WHEN IS A POSITIVE ANTI-TG, ANTI-TPO OR ANTI-TSH-RECEPTOR TITER CLINICALLY USEFUL?

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BACKGROUND

Antithyroid antibodies are often present in the serum by the time a patient is diagnosed with either Graves' disease or Hashimoto's thyroiditis. The authors measured antithyroid peroxidase (TPO), antithyroglobulin (Tg) and anti-TSH receptor (TSH-R) levels in serum samples drawn years earlier from women now 23 to 50 years of age in whom Graves' or Hashimoto's disease developed in an attempt to find out when the antibodies first began to appear.

METHODS

Between 1998 and 2007, 1684 (of more than 540,000) female active-duty U.S. military personnel who were seen in a rheumatology, family medicine, obstetrics-gynecology, internal medicine, or endocrine clinic were given a new diagnosis of Hashimoto's thyroiditis or Graves' disease. A blood sample drawn within 6 months before or after the diagnoses, plus three earlier serum samples had to be available. The four samples from each randomly selected patient with Hashimoto's thyroiditis or Graves' disease (87 each), and from 348 age-matched controls were assayed for anti-TPO and anti-Tg (both by enzyme-linked immunosorbent assay [ELISA]). TSH-R antibody

levels were assayed (by ELISA) in all the patients with Graves' disease and in some controls.

Clinical

THYROIDOLOGY

RESULTS

Anti-TPO, anti-Tg, or both were positive in 50 of the controls. In the pre-Hashimoto's samples, the percent that were positive did not change over 5 to 7 years: 66% had positive anti-TPO titers and 50% had positive anti-Tg titers at 5 to 7, 3 to 5, and 0.5 to 2 years before, as well as at the time of diagnosis. No TSH-R antibodies were found in 17 pre-Hashimoto's serum samples drawn 5 to 7 years before the diagnosis was made. In the pre-Graves' samples, the mean anti-Tg and anti-TPO levels were not significantly different from controls at any individual time point before the diagnosis, although the rate of increase was significantly higher than in controls. TSH-R antibodies were detected in only 2% of samples drawn 5 to 7 years before the diagnosis was made, in 7% of samples at 3 to 5 years, in 20% of samples at 6 to 24 months before diagnosis, and in 55% at the time of diagnosis ± 6 months.

CONCLUSIONS

The authors conclude that thyroid antibodies in apparently healthy individuals should not be neglected and may serve as a useful tool to screen for autoimmune thyroid diseases before clinical diagnosis.

COMMENTARY • • • • • • • • • • • • • • • • •

In general, the most sensitive test of thyroid hormone status is the TSH level, recognizing that after treatment of either Hashimoto's thyroiditis or Graves' disease, the TSH level can lag behind the normalization of thyroxine (T_4) and triiodothyronine (T_3) levels (TSH values were not provided in the present study). Antibodies to TPO and TG are not uncommon in euthyroid individuals. When the thyroids of such individuals have been examined, foci of lymphocytic infiltration have been found. Such foci are also found in thyroids of patients with Graves' disease as well as in or near benign and malignant thyroid tumors, but generally are more extensive in Hashimoto's thyroiditis. The epitopes on TPO and TG that are recognized by antibodies can change with time, and the balance between antibodies that stimulate and those that block the TSH receptor can shift, influencing thyroid size or nodularity as well as hormone levels.

continued on next page

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Hashimoto's thyroiditis often presents as a goiter in adolescents and young adults, and these patients often remain euthyroid, whereas some whose TSH was initially above normal or who were overtly hypothyroid subsequently return to euthyroidism, and yet others continue to or subsequently have hypothyroidism (1). Adult patients with Hashimoto's thyroiditis often do not have a goiter (clinical information about the patients was not provided in the present study). A common diagnostic and clinical problem is the patient who has symptoms that might indicate hypothyroidism but who has no positive physical findings. When tests for $T_4/$ free T₄, T₃, and TSH are ordered, they turn out to be normal. However, if antithyroid antibodies are also ordered and they turn out to be positive, what should the physician do? Most will follow the patient's TSH level closely. However, if you simply assume that the diagnosis is Hashimoto's thyroiditis and put the patient on levothyroxine therapy, then even if the patient's symptoms improve, you have not established that your diagnosis is correct. On the other hand, a euthyroid woman with positive antibodies and a TSH that is within the normal range

but >2.5 mU/L is more than four times as likely to have hypothyroidism over the next 13 years than if her TSH is ≤ 2.5 mU/L (2).

Only 55% of the patients with Graves' disease had positive anti-TSH-R antibodies in this study, perhaps because samples could be drawn 6 months after the diagnosis was made, and antithyroid therapy can reduce mean anti-TSHR-stimulating antibody levels by more than half (and anti-TPO titers by two-thirds) in adults within 6 months (3). Anti-TSH-R assays can be useful in evaluating pregnant women who currently have or previously had Graves' disease; in newborns with possible neonatal hyperthyroidism or who may be transiently hypothyroid because of blocking antibodies; in patients in whom euthyroid Graves' ophthalmopathy is suspected; in confirming Graves' disease in hyperthyroid patients in whom a radioiodine uptake and scan should not or cannot be performed; and possibly in determining the likelihood of a recurrence of Graves' disease before discontinuing antithyroid drug therapy.

— Stephen W. Spaulding, MD

References

- 1. Demirbilek H, Kandemir N, Gonc EN, et al. Assessment of thyroid function during the long course of Hashimoto's thyroiditis in children and adolescents. Clin Endocrinol 2009;71:451-4.
- 2. Walsh JP, Bremner AP, Feddema P, et al. Thyrotropin and thyroid antibodies as predictors of hypothyroidism: a 13-year, longitudinal study of a community-based cohort using current

immunoassay techniques. J Clin Endocrinol Metab 2010;95:1095-104.

3. Guilhem I, Massart C, Poirier JY, Maugendre D. Differential evolution of thyroid peroxidase and thyrotropin receptor antibodies in Graves' disease: thyroid peroxidase antibody activity reverts to pretreatment level after carbimazole withdrawal. Thyroid 2006;16:1041-5.