Ref: Ro Med J. 2018;65(2)
DOI: 10.37897/RMJ.2018.2.10

ANTIBODIES AGAINST THYROID AND THYROID STIMULATING HORMONE (TSH): WHO'S WHO?

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ABSTRACT

This is a 67-year old male who was referred for autoimmune myxedema after prior presentation in different departments. This real life case introduces the discussion related to relationship TSH and specific thyroid antibodies against thyroid. Despite relative high frequency, autoimmune thyroiditis may be under diagnosed until myxedema is recognised, challenging various differential diagnoses, as in our case. Male are rarer affected than women. Overall, the levels of thyroid antibodies are not correlated with TSH; neither they predict the pattern of response to levothyroxine substitution.

Keywords: thyroid, myxedema, antibodies, ultrasound

INTRODUCTION

Chronic autoimmune thyroiditis (CAT) is caused by antibodies against thyroid like anti-thyroperoxidase (TP) and anti-thyroglobulin (TG) antibodies (1-3). They cause primary hypothyroidism, but the increase of TSH (Thyroid Stimulating Hormone) is not directly correlated with the level of antibodies which actually do not represent a prognosis factor according to most of the studies, but a correlation with differentiated thyroid cancer, breast cancer in females or metabolic complications have been observed (1-4). We aim to introduce an adult case who was first diagnosed with CAT because of severe myxedema symptoms. This is a case report. The patient agreed for anonymously use of his medical records.

CASE PRESENTATION

This is a 67-year old former smoker coming from non-endemic area, who accused breathing difficulties and palpitations. His medical family history is negative, so is his personal and medical history. He was first seen at cardiology and then referred to pneumology and then to endocrinology. On admission, typical presentation of myxedema was found; slow speech and movements; dry skin, sinus bradicardia. Blood tests showed high TP, of 855 UI/ml (normal levels less than 35 UI/ml), and primary hypothyroidism based on low FreeT4 levels (of 3.8 pmol/l, normal ranges between 10.3 and 24.4 pmol/l), and very high TSH, of 75 µUI/ml (normal levels between 0.5 and 4.5 µUI/ml). Thyroid ultrasound showed a right lobe of 1.8 by 1.5 by 3.5 cm (centimetre), an isthmus of 0.29 cm, a left lobe of 1.3 by 1.22 by 3.4 cm, of hypoechoic, inhomogeneous pattern, and normal Doppler signal on both lobes, without thyroidnodules, but a left lymph node enlargement of 0.8 by 0.4 cm (probably of reactive type) (Fig. 1). Electrocardiogram confirmed slow cardiac rhythm, of 49 beats per minute, diffuse hypo voltage of T wave (Fig. 2). The patient was offered low dose of daily levothyroxine (starting with 25 µg per day and progressively increasing to daily 50 µg) with mild progressive clinical improvement. Within two months, thyroid ultrasound was stationary but TSH decreased to 36.8 µUI/ml (normal values between 0.5 and 4.5 µUI/ml), with FreeT4 of 9.16 pmol/l (normal ranges between 10.3 and 24.4 pmol/l), and similar values of TP (of 815 UI/ml, normal ranges below 35 UI/ml) (Fig. 3). TSH normalized within 2 months after extra 25 µg added per day.

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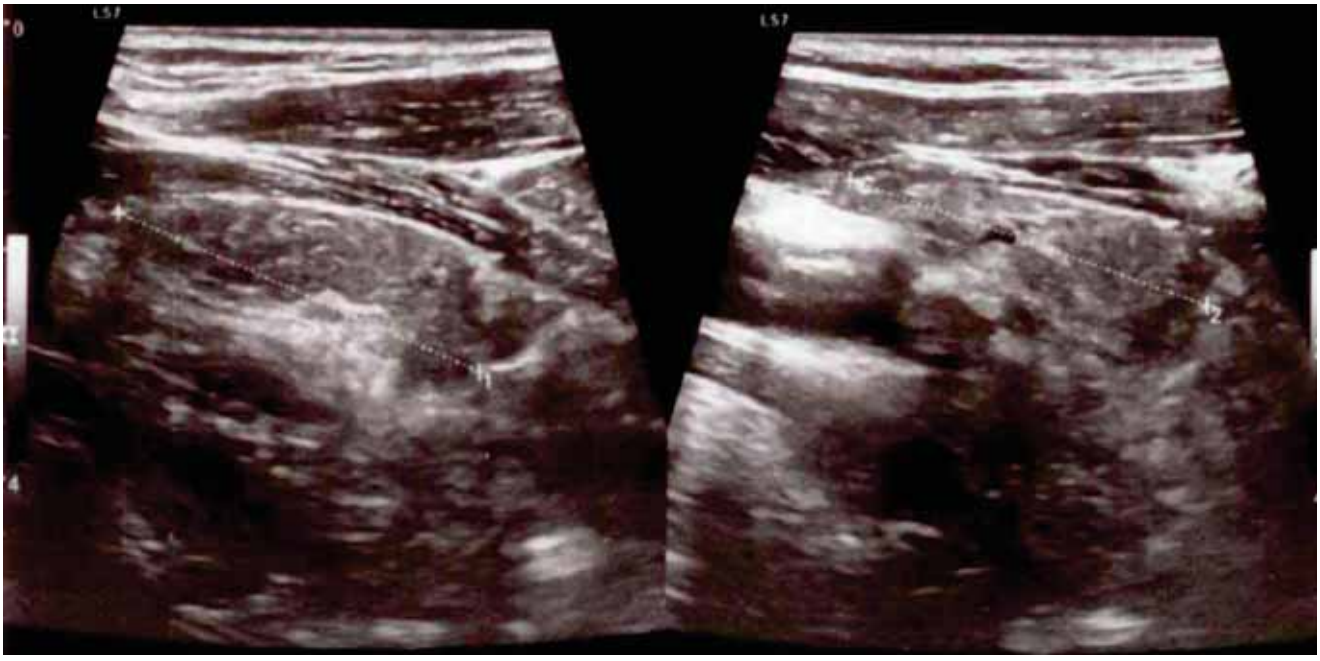

FIGURE 1. *Thyroid ultrasound on a 67-year old adult with autoimmune myxedema reveals a right lobe of 1.8 by 1.5 by 3.5 cm (centimetre), an isthmus of 0.29 cm, a left lobe of 1.3 by 1.22 by 3.4 cm, of hypoechoic, inhomogeneous pattern, and normal Doppler signal on both lobes, without thyroid nodules and a left lymph node enlargement of 0.8 by 0.4 cm.*

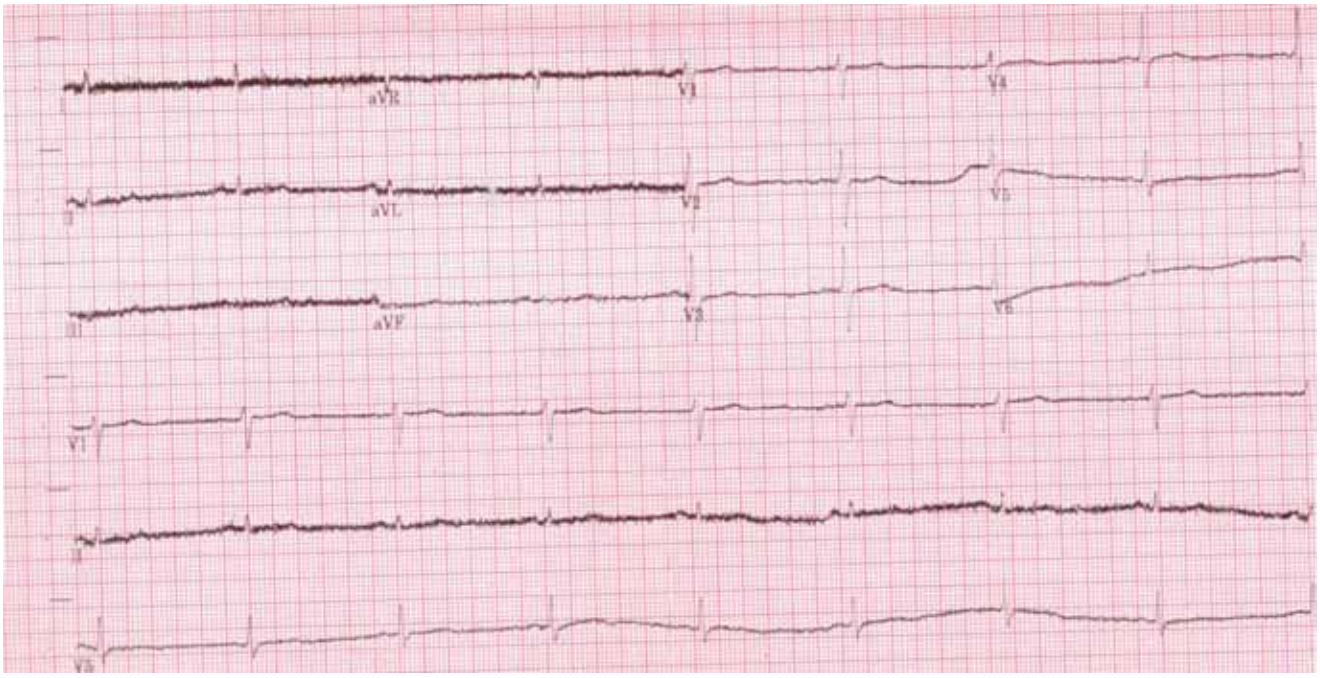

FIGURE 2. *67-year old male; suggestive electrocardiogram findings for myxedema - slow cardiac rhythm, of 49 beats per minute, diffuse hypovoltage of T wave*

DISCUSSION

Autoimmune chronic Hashimoto thyroiditis is a relatively frequent condition of modern society because of environmental triggers and easy access to thyroid antibodies blood assays (5). The etiology is mixed: genetic and environmental elements; men are less affected than women, as seen in this case (5). Thyroid antibodies do not predict with precision the moment of hypothyroidism onset, neither the highest values of TSH (6). Genetic background has been studied to sustain the autoimmune versus functional profile, including what kind of patients display a higher risk of hypothyroidism (5,6). No clear conclusion is yet used in daily practice. The abnormal function is actually the only therapeutic

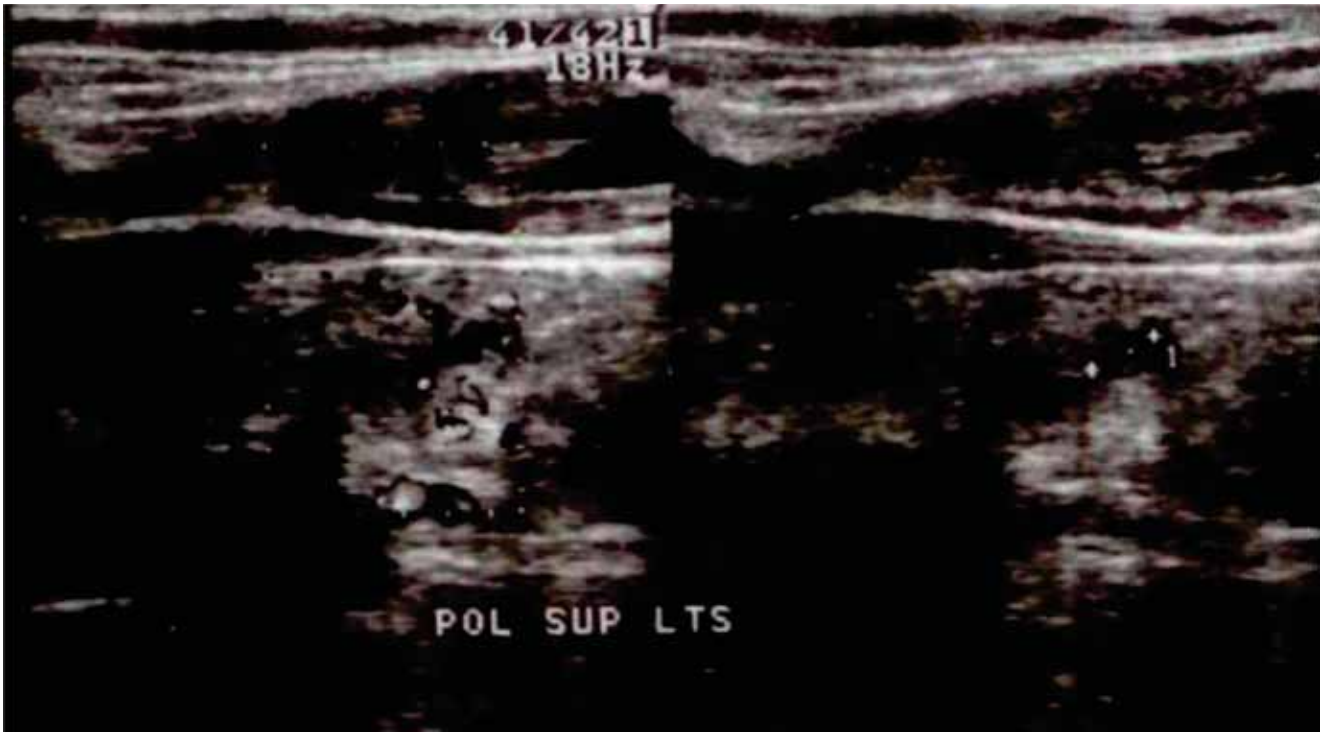

FIGURE 3. *Thyroid ultrasound on a patient with treated autoimmune myxedema; stationary aspects which are highly suggestive for an autoimmune thyroid condition (hypo-echoic, inhomogeneous)*

target, not the antibodies themselves (opposite to other non-endocrine conditions like most of rheumatologic diseases) (5,6). Some studies support the idea of selenium supplementation as single therapy in euthyroid subjects or in combination with levothyroxine substitution in patients with hypothyroidism but selenium as therapeutic option did not actually reach guideline indication up to this moment due to heterogenous evidence based medicine data (7-10). Neither we used selenium in this case of autoimmune myxedema despite elevated levels of TP. Actually, a third type of antibodies against thyroid a part from TP and TG may be found in chronic thyroiditis, especially in cases with atrophic gland at ultrasound and myxedema: TSH receptor blocking antibodies which are opposite to TSH receptor stimulating antibodies, typically for Basedow-Graves's disease (11,12). These antibodies are not assessed on every day practice (11,12).

CONCLUSION

Despite relative high frequency, autoimmune thyroiditis may be under diagnosed until myxedema is recognised, challenging various differential diagnoses, as in our case. Male are rarer affected than women. Overall, the levels of thyroid antibodies are not correlated with TSH, neither predict the pattern of response to levothyroxine substitution.

REFERENCES

1. **Bircan H.Y., Koc B., Akarsu C., Demiralay E., Demirag A., Adas M., Alis H., Kemik O.** Is Hashimoto's thyroiditis a prognostic factor for thyroid papillary microcarcinoma? *Eur Rev Med Pharmacol Sci.* 2014 Jul; 18(13):1910-5.
2. **Valea A., Albu S.E., Petrescu R., Carsote M.** Chronic thyroiditis and differentiated thyroid cancer: From overlapping high prevalence to a shift on multifocal intra-thyroid papillary thyroid carcinoma. *Journal of Surgical Sciences.* 2017; 4(1):38-45.
3. **Valea A., Ghervan C., Morar A., Pop D.D., Carsote M., Albu S.E., Georgescu C.E., Chiorean A.** Hashimoto's thyroiditis and breast cancer: Coincidence or correlation? *Archives of Balkan Medical Union*. 2016; 51(1):129-132
4. **Valea A., Carsote M., Morar A., Mihalca D., Tarau R., Marcusanu A., Talpasanu A., Chereji A., Georgescu C.E.** High cardio-metabolic risk parameters: A cross-sectional study in 80 women and men diagnosed with chronic thyroiditis (an age decades analysis). *Current Health Sciences Journal.* 2015. 41 (Suppl. 1):101-104.
5. **Dong Y.H., Fu D.G.** Autoimmune thyroid disease: Mechanism, genetics and current knowledge. *Eur Rev Med Pharmacol Sci.* 2014; 18(23):3611-8.
6. **Brčić L., Gračan S., Barić A., Gunjača I., Torlak Lovrić V., Kolčić I., Zemunik T., Polašek O., Barbalić M., Punda A., Boraska Perica V.** Association of Established Thyroid-stimulating Hormone and Free

Thyroxine Genetic Variants with Hashimoto's Thyroiditis. *Immunol Invest.* 2017 Aug; 46(6):625-638.

7. **van Zuuren E.J., Albusta A.Y., Fedorowicz Z., Carter B., Pijl H.** Selenium supplementation for Hashimoto's thyroiditis. *Cochrane Database Syst Rev.* 2013 Jun 6; (6):CD010223.
8. **Yu L., Zhou L., Xu E., Bi Y., Hu X., Pei X., Jin G.** Levothyroxine monotherapy versus levothyroxine and selenium combination therapy in chronic lymphocytic thyroiditis. *J Endocrinol Invest.* 2017 Nov; 40(11):1243-1250.
9. **Drutel A., Archambeaud F., Caron P.** Selenium and the thyroid gland: More good news for clinicians. *Clin Endocrinol* (Oxf). 2013 Feb;78(2):155-64.
10. **Radetti G.** Clinical aspects of Hashimoto's thyroiditis. *Endocr Dev.* 2014; 26:158-70. doi: 10.1159/000363162.
11. **Diana T., Krause J., Olivo P.D., König J., Kanitz M., Decallonne B., Kahaly G.J.** Prevalence and clinical relevance of thyroid stimulating hormone receptor-blocking antibodies in autoimmune thyroid disease. *Clin Exp Immunol.* 2017 Sep; 189(3):304-309.
12. **Morgenthaler N.G., Ho S.C., Minich W.B.** Stimulating and blocking thyroid-stimulating hormone (TSH) receptor autoantibodies from patients with Graves' disease and autoimmune hypothyroidism have very similar concentration, TSH receptor affinity, and binding sites. *J Clin Endocrinol Metab.* 2007 Mar; 92(3):1058-65.