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A Case of Plummer Disease Treated With Radioiodine Therapy

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A case of Plummer disease treated with radioactive iodine was described. A 74-year-old woman was examined for her thyroid mass, which had been unattended for 7 years, and was diagnosed as having Plummer disease. Laboratory tests showed high and low levels of thyroid hormones and TSH, respectively, but no clinical manifestation of hyperthyroidism was observed. Technetium 99m scintigraphy showed strong accumulation to the mass and suppressed accumulation to the normal part of the thyroid. Ultrasonography revealed apparent cystic change but no calcification. Malignancy of the lesion was excluded by cytological examination. The patient was administered 481 MBq of radioactive iodine 131 without restriction of iodine intake before the treatment. The hormone levels have been normalized in one after treatment, and abnormal intake of the radioisotope into the lesion has been normalized. Amongst possible treatments for the disease, radioiodine therapy, but not radical surgery, was chosen based on the patient's wishes.

Key words: Hyperthyroidism, Plummer disease, Radioiodine therapy

INTRODUCTION

Hyperthyroidism is a disease group in which hormone synthesis and its secretory function are enhanced in the thyroid gland. Plummer disease, rarely found in Japan, is evidenced by the formation of autonomous thyroid hormone-producing nodules. For treatment, surgical removal of the thyroid lesion with expectation of complete cure is often selected from among the possible choices, such as percutaneous ethanol injection therapy（PEIT）, antithyroid medication and radioiodine therapy. Our experience in radioiodine therapy for this disease is limited, although the treatment is listed as recommendation grade B in the American and European guidelines for treatment of the disease. Here we report a case of a 74 year old woman with Plummer disease successfully treated with radioactive iodine 131.

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CASE PRESENTATION

Clinical history

The patient: a 74 year old woman. Her thyroid mass had been noted and pointed out seven years previously, but she left it unattended as there had been no tendency of a goitrous increase, and no symptom of goiter. However, she had recently been advised by her urologist to have a thorough check-up because of goiter and abnormal levels of thyroid hormone.

Physical examination

The right lobe of the thyroid gland had grown to 3.5 cm in size, with hard elasticity and no tenderness. The left lobe had no abnormality by palpation.

Blood pressure was 132/76 mmHg; heart rate, 86/min; and, respiratory rate, 18/min. An electrocardiogram showed normal finding.

There was no exophthalmos, abnormal sweating, abnormality in breath sound or heartbeat, and no neurological abnormality was observed.

Blood findings

Because of the patient's history of diabetes, blood glucose level and HbAlc were high. In addition, CRP was at a high level. There were increased levels of thyroid hormones FT3 and FT4, and a decreased

level of thyrotropin TSH; however, an increase of thyroid autoantibodies was not seen (Table 1).

Table 1. Blood test results at first examination

RBC	421×10^4/μl
Hb	12.8 g/dl
Plt	16.3×10^4/μl
WBC	5830 /μl
BS	191 mg/dl
HbA1c	6.9%
LDH	212 IU/l
AST	20 IU/l
ALT	20 IU/l
T-bil	0.5 mg/dl
Amy	79 IU/l
BUN	18.0 mg/dl
Crea	0.48 mg/dl
TP	6.7 g/dl
CRP	1.51 mg/dl
HDL-C	45 mg/dl
LDL-C	142 mg/dl
TG	93 mg/dl
FT3	4.8 pg/ml (2.1-3.8 pg/ml)
FT4	1.7 ng/ml (0.8-1.5 ng/ml)
TSH	0.02 μU/ml (0.5-3.0μU/ml)
Thyroglobulin	430 ng/ml
Antithyroid antibody	Negative

Image findings

Cervical ultrasonography imaging found, in the right lobe of the thyroid gland, a mass having a longer axis of 3.5cm and a heterogeneous internal echogenicity. Cystic degeneration often occurs in the mass (Fig. 1). The estimated weight of the mass by measurement with ultrasonograpy was 30 g. Blood flow confirmation by ultrasonic color doppler showed an increase of macular blood flow (Fig. 2). The outline of the thyroid gland was undetectable due to the exclusion of the thyroid capsule by the mass. Contrast enhanced CT showed a mass 3.5 cm in size with internal heterogeneity and strong cystic degeneration in the right lobe of the thyroid gland. The mass had not infiltrated other organs clearly, yet it was as difficult to confirm the thyroid capsule as it was by ultrasonography findings. The mass had clear demarcation, so there was no doubt that it was malignant (Fig. 3). There was a significant accumulation in the right lobe and a reduced accumulation in the left lobe in the thyroid technetium 99m scintigraphy. Our reference value of uptake rate in the thyroid technetium 99m scintigraphy was 0.5-4%, and, from this point of view, the result was certainly within the criteria. But the uptake rate of our patient showed an abnormal laterality with 2.6% in the right lobe and 0.1% in the left, and

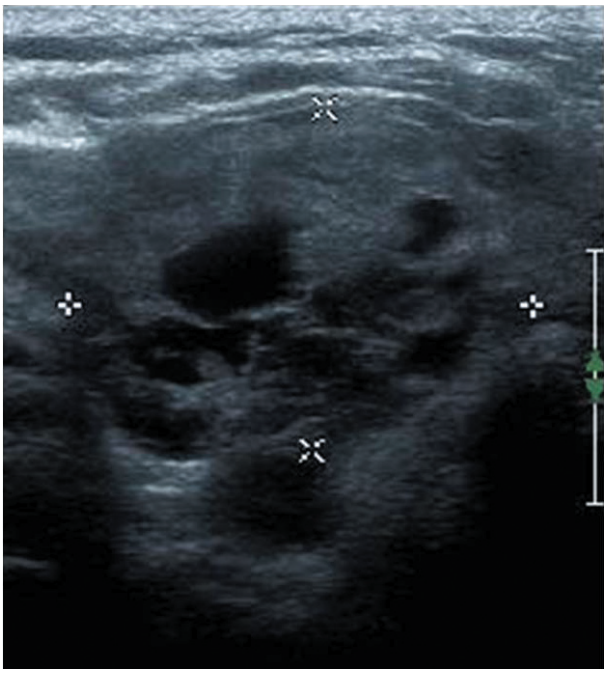

Fig. 1. Ultrasonography image. The mass 3.5cm in size is found in the right lobe of thyroid gland, and cystic degeneration is obvious within it.

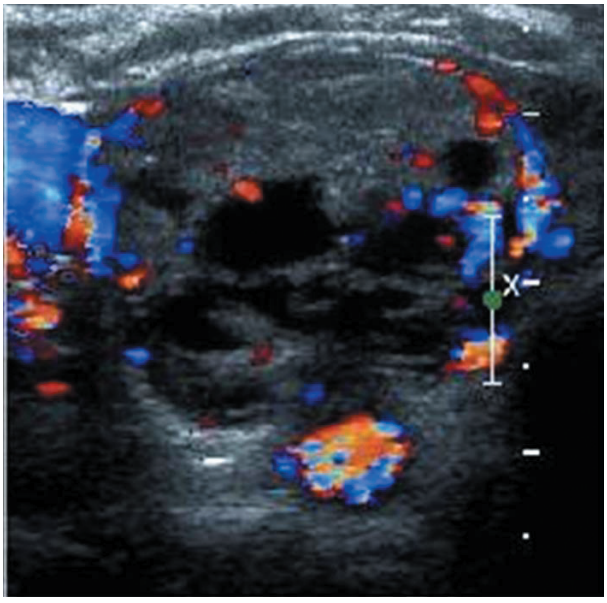

Fig. 2. Neck ultrasonography color Doppler. Increased vascular flow inside the mass.

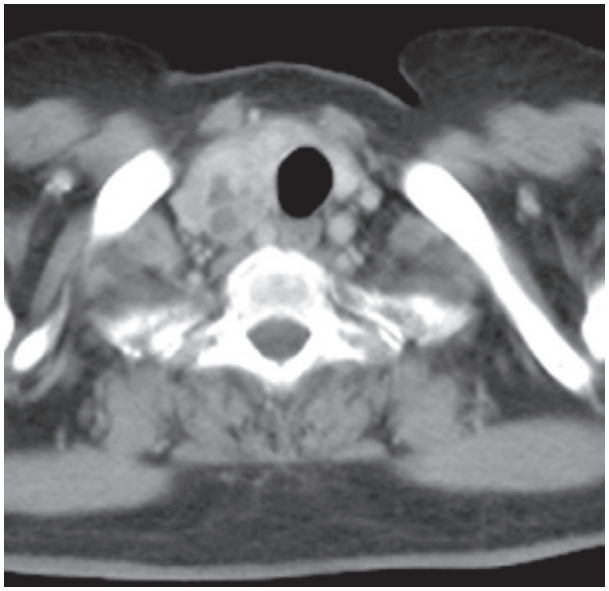

Fig. 3. Neck enhanced CT. A mass 3.5cm in size is visible in the right lobe of thyroid gland. It excludes the thyroid capsule, although the boundaries are clear. The mass inside shows conspicuous cystic degeneration is with a slight tracheal midline displacement.

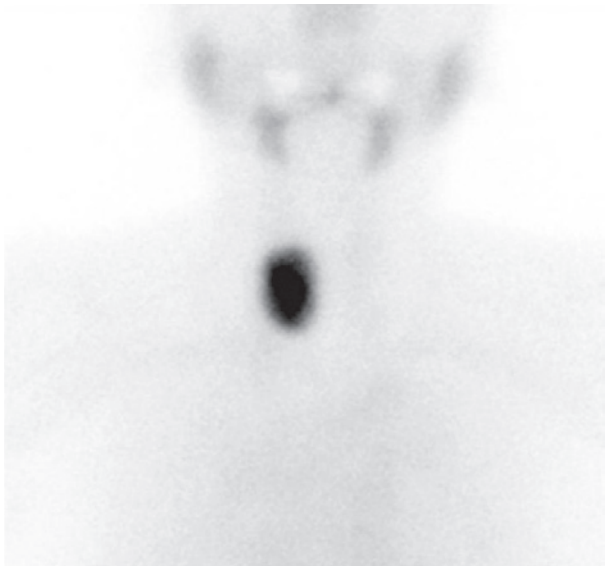

Fig. 4. Thyroid gland technetium 99m scintigraphy. The accumulation of the isotope is observed in the same location as the mass in the right lobe of thyroid gland, with almost no accumulation in the left. The abnormal accumulation indicative of an aberrant thyroid is absent.

also showed particularly strong accumulation in the nodule（Fig. 4）.

Thyroid gland aspiration cytology test

Malignancy was excluded by aspiration cytology, as reported class 3.

Treatment

Because the patient had no subjective symptoms, and clinical manifestations such as tachycardia or exophthalmos associated with hyperthyroidism were absent, she was not given an antithyroid agent. Instead, we considered other therapeutic approaches, taking the American Association of Clinical Endocrinologists guidelines into account. In our case, the mass size was large, so PEIT was considered inadequate. Of other potentially effective therapies, including surgery and radioiodine therapy, we chose the latter as the patient did not want the surgery.

Radioiodine therapy for hyperthyroidism due to Basedow's disease commonly includes a restricted iodine intake for about two weeks before the administration of radioactive iodine to prevent competitive accumulation of iodine. In case of radioiodine therapy for Plummer disease, the 2-week restriction of iodine intake in preparation is not required, and the administration of antithyroid drug is unnecessary, as maintaining the hyperthyroid state is essential to obtain an adequate accumulation of radioactive iodine.

Therefore, without particular preparation, we gave the patient 481 MBq of radioactive iodine 131 orally for a radiation dose. We imaged the iodine 131 by scintigraphy to confirm the radioactive iodine accumulation three days after the administration. Just like the technetium 99m scintigraphy before the treatment, we found a strong accumulation in the right lobe of the thyroid gland, and no accumulation in the left lobe（Fig. 5）. After administering

Fig. 5. Scintigraphy three days after the radioiodine therapy. Strong accumulation is detected in the right lobe of thyroid gland.

Table 2. Thyroid-related hormone levels before and after therapy.

	Before	9 months later
FT3	35.9 pg/ml	1.8 pg/ml
FT4	1.8 ng/ml	1.0 ng/ml
TSH	<0.01 μU/ml	2.02 μU/ml

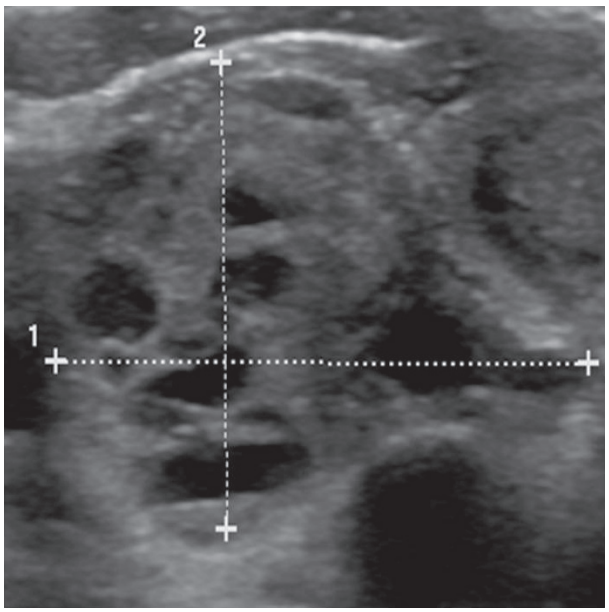

Fig. 6. Neck ultrasonography image nine months after the treatment. The maximum dimension of the mass is 3.0cm---slightly smaller.

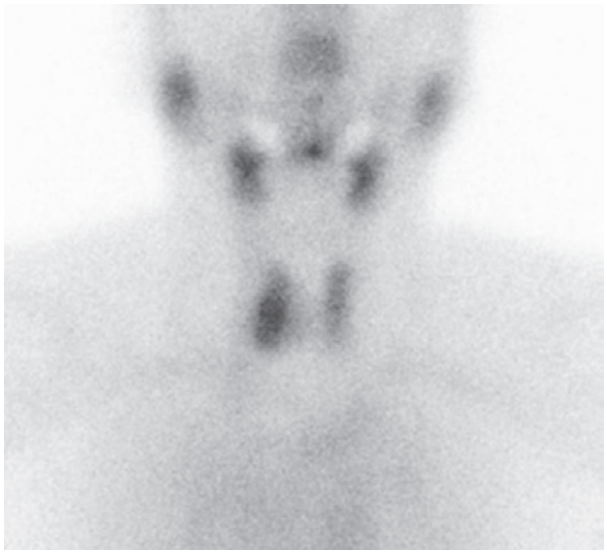

Fig. 7. Thyroid gland technetium scintigraphy nine months after the treatment. The abnormal accumulation in the right lobe has decreased and accumulation in the left lobe is apparent.

the radioactive iodine, there was no thyrotoxic crisis or radiation sickness, and treatment procedures were continued with no abnormality in thyroid function or side effects.

It has now been more than nine months since treatment, and the thyroid function has returned to normal (Table 2). The mass size in ultrasonography has become slightly smaller (3.0cm) and its hardness has decreased (Fig. 6). Also, thyroid technetium 99m scintigraphy shows that the abnormal accumulation in the right lobe has been normalized, and the abnormally reduced accumulation in the left lobe has been improving. The uptake rate is 0.3% in the right lobe, and 0.2% in the left, both improving (Fig. 7)

DISCUSSION

Plummer disease, also called autonomously functioning thyroid nodule (AFTN), is caused by the functioning nodules and is more common in elderly people and women. Its frequency is reported to be less than 0.5% of all cases of hyperthyroidism in Japan, making it a rare disease. On the other hand, the frequency in Europe and America is said to range from 5~20%. To date, the etiology and clinical condition are not fully understood. Diagnosis requires the measurement of thyroid-related hormones and thyroid autoantibodies. The functioning nodules in general show a mild increase of thyroid hormone. Various imaging studies such as ultrasonography, ultrasonic color Doppler, CT, and MRI are normally necessary. For confirmation of diagnosis, scintigraphy of radioactive iodine accumulation to the thyroid nodule is required [1, 2]. Aspiration cytology examination is performed to determine whether the nodule is malignant or not. Our patient was diagnosed as typical Plummer disease according to the results of these examinations.

The treatment for Plummer disease includes antithyroid drugs, surgery, PEIT, and radioiodine therapy. Case conference was held by members of our otolaryngology, endocrinology and metabolism, and radiation oncology departments. As the patient had almost no hyperthyroid symptoms, we disregarded the use of antithyroid drugs. Though PEIT is adaptable for small nodules (approx. 20 g or less) [3,

4], our case was 30 g, too large for adaptation. Surgical removal of the lesion commonly has immediate effects on hyperthyroidism and goiter [5]. However, our patient refused such a procedure for her benign thyroid lesion. Therefore, we decided to perform radioiodine therapy. Medical consensus on the dosing of radioactive iodine isotope has not yet been achieved, thus optimum dosages are not clear Tajiri indicated that 481 MBq of radioiodine with TSH suppression may be an optimum dose [6]. Prior to treatment, we fully explained to the patient that an insufficient dose would be ineffective, while an excessive dose might invite hypothyroidism after treatment. Treatment began by repeatedly administering small doses [7], closely monitoring their effect, until achieving the desired result with little hypothyroidism after the treatment. Prior reports have noted that, by keeping TSH at a low level before treatment and not giving antithyroid drugs, the possibility of post-treatment hyperthyroidism is reduced [8, 9]. Following this advice, we did not limit iodine intake or use antithyroid drugs that would otherwise cause higher TSH levels. It was also reported that thyroid function abnormality can be controlled in most cases [2-9]. In our case, thyroid function abnormality improved rapidly after the treatment, with a normal level now being maintained. Ultrasonography has shown a decrease of the mass size, a positive benefit of the radioiodine therapy. Patients with Plummer disease sometimes (about 20 %) have coexisting thyroid cancer [10, 11]. Our patient in this case now undergoes intensive and regular check-ups for cancer detection, due to the prior class 3 pathological diagnosis by aspiration cytology.

According to the guidelines of the American Association of Clinical Endocrinologists, radioiodine therapy for Plummer disease is recommended as Grade B (http://www.aace.com/pub/guidelines/index.php). This treatment is rarely adopted in Japan, as the disease itself is rare and patients are usually opposed to radiation treatments. To our knowledge there have been *few* reports in Japan of radioactive isotopic treatments of this disease. However, the treatment would appear to be preferable to surgery in that it is pretreatment-free and less invasive. Radioiodine therapy should be considered as a choice of therapy for a case of Plummer disease.

In conclusion, Plummer disease is caused by the formation of thyroid hormone-producing nodules, the nature of which in most cases is thyroid adenoma, and it is a rare disease in Japan. The case of a 74-year-old woman treated with the radioiodine therapy with remarkable results is reported, although surgical treatment of this disease is commonly preferred in Japan.

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