Case Report

iMedPub Journals
http://www.imedpub.com/

Journal of Clinical and Molecular Endocrinology
ISSN 2572-5432

2016
Vol.2 No.1:7

DOI: 10.21767/2572-5432.10043

False Positive TSH Receptor Binding Inhibitory Immunoglobulin in a Patient with Overt Hyperthyroidism Caused by Painless Thyroiditis

Run Yu

Division of Endocrinology, Diabetes, and Metabolism, UCLA David Geffen School of Medicine, Los Angeles, CA 90095, USA

Corresponding author: Yu R, Division of Endocrinology, Diabetes, and Metabolism, UCLA David Geffen School of Medicine, Los Angeles, USA; Tel: 310-825 7922; E-mail: runyu@mednet.ucla.edu

Rec date: Oct 28, 2016; **Acc date:** Dec 02, 2016; **Pub date:** Dec 05, 2016

Citation: Yu R (2016) False Positive TSH Receptor Binding Inhibitory Immunoglobulin in a Patient with Overt Hyperthyroidism Caused by Painless Thyroiditis. J Clin Mol Endocrinol 2: 7.

Abstract

The diagnosis of Graves's disease (GD) can be challenging in patients with atypical presentations of hyperthyroidism. Recently, TSH receptor antibody assays are proposed as first-line test for suspected GD. I here report a case of false positive TSH receptor binding inhibitory immunoglobulin (TBII) in an elderly male patient with overt hyperthyroidism caused by painless thyroiditis. This case highlights the fallacy of overreliance on TBII in making the GD diagnosis. The differential diagnosis of hyperthyroidism should not rely solely on TSH receptor antibody assays to confirm or rule out GD because false positive results are possible in patients with other causes of hyperthyroidism, like the patient reported here. Radioactive iodine uptake and scan is likely the best diagnostic test for patients with atypical presentation of hyperthyroidism.

Keywords: TBII, Graves' disease, false positive, painless thyroiditis

Introduction

The diagnosis of Graves' disease (GD) is usually straightforward in patients with typical clinical presentation of persistent hyperthyroidism and ophthalmopathy. The diagnosis of GD can be challenging in patients with subacute or subclinical hyperthyroidism, atypical symptoms of hyperthyroidism, or drug-induced hyperthyroidism [1,2]. The "gold criteria" for the diagnosis of GD traditionally have been radioactive iodine uptake and scan in a patient with clinical hyperthyroidism [1,3]; recently, TSH receptor antibody (TRAb) assays are proposed as first-line test for suspected GD [2,4]. Two types of TRAb assays are available: bioassay of thyroid-stimulating immunoglobulin (TSI) and binding assay of TSH receptor binding inhibitory immunoglobulin (TBII) [5,6]. Most experts consider that the two types of assays are equivalent for the diagnosis of GD in patients with hyperthyroidism and either test can be used alone [1-6]. I here report a case of false positive TBII in a patient with overt hyperthyroidism caused by painless thyroiditis.

Case report

A 73-year-old man had a weight loss of 25 lbs in a month, accompanied with fatigue, anxiety, and short temper. His thyroid function had been normal one and half years before presentation. He had a pacemaker due to heart block but had never taken amiodarone or had any recent exposure to iodine-containing radiocontrast or topical iodine. He had no preceding viral illness and denied anterior neck pain or tenderness or eye discomfort. His vital signs were normal. His height was 1.85 m, weight 71.22 kg (157 lbs), and body mass index (BMI) 20.72 kg/m^2. He appeared well and had no proptosis. His thyroid was grossly enlarged and non-tender, and felt lumpy-bumpy without clear palpable thyroid nodules or neck lymph nodes. Hyperthyroidism was suspected and confirmed by thyroid function tests: TSH 0.01 µIU/mL (normal 0.35-4.94), and free T4 5.1 ng/dL (0.70-1.48). Erythrocyte sedimentation rate (ESR) was 13 mm/h (0-15).

GD was considered and thyroid antibody tests performed. In the first laboratory, thyroid peroxidase (TPO) antibody titer was 21 IU/mL (<9), and TSI <89% (<140%). The thyroid antibody tests were then sent to a second laboratory and the results were: TPO antibody titer 15.6 IU/mL (<9), TSI 94 (<=122%), and TBII 7.07 IU/L (<=1.75). To resolve the discrepancy between TSI and TBII in this hyperthyroid patient, radioactive iodine uptake and scan was done which showed uptake of 1.3% at 4 h (4-18%) and 1.1 % at 24 h (8-33%). Painless thyroiditis was diagnosed and patient treated with propranolol.

Discussion

This case highlights the fallacy of overreliance on TBII in making the GD diagnosis. This patient had high titers of TBII but he was finally diagnosed with painless thyroiditis based on very low radioactive iodine uptake and negative TSI. Had only the TBII assay been ordered, he would have been misdiagnosed with GD. The differential diagnosis of hyperthyroidism includes GD, hot nodule, iodine exposure, thyroiditis, and other rare causes [1,2]. It is important to differentiate GD from other causes of hyperthyroidism as the natural history and management of GD are different. Traditionally, radioactive iodine uptake and scan

has been the preferred study for confirming or ruling out GD in a patient with clinical hyperthyroidism because the single test can make the diagnosis of not only GD but also hot nodule, iodine exposure, and thyroiditis [1,3].

The radioactive iodine uptake and scan, however, is expensive and requires two visits within 24 h, is contraindicated in pregnant or breast-feeding females or in patients with iodine allergy, and requires careful interpretation if iodine uptake is low which is not only caused by thyroiditis but also by non-thyroidal, factitious or ectopic, thyrotoxicosis. TRAb assays directly address the etiology of GD, require only one blood draw, and become more accurate and standardized and less expensive in recent years [5,6]. Authoritative reviews have called for the use of TRAb assays as the initial diagnostic test for GD and considered the two types of TRAb assays, TSI and TBII, as approximately equivalent in hyperthyroidism differential diagnosis [2,4].

TBII is slightly favored over TSI because the former is technically less complicated, can be automated, and is less expensive and more widely available [5,6]. There have been a few studies directly comparing the performance of TSI and TBII in diagnosing GD but none of them is performed prospectively in patients with known hyperthyroidism (so as to determine the etiology of hyperthyroidism) [7-10]. The often-touted high sensitivity and specificity of TSI and TBII (each approaching 99%) are more theoretical calculations than values determined by prospective trials [4,5]. Both TSI and TBII can be false positive in thyroiditis [8,9,11]. In elderly patients like the one reported here, GD is relatively less common than in younger patients [12], making the positive predictive value of TSI or TBII lower and the probability of alternative causes of hyperthyroidism higher. Painless thyroiditis usually causes mild hyperthyroidism but can cause overt, symptomatic hyperthyroidism in some patients [13], as seen in the case reported here.

In summary, the differential diagnosis of hyperthyroidism needs to consider the patient's demographics and clinical presentation and should not rely solely on TRAb assay to confirm or rule out GD. False positive TRAb results are possible in patients with other causes of hyperthyroidism, like the patient reported here. Radioactive iodine uptake and scan is likely the best diagnostic test for patients with atypical presentation of hyperthyroidism.

References

1. Brent GA (2008) Clinical practice. Graves' disease. N Engl J Med 358: 2594-2605.
2. Smith TJ, Hegedüs L (2016) Graves' Disease. N Engl J Med 375: 1552-1565.
3. Bahn RS, Burch HB, Cooper DS, Garber JR, Greenlee MC, et al. (2011) Hyperthyroidism and other causes of thyrotoxicosis: management guidelines of the American Thyroid Association and American Association of Clinical Endocrinologists. Endocr Pract Thyroid 21: 593-646.
4. Barbesino G, Tomer Y (2013) Clinical review: Clinical utility of TSH receptor antibodies. J Clin Endocrinol Metab 98: 2247-2255.
5. Zöphel K, Roggenbuck D, Schott M (2010) Clinical review about TRAb assay's history. Autoimmun Rev 9: 695-700.
6. Kamath C, Adlan MA, Premawardhana LD (2012) The role of thyrotrophin receptor antibody assays in graves' disease. J Thyroid Res 2012: 525936.
7. Morris JC 3rd, Hay ID, Nelson RE, Jiang NS. (1988) Clinical utility of thyrotropin-receptor antibody assays: comparison of radioreceptor and bioassay methods. Mayo Clin Proc 63: 707-717.
8. Schott M, Hermsen D, Broecker-Preuss M, Casati M, Mas JC, et al. (2009) Clinical value of the first automated TSH receptor autoantibody assay for the diagnosis of Graves' disease (GD): an international multicentre trial. Clin Endocrinol (Oxf) 71: 566-573.
9. Kamijo K, Murayama H, Uzu T, Togashi K, Olivo PD, et al. (2011) Similar clinical performance of a novel chimeric thyroid-stimulating hormone receptor bioassay and an automated thyroid-stimulating hormone receptor binding assay in Graves' disease. Thyroid 21: 1295-1299.
10. Leschik JJ, Diana T, Olivo PD, König J, Krahn U, et al. (2013) Analytical performance and clinical utility of a bioassay for thyroid-stimulating immunoglobulins. Am J Clin Pathol 139: 192-200.
11. Dow A, Azer P, Yu R (2014) Subacute thyroiditis metamorphosing into Gravesâ€™ disease. Endocrinol Nutr 61: 171-172.
12. Boelaert K, Torlinska B, Holder RL, Franklyn JA. (2010) Older subjects with hyperthyroidism present with a paucity of symptoms and signs: a large cross-sectional study. J Clin Endocrinol Metab 95: 2715-2726.
13. Schwartz F, Bergmann N, Zerahn B, Faber J. (2013) Incidence rate of symptomatic painless thyroiditis presenting with thyrotoxicosis in Denmark as evaluated by consecutive thyroid scintigraphies. Scand J Clin Lab Invest. 73: 240-244.