carcinoma of the thyroid gland. Serum levels of calcium, phosphorus, alkaline phosphatase, BUN, creatinine, and PTH are shown in Table l. In 1993, a total thyroidectomy with a modified radical neck dissection was done. During the same operation, two enlarged parathyroid glands on the right side were removed. The glands weighed 150 and 200 mg. The final pathologic diagnosis documented the papillary thyroid carcinoma, which was 3 ↔ 2 ↔ 1 cm in size and in the right lobe. There were metastases in 5 of 19 lymph nodes. No pathologic diagnosis was rendered on the parathyroid glands, which were grossly enlarged. Three weeks later, treatment with radioiodine was begun with a dosimetric approach to determine the appropriate dose of radioiodine. The patient was put on a low phosphate and iodine-free diet for 3 wk prior to the start of treatment. Hemodialysis was then converted to continuous ambulatory peritoneal dialysis (CAPD). Two millicuries of ^{131}I was initially given and CAPD was begun. Six hours later, the dialysate was collected and a count was done. The identical procedure was then repeated. The counts in the dialysates showed that approx 60% of the initial dose of radioiodine was removed by each period of CAPD. At 18 and 24 h after administration of radioiodine, retention of ^{131}I sodium iodide is 6.4% and 2.6%, respectively . In addition, the whole body scan for ^{131}I on the same day showed two foci of avid uptake of ^{131}I in the thyroid bed and another focus in the right lower neck. Four days later, a therapeutic dose of 100 mCi of ^{131}I was administered. CAPD was then repeated every 6 h. A whole body scan done 10 d after the administration of ^{131}I showed that the areas of uptake demonstrated on the previous scan was the same (Fig. 1, left). A whole body scan done 6 months later revealed no demonstrable areas of uptake (Fig. 1, right). The patient appeared well at the follow-up examinations and the latest serum human thyroglobulin (hTG) level was below 0.5 ng/mL (Fig. 2).

Case B

A 54-yr-old male developed two masses in his right neck during a period of 1 yr. In 1985, the patient had bilateral

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Table 1
Laboratory Data of the Two Patients with ESRD and Thyroid Cancer During Hospital Course

	Total calcium (n = 8.4–10.6 mg/dL)	Phosphate (n = 2.1–4.7 mg/dL)	Intact-parathyroid hormone (n < 35.3 pg/dL)	Blood urea nitrogen (n = 7–20 mg/dL)	Creatinine (n = 0.5–1.5 mg/dL)	Alkaline phosphatase (n = 10–100 U/L)
Patient A						
Preoperation[a]	9.2	5.8	520	58	9.8	78
Postoperation	9.0	6.7	<15.5	72	14.3	65
Posttransplant[b]	7.7	2.1	<20.2	31	2.8	
Patient B						
Preoperation[c]	9.1	4.3	2.51*	52	7.7	118
Postoperation	7.8	2.9	0.20*	35	6.6	101

[a] 10/12/93, total thyroidectomy and right parathyroidectomies.
[b] 6/30/95, renal transplant.
[c] 7/24/85: subtotal parathyroidectomy.
*PTH-MM (n = 0.14–0.21 ng/mL).

renal calculi with secondary hyperparathyroidism and chronic renal failure. During that admission, serum levels of parathyroid hormone–mid-molecular (PTH-MM) was 2.51 ng/mL (n = 0.13-0.2 ng/mL). Serum levels of calcium and phosphorus were within normal limits, while serum levels of alkaline phosphatase, BUN, and creatinine were elevated (Table 1). A subtotal parathyroidectomy with preservation of half of the right superior parathyroid gland was done in 1985. Serum level of PTH-MM remained normal postoperatively. The pathologic diagnosis on the resected parathyroid glands was hyperplasia with a combined weight of 1800 mg. His renal function continued to deteriorate and a regular program of dialysis was initiated in 1988. The patient was readmitted to the hospital in 1995 because of the two stony hard nodules in his right neck. A fine needle aspirate of one of the nodules revealed a papillary thyroid carcinoma. A total thyroidectomy with dissection of the right cervical lymph nodes was then done. Pathologic examination showed metastases in four of seven lymph nodes. Treatment with radioiodine was initiated and the dose was determined by an empirical approach. After a low phosphate, iodine-free diet for 3 wk, the patient received an oral dose of 30 mCi of ^{131}I. The patient was then converted to a self-administered program of CAPD. The protocol for CAPD was similar to the one used with patient A. Following the oral dose, a whole body scan was done 10 d later. The scan showed several "hot spots" low in the right anterior neck and the superior mediastinum and diffuse uptakes in both lungs (Fig. 3, left). A therapeutic dose of 150 mCi of ^{131}I was then given. A whole body scan repeated 12 d later showed nearly complete resolution of the "hot spots" in the neck and mediastinum. The lungs continued to show a diffuse uptake (Fig. 3, right). The patient continues to be followed as an outpatient and is receiving thyroxine suppression of the thyroid gland. The last determination of serum levels of human thyroglobulin was low, <3-15 ng/mL. Serum Ca and i-PTH were within normal limits (Fig. 2).

Discussion

Patients with end-stage renal disease are susceptible to the development of malignant tumors, including thyroid cancers *(1–3)*. Probable explanations for this phenomenon include impaired function of the immune system, impaired DNA repair, and high serum levels of PTH. The increased risk for the development of thyroid cancers can also be attributed to the exposure of the structures contained within the neck to relatively high levels of radioactivity. Imaging techniques, in which radionuclides are used, are commonly employed during the management of patients with secondary hyperparathyroidism. In our patients, patient A had no clinical hyperparathyroidism, while in patient B hyperparathyroidism had been diagnosed 10 yr prior to the establishment of the diagnosis of thyroid cancer. The current consensus for the treatment of well-differentiated thyroid cancer with metastases in regional lymph nodes is total thyroidectomy with dissection of the neck for lymph nodes followed by radionuclide ablation therapy *(4)*. ^{131}I is predominantly excreted by the kidneys into the urine. The ideal dosage for radionuclide therapy in patients with normal renal function is controversial. The currently accepted dosage is 30 mCi for ablation of thyroid tissue, 75–100 mCi for metastases in regional lymph nodes, and 150–200 mCi for distant metastases. However, the treatment with similar doses of radionuclides in patients with end-stage renal disease could result in excessive exposure to radiation if immediate dialysis is not employed. Therefore, the dosage and the timing of the dialysis needs to be modified. Recent reports of the manage-

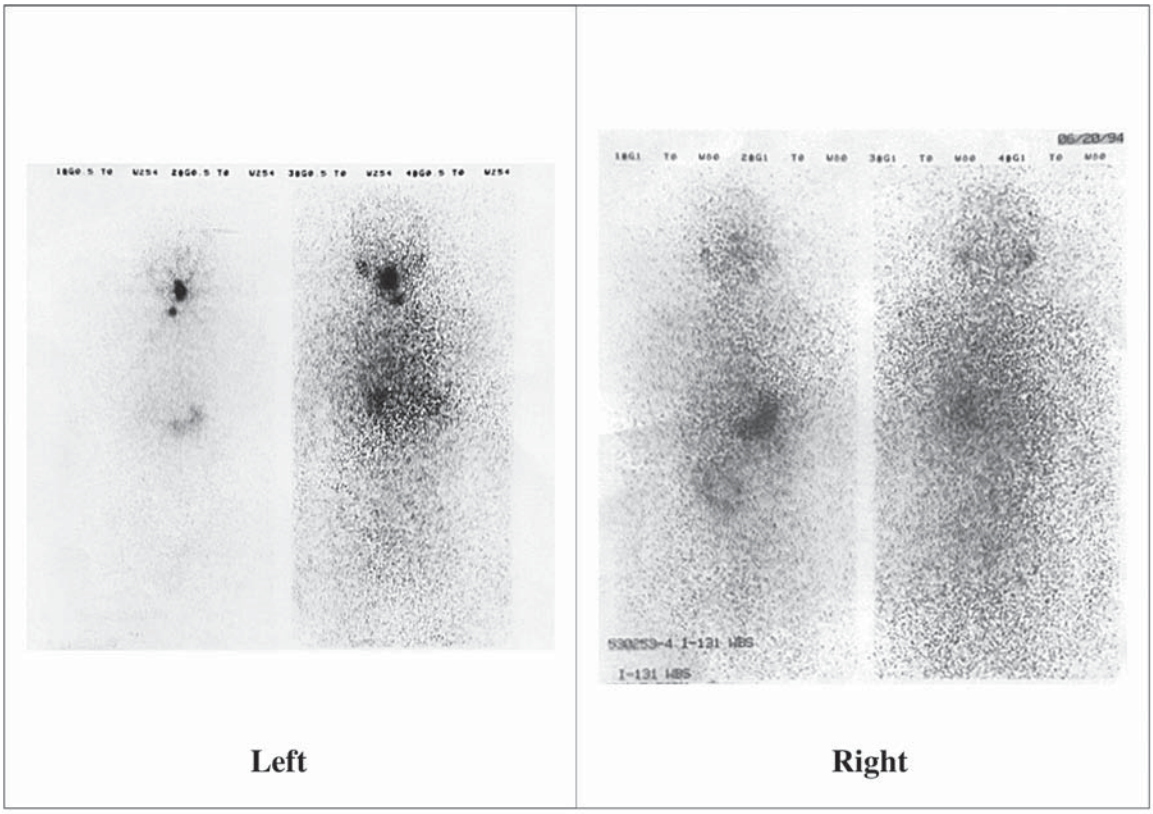

Fig. 1. ^{131}I whole body bone scans in a 48-yr-old male patient before (left) and after (right) radioiodine treatments. Left, whole body scan on 1994/1/4 showed uptake of ^{131}I in the thyroid bed and in the right lower neck (arrow). Right, whole body scan on 1994/6/20 revealed no demonstrable areas of uptake.

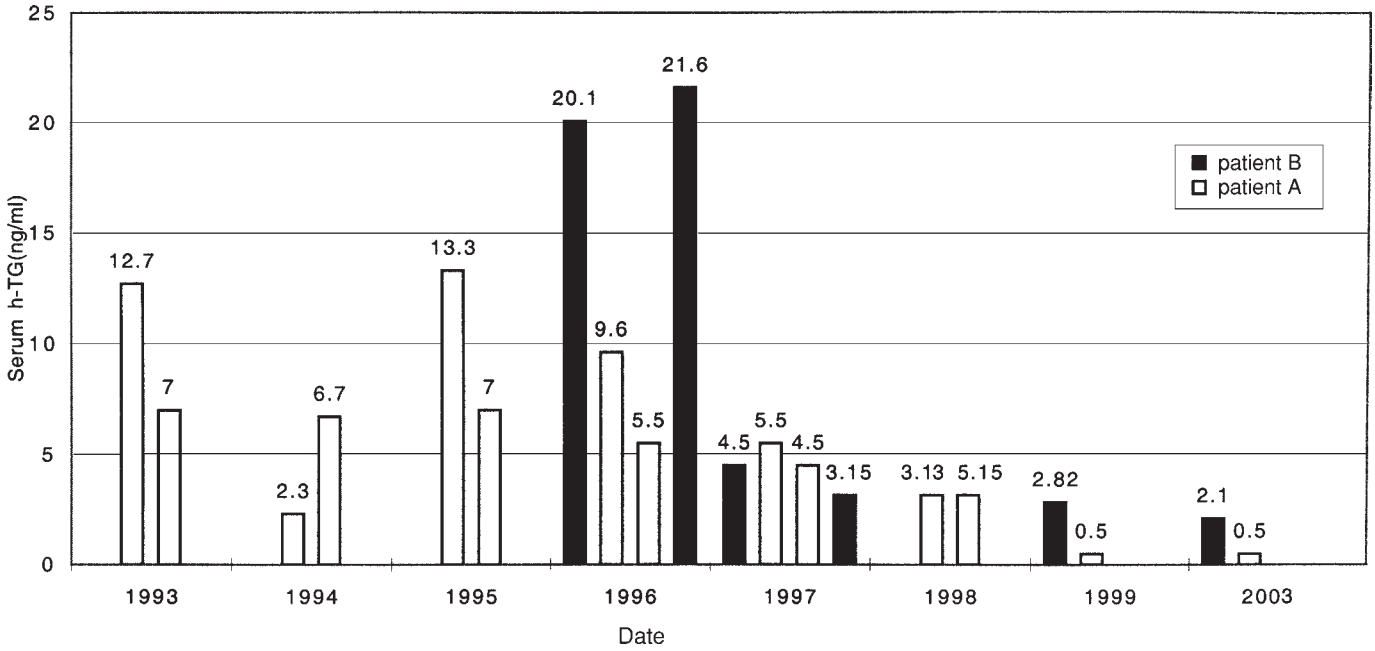

Fig. 2. The change of serum h-TG (off T4) level in the two patients of end stage renal disease with thyroid cancer.

ment of such patients indicate that the dosage of ^{131}I in patients treated by hemodialysis remains controversial *(5–7)*. The half-life of ^{131}I in patients with normal renal function is 8–11 h, and, according to Mello et al. *(5)*, with the use of intermittent hemodialysis at fixed intervals, the ideal dosage of radiation energy could be delivered to targeted lesions.

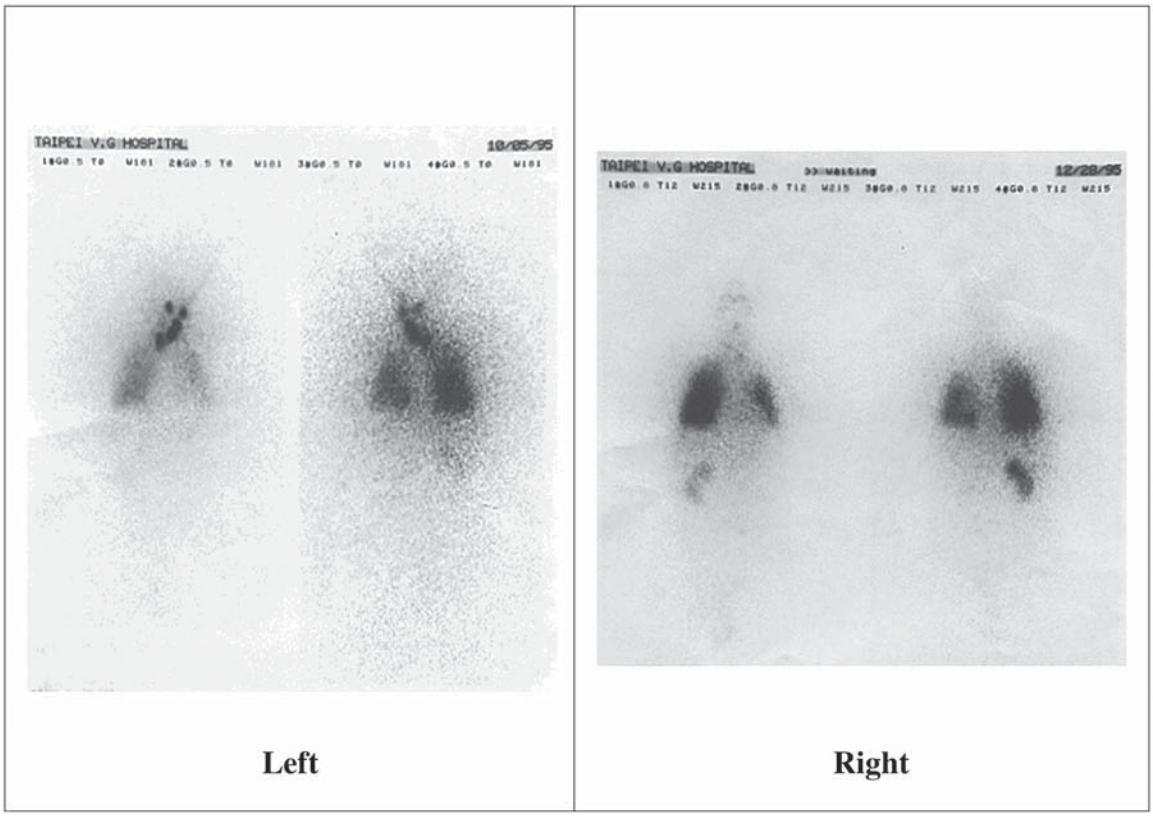

Fig. 3. ^{131}I whole body scan in a 54-yr-old male patient before (left) and after (right) radioiodine treatment. Left, whole body scan on 1995/10/5. Note there were several hot spots over neck (arrow) and both lungs. Right, whole body scan on 1995/12/28 revealed almost complete resolution.

In our scheme, by using 2 mCi of radioiodine and CAPD, the dose was similar but the time intervals were shorter, and the procedure could be performed in 1 d. Uptake of radioiodine by functioning thyroid tissue may reach the plateau at 18–24 h after treatment. The conservative estimation of retention of radioiodine in our cases is around 2.6–6.4%, which is much higher than the usual retention of 0.6% of administered dose in the thyroid remnants *(8)*. We used CAPD in preference to hemodialysis because of the ease with which contamination of the environment by radiation could be prevented. The management and disposal of radioactive dialysates were also simplified. Our procedure called for the first course of CAPD, followed by the oral administration of the ^{131}I. This was followed by three more courses of CAPD, each performed at intervals of 6 h. Both patients resumed hemodialysis after the treatment utilizing CAPD. They are both well with their serum levels of hTG at very low levels, suggesting successful management of their thyroid cancers.

Reactive enlargement of parathyroid glands is commonly seen in patients with ESRD. There is general agreement that parathyroidectomy is indicated in patients with calcification of soft tissue, osteodystrophy, bone pain, and other indicators *(9,10)*. However, there is much controversy concerning parathyroidectomies done in patients in whom the only indication is elevation of serum PTH (10), because normal serum PTH can be restored after successful renal transplantation unless autonomous parathyroid function develops *(11)*. Patients with ESRD are treated by life-long hemodialysis in countries with fewer available donated organs. However, secondary hyperparathyroidism is likely to occur under these circumstances *(12,13)* and some of these patients might need operations. To prevent increased risk of surgical complications in a patient with previous neck explorations, it may be wise to remove the bulk of the enlarged parathyroid glands, which are potentially more autonomous, and mark the remnants in case there is a second attempt at parathyroidectmy *(14,15)*. In patient A, no pathologic diagnosis was rendered on the parathyroid glands despite their evident size enlargement, but the patient was relieved of muscle aches after the bulk of the parathyroid glands was removed. Portions of the parathyroid glands were cryopreserved to be used if hypoparathyroidism developed from excessive resection of the glands.

In summary, these two case reports demonstrate the feasibility of an empirical and dosimetric approach in the treat-

ment of metastatic thyroid cancers after total thyroidectomy for well-differentiated cancers in patients with ESRD. To minimize contamination by radioactive materials, short-term CAPD is recommended.

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