

Case Report

Carcinomas in the remnant thyroid after thyroidectomy for Graves' disease: report of a case

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A 52-year-old female who had undergone subtotal thyroidectomy for Graves' disease 20 years previously was referred to us with nodules in both lobes in her remnant thyroid. Although benign follicular tumors were most likely to be considered on further examinations, total remnant thyroidectomy was performed due to the increasing size of the nodules. Diagnoses of papillary carcinoma (follicular variant) and minimally invasive follicular carcinoma were strongly suspected based on the findings of the histological examination. In follow-up examinations after subtotal thyroidectomy for Graves' disease, not only function but also structure of the remnant thyroid, should be focused on. Although rare, the possibility for carcinoma should be considered if nodules present in the remnant thyroid.

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Introduction

Surgical approaches for treating Graves' disease include total and subtotal thyroidectomy. After undergoing subtotal thyroidectomy, patients sometimes suffer from recurrence of hyperthyroidism and increases in the size of the remnant thyroid (1, 2). Thyroid carcinoma occurring in patients with Graves' disease has been investigated, and, in most reports, there seems to be no relationship between the prevalence of thyroid carcinoma and Graves' disease (3, 4). We herein report a case of nodules developing in each lobe of the remnant thyroid in a patient with a normal thyroid function following thyroidectomy for Graves' disease. Although preoperative aspiration cytology showed no malignancies, the final histological findings revealed that both nodules were carci-

nomas with different histological types. To our knowledge, there have been no other reports of carcinomas occurring in the remnant thyroid after thyroidectomy for Graves' disease.

Patient

A 52-year-old female who had undergone subtotal thyroidectomy at another hospital 20 years previously visited a private hospital with a palpable nodule in the neck. Although ultrasonography revealed a nodule measuring 19.5 mm in diameter in the right lobe of the remnant thyroid, the patient did not undergo any other examinations. Three years later, she visited the hospital, and thyroid ultrasonography showed enlargement of the nodule in the right lobe and the appear-

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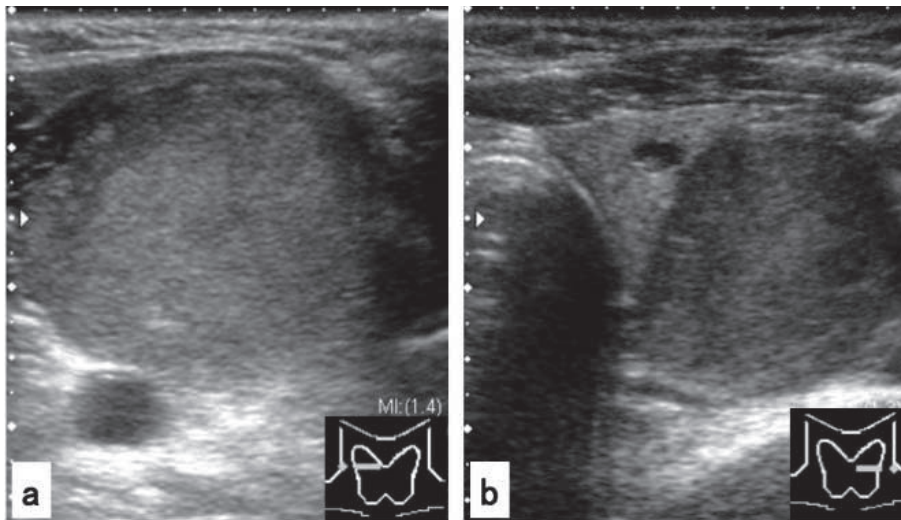


Figure 1. On ultrasonography, well-circumscribed homogeneous low-echoic lesions were seen in both lobes of the remnant thyroid, measuring $18 \times 18 \times 40$ mm in the right lobe (a) and $26 \times 23 \times 25$ mm in the left lobe (b). The nodules were encapsulated and did not have calcifications.

ance of a second nodule in the left lobe with a normal thyroid function. The patient was then referred to us for further investigation and treatment. A cervical examination revealed nodules in both lobes of the remnant thyroid. The patient's thyroid function was normal (free T3: 2.69 pg/ml (normal value: 2.37-3.91 pg/ml), free T4: 0.97 ng/dl (normal value: 0.95-1.57 ng/dl), TSH: 2.01 mU/ml (normal value: 0.48-5.08 mU/ml)); however, the level of serum thyroglobulin was above normal at 76.8 ng/ml (normal value: ≤ 32.7 ng/ml). Ultrasonography showed two well-circumscribed homogeneous low-echoic lesions, one measuring $18 \times 18 \times 40$ mm in the right lobe and one measuring $26 \times 23 \times 25$ mm in the left lobe, of the remnant thyroid, both of which were encapsulated, did not have calcifications and were compatible with diagnoses of adenoma or adenomatous goiter (Figure 1). On computed tomography, the nodular lesions showed strong and heterogeneous enhancement without evidence of invasive growth or lymphadenopathy (Figure 2). Although ultrasound-guided fine needle aspiration cytology of both lobes showed normal or benign follicular cells, surgery was scheduled due to the increasing size of the nodules. Intraoperatively, there were tumors in both lobes of the remnant thyroid, with no evidence of tumor invasion, and the patient underwent total remnant thyroidectomy. On histological examination, the nodule in the right thyroid lobe showed microfollicular proliferation and vascular invasion (Figure 3a, b). The nodule in the left lobe consisted of proliferation of small follicles surrounded by a thin capsule. The nuclei were enlarged with a ground glass appearance, nuclear grooves and intranuclear cytoplasmic inclusions

(Figure 3c). Immunohistochemically, the atypical cells were positive for cytokeratin 19 (Figure 3d). The nodule of the

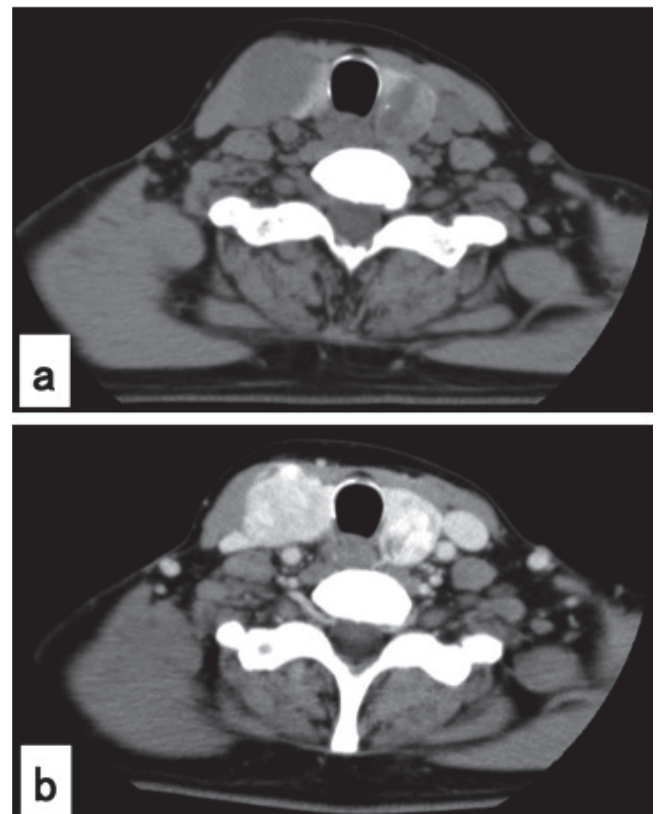


Figure 2. A plain computed tomography scan showing low density nodules in both lobes of the remnant thyroid (a). On contrast-enhanced computed tomography, the nodules showed strong and heterogeneous enhancement without evidence of invasive growth or lymphadenopathy (b).

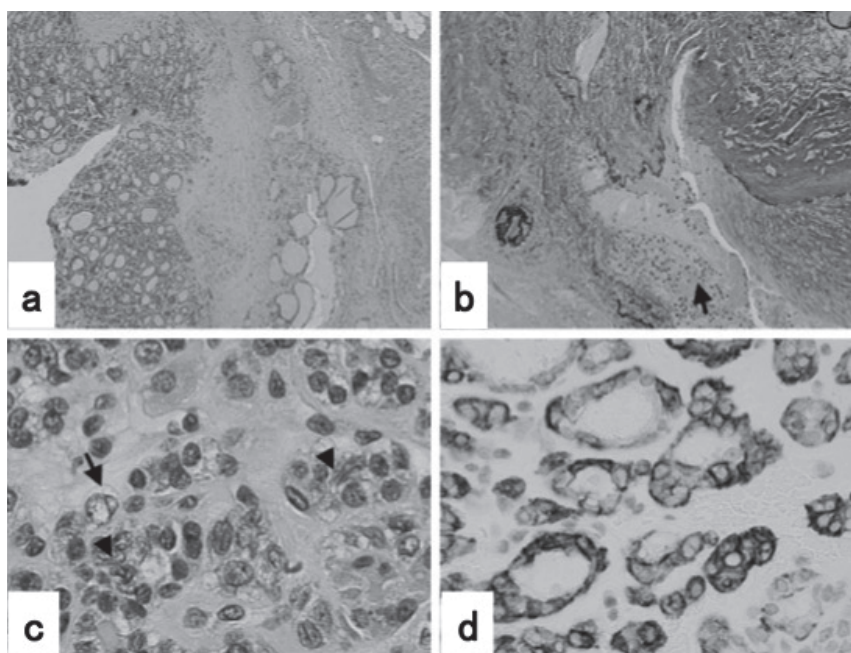


Figure 3. The nodule in the right thyroid lobe showed proliferation of follicles. Capsular invasion was not identified (a, hematoxylin and eosin, $40\times$). There were tumor cells between the elastic membrane and the endothelium (arrow) (b, Elastica van Gieson stain, $100\times$). The nodule in the left lobe also consisted of small follicles. The enlarged nuclei exhibited grooves (arrow) and cytoplasmic inclusions (arrowhead) (c, hematoxylin and eosin, $400\times$). Immunohistochemically, the cytokeratin 19 expression was positive in the cells with enlarged irregular nuclei (d, $400\times$).

right lobe was considered to most likely be a follicular carcinoma, while that of the left lobe was diagnosed as a papillary carcinoma (follicular variant).

The patient's postoperative course was uneventful. Ten months after surgery, she remains well, is currently taking levothyroxine and has no signs of recurrence and a normal serum thyroglobulin level.

Discussion

Papillary carcinoma is the most predominant type of malignancy of the thyroid. In a study of 408 consecutive autopsy cases in Japan, the prevalence of this condition was found to be 11.3% (5). Bradley et al. reported that performing total thyroidectomy is reasonable in patients with Hashimoto's thyroiditis when the involvement is diffuse due to the high frequency of incidental papillary carcinoma in patients with that disease (28%) (4). However, the prevalence of papillary carcinoma of the thyroid has been reported to range from 2.2% to 8% in patients with Graves' disease, which suggests that no definite correlation exists between the two diseases (3, 4). Additionally, among Graves' disease patients, the proportion of patients with papillary carcinoma is

much higher than that of patients with follicular carcinoma, similar to that observed in non-Graves' patients (3). In this case, different situations are possible with regard to the timing of the development of the carcinomas: either the nodules already existed as incidental carcinomas during the initial thyroidectomy performed 20 years previously or they developed as "de novo" carcinomas after thyroidectomy. As is well known, differentiated thyroid cancers express TSH receptors (6). It has been reported that high levels of serum TSH are associated with a high risk of developing differentiated thyroid cancers and advanced cancer staging (7). This patient had not undergone check-ups for a long time, approximately 20 years, since the initial thyroidectomy; therefore, whether she had been under stimulation by continuously high levels of TSH remains uncertain.

Surgical approaches for treating Graves' disease are roughly classified as either total or subtotal thyroidectomy, the latter of which is subdivided into surgeries leaving behind bilateral or unilateral remnants (1). Some patients who undergo subtotal thyroidectomy suffer from recurrent hyperthyroidism (1, 2). Follow-up examinations after subtotal thyroidectomy for Graves' disease primarily focus on the function of the remnant thyroid, and structural examinations are rarely performed, unless the function fluctuates.

Although only a small proportion of patients with remnant thyroid tissue, from which carcinomas derive, develop thyroid carcinomas after undergoing subtotal thyroidectomy for Graves' disease, imaging modalities such as ultrasonography should be used during the postoperative follow-up. The follicular variant of papillary carcinoma and minimally invasive follicular carcinoma are sometimes difficult to distinguish from benign follicular tumors, even when using fine needle aspiration cytology (8, 9). However, if increases in the size of nodules in the remnant thyroid are detected, the possibility for carcinoma should be taken into account.

Conflict of Interest

No competing financial interests exist.

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