Title of dissertation: Endoscopic decompression of orbit in Graves' orbitopathy: treatment results and attempt at identification of new biomarkers of Graves' orbitopathy

ABSTRACT

Graves' orbitopathy is extra-thyroidal demonstration of Graves' disease (in rare cases Hashimoto thyroiditis) that impairs the function of an organ of sight causing its temporary or permanent dysfunction. It manifests with ocular signs disruptive for patients (diplopia, exophthalmos, blurred vision and color vision deficiency), which in severe cases can lead to vision loss. The autoimmunological reaction with production of proinflammatory cytokines and glycosaminoglycans by fibroblasts activated by anti - TSH (thyroid stimulating hormone) receptor antibodies seems to be the causative factor of Graves' orbitopathy.

In the aforementioned reactions, there is a chronic inflammation of soft tissues of orbit, which in consequence causes oedema of extraocular muscles and orbit's tissue degeneration (fibrosis). Recommended first line therapy consists of immunosuppressants – glicocortycosteroids. The progress in endoscopic endonasal surgery influenced an attitude to surgical treatment of an orbit's diseases, including indications to its endoscopic endonasal decompression. According to EUGOGO's (European Group On Graves' Orbitopathy) recommendations, orbital decompression should be considered in the inactive phase of disease as well as in the severe form of Graves' orbitopathy in case of no improvement in response to conservative treatment.

A review of available literature concerning effects of surgical treatment of Graves' orbitopathy served for us to write the review article „Endoscopic decompression of orbit in Graves' orbitopathy". General characteristics of Graves' orbitopathy, as well as surgical steps crucial for understanding the idea of this surgical procedure, indications, possible complications, initial results - all have been described in previously mentioned articles.

Due to the lack of a biomarker in the course of Graves' orbitopathy, that would be used for monitoring of the disease itself and the progress of treatment, an assumption was made about the potential usage of the assessment of HMGB1 (high mobility group box 1) and RAGE (receptor for advanced glycation end products) in disease monitoring.

RAGE poses as a receptor for products of advanced glycation. It is a member of a group of pattern recognition receptors (PRRs). It performs an important role in the body's

innate immunity. Endogenous HMGB1 protein, released during cellular stress, tissue injury and tissue death, is an essential RAGE ligand. The HMGB1 protein belongs to the so-called damage associated molecular patterns (DAMPs). An inflammation along with initiated tissue repair mechanisms are present due to the stimulation of PRRs by DAMPs.

For the above reasons, in the next original publication from the series, entitled: „RAGE and HMGB1 Expression in Orbital Tissue Microenvironment in Graves' Ophthalmopathy" an attempt was made to determine a new biomarker of the disease. As part of the conducted research, an increase in the expression of the tested proteins in the orbital fat tissue in patients with GO was demonstrated compared to the control group. It has also been proven that there is a statistically significant relationship between RAGE expression and the presence of optic neuropathy (DON - dysthyroid optic neuropathy) and the increased level of antibodies directed against TSH receptor (TRAb - anti - TSHR antibodies).

RAGE (+) and HMGB1 (+) inflammatory cells have been demonstrated to exist near blood vessels which supports the thesis about the possible involvement of the above proteins in the progression of the inflammatory process in GO. In the following research paper entitled „Treatment Results of Endoscopic Transnasal Orbital Decompression for Graves' Orbitopathy — A Single - Center Retrospective Analysis in 28 Orbits of 16 Patients" efficacy data was collected and presented concerning also the issue of safety of TEOD (transnasal endoscopic orbital decompression) - the procedure performed in the Department of Otolaryngology, Centre of Postgraduate Medical Education in 2017-2020. Surgical procedures with the usage of TEOD method were performed in 28 orbits in 16 patients.

In the summary of the publication the following conclusions were presented: after the completed surgical treatment with the usage of TEOD in patients with Graves' orbitopathy the follow-up results were indicated: proptosis decrease, an increase in best corrected visual acuity, reduction of intraocular pressure and severity reduction of the disease expressed by CAS (clinical activity score).