

# Thymic Hyperplasia Presenting as a Neck Mass in Graves Disease

## *Graves Hastalığında Boyunda Kitle Şeklinde Görülen Timus Hiperplazisi*

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### Abstract

We describe a female patient who presented with Graves disease and a neck mass. Radiological characteristics of the mass suggested thymic hyperplasia. She was treated with methimazole, and because the mass did not regress after six months of therapy, the patient had total thyroidectomy and thymectomy. Pathological examination was consistent with chronic lymphocytic thyroiditis and thymic hyperplasia. Microscopic changes in the thymus can be detected in one third of patients with Graves disease, but massive enlargement is rare. It has been reported that regression occurs in most patients after a euthyroid state has been achieved; however, in some patients, thymectomy may be indicated. *Turk Jem 2009; 13: 11-2*

**Key words:** Graves disease, thymus hyperplasia

### Özet

Bu yazıda Graves hastalığı ve boyunda kitle ile başvuran bir bayan hasta sunulmaktadır. Kitlenin radyolojik özellikleri timus hiperplazisini düşündürmekteydi. Hastaya metimazol tedavisi başlandı ve kitle boyutlarında gerileme olmaması nedeni ile tedavinin 6. ayında total tiroidektomi ve timektomi uygulandı. Patolojik incelemede kronik lenfositik tiroidit ve timus hiperplazisi saptandı. Graves hastalarının üçte birinde timusta mikroskopik değişiklikler olabilir, ancak masif büyüme nadirdir. Vakaların çoğunda ötiroidi ile timusta regresyon gösterilmiştir. Ancak, bazı hastalarda timektomi gerekli olabilir. *Turk Jem 2009; 13: 11-2*

**Anahtar kelimeler:** Graves hastalığı, timus hiperplazisi

### Introduction

Thymic hyperplasia is not an ordinary manifestation of Graves disease (GD). The exact pathophysiology has not been determined. The thymus has no proven etiologic role in GD; thymectomy is not a curative therapeutic option. Few patients with Graves-disease-associated thymic hyperplasia have been described in the literature. In this report, we describe a female patient who presented with thymic hyperplasia attributable to Graves disease.

### Case Report

A 28-year-old woman was referred to our division for the evaluation of a one-month history of palpitations, hand tremor, and

weight loss. The patient's medical history was otherwise unremarkable. She had no symptoms related to myasthenia gravis, lymphoproliferative disease, or autoimmune disease, and her family history was negative for these conditions.

Physical examination revealed resting tachycardia (106 beats/min) and diffusely enlarged thyroid gland (Grade 1b). Results of routine laboratory studies were all normal. Thyroid function tests were as follows; free T<sub>3</sub>: 7.48 pg/mL (normal range, 1.57-4.71 pg/mL), free T<sub>4</sub>: 3.97 pg/mL (normal range, 0.8-1.9 pg/mL) and thyroid stimulating hormone (TSH): 0.007 IU/mL (normal range: 0.4-5.0 IU/mL). Sonography of the neck showed bilateral enlargement of thyroid lobes, typical "thyroid inferno" pattern, and a 10x15x25 mm homogenous mass at the inferior portion of the thyroid, just at the level of the suprasternal area (Fig. 1). Magnetic resonance (MR)

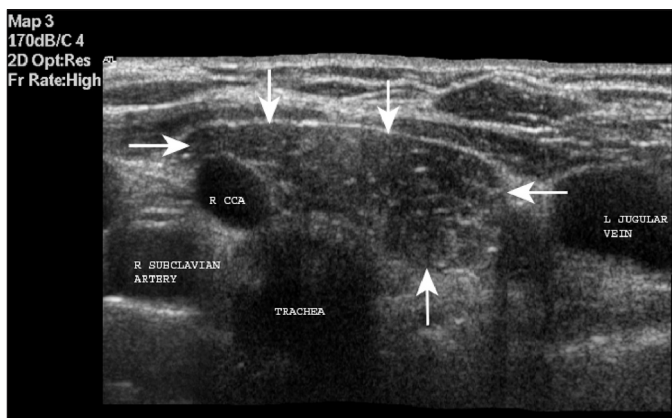
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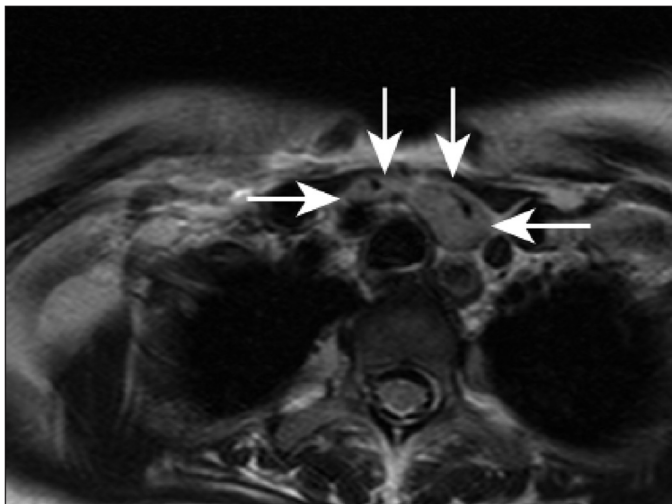
imaging demonstrated that the neck mass detected on sonography was a homogenous anterior mediastinal lesion extending to the neck, compatible with hyperplasia of the thymus (Fig. 2).

Radiological features of the mass were not suggestive of malignancy. Radioiodine (I-131) uptake was increased in the diffusely enlarged thyroid gland, but no uptake was detected in the mass. Thyroid receptor antibody (TRAb) was 22.3 U/l (positive: >14 U/l). Based on these findings, the patient was diagnosed with GD. She did not have ophthalmopathy.

Thymic hyperplasia related to GD was suggested, and follow up was recommended. The patient was treated with methimazole. After three months of therapy, a euthyroid state was achieved, and a neck ultrasonography was performed. There was no significant change in either the size or the sonographic characteristics of the mass. After six months of therapy, the patient was euthyroid and was totally asymptomatic. Neck ultrasonography did not reveal any regression of the mass. Total thyroidectomy and mass resection were performed, and pathological examination was consistent with chronic lymphocytic thyroiditis and thymic hyperplasia. The patient has been in good health since the operation. She continues to be treated with levothyroxine 150 µg/day.



**Figure 1.** Axial panoramic sonography of the neck at the level of the suprasternal area, demonstrating a midline mass predominantly to the left side of the trachea (arrows)



**Figure 2.** Axial T1W MR image demonstrating a homogenous anterior mediastinal mass at the midline

## Discussion

Few cases of hyperplasia of the thymus during the course of GD are reported in the literature (1). The etiologic role of GD in thymic hyperplasia is not clear. Fabris et al. demonstrated that thymic endocrine activity is positively correlated with thyroid function (2). In animal models, exogenous thyroid hormone administration has resulted in an increase of both medullary and cortical components of thymus (3), while thyroidectomy has resulted in reduction of the size of the thymus (4). In a more recent study, Murakami et al. have identified thyrotropin receptors in the human thymus (5). In addition, they have demonstrated that therapy with anti-thyroid drugs produces a reduction in thymic size and density, with a concomitant decrease in thyrotropin receptor antibodies. In GD, a decrease in thymic size with treatment is reported to be associated with the immunosuppressive effects of anti-thyroid drugs, and with a reduction in the levels of circulating thyroid hormones.

It must be noted that microscopic changes in the thymus can be detected in one third of patients with GD but that massive enlargement is rare. In the literature, the reports regarding massive thymic hyperplasia due to GD include patients who present with mediastinal masses (1,6,7). Thymic hyperplasia presenting as a neck mass has not been reported previously in GD. A possible explanation for the unexpected finding in our patient may be the unusual growth pattern of the thymus, from the mediastinum towards the cervical area.

Another feature of this patient inconsistent with the literature is the unresponsiveness of thymic hyperplasia to six months of treatment with methimazole. In most of the cases reported previously, regression of thymic hyperplasia was achieved with anti-thyroid treatment (1,6). It may be inferred that factors other than the level of circulating thyroid hormones may be involved in the pathogenesis of thymic hyperplasia in GD.

Clinicians should be aware of thymic hyperplasia associated with GD. In most cases, hyperplasia is in the mediastinum, but exceptional localizations may be seen. The course is usually benign, and follow up should be recommended. It has been reported that a euthyroid state can achieve regression in most patients. However, in some patients thymectomy may be indicated.

## References

1. Budavari AI, Whitaker MD, Helmers RA. Thymic hyperplasia presenting as anterior mediastinal mass in 2 patients with Graves disease. *Mayo Clin Proc* 2002; 77: 495-9.
2. Fabris N, Mocchegiani E, Mariotti S, Pacini F, Pinchera A. Thyroid function modulates thymic endocrine activity. *J Clin Endocrinol Metab* 1986; 62: 474-8.
3. Ban T, Kosugi S, Kohn LD. Specific antibody to the thyrotropin receptor identifies multiple receptor forms in membranes of cells transfected with wild-type receptor complementary deoxyribonucleic acid: characterization of their relevance to receptor synthesis, processing, structure, and function. *Endocrinology* 1992; 131: 815-29.
4. Fabris N. Immunodepression in thyroid-deprived animals. *Clin Exp Immunol* 1973; 15: 601-11.
5. Murakami M, Hosoi Y, Negishi T, Kamiya Y, Miyashita K, Yamada M, Iriuchijima T, Yokoo H, Yoshida I, Tsushima Y, Mori M. Thymic hyperplasia in patients with Graves' disease. Identification of thyrotropin receptors in human thymus. *J Clin Invest* 1996; 98: 2228-34.
6. Goichot B, Vinzio S, Massard G, Thompson M. An unusual cause of anterior mediastinal mass: thymic hyperplasia resulting from Graves disease. *Am J Clin Oncol* 2006; 29: 322-3.
7. Kirkeby KM, Pont A. Image in endocrinology: thymic hyperplasia in a patient with Graves' disease. *J Clin Endocrinol Metab* 2006; 91: 1.