

# A case of Graves disease with negative thyrotropin stimulating antibodies in a pediatric patient with type 1 diabetes

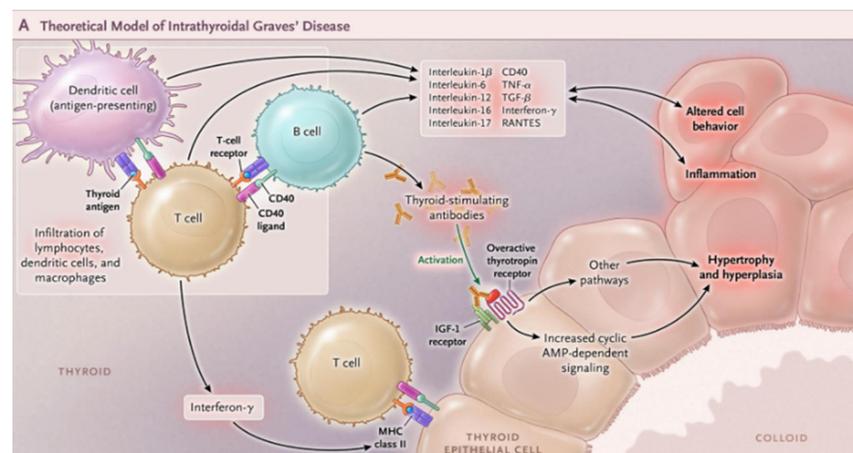
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## INTRODUCTION

Graves disease (GD) is an autoimmune condition caused by direct stimulation of the thyroid epithelial cells by thyrotropin (TSH) receptor antibodies (TRAb). The action of TRAb can be stimulating, blocking or neutral. Antibodies with agonist action are also called thyroid stimulating immunoglobulins (TSI).

The diagnosis of GD is typically confirmed with TSI titer which is positive in >90% of patients. In patients that have negative TSI, highly sensitive and specific assays for detecting TRAb antibodies are available but they are rarely ordered.



## CASE

The patient is a 14-year male with type 1 diabetes mellitus that was found to have a suppressed thyroid stimulating hormone (TSH) <0.002 uIU/mL (0.350-4.94), elevated free thyroxine (FT4):1.8 ng/dL (0.7-1.5) with elevated total triiodothyronine (T3):1.9 ng/dL (0.6-1.6), negative thyroid-stimulating immunoglobulin (TSI) <89 (<140%), positive antithyroid peroxidase antibodies (antiTPO)-50.4IU/mL (0.0-5.6) and positive anti-thyroglobulin antibodies-43.2IU/L (0.0-4.1). Based on these studies he was diagnosed with hyperthyroidism due to Hashimoto thyroiditis.

Initially, he was asymptomatic, and he was not placed on any antithyroid medication. Two months later due to weight loss and elevated FT4-2.0 ng/dL, he was started on methimazole (MMI) 2.5 mg daily, adjusted to 5mg daily. Seven months after starting MMI, FT4 had normalized. He developed neutropenia and MMI was discontinued. One month later, FT4 increased to 2.1ng/dL and T3 -2.1 ng/dL, TSI negative and TRAb: 6.93 IU/L (0.00 - 1.75). He was diagnosed with hyperthyroidism due to GD.

The decision was made to restart him on MMI and propranolol. We consulted hematology-oncology regarding his mild neutropenia, and it was thought that most likely it was due to ethnic variation. An anti-neutrophil antibody level was obtained and was negative. Parents discontinued propranolol and were not comfortable with a higher dose of MMI.

Currently, he is on low dose MMI 5mg daily and his FT4 continues to be elevated. Permanent treatment for his autoimmune hyperthyroidism has been discussed with family.

## CONCLUSION

This was an interesting case of TSI negative, TRAb-positive Graves disease in a pediatric patient with type 1 diabetes. Initially, his hyperthyroidism was thought to be due to Hashitoxicosis, based on his clinical presentation and laboratory studies with negative TSI. When his hyperthyroidism was not improving, TSI was remeasured and continued to be negative, TRAb was measured and was positive.

Both TSI and TRAb measure the stimulating TSHR antibodies but they are using different bioassays. Widely available TRAb measurement methods have been significantly improved recently. However, TRAb is not always used in the United States as a first-line test in the differential diagnosis of hyperthyroidism

## REFERENCES

1. Giuseppe Barbesino, Yaron Tomer. Clinical Utility of TSH Receptor Antibodies. *JCEM, Volume 98, Issue 6, 1 June 2013, Pages 2247-2255*
2. Smith TJ, Hegedus L. Graves' disease, *NEJM* 2017 Jan 12;376(2):185. doi: 10.1056/NEJMc1614624.
3. McLachlan SM, Rapoport B. Thyrotropin-blocking autoantibodies and thyroid-stimulating autoantibodies: Potential mechanisms involved in the pendulum swinging from hypothyroidism to hyperthyroidism or vice versa. *Thyroid* 2013;23:14-24.
4. Lytton SD, Kahaly GJ. Bioassays for TSH-receptor autoantibodies: An update. *Autoimmun Rev* 2010;10:116-22.

## DISCLOSURES

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