Streszczenie w języku angielskim

THE KYNURENINE PATHWAY IN YOUNG WOMEN WITH AUTOIMMUNE THYROIDITIS

Autoimmune diseases result from the loss of immunotolerance, which leads to the generation of self-reactive lymphocytes and the production of autoantibodies that cause tissue damage. The kynurenine pathway (KP) of tryptophan (TRP) metabolism plays a crucial role in regulating immune responses, thereby influencing long-term immunotolerance by linking various components of innate and adaptive immune systems, whose proper function is essential for maintaining long-term immunotolerance.

Autoimmune thyroiditis (AIT) ranks as the second most prevalent thyroid disease, constituting around 20% of all cases of thyroid dysfunction. Hashimoto's disease (HD) is the prevailing form of AIT. It is characterised by thyroid follicular cell atrophy, lymphocytic infiltration, and progressive fibrosis, leading to hypothyroidism, with a higher incidence in women.

The presented study aimed to evaluate changes in KP metabolites in young women with autoimmune thyroiditis (AIT) and their association with thyroid function. Until now, no data regarding the kynurenine pathway in AIT have been published in the available literature, which inspired the research that underpins the doctoral thesis.

The study comprised 57 young women with AIT (mean age of 32.45 ± 10.78 years) and 38 age- and BMI-matched healthy women (controls). In all participants, thyroid-stimulating hormone (TSH), free thyroxine (fT4), free triiodothyronine (fT3) levels, anti-thyroglobulin (anti-TG) and anti-thyroperoxidase (anti-TPO) antibodies titer in serum were measured. Moreover, in all patients, the ultrasound examination of the thyroid gland was performed by the ultrasound system. To assess the activity of peripheral deiodinases, the SPINA-GD was calculated. Tryptophan and KP metabolites levels in serum were determined by high-performance liquid chromatography (HPLC), and the activity of KP enzymes was calculated indirectly as product-to-substrate ratios.

The obtained results confirm the activation of the KP in young women with AIT and significant shifts in TRP metabolism through the KP, expressed by an increase in the concentration of kynurenine (KYN, $p<0.01$) and anthranilic acid (AA, $p<0.001$)

with a simultaneous decrease in the concentration of kynurenic acid (KYNA, $p<0.05$) levels in serum. Moreover, it has been proven that KP metabolites may play an important role in maintaining the proper function of peripheral deiodinases represented by changes in SPINA-GD. In addition, a positive correlation between anti-TPO antibody concentrations and increased AA synthesis, inhibiting transformation towards 3-hydroxyanthranilic acid (3-HAA), was observed in healthy individuals. Whereas, a positive relationship was found between anti-TPO antibody concentrations and changes in the quinolinic acid (QA) levels in the serum of women with AIT. The above results suggest a close link between KP activation and the immunological status of the thyroid gland.

Based on the acquired results, it was shown that changes in serum AA and QA concentrations and the AA/KYNA ratio, especially in combination with the SPINA-GD, could become a helpful diagnostic tool supporting the prediction of AIT at an early stage of the disease, even before classic symptoms of hypothyroidism are revealed.

Anna Trzepla