Sera from patients with Hashimoto’s disease impair TSH signaling in a TSH receptor bioassay, and coexisting TRAb are identified as stimulating

DGE 2017 Würzburg

Ulrich Loos¹, Sigrid Bräth¹, Johannes W. Dietrich²

¹. KreLo GmbH Medical Diagnostics, Ulm, Germany. 2. Medical Hospital I, Bergmannsheil University Hospitals, Bochum, Germany

Introduction: TPO-Ab and TRAb are biomarkers of thyroid autotimmunity. Here we measured biological activity of thyroid autotimmunity (TA) by a TSH receptor bioassay in sera from patients with Hashimoto’s disease (HD).

Methods: fT4, fT3, TSH, TPO-Ab, TRAb (Thermo Fisher) and sTRAb [1] were tested to confirm the diagnosis. Stimulating (sBioTRAb positive >approx. 1.2–1.3 stimulation index = SI) and blocking (bBioTRAb positive <approx. 0.7 SI) activity were measured by a TSH receptor CRE reporter gene bioassay in HEK cells [2]. Groups of patients with TA: 1. Hypothyroid and only TPO-Ab extremely positive 2. Hypothyroid and TPO-Ab moderately positive, TRAk and sTRAb negative or slightly positive 3. Hypothyroid and TPO-Ab, TRAk and sTRAb clearly positive 4. In an extended collective of G1 and G2 (52 TPO-Ab positive patients) the correlation between TPO-Ab and bBioTRAb values was studied. Statistical distributions were compared with Welch’s t test and Pearson’s correlation.

Results: Signal tranduction was impaired in sera with high TPO-Ab titers in G1 (p<0.01) as compared to G2 and in total there was a significant correlation between TPO-Ab titers and inhibition of TSH signaling in the blocking assay (G4, r=04691, p<0.001, n=52). Interestingly, in G1 TRAk and sTRAb were negative, however, in G2 two cases were slightly sTRAb-positive; 7 cases were in grey zone of TRAk. In G3 CRE signaling could be stimulated by sera containing high TRAb (p<0.01) showing stimulatory character of coexisting TRAb values.

Conclusion: Sera in HT inhibit cAMP accumulation increasingly with the height of TPO-Ab titers in none thyroidal cells haroring the TSHR and CRE-AP suggesting cAMP pathway may be involved in the pathogenesis of hypothyroidism in HD. Increasing TRAb may lead to hyperthyroidism.

References:
1. Horm Metab Res. 2015 Nov;47(12):880-8