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Case Report
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Graves' Ophthalmopathy Induced by Radioiodine Therapy for Toxic Thyroid Adenoma

Laura Delegido-Gomez[1#], Soledad Serrano Corredor[2], Paula Revert[2] and Ruth Sanchez-Ortiga[2#]*

[1]*Department of Endocrinology, Hospital Marina Baixa, Spain*

[2]*Department of Endocrinology, Hospital General Universitario de Alicante, Spain*

[#]*These authors equally contributed to this work*

Abstract

Graves's Disease (GD) may develop as an infrequent adverse effect after radioiodine therapy for toxic thyroid adenoma and toxic multi nodular goiter. We present a case of a 64- year-old female treated with radioiodine therapy for toxic adenoma and subclinical hyperthyroidism, whose antithyroid peroxidase and TSH-Receptor Antibodies (TRAbs) were negatives. She didn't smoke. After therapy, the patient became hyperthyroid and presented ophthalmopathy with positive TRAb. She underwent to corticosteroid and anti-thyroid treatment. After eighteen months of treatment, she maintained asymptomatic and TRAb were negatives. The radioiodine therapy for toxic adenoma may induce GD and thyroid ophthalmopathy even in absence of classical risks factors.

Keywords: Thyroid-associated orbitopathy; Graves's disease; Radioiodine therapy; Thyroperoxidase antibody; Thyrotropin receptor antibodies; Thyroid toxic adenoma

Introduction

The most common causes of primary hyperthyroidism are Graves' Disease (GD), Toxic Multi-Nodular Goiter (TMNG), and Toxic Adenoma (TA). GD is an autoimmune disease due to elevation of TSH-receptor antibodies (TRAbs) and/or Antithyroid Peroxidase Antibodies (TPOAb), whereas TMNG and TA are caused by autonomous function of thyroid nodules that can be evidenced on scintigraphy [1]. Actual guidelines suggest treating with Radioiodine Therapy (RAI) or surgery hyperthyroidism caused by Toxic Adenoma (TA). Overall, the success rate of RAI (definitive hypothyroidism or euthyroidism) is 93.7%. However, following RAI therapy there have been reports of new-onset GD (up to 4% prevalence) as well as concern for thyroid malignancy and a very minimal increase in late non-thyroid malignancy [1].

Clinical Case

We presented a 64 year old woman with primary hyperthyroidism. She was referred by digestologist who treated her for cholelithiasis and positive Antinuclear Antibodies (ANA). She didn't have symptoms of thyroid hyperfunction or local compression. TSH, Free T4, TRAbs and TPOAbs values are summarized on Table 1. Two solid hypoechoic nodules on right lobe of 14 mm × 12 mm × 20 mm and 23 mm × 17 mm × 23mm, well-defined, with peripheral and intranodular vascularity were described on ultrasound. Therefore we performed a scintigraphy ^{99m}Tc pertechnetate that showed focal enhancement on right lobe and suppression of extra nodular tissues. After discussion of treatment possibilities, the patient underwent to RAI therapy without immediately adverse effects. However, forty five days after RAI she complained about palpitations, insomnia, excessive tearing and ocular pain. On physical examination we found elevated cardiac rate, swelling of eyelids, redness of conjunctiva and chemosis. We assessed activity by the Clinical Activity Score (CAS) as 4/7. Exophthalmos plus thickening of both inferior rectus were described by orbital MRI (Figure 1). At that moment, she had clinical hyperthyroidism with positive-TRAbs on laboratory tests (Table 1). We started tiamazol 2.5 mg per day, selenium supplementation and propanolol. After no-improvement, she needed i.v. methylprednisolone bolus (protocol 0.5 g i.v. methylprednisolone once weekly for 6 weeks, followed by 0.25 g once weekly for 6 weeks). However due to adverse effects she only received 2.5 g of methylprednisolone, with clinical complete ocular response (CAS 0). She completed eighteen months of tionamides achieving euthyroidism (Table 1).

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Correspondence:
Ruth Sanchez-Ortiga, Department of Endocrinology, Hospital General Universitario de Alicante, Alicante 03010, Spain,
E-mail: ruthsanchez@coma.es

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Table 1: Laboratory test.

	Reference range	Before RAI therapy	2 months after RAI	6 months after RAI	18 months after RAI
TSH mU/L	0.38-4.84	<0.2	0.15	2.27	4.63
FT3 pg/mL	1.6-4.6	6.3	5	2.8	3.6
Ft4 pg/mL	0.8-2.0	1	1.6	1.3	1.1
TRAb UI/mL	0.0-1.5	0.5	102.1	4.3	0.8
TPOAb UI/mL	0.0-16.0	5.0	3.0	na	na

RAI: Radioiodine Therapy; TRAbs: TSH-Receptor Antibodies; TPOAb: Antithyroid Peroxidase Antibodies; na: non-available

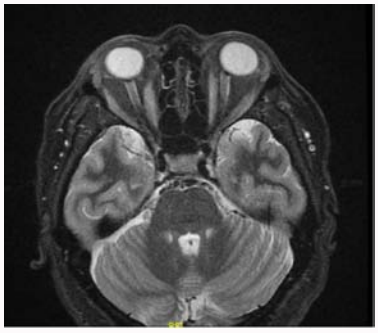

Figure 1: Orbital MRI showing hyperintensity in the inferior rectus and contrast enhancement along with bilateral exophthalmos.

Discussion

Our patient developed Graves' Ophthalmopathy (GO) and GD after RAI therapy for subclinical hyperthyroidism due to toxic adenoma. New-onset GD following RAI therapy is infrequent (less than 4%) and its risks factors are the presence of TPOAbs (incidence up to 22%) [1-10]. The presence of circulating TRAbs in patients with TMNG or TA points to a diagnosis of Marine-Lenhart's syndrome [3] and it should be excluded before RAI therapy. Other rare causes of new-onset GD are percutaneous ethanol injection, parathyroidectomy or thyroid surgery [11-13]. It has been proposed that these situations would release TSH receptor of follicular cells, which would cause an immune reaction and TRAbs activation [8,12]. Furthermore radiation would deteriorate balance between T-helper and suppressor lymphocytes [4]. Although the patient had negative TPOAbs or TRAbs prior to RAI therapy, she had autoimmune background as ANA were positive. New-onset GD was treated with anti-thyroid drugs along 18-months due to the presence of GO and patient' preferences. On the other hand, it is well- known that RAI-treated GD patients are at risk of progression or de novo development of GO. To date, risks factors are smoking, severe/unstable hyperthyroidism and high serum TRAbs [1,14,15]. In these cases, guidelines recommended concomitant short-term course of oral prednisone in order to prevent RAI-associated [15]. Nevertheless the patient described did not have any risk factors but she developed of moderate-to-severe GO after RAI therapy for non-GD disease. In the literature, there has been described one case of OG after RAI therapy for TMNG [2]. However, that patient turned positive-TRAbs after first dose of I-131 and developed OG after second dose of I-131.

As conclusion, clinicians must be aware of risk of GD and GO development after RAI therapy of thyroid dysfunction even in subjects with negative TPOAbs and TRAbs. The role of other autoimmune factors, as ANA, should be confirmed.

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