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Wpływ stanu zapalnego na metabolizm tryptofanu w przewlekłych chorobach reumatycznych

Abstract

Tryptophan, which is an endogenous amino acid, under physiological conditions is a substrate for the production of serotonin, a neurotransmitter responsible, among others, for mood and anxiety. In inflammation, its metabolism via the kynurenine pathway is dominant. This is caused by the activation by pro-inflammatory cytokines, such as tumor necrosis factor alpha (TNF-α), of the first of the kynurenine pathway enzymes: indoleamine 2,3-dioxygenase (IDO), which catabolizes the synthesis of kynurenine from tryptophan. Increased tryptophan metabolism through the kynurenine pathway results in the reduction of tryptophan's availability for serotonin synthesis, which can lead to lowering of mood and the occurrence of depressive disorders. Ankylosing spondylitis (AS) belongs to chronic rheumatic diseases and is therefore characterised by increased levels of inflammatory parameters, including TNF-α. Currently, in this group of patients, one of the most effective forms of therapy is the use of biological drugs – TNF-α inhibitors (adalimumab, etanercept, certolizumab, infliximab or golimumab).

The aim of this dissertation was to evaluate the impact of inflammation on tryptophan metabolism in chronic rheumatic diseases. The effect of biological treatment with TNF-α inhibitors on tryptophan metabolism in patients with ankylosing spondylitis has been assessed, as well as the relationships between disease activity, inflammatory markers, depressive symptoms and tryptophan metabolites.

The above-described objectives have been realised and presented in the three articles discussed, which constitute the dissertation. The following conclusions have been drawn from the research:

- Six-month biological treatment with TNF-α inhibitors in patients with ankylosing spondylitis resulted in a significant improvement, i.e. a reduction in the disease activity – a favourable response have been reflected in both clinical and biochemical criteria.
- The results confirmed altered tryptophan metabolism with a predominance of the kynurenine pathway in patients with ankylosing spondylitis, compared to the control group. However, concentrations of tryptophan and its metabolites did not correlate significantly with the clinical disease activity or laboratory markers of inflammation. The effect of biological treatment with TNF-α inhibitors on tryptophan metabolism has also not been confirmed. Although, as originally assumed, the patients with AS have higher concentrations of tryptophan and metabolites of the kynurenine pathway and reduced levels of serotonin, the blocking TNF-α does not affect tryptophan metabolism, demonstrating the predominance of other inflammatory pathways in IDO activation.
- Even though the groups of AS patients with and without depression have not differed significantly in terms of disease activity, inflammatory parameters or tryptophan metabolite concentrations, a statistically significant improvement in depressive symptoms as measured by the Beck Depression Inventory (BDI) has been observed after a treatment with TNF-α inhibitors. The results of the study therefore support previous reports on the possible use of biological treatment in patients with depression.

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