

Toxic multinodular goiter Description of a short case series.

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Abstract

Hyperthyroidism is defined as increased thyroid function produced by the thyroid gland. Common causes of hyperthyroidism include Graves' disease, toxic multinodular goiter, and toxic adenoma. Toxic multinodular goiter is the enlargement of the thyroid gland with nodules associated with hyperthyroidism.

Once the biochemical and structural diagnosis has been made, the most appropriate treatment must be chosen. It is considered that this treatment should be individualized; In many cases it is thyroid surgery and thus the thyroid dysfunction and the structural problem caused by the nodules are resolved.

A brief series of cases of five women with goiter associated with hyperthyroidism is presented: the first in a young adult with multinodular goiter of more than a decade of evolution with great tracheal compression; another in an older adult with previous partial thyroidectomy; the third with a large dominant nodule, the next with toxic multinodular goiter with incidental carcinoma and finally a patient with persistent hyperthyroidism after radioiodine.

Keywords: Goiter, Hyperthyroidism, Multinodular, Thyroidectomy

Introduction

In the United States, the prevalence of hyperthyroidism is approximately 1.2% (0.5% overt and 0.7% subclinical); the most common causes include Graves' disease (GD), toxic multinodular goiter (TMNG), and toxic adenoma (TA) [1].

Goiter associated with hyperthyroidism is a disorder that generally arises from multinodular goiter of several years' duration. The incidence is highly variable and depends, to a large extent, on the iodine intake of the population.

Clinical manifestations vary with thyroid function and goiter. If hyperthyroidism is manifest (low TSH with high FT3 and/or FT4) it is more symptomatic and may appear: palpitations, insomnia, restlessness, weight loss, among other symptoms) and if it is subclinical (low TSH with normal FT3 and FT4) it may be asymptomatic and even more so at an older age.

Treatment can be radioiodine (RAI) or surgery, and treatment with synthetic antithyroid drugs can sometimes be considered [2].

If surgery is chosen as a treatment for TMNG, a near-total or total thyroidectomy should be performed. Recurrence can be avoided in TMNG if a near-total or total thyroidectomy is performed initially [3].

In the case of total thyroidectomy, remission of hyperthyroidism and solution of the gland's structure is achieved in all patients, although they will remain with hypothyroidism.

In the case of radioiodine, control of thyroid function is generally achieved, it improves the structure many times and can remain in thyroid eu-function at times.

Cases

Case 1

A 58-year-old woman with a history of breast carcinoma treated with chemotherapy and radiotherapy. During the preoperative assessment of his oncological disease, he reported a multinodular goiter of 10 years' evolution, recently added a bitonal voice, accompanied by insomnia, irritability, heat intolerance, palpitations, and muscle weakness.

On examination: BMI 19Kg/m², grade IV goiter was found (figure 1A) with a firm-elastic tumor of approximately 1.5 cm in diameter in the left thyroid lobe (LTL). The lower border of the right thyroid lobe (RTL) was not palpable; dullness to percussion of the suprasternal foramen and positive Maranon-Pemberton maneuver. Heart rate 102 beats/minute.

Laryngoscopy showed a rotated larynx to the left with a good glottic lumen, normal motility of the vocal cords. Tracheal stenosis of 70-75% due to extrinsic compression of the thyroid goiter from the second to the fifth tracheal ring.

Neck and chest tomography: enlarged thyroid gland with multiple hypodense nodules and calcifications with intrathoracic extension, at the expense of the LTR. Trachea displaced to the left, determining a 2mm stenosis (figure 1B). Compresses and displaces esophagus to the left. On the right, a patent superior vena cava with decreased caliber.

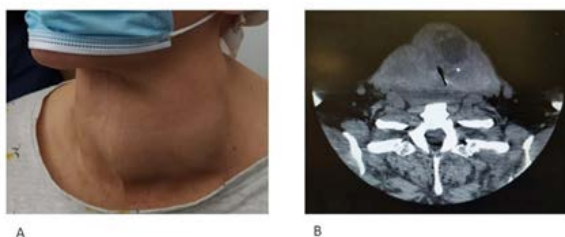


Figure 1: A. Grade IV Goiter, Heterogeneous. B. Computed Tomography where the Great Decrease in the Tracheal Lumen Due to Goiter is Observed.

From the laboratory: TSH <0.005uU/ml (NR 0.27 -4.2); T4L 1.44 ng/dL (NR 0.93 – 1.70); T3L 6.95pg/dL (NR 2 – 4.40). Due to multinodular goiter associated with hyperthyroidism (toxic multinodular goiter), surgical treatment was decided. Methimazole and propranolol were started and with a normal thyroid profile, a mastectomy + total thyroidectomy was performed simultaneously without complications.

A 70 x 55mm follicular variant papillary carcinoma in the right lobe stands out from the pathology of the thyroid; 5% necrosis, without capsule involvement or vascular invasion (T3a N0 M0; Stage II). Later he received 150mCi of radioiodine.

Currently, ultrasound without structural remnant, under treatment with levothyroxine and profile target thyroid.

Case 2

A 74-year-old woman with a history of hypertension and dyslipidemia. At 33 years of age, a subtotal thyroidectomy was performed for MNG without elements of malignancy. In the last year, he developed hoarseness, cough, and intermittent dysphagia.

On BMI examination: 27kg/m², grade III goiter, arcuate scar, retrosternal dullness (Figure 2A). Heart rate of 94 beats/minute.

The thyroid ultrasound reported a gland with an 81cc intrathoracic component; shifts airway to the right. Left lobe: ovoid

nodule, solid cystic, 34x17x18mm. Right lobe: predominantly solid isoechoic mixed nodule that completely replaced the right lobe measuring 33x28x24mm and another predominantly cystic mixed nodule 13x18x12mm.

The Airway X-Ray Showed Tracheal Compression and Deviation to the Right (figure 2B)

The tomography (figure 2C) showed plungent MNG with a predominance of the LTL (103x50x66mm). It presents irregular borders with heterogeneous make and some calcifications of different sizes and shapes. Does not infiltrate adjacent structures. Diverts and compresses the trachea to the right with a maximum stenosis of 6mm. High right lateral-tracheal adenomegaly with low lateral-tracheal extension 60 x 18 x 25mm, heterogeneous density, characteristic similar to gland. Permeable vascular structures, without alteration in caliber.

From the laboratory: TSH: 0.01 (NR 0.27 -4.2uU/ml), T4 L 1.2 (NR 0.93 – 1.70 ng/dl); T3 L 3.3 (NR 1.4 – 4.40).

Due to intrathoracic involvement and the patient's decision, total thyroidectomy was completed without complications. She is currently receiving levothyroxine and is in eu-function.

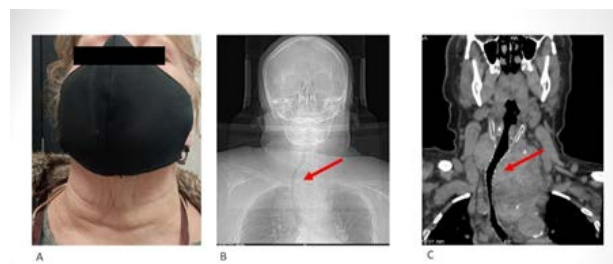


Figure 2: A. Grade iii Goiter. B. Chest X-Ray And C: Computed Tomography, in which the Deviation and Compression of the Tracheal Lumen is Observed (Red Arrow).

Case 3

Woman, 46 years old with a history of schizophrenia and smoking since she was 18 years old. MNG of 20 years of evolution without controls, consultation due to progressive increase in its size in 5 years. No symptoms of thyroid dysfunction or locoregional compression. No elements of ophthalmopathy.

From the Grade III goiter examination at the expense of the left lobe (LL), the lower edge and firm-elastic nodule of 6 x 5 cm were palpable. No adenopathy's. Negative Maranon-Pemberton maneuver. Normal heart rate.

The ultrasound reported: enlarged gland with a predominance of the left lobe (LL), which measured 70x45x32mm, completely replaced by a 68x44x30 mm nodule that displaces the homolateral vascular axis outward, it is heterogeneous and predominantly solid, isoechoic, with a hypoechoic halo. Several cystic images in the upper sector and scattered macrocalcifications. Right lobe (RL) of 43x13x15mm. Several mixed nodules, some of them larger than 7 and 8mm.

From the laboratory: TSH 0.004, it was reiterated and subclinical hyperthyroidism was diagnosed;

TSH: 0.003 (NR 0.27 -4.2uU/ml), T4 L 0.95 (NR 0.93 – 1.70 ng/dl); T3 L 3.14 (NR 1.4 – 4.40pg/dl).

Thyroid scintigraphy with SPECT-CT (figure 3A): hyper-uptake nodule with central low-uptake areas covering the entire LI measuring 72x41x40mm and one in the right lobe of less intensity and irregular uptake. Airway deviation to the right with a minimum diameter of 12mm. PAAF of the low-enhancement sector was indicated and the patient refused. Methimazole 10mg/day was started and due to the size of the larger nodule, total thyroidectomy was performed without complications. From the pathology there was no evidence of malignancy (figure 3B). Currently replaced with Levothyroxine in eu-function.

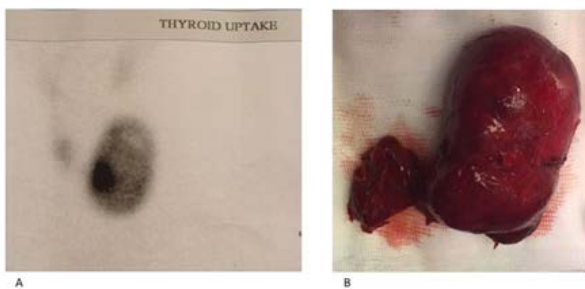


Figure 3: A. Thyroid Scintigraphy and B: Macroscopy of a Thyroidectomy Specimen Showing the Great Asymmetry of the Gland with a Clear Predominance of the Left Lobe.

Case 4

Woman, 57 years old. Type 2 diabetic with 5 years of evolution with insulin therapy, without repercussions. Hypertensive and smoker since the age of 34. MNG of 5 years of evolution. Clinical and biochemical eu-function up to the time of consultation, presenting: weight loss of 30 kg, muscle fatigue and insomnia of 8 months of evolution. He referred progressive increase in goiter, dysphagia for some solids. No elements of orbitopathy.

On examination: BMI 18.3 kg/m². Grade III goiter, firm consistency, irregular at the expense of thyroid nodules, the largest in the left lobe of 3 cm in diameter (figure 4). No adenopathy's. Negative Pemberton cashew maneuver. Regular rhythm of 100cpm, without murmurs.

Ultrasound: 42cc enlarged thyroid gland, heterogeneous at the expense of multiple mixed nodules with echogenic focus, which completely replaced the glandular parenchyma. RL: 13x1mm nodule and 12x10mm in the lower third. In LL: larger nodule of 37x24x29mm. They present predominantly peripheral vascularization on color Doppler. No lymph nodes.

Hyperthyroidism was diagnosed: TSH <0.005 (NR 0.27-4.2uU/ml), FT4 3.11 (NR 0.9-1.7 ng/dl), FT3 9.01 (NR 1.4-4.4pg/dl). Methimazole 20mg/day and propranolol 30mg/day were started, with great difficulty in reaching thyroid eu-function.

Thyroid scan with Tc99: pattern compatible with hyperfunctioning multinodular goiter with areas of low uptake in the upper and middle third of the right lobe.

Neck tomography: airway centered with caliper and visceral axis preserved and centered. No lymph nodes. The patient requested surgery as treatment and a total thyroidectomy was performed without complications. Of the pathology: multifocal papillary carcinoma with a larger focus of the invasive follicular type of 11x7mm, without evading the organ capsule. No necrosis. No vascular-lymphatic emboli or perineural invasion. Lymph node without neoplastic involvement (1/1) (T1b N0 M0; Stage I).

Five months after surgery, he received 30mCi of Radioiodine. Currently post-surgical hypothyroidism in replacement treatment with levothyroxine in eu-function.



Figure 4: A. Photograph of the Neck where the Goiter with Left Thyroid Nodule Can Be Seen.

Case 5

Woman, 42 years old with no outstanding history. It began 6 years prior to the consultation with palpitations, sweating, insomnia. He received methimazole, without achieving thyroid eu-function and in the evolution, he noted growth of the neck: anterior, lateral and circumferential (figure 5). He denied symptoms of locoregional compression and 25mCi of Iodine 131 was administered. He persisted with hyperthyroidism and methimazole 40mg/day was reinstated to achieve eu-function. He did not present elements of ophthalmopathy at any time.



Figure 5: A, B Y C: Evolution of the Change at the Neck Level with Clear Growth of the Thyroid Gland.

On examination: Grade IV goiter, asymmetric with a 2-3cm nodule in the left lobe. The lower border was not defined, sternal dullness and the Maranon-Pemberton maneuver was positive. On ocular examination: slight palpebral edema of the left eye. We do not exophthalmos. Thyroid ultrasound: goiter with an estimated volume of 200cc and multiple nodules. Right: predominantly solid, hyperechogenic, well-defined, fine cystic halo and peripheral vascularity. The largest of 19x15mm. Left: upper sector: 22x20x14 mm nodule, predominantly solid, central and peripheral vascularization; In the lower sector: a 29x28x20mm nodule, mixed, predominantly solid, hyperechogenic, peripheral vascularization. No cervical lymph nodes.

Neck and chest tomography: markedly enlarged thyroid displacing adjacent structures. Compresses and displaces the trachea in a right posterolateral direction, with a residual lumen of 24mm x 12mm. Inferiorly it contacts the thoracic outlet. No lymph nodes or lymph node conglomerates. Mouth, floor of the mouth, tongue, fatty spaces and paravertebral spaces without lesions. Thorax: s/p.

From the laboratory TSH 0.01 (NR 0.27 -4.2uU/ml), T4 L 0.97 (NR 0.93 - 1.70ng/dl) and T3L 2.1 (NR 1.4-4.4pg/dl). Total thyroidectomy was performed without complications. He is currently receiving levothyroxine and is in eu-function.

Hyperthyroidism is considered overt or subclinical, depending on the biochemical severity of hyperthyroidism, already defined above. Manifest hyperthyroidism occurred in cases 1 and 4 and was symptomatic as usually described, and both presented with low weight according to the WHO classification by BMI.

Toxic nodular goiter may be more common than Graves' disease in older patients, especially in iodine-deficient regions [4,5].

Once the presence of TMNG is confirmed, a thyroid scan should be performed to define the therapeutic approach. In our series in case 1 due to the urgency of solving her breast cancer and the great tracheal compression; in case 2 for having a plongeant goiter and in case 5 for the volume of 200cc. Since total thyroidectomy was proposed, the scintigraphy was not performed.

Regarding TMNG therapy, beta-adrenergic blockade is recommended in all patients with symptomatic thyrotoxicosis, especially in advanced age and those presenting with thyrotoxicosis and resting heart rates greater than 90 beats per minute or coexisting cardiovascular disease. In these cases, cases 1 and 4 were symptomatic hyperthyroidism and case 2 was an older adult patient (over 65 years of age) with arterial hypertension and dyslipidemia, in addition to having a heart rate greater than 90 beats/minute.

Toxic nodular goiter is generally progressive and does not resolve spontaneously, as can happen in mild GD, which can remit in up to 30% of patients without treatment [6].

For this reason, an adequate and individualized treatment must be offered to each patient, according to their preference. Its objective is the rapid and sustained elimination of hyperthyroidism.

Occasionally treatment with methimazole may be appropriate, for example, to achieve thyroid eu-function prior to surgery, as occurred in cases 1 and 4, or in patients with other medical complications in whom long-term treatment with low doses of methimazole may be considered.

There are two effective and relatively safe definitive treatment options for MNG: RAI therapy and thyroid surgery.

In MNG, the risk of retreatment or need for retreatment is <1% after near-total and/or total thyroidectomy, compared with a 20% risk of retreatment need after RAI therapy [2].

In cases 1 and 2, compressive elements were present, which determined the choice of surgical treatment. In a retrospective study of patients with MNG who presented compressive symptoms, in all cases that underwent total thyroidectomy there was resolution of these symptoms after treatment, while in 46% of the patients who underwent RAI these symptoms improved [7]. In very large goiters treated with RAI, they decrease in size between 30% and 50% [8].

To minimize the risks of thyrotoxic crisis, patients must reach eu-thyroidism prior to surgery. In our cases with manifest hyperthyroidism (1 and 4), methimazole was used for this purpose; in the others beta blockers were used.

All patients in this series were left with hypothyroidism, as described in all cases of near-total or total thyroidectomy.

In RAI therapy, hypothyroidism appears sometimes, with variable figures such as 50% to 60% at 3 months and 80% at 6 months [2].

In case 5 the patient had already received a dose of RAI that was not curative. The success rate of RAI (definitive hypothyroidism or eu-thyroidism) is 81.1% in patients with MNG [9].

In the following circumstances, surgery is considered more appropriate as definitive treatment, such as: the presence of compressive symptoms or signs in the neck (case 1), large goiter (>80 g), as in case 5, substernal or retrosternal extension (case 2) or the need for rapid correction of the thyrotoxic state (case 1). In case 3, thyroidectomy was performed due to the presence of a 7.5 cm nodule and in case 4 at the patient's request [7].

In case 4 there was an incidental finding of differentiated thyroid cancer. The prevalence of thyroid cancer in MNG can reach 9%, which is similar to the 10.6% prevalence observed in nontoxic MNG [10].

Conclusion

Toxic multinodular goiter is an entity that determines considerable morbidity and mortality, especially in elderly patients.

In cases where there are compressive elements, intrathoracic goiter or large thyroid volumes, surgical indication prevails over radioiodine therapy.

Near-total or total thyroidectomy is the technique of choice in experienced surgeons and in patients in whom eu-function has been achieved with antithyroid drugs.

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