Background knowledge

Hashimoto’s Thyroiditis (HT) is a relatively common autoimmune disorder that involves both cellular and humoral immunity, the latter characterized by the presence of antithyroid antibodies (ATA). Nevertheless, despite the large number of relevant studies, the underlying pathogenetic mechanisms still remain unclear; evidence and indications pointing to both genetic and environmental components.

Genetic studies have uncovered molecular associations that include immunoregulatory and thyroid specific genes. Possible environmental triggers and effectors of the autoimmune process have included the hygienic conditions, selenium and vitamin D deficiency, drugs, stressors, smoking, alcohol, toxins and infections such as HHV-6, Yersinia and the Hepatitis C virus.

Streptococcal infections are known triggers of autoimmune processes such as rheumatic fever, glomerulonephritis and CNS autoimmune disorders. Moreover, in a 1978 animal study by Tonooka N et al (Am J Pathol 92:681-690, 1978), severe lymphoid thyroiditis with detectable antithyroglobulin antibodies and associated hypothyroidism occurred in all male and female rats immunized against Group A streptococci for seven successive generations.

Patients and Methods

The study group included a total of 106 children (73 females and 33 males), aged 9.9±2.9 years, initially examined for various reasons in a pediatric endocrinology setting (idiopathic short stature, early puberty, premature adrenarche, elevated TSH levels in warm months: April through September). Nevertheless, among children with negative ATA antibodies the percent of ASO-positive children was 36.3%.

Antithyroid antibodies (ATA, i.e., antiTPO and antiTg) and Antistreptolysin O (ASO) titer, a toxic enzyme used as a marker of Streptococcal infection, were determined. For ASO, a titer >200 IU was characterized as positive.

Statistical analysis: Results are presented as mean±SD for quantitative variables, and as absolute and relative (%) frequency for qualitative variables. We used the X² test to investigate the relationship between categorical variables. Differences in the levels of a quantitative parameter between two groups were investigated with either t-test or Mann-Whitney test, as appropriate. Additionally, we used multiple logistic regression to investigate the association between ATA positivity, while adjusting for potential confounders (e.g. age, season). Two-tailed p-values<0.05 were considered statistically significant. All statistical analyses were performed in IBM SPSS (v. 25).

Table 1: Comparison of ASO titers measured in the negative and positive antithyroid antibodies (ATA) subgroups. ASO titers were significantly increased in children and adolescents with positive ATAs with respect to the negative antithyroid antibodies group (p<0.001).

Table 2: Percent of patients with positive ASO titers: In the group of children and adolescents with a positive ASO titer, positive antithyroid antibodies were observed in a significantly higher percent of children (in 63.6 %) compared to those with a negative ASO titer (in 31.4%, p = 0.001). With respect to gender, the difference in positive antithyroid antibodies was significant only in females (p=0.002 in girls and 0.282 in boys).

Conclusions

We attempted to examine whether the range of autoimmune disorders associated with streptococcal infections includes Hashimoto’s Thyroiditis. A significant association of ASO positivity with the presence of antithyroid antibodies (ATA) was revealed in females.