

## Plummer's disease with spontaneous progression to hypothyroidism

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A case of Plummer's disease that spontaneously progressed to hypothyroidism is presented. A 49-year-old female visited our hospital because of a 3 kg decrease in body weight during the previous month and a painless nodule in the right anterior area of her neck. A diagnosis of Plummer's disease was made based on the results of thyroid function tests, thyroid scintigrams, and an ultrasonogram, but the patient's disease followed an usual clinical course. About two months later, she gradually developed manifestations of permanent hypothyroidism, and anti-thyroid autoantibodies became positive. In spite of continuous administration of levothyroxine sodium, uptake of  $^{99m}\text{TcO}_4^-$  to the nodule was unchanged or rather increased according to the consecutive thyroid scintigraphies. These results suggested that this case represented an autonomously functioning nodule with underlying silent thyroiditis and Hashimoto's disease.

**Key words:** Plummer's disease, hypothyroidism, Hashimoto's disease, silent thyroiditis, autonomously hyperfunctioning nodule

### INTRODUCTION

PLUMMER'S DISEASE is characterized by the presence of autonomously functioning nodules that hypersecrete thyroid hormones, resulting in hyperthyroidism. Diagnosis requires demonstration of selective radioiodine accumulation in the nodules and suppressed uptake in non-nodular tissues.<sup>1</sup> After our patient was diagnosed as having Plummer's disease, her hyperthyroid state spontaneously changed to permanent hypothyroidism in the absence of any treatment. But, even though levothyroxine sodium was given continuously,  $^{99m}\text{TcO}_4^-$  uptake to the nodule was either unchanged or increased slightly. To our knowledge, spontaneous progression of Plummer's disease to continuous hypothyroidism has never been reported. This rare case is presented below.

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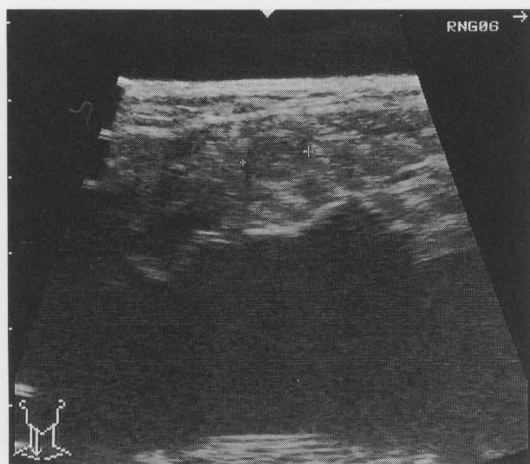
### CASE REPORT

In January 1997, a 49-year-old woman visited our hospital because of a 3 kg decrease in body weight during the previous month and a painless nodule in the right anterior area of her neck. Until then she had been healthy, and her family history was unremarkable. Physical examination revealed a non-tender, non-adherent solitary nodule, 1.2 × 1.4 cm in diameter, in the right anterior area of her neck. There was no exophthalmos. Neither profuse sweating nor palpitation was noted. Body temperature was 36.5°C, the pulse rate 84/min, and blood pressure was 120/74 mm Hg. Thyroid function tests yielded the following values: free triiodothyronine (FT<sub>3</sub>), 5.4 pg/ml (normal range, 2.3-3.7); free thyroxine (FT<sub>4</sub>), 2.2 ng/dl (normal, 1.0-1.8); thyroid-stimulating hormone (TSH), 0.09 μU/ml (normal, 0.6-5.5); thyroglobulin (Tg), 375.6 ng/ml (normal, < 25.0); anti-thyroid peroxidase antibody (TPOAb), < 0.3 U/ml (normal, < 0.3); anti-thyroglobulin antibody (TgAb), < 0.3 U/ml (normal, < 0.3); thyroid stimulating antibody (TSAb), 143% (normal, < 180). Ultrasonography revealed a mass lesion in the right lobe of the thyroid gland (Fig. 1). Thyroid scintigraphy was performed by intravenous injection of 370 MBq of Tc-99m pertechnetate ( $^{99m}\text{TcO}_4^-$ ), and administration of 7.4 MBq of I-123 after a low-iodine diet for a period of two weeks. Thyroid

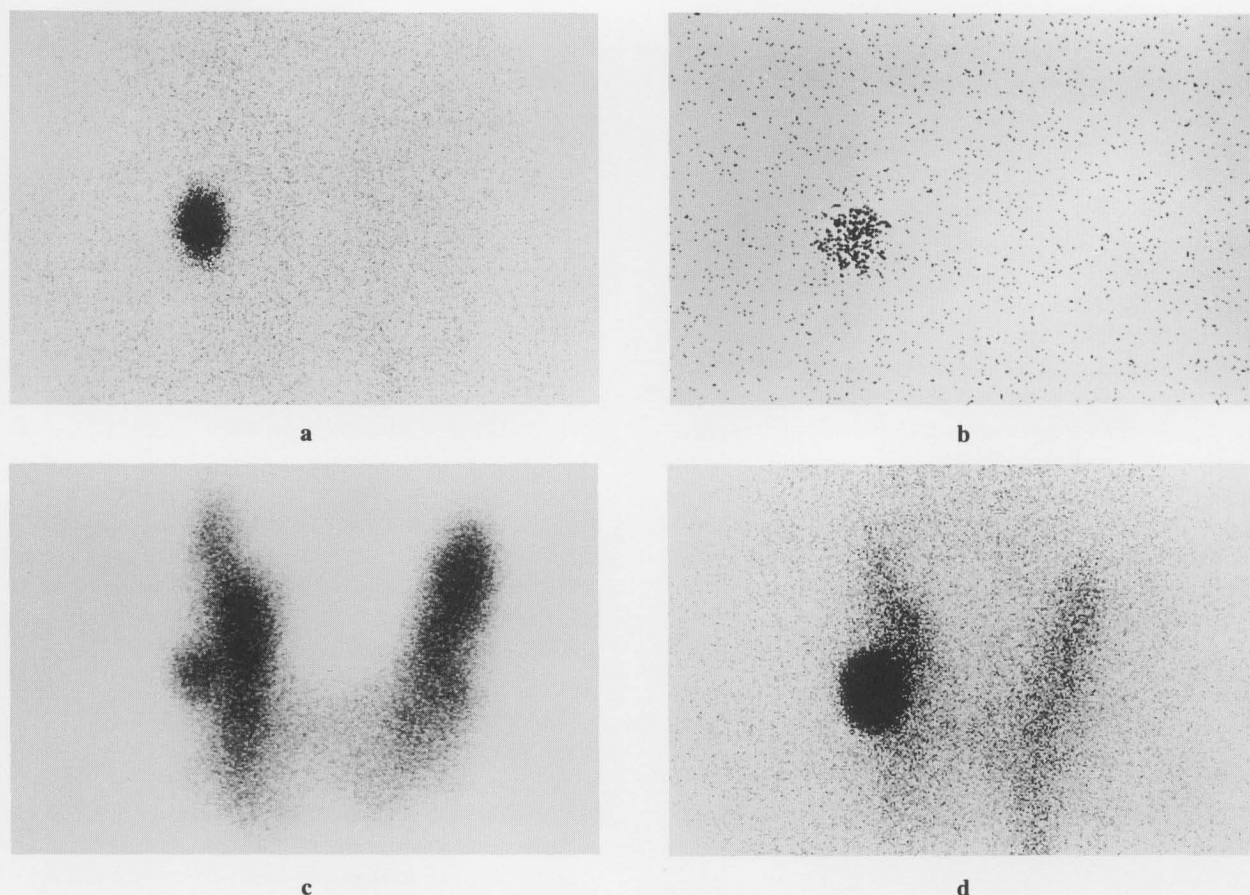
scintigraphy with a gamma camera with a pinhole collimator demonstrated selective accumulation of I-123 in the nodule corresponding to the mass on the ultrasonogram (Fig. 2a, b), and the  $^{99m}\text{TcO}_4^-$  thyroidal uptake value 30 minutes after intravenous injection was 1.9% (nor-

mal, 0.3–3.3). These findings suggested that the patient had an autonomously hyper functioning nodule, namely Plummer's disease. A  $\beta$ -blocker (propranolol 20 mg/day) was prescribed.

Over the next two months the patient gained 5 kg in weight. The hyperthyroid state caused by Plummer's disease was converted to a hypothyroid state ( $\text{FT}_3$ : 1.8 pg/ml;  $\text{FT}_4$ : 0.4 ng/dl; TSH: 67.04  $\mu\text{U}/\text{ml}$ ; Fig. 3, Tg: 82.3 ng/ml), with positive anti-thyroidal autoantibodies (TPOAb: 0.8 U/ml, TgAb: 1.0 U/ml). Propranolol was withdrawn and levothyroxine sodium (Thyradin S) was given, first at a dose of 50  $\mu\text{g}/\text{day}$ , and then at a maintenance dose of 100  $\mu\text{g}/\text{day}$ . The thyroid function test rapidly became normal (Fig. 3), and the Tg value decreased to 5.2 ng/ml. Thyroid scintigraphy performed after development of the hypothyroid state showed diffuse uptake of  $^{99m}\text{TcO}_4^-$  throughout the thyroid gland, but a hot nodule on the pinhole collimator was still observed, indicating the presence of Plummer's disease (Fig. 2c). Levothyroxine sodium (Thyradin S) with a maintenance dose of 100  $\mu\text{g}/\text{day}$  was continued and her thyroid function remained within the normal range, but anti-thyroidal autoantibodies remained positive at low titer levels (data not shown).



**Fig. 1** Thyroid ultrasonogram, showing a mass in the right lobe of the thyroid gland.



**Fig. 2** Thyroid scintigrams at the first visit (a:  $^{99m}\text{TcO}_4^-$  and b:  $^{123}\text{I}$ ) and after development of the hypothyroid state (c and d:  $^{99m}\text{TcO}_4^-$ ).  $^{99m}\text{TcO}_4^-$  thyroidal uptake values (30 minutes) were reduced to 1.9% on 97, Feb. 24, 0.8% on 97, Apr., and 0.37% on 98, May 16 (normal, 0.3–3.3).

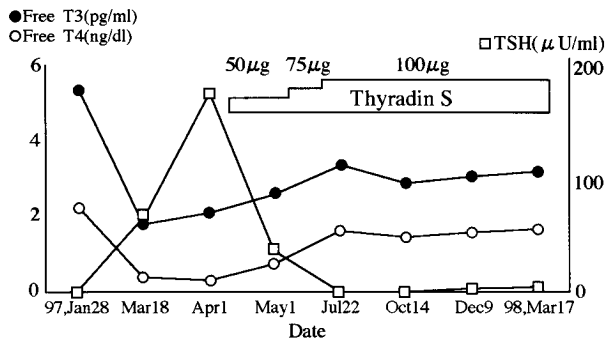


Fig. 3 Changes in serum FT<sub>3</sub>, FT<sub>4</sub>, and TSH levels.

## DISCUSSION

The solitary autonomous nodule is one form of a broader disorder, Plummer's disease, which can be characterized functionally as follows: (a) the autonomous tissue is non suppressible by thyroid hormones, and (b) cannot be stimulated by TSH, (c) suppressed, extranodular tissue is always present and can be stimulated by TSH.<sup>2</sup> Our patient first presented with a solitary hot nodule on a thyroid scintigram, but with suppressed radioiodine uptake in the remainder of the thyroid (Fig. 2a, b). These findings are consistent with Plummer's disease with hyperthyroidism. It is possible for Hashimoto's disease to resemble Plummer's disease on thyroid scintigrams, since a greater part of the thyroid gland is destroyed in Hashimoto's disease, and consequently, radioiodine may accumulate in the remainder of the normal thyroid tissue. But this can be fully excluded by the finding of a nodular lesion on the ultrasonogram (Fig. 1).

This case spontaneously progressed to hypothyroidism. Huysmans et al.<sup>3</sup> have reported that it is improbable that radioiodine treatment of Plummer's disease with hyperthyroidism would induce hypothyroidism.<sup>4</sup> Our findings therefore suggest that this patient may have had masked Hashimoto's disease that preceded the Plummer's disease insidiously. Although histopathological examination is preferable to make a definite diagnosis, a percutaneous thyroid biopsy could not be performed because the patient refused it. The patient was thought to have experienced sudden exacerbation of Hashimoto's disease with hypothyroidism, since the anti-thyroidal autoantibodies became positive, after having been negative at the first visit.

Very rare cases of Plummer's disease that progressed to hypothyroidism due to isotope therapy,<sup>3</sup> or that spontaneously changed from hyperthyroidism to normothyroidism, or to transient thyrotoxicosis due to hemorrhagic infarc-

tion or necrotic change in nodules<sup>5</sup> have been reported.

Moreover, Kasagi et al.<sup>6</sup> reported a rare case of transient thyrotoxicosis together with a functioning nodule. They were more convinced of a diagnosis of silent thyroiditis with functioning nodule based on the course of the case, serial changes in the serum thyroid hormone concentrations, the I-123 thyroidal uptake value, and the thyroid scan image which seemed to reflect the healing process of silent thyroiditis. The clinical course of the case with transient thyrotoxicosis appeared to resemble our case. It is more likely that hyperthyroidism in the present case was also mainly induced by silent thyroiditis, because (a) the thyroidal nodule was rather small and solitary as compared to previous cases of Plummer's disease, and the Tg value increased in relation to transient hyperthyroidism, (b) our case gradually developed manifestations of hypothyroidism, (c) anti-thyroid autoantibodies became positive, and (d) <sup>99m</sup>TcO<sub>4</sub><sup>-</sup> uptake by the nodule was unchanged or increased slightly in spite of continuous administration of levothyroxine sodium (Fig. 2c, d). From these findings, our patient was diagnosed as having Plummer's disease with silent thyroiditis.

To our knowledge, an autonomously hyperfunctioning nodule which spontaneously progressed to continuous hypothyroidism has never been reported previously.

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