

Unilateral Graves' Disease in a Bilobar Thyroid Gland: A Very Unusual Cause of Hyperthyroidism

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Abstract

Graves' disease (GD) is an autoimmune condition that affects both thyroid gland lobes. Patients with GD with unilateral thyroid scan uptake are rare. These patients present with classic Graves' symptoms, occasionally with Graves' ophthalmopathy characteristics and increased thyroid hormones, and scintigraphic assessment reveals radiotracer uptake in only 1 lobe of the thyroid gland. In this case, a 48-year-old female presented with symptoms and signs indicative of thyrotoxicosis. Laboratory results revealed that TSH was undetectable, whereas free thyroxine and free triiodothyronine were in the high-normal range. Positive results were observed for both thyroid-stimulating Ig and TSH receptor antibodies. Ultrasonography of the thyroid gland revealed an enlarged left lobe with heterogeneous echotexture and a hyperemic gland without any focal lesions, distinct nodules, or cysts. Thyroid scintigraphy revealed enlarged and increased radioisotope uptake in the left lobe and decreased uptake in the right lobe, with no hot or cold nodules. The most likely diagnosis was unilateral GD. The patient was administered carbimazole and within 8 weeks had improved clinically and biochemically.

Key Words: thyroid, Graves' disease, autoimmune, unilateral, carbimazole

Abbreviations: ATD, antithyroid drug; GD, Graves' disease; NIS, Na (+)-I⁻ symporter; T3, triiodothyronine.

Introduction

Graves' disease (GD), first described by Dr Robert J. Graves in 1835, is the leading cause of hyperthyroidism, accounting for 50% to 80% of cases [1]. The incidence of hyperthyroidism in the United States ranges from 20 to 50 per 100 000 people, with a prevalence of 1.2% [1]. It is particularly prevalent in those aged 40 to 60 years and in females more so than males [1].

The thyroid uptake scan in patients with GD typically reveals bilateral, diffuse radioactive uptake. However, unilateral lobe involvement in a bilobar thyroid gland is uncommon. Unilateral GD can present clinically the same way as bilateral GD, yet the scintigraphic evaluation indicates radiotracer uptake in only 2 lobe of the thyroid gland. There is no clear explanation for unilateral GD. Involvement of the right thyroid lobe is more common than the left lobe, which could be because the right lobe is larger in size and more commonly affected by nodular disease, as proposed by Bolognasi and Rossi [2]. On thyroid ultrasound, nodules or cysts should be ruled out before confirming the diagnosis of unilateral GD.

One of the known causes of unilateral GD is thyroid hemiagenesis. Hemiagenesis of the thyroid is an extremely uncommon form of congenital malformation that occurs when 1 of the thyroidal lobes fails to develop. The majority of patients with hemiagenesis are euthyroid and have no clinical signs. Consequently, thyroid hemiagenesis is typically discovered incidentally while evaluating concurrent disorders of thyroid function or a suspected structural abnormality [3]. Unilateral Graves' hyperthyroidism is the most commonly described pathology associated with thyroid hemiagenesis [4].

Once the cause of hyperthyroidism is determined to be GD, the patient and physician should discuss the 3 available treatment options: 131I therapy (radioiodine), antithyroid drugs (ATDs), or thyroidectomy [5]. If surgery has been chosen as the treatment for unilateral GD, total thyroidectomy is the procedure of choice, whereas unilateral hemithyroidectomy is generally avoided [6].

Case Presentation

We present the case of a 48-year-old woman who was referred to the thyroid clinic with a 4-week history of palpitation, heat intolerance, insomnia, and sweating. There was no history of thyroid or autoimmune disease in the family. There was no history of thyroid surgery or ATD use. On examination, thyroid gland palpation revealed a nontender, enlarged left thyroid lobe that moved with swallowing but had no definite nodules. The right lobe appeared to be normal in size and consistency. Pemberton sign was negative. There was no exophthalmos, acropachy, or pretibial myxedema.

Diagnostic Assessment

Laboratory results revealed an undetectable TSH level of <0.01 μ IU/mL (normal reference range, 0.35–4.94 μ IU/mL), an upper normal free thyroxine level of 17 pmol/L (1.3 ng/dL; normal reference range, 9.0–19.0 pmol/L [0.7–1.9 ng/dL]), and a normal free triiodothyronine (T3) level of 6.9 pmol/L (0.53 ng/dL; normal reference range, 5.8–14.350 pmol/L [0.4–1.1 ng/dL]). Thyroid-stimulating Ig and TSH receptor

autoantibodies were both positive. High-resolution ultrasonography of the thyroid gland revealed an enlarged left lobe ($1.9 \times 2 \times 4.9$ cm) with heterogeneous echotexture and hypervascularity. The size of the right lobe was normal ($1 \times 0.7 \times 2.6$ cm). There were no focal lesions, discrete nodules, or cysts in either lobe (Fig. 1). Nuclear medicine technetium-99M thyroid scintigraphy showed enlarged and increased radiotracer uptake within the left thyroid lobe, whereas the right thyroid lobe showed suppressed uptake with no hot or cold nodules. The calculated thyroid uptake was 4.5% (normal range, 0.5%-3.5%) (Fig. 2). Unilateral GD was the most likely diagnosis.

Treatment

The patient was administered carbimazole 10 mg twice daily and propranolol 10 mg twice daily as needed for palpitations.

Outcome and Follow-Up

Eight weeks after starting treatment, the patient's clinical symptoms and thyroid function test results improved. Free thyroxine, T3, and TSH levels improved to 9.10 pmol/L, 3.30 pmol/L, and 0.16 μ IU/mL, respectively. The carbimazole dosage was decreased every 2 months. The patient went into remission after 6 months of antithyroid therapy. Her symptoms resolved, and her laboratory tests normalized (TSH, 4.3 μ IU/mL; free thyroxine, 10.4 pmol/L; and T3, 4.2 pmol/L). No adverse effects were reported during treatment.

Discussion

During our review of the literature, we identified 14 published clinical cases of unilateral GD. Three patients had involvement in the left lobe and 11 had involvement in the right lobe. Four patients were male and 10 were female. The ages ranged from 18 to 63 years, with the majority in their 40s and 50s. Based on clinical presentation, positive TSH receptor antibodies, and imaging, all patients were diagnosed with hyperthyroidism resulting from unilateral GD. According to the findings of Sakata et al [6], the patients in the first 2 cases published in the literature were treated with right hemithyroidectomy; however, they later developed thyrotoxicosis because of left lobe hyperfunction and required methimazole. Twelve patients were treated with ATDs, whereas radioactive iodine was used to treat 1 patient. This case report is thought to describe the first patient diagnosed with subclinical hyperthyroidism caused by unilateral GD.

The exact cause of GD with unilateral lobe involvement is unknown. There are several possibilities that could explain why only 1 thyroid lobe is affected: first, unilateral GD may be an early phase of bilateral GD, as suggested by the first 2 cases reported by Sakata et al [6]. In these cases, both patients were initially treated with hemithyroidectomy and later developed thyrotoxicosis in the other lobe. This suggests that unilateral GD may be an early phase of bilateral GD. Second, there may have been a history of unilateral thyroiditis in the unaffected lobe, resulting in thyroid cell destruction and unilateral radioisotope uptake. Third, the intrinsic membrane protein Na (+)-I⁻ symporter (NIS) mediates active iodide transport into the thyroid. NIS is important in thyroid pathophysiology because it is the route by which iodide (I⁻) reaches the gland for thyroid hormone biosynthesis. Differential expression of the NIS gene between the 2 lobes and its function

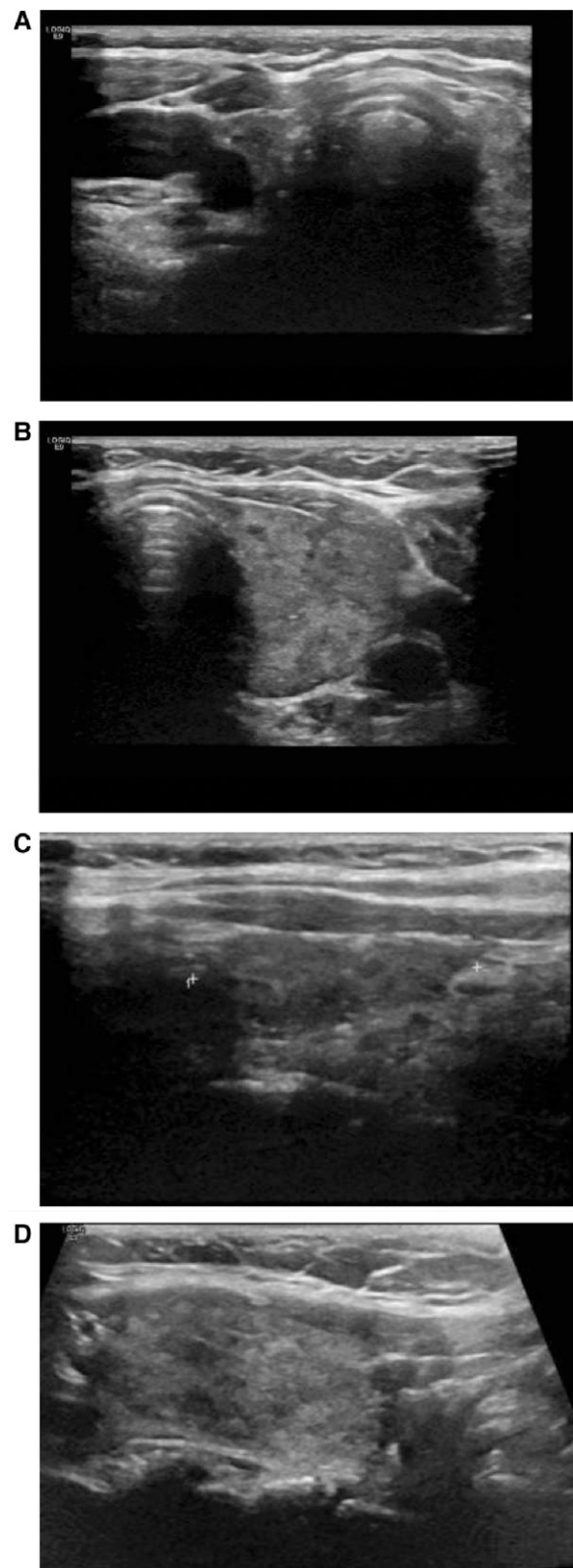


Figure 1. Thyroid ultrasound. (A) Transverse view and (C) sagittal view show a normal right thyroid lobe with no nodules or cysts. (B) Transverse view and (D) sagittal view show an enlarged left lobe with heterogeneous echotexture and hypervascularity, with no nodules or cysts.

may be responsible for the occurrence of impaired radioisotope uptake by thyroid tissue [7]. Fourth, according to Bolognasi and Rossi [2], the right lobe is larger and more

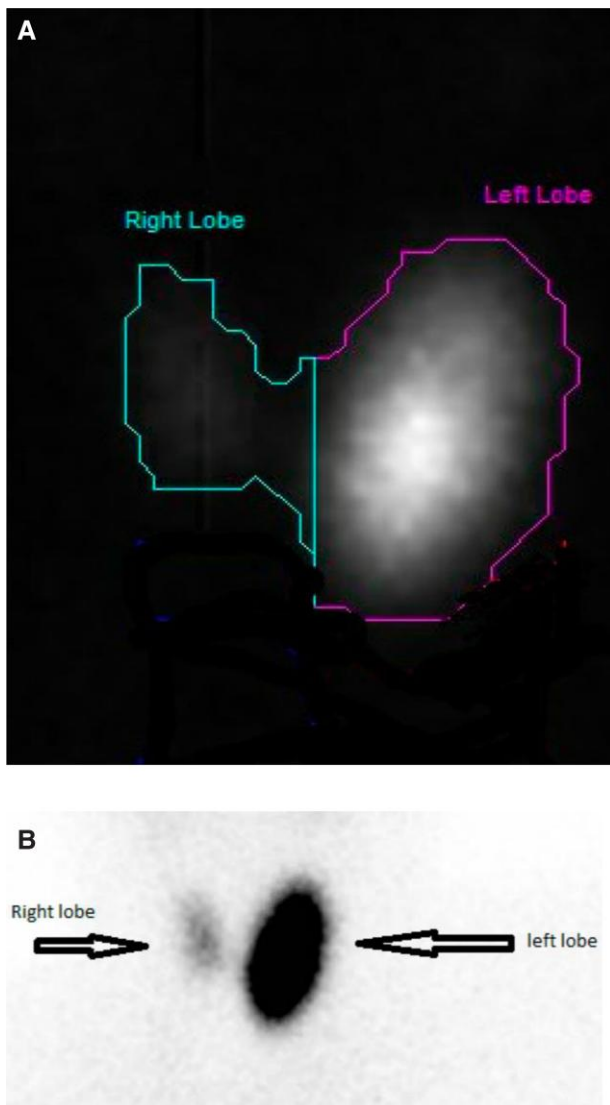


Figure 2. Nuclear medicine technetium-99M thyroid scintigraphy showing increased radiotracer uptake within the left thyroid lobe, whereas the right thyroid lobe shows suppressed uptake with no hot or cold nodules.

frequently affected by nodular disease. Our review of the literature confirmed that more cases involved the right lobe (11 cases) than the left lobe (3 cases) [8-10], and our case was thought to be the fourth case. A differential diagnosis of unilateral GD could be hemi- aplasia of the thyroid gland lobe, and there are multiple cases of this condition that have been published in the medical literature. Other possible explanations include a history of hemithyroidectomy or the expansion of a toxic nodule throughout the entire thyroid lobe.

Learning Points

- Graves' disease (GD) can present in the bilobar thyroid gland with unilateral thyroid gland involvement; clinicians should be aware of this possibility.
- Unilateral GD should be treated in the same manner as bilateral GD with antithyroid drugs, radioactive iodine, or

total thyroidectomy because recurrence in the unaffected lobe is possible after hemithyroidectomy.

- Unilateral GD is uncommon, and its pathophysiology is poorly understood.

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Informed Patient Consent for Publication

Signed informed consent obtained directly from the patient.

Data Availability Statement

Original data generated and analyzed during this study are included in this published article.

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