INVESTIGATION OF INFLAMMATORY DISEASES BY MODERN OPHTHALMOLOGICAL DIAGNOSTIC TOOLS

Summary of Ph.D. Thesis

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1. Publications related to the subject of the thesis

1. Lilla Smeller, Edit Toth-Molnar, and Nicolette Sohar

Optical Coherence Tomography: Focus on the Pathology of Macula in Scleritis Patients

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2. Lilla Smeller, Edit Toth-Molnar, Nicolette Sohar

White Dot Syndrome Report in a SARS-CoV-2 Patient

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A biológiai terápia helye a gyermekkori uveitis ellátásában

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List of abbreviations

BCVA best corrected visual acuity

CME cystoid macular edema

CRT central retina thickness

DMARD disease-modifying antirheumatic drugs

DME diffuse macular edema

ERM epiretinal membrane

ETDRS early treatment of diabetic retinopathy study

FAF fundus autofluorescence

FLAG fluorescein angiography

IUSG International Uveitis Study Group

JIA juvenile idiopathic arthritis

ME macular edema

MEWDS multiple evanescent white dot syndrome

MTX methotrexate

OCT optical coherence tomography

RPE retinal pigment epithelium

SARS-CoV-2 severe acute respiratory syndrome coronavirus

SD-OCT spectral-domain optical coherence tomography

SRD serosus retinal detachment

TA triamcinolone-acetonide

TNF tumor necrosis factor

UWFI Ultra widefield imaging

VA visual acuity

1. Introduction

The global prevalence of inflammatory diseases is increasing. As a result, the number of eye complications related to these diseases has also increased, ranging from minor symptoms to vision-threatening complications. These ocular manifestations may result from the disease itself or from treatments that are used to treat the primary disease.

The field of ophthalmic imaging has been revolutionized over the past 30 years, particularly with the introduction of optical coherence tomography (OCT), which has since become the standard of care for many diseases. Significant advances in both hardware and software have enabled the emergence of multiple imaging techniques for increasingly high-resolution and high-contrast imaging of both anterior and posterior part of the eye.

Ultra widefield imaging (UWFI) systems can produce up to 200-degree images. It is a non-contact diagnostic tool for taking fundus photographs, autofluorescent photos, and making fluorescent angiography or indocyanine-green angiography.

All of these ophthalmic imaging methods are increasingly being used and translated into the clinical setting, where initial results are promising to use them in patient care. By revealing the pathophysiological structures and functions of the eye's complex neurovascular network, the development of imaging technology can lead to earlier detection of diseases, more accurate diagnosis and treatment monitoring, and better treatment of many ophthalmic diseases, among them uveitis. The prognosis in cases of uveitis could be good for those who receive prompt diagnosis and treatment, but serious complications may result in permanent vision loss if left untreated. Diagnostic tools like OCT, UWFI can play an important role in the diagnosis and management of the uveitis.

2. Aims of the thesis

The aims of the thesis were:

1. To examine patients with anterior scleritis and to investigate the changes of their macula using OCT: to find correlation between the images and the clinical symptom, too.

2. To determine whether the macular complications would affect the prognosis and the treatment of scleritis, and wheather the OCT results might be applied as biomarkers in ophthalmology.

3. To present the results of ophthalmic examinations of pediatric and adult uveitic patients treated at our Department with the newest treatments and to find possible correlations between their therapy and the prognosis of the disease. In addition, to determine the visual acuity of juvenile uveitic patients treated with adalimumab.

4. To find out how the macular complications could affect the prognosis and the treatment to be applied in uveitic patients (children and adults).

5. To present a bilateral multiple evanescent white dot syndrome (MEWDS) case caused by severe acut respiratory syndrome coronavirus (SARS CoV2) and to prove that modern imaging procedures are irreplaceable in time of SARS CoV2 pandemic.

3. Background

3.1. Scleritis

Scleritis is a chronic, painful, vision-threatening inflamed disease that is characterized by edema and cellular infiltration of the scleral and episcleral tissues. The most common

etiology is inflammatory (noninfectious in 90% of all scleritis patients), either idiopathic or in the context of a systemic disease. Scleritis is commonly associated with systemic autoimmune disorders.

Based on the anatomical location of the inflammation, scleritis may be classified as anterior and posterior ones.

Scleritis is a rare disease, the prevalence is estimated to be six cases per 10,000 people. Anterior scleritis is demonstrated in 94% of the cases, and posterior scleritis is diagnosed only in 6% of the patients.

Scleritis is usually painful and can lead to vision loss due to progressive inflammation and destruction of the ocular tissues or even to morbidity and mortality due to an underlying collagen vascular disease.

Scleritis may often pose a diagnostic challenge since the clinical features are subtle and diagnostic modalities are limited. The diagnosis of scleritis is usually based on clinical assessment and ultrasonography. B-scan ultrasound is the most useful confirmatory analysis method for the diagnosis of posterior scleritis.

Generally, scleritis requires systemic therapy. Nonsteroidal anti-inflammatory drugs (NSAIDs), corticosteroids, or immunomodulatory drugs can be indicated. The treatment must be individualized according to the severity of scleritis, response to treatment, adverse effects, and presence of associated diseases

3.2. Uveitis

Uveitis is a common, sight-threatening group of disorders, characterised by inflammation of the uveal tract.

According to the underlying etiology, uveitis could be clinically categorized as idiopathic, infectious, non- infectious and masquerade uveitis.

In pediatric uveitis the most common cause of the inflammation is juvenile idiopathic arthritis (JIA), in adult patient it is idiopathic uveitis.

Treatments of uveitis are based on the degree of inflammation and the presence of risk factors and complications.

First-line treatment for non-infectious uveitis is represented by corticosteroid monotherapy. Immunosuppressive agents represent the therapeutic option when quiescence is

not obtained with corticosteroids, or in cases of reactivation or new complications, and are used as corticosteroid-sparing drugs to reduce inflammation and control the disease. There are four types of immunmodulator therapy: 1. antimetabolites, 2. T-cell inhibitors, 3. alkylating agents with cytotoxic effect, and 4. biological therapies.

The most widely used biologic compounds for treating uveitis are represented in adults by the tumor necrosis factor alpha inhibitors (anti-TNF-α) in intermedier, posterior, and panuveitis. Anti-TNF-α is also recommended for children in cases of anterior uveitis.

3.2.1. Pediatric uveitis

Uveitis in children accounts for 5 - 10% of total uveitis cases. Of all diagnosed children, anterior uveitis cases are 40%, posterior cases are 40%, intermediate cases are 15%, and panuveitis is 5%. The visual complications can be more severe in the pediatric group due to a higher prevalence of posterior uveitis. Among the non-infectious causes of uveitis, JIA is the most common systemic disease. Even though uveitis is less common in children than in adults, juvenile uveitis causes a higher rate of vision loss and secondary complications than in adults because uveitis is diagnosed late in these cases.

3.2.2. Uveitis in adults

The most common non- infectious uveitis in the developed world is HLA-B27 associated uveitis. The most common location of non- infectious uveitis is anterior, representing from 47.5 to 93% of all cases. The incidence of panuveitis and posterior uveitis is similar: about 20% of all uveitis cases, and intermediate uveitis is the least frequent form of uveitis, about 10–15% of all cases.

3.3. Rare bilateral uveitis in SARS CoV2 (severe acute respiratory syndrome coronavirus) pandemic

In March 2020, the World Health Organization (WHO) declared the COVID-19 outbreak as pandemic. The virus would spread to the respiratory system of the same individual with the ocular system acting as a passage. The SARS-CoV-2 may also constitute the risk factor for reactivation of the herpes family viruses.

White dot syndromes are a group of inflammatorical chorioretinopathies in which the common defining clinical feature is the presence of multiple discrete white lesions located at deeper levels of the retina and choroid.

Multiple evanescent white dot syndrome (MEWDS) is a rare posterior uveitis where numerous white dots can be seen in the posterior pole and midperiphery.

3.4.: Modern ophthalmic imaging - Imaging procedures used in patients with inflammatory diseases

3.4.1. Optical coherence tomography (OCT)

Second-generation OCT is the spectral domain OCT (SD-OCT), based on the Fourier transformation principle. By eliminating the moving reference mirror, the number of A-scans increases significantly, which results in faster imaging and higher resolution. SD-OCTs axial resolution is 4-6 μm. The scanning speed of SD-OCT can exceed 100,000 A-scans per second. These systems operate at scanning rates of approximately 27,000–70,000 A-scans per second. As the A-scan density increases, resolution becomes higher, and SD-OCT produces better quality B-scans. Higher scanning speed reduces the effect of artifacts made by eye motion and produces images that provide a true picture of the retina. The large, dense raster scans make it possible to obtain detailed surfaces of individual retina layers over large areas resulting in segmentation maps.

OCT imaging also has limitations. Since OCT utilizes light beams, media opacities can interfere with optimal imaging opposite to ultrasound's sound waves.

3.4.2. Ultra widefield fundus imaging (UWFI)

It can produce up to 200-degree images. More than 80% of the surface of the retina can be imaged. The peripheral retina can be photographed through small pupils in cases where examination of the peripheral fundus may be limited due to pupil size. In addition to imaging, UWFI also provides valuable information about the peripheral vasculature and other changes in the retina that would be overlooked by traditional imaging systems.

3.4.3.Ultra widefield fundus autofluorescence (FAF)

This method maps the fluorescent property of lipofuscin, a breakdown product of retinal proteins within the retinal pigment epithelium (RPE). Hyperautofluorescence shows the increased metabolic activity of the RPE due to the loss of photoreceptors, and hypoautofluorescence occurs with loss or blockage of RPE cells.

3.4.4. Ultra widefield fluorescein angiography (FLAG)

FLAG is an essential imaging modality for evaluating eyes with chorioretinal disease and structural complications caused by posterior uveitis. After injecting fluorescein dye intravenously, a series of filtered posterior segment images provides a functional and structural view of retinal (and choroidal) vasculature and anatomy. Wide and

ultra-wide-field FLAG can identify retinal vascular pathology that can not be noted by clinical examination.

4. Patients and methods

4.1 Patients

4.1.1. Scleritis patients

We analyzed retrospectively the data of patients with scleritis at the University of Szeged in the Department of Ophthalmology between January 1, 2017 and December 31, 2021. Twenty-seven eyes of 24 patients (7 males and 17 females) were included in this study, who were diagnosed with non-infectious scleritis. The mean age of the patients was 57.75 years (range: from 30 to 77 years).

Scleritis was diagnosed by the presence of the following parameters: (1) acute or subacute symptom onset; (2) eye pain with or without decreased visual acuity; (3) posterior sclerochoroidal wall thickening. Scleritis was classified as diffuse, nodular, or necrotizing. The location of inflammation was also recorded.

4.1.2. Juvenile uveitic patients

We analyzed retrospectively the data of children with uveitis at the University of Szeged in the Department of Ophthalmology between January 1, 2017 and May 31, 2021. Childhood uveitis of non-infectious origin was also analyzed in those cases when adalimumab therapy was immidiately started with the indication of the uveitis. We did not select those patients for the study whose indication for treatment was their underlying systemic disease.

Adalimumab therapy for uveitis was initiated for 11 of the 46 children (23.9%). The average age of patients at the start of adalimumab treatment was 10 (4–13) years. Three boys (27%) and eight girls (73%) were treateted with adalimumab.

4.1.3. Adult uveitic patients

In our study, we examined retrospectively the data of adult non-infectious uveitic patients treated with adalimumab at our Department between January 2017 and December 2021. Those patients were included in our study who received adalimumab, that was given with the indication of non-infectious uveitis after steroid therapy failure, and the patients received the medication at least for 3 months.

The average age was 51 years, the youngest patient was 20 years old and the oldest one was 80 years old at the beginning of therapy.

4.1.4. MEWDS patient

A 47-year-old female patient was examined in our department because of bilateral photophobia and blurred vision in both eyes and decreased vision in her left eye. She visited our department in November 2020, that was the peak year of Covid.

4.2 Methods

4.2.1 Ophthalmologic examinations

Patients with scleritis, as well as adult and pediatric uveitic patients underwent standard ophthalmic examinations including visual acuity test (using Kettesy's decimal visual chart or early treatment of diabetic retinopathy study (ETDRS) visual chart), intraocular pressure with applanation tonometer or non-contact tonometer (iCare), slit-lamp biomicroscopic examination of the anterior segment of the eye using Haag-Streit (Liebefeld-Bern, Switzerland) slit-lamp, and fundus ophthalmoscopic examination with 90 or 78 D ocular lenses (060123, Bellevue, WA,USA). Examination before the authorization of biological therapy was carried out as specified in the prescription .

4.2.2 OCT

OCT examinations were taken by SD-OCT Spectralis OCT system (Heidelberg Engineering, Heidelberg, Germany, Software version: Heidelberg Eye Explorer 1.9.13.0). OCT scan parameters were as follows: infrared scan; pattern size: 20◦ × 20◦; 25 sections; 240 μm between B-scans; 512 A-scans. OCT examination was performed in all of the cases at the time of their check-in at our uveitis outpatient clinic. For standardization, all examinations were performed by the same technician. The thickness of the retina was measured between the inner limiting membrane and Bruch's membrane in the central macular region.

4.2.3 UWFI

UWF images (colour and FAF) were taken by Optos, California (Optos, Marlborough, MA, USA Software version: Window Server 2008 (R 3.1-4.1) or Windows 7 SP 64-bit) by the same technician. The Optomap obtained with the patients' eyes in the primary position, were acquired at the same visit. The instrument is able to obtain wide-field images of approximately 180–200 degrees.

4.3 Ethics

Our studies were conducted according to the guidelines of the Declaration of Helsinki and approved by the Institutional Review Board (or Ethics Committee) of Human Investigation Review Board at the University of Szeged, Albert Szent-Györgyi Clinical Center (protocol code 4693 and date of approval 20/Jan/2020).

5. Results

5.1 Scleritis patients

Twenty-four anterior and three posterior scleritis was diagnosed at the patients in our Department. Among the twenty-four eyes diagnosed with anterior scleritis, there were 16 with diffuse scleritis and 8 with nodular anterior scleritis. One patient had peripheral ulcerative keratitis, one had retinal detachment, and one had hydro-keratopathy. Bilateral disease was found at three patients.

The overall mean VA of all of our scleritic patients was 28 + 30 letters with correction, and the mean CRT at the central fovea was 291.7 μm.

The mean VA was 22 + 30 letters, 19 + 30 letters, and 33 + 30 letters in patients with CME, DME, and SRD, respectively.

The mean CRT was 558 μm, 328 μm, and 288 μm in our patients with CME, DME, and SRD, respectively. CRT was the thickest in cases of CME and thinnest in the case of SRD. The macular thickness, as seen on OCT, is objective and correlates with BCVA.

The patients with CME were treated with triamcinolone (TA) injection sub-tenonly when topical non-steroid eye drops were ineffective.

OCT examinations showed ERM in three patients (12%). None of our patients with ERM needed vitrectomy surgery so far due to the close OCT follow-up and the adequate treatment.

5.2 Pediatric uveitic patients

The average age of the children with uveitis at the beginning of adalimumab therapy was 10 (4–13) years.

We initiated adalimumab for 11 of the 46 children (23.9%) to treat their uveitis. Before starting the treatment with adalimubab (according to the protocol), all patients received systemic steroid treatment. It was followed by disease-modifying antirheumatic drugs

(DMARD), since various complications resulting from uveitis had already appeared at couple of children in this group: in 2 children (18%) "band" keratopathy, in 2 patients (18%) secondary glaucoma that was controlled with eye drops, in 2 cases (18%) cataract, and in 2 children (18%) cystoid macular edema (CME). Unfortunately one child was diagnosed with Hodgkin's lymphoma during his treatment, hence his adalimumab therapy was immediately stopped. The 10 patients who are currently being treated with adalimumab, also receive methotrexate therapy as stated in the protocoll.

The average of the best corrected VA at the start of the adalimumab treatment on the right eye was 0.71, and on the left eye it was 0.83. This value improved to 0.96 in both eyes by the end of the follow-up period. Within a month after starting treatment, we found complete remission in all 10 patients.

5.3 Adult uveitic patients

We examined the data of those patients who received adalimumab, which was given with the indication of non-infectious uveitis, and those patients got the adalimumab at least for 3 months. Eighteen people (12 women, 6 men) met our criteria. The average age was 51 years, the youngest patient was 20 years old, and the oldest one was 80 years old at the beginning of the therapy.

The uveitis was intermediate in 7 (39%) patients, and in 3 (17%) and 8 (44%) cases posterior uveitis and panuveitis was detected, respectively.

Unilateral uveitis was found in 6 of 18 patients (33%), and the uveitis was bilateral in 12 (67%) cases.

Fourteen (77%) patients received corticosteroid systemically. Six (33%) patients received systemic immunosuppressive treatment prior to adalimumab therapy, most often cyclosporin and/or methotrexate.

Side effects occurred in 5 (28%) patients during adalimumab therapy in the follow-up period.

At the beginning of our study, the average best corrected visual acuity (BCVA) of the right eye was 0.63, and the left eye was 0.67. Average VA measured at the end of the follow-up period became less in both eyes, 0.55 in the right eye and 0.63 in the left eye. Despite the adalimumab therapy, the VA decreased in 3 eyes because of band keratopathy, in 4 cases because of cataract, and in 2 eyes irreversible damage of the macula was responsible for the decrease.

5.4 MEWDS patient

One patient was diagnosed with MEWDS during SARS-CoV-2 at our Department.

Funduscopic examinations with dilated pupils showed mild vitritis on both sides. The optic disc was normal on both sides, and no swelling was detected. Multifocal, flat, and grayish-white placoid lesions in the retinal pigment epithelium (RPE) level of the retina on both sides were revealed. In addition, the macular region was also involved on the left side. OCT image showed swelling of the outer retinal layers and granules at the level of RPE. Discontinuities in the inner segment - outer segment junction and mild attenuation of the external limiting membrane have been reported in acute phase. Recurrent episodes may result in the thinning of the outer nuclear layer.

On the FLAG picture early and late hyperfluorescence of the white spots could be seen. In addition, diffuse and patchy late stainings were detected at the level of RPE and retina.

Our patient received corticosteroid injection (1 mg, dexamethasone, ratiopharm) into the orbital floor of both sides every other day, and corticosteroid drops five times a day. In order to prevent severe ciliary spasm and synechiae formation, dilatation of the pupil was initiated (cycloplegicedol eye drops 5 times a day). In addition, we gave her acyclovir orally (5 × 800 mg/day) as her test was positive for acut herpes simplex infection.

The clinical symptoms regressed completely in 4 weeks and at the 1-month follow-up visit, the whitish inflammatory dots regressed, but did not disappear totally.

6. Discussion

6.1. Examination of scleritic patients

Although scleritis is a rare disease characterized by inflammation of the sclera and adjacent ocular structures, its complications are vision-threatening.

Using OCT, we could find the adequate diagnosis leading to the best, complex treatment and follow-up of the disease. OCT can give more information about the depth of the inflammation and the prediction of visual outcomes than previous examinations e.g. ultrasound. The thickness of the retina and macula measured by OCT is a potential indicator of retinal inflammation. Four studies used OCT to measure retinal/macular thickness and compared it with the presence of retinal vasculitis. Their results suggest that increased retinal/macular thickness correlates with retinal vasculitis. There is no report in the literature about using OCT to detect any macular entity in cases of scleritic patients.

The most common and vision-decreasing complication of inflammation is ME, which can persist or recur despite improvement or resolution of the ocular inflammation.

ERM is also commonly seen in recurrent uveitis or other ocular inflammation.

The OCT data of our scleritis series showed three patients had CME (12%), one patient (4%) had DME, and one patient (4%) had SRD among all scleritic patients. CME and DME lead to reduced VA, which can affect patients' quality of life. The vision was 22 + 30 in the case of CME and 19 + 31 in DME. The central retina thickness was the thickest in cases of CME and the least thick in cases of SRD.

ERM occurs in approximately 6% of patients over the age of 60. Although none of the patients was older than 60 years in our study, OCT examinations showed ERM in three patients (12%), and their vision remained stable at 45 + 30.

We can state that OCT findings help ophthalmologists determine visual outcomes. ME and ERM can make vision worse, but visual improvement can be achieved by systemic and additional ophthalmologic therapy.

CME, SRD, DME, and ERM negatively affect VA. Especially in chronic scleritis cases, ME and ERM could work as biomarkers since they provide an objective, measurable method for evaluating the disease process.

6.2 Examination of uveitic patients

Uveitis can develop in all age groups and it is one of the leading causes of preventable blindness in the world. It frequently takes a chronic course and presents bilaterally with recurrent inflammation.

Biologic therapies such as adalimumab have revolutionized the treatment of severe, sight-threatening uveitis.

Within a month after starting the adalimumab treatment, we found complete remission in all 10 pediatric patients. In adults, 4 patient (22%) still had posterior uveitis, and 14 patients (78%) were in remission durig the follow-up period.

Side effects occurred in 5 (28%) patients during adalimumab therapy in the follow-up period in adults. In case of 2 patients, paradoxical psoriasis developed. Fever occurred several times during the use of the therapy in one patient, hence the therapy was stopped. In another patient red, non-itchy spots appeared all over her body, but mainly on the upper body that was associated with a burning sensation. The spots disappeared in a few days without therapy. One

patient reported local erythema at the subcutaneous injection site, but redness and swelling disappeared.

The use of biologics has greatly improved the outcome of non-infectious uveitis.

In children: the average of the best corrected VA at the start of the adalimumab treatment in the right eye was 0.71, and in the left eye was 0.83. This value improved to 0.96 in both eyes by the end of the follow-up period. In adults at the beginning of our study, the averaged best corrected visual acuity (BCVA) in the right eye was 0.63, and in the left eye was 0.67. The average VA measured at the end of the follow-up period became less in both eyes, 0.55 in the right eye and 0.63 in the left eye. The cause of the deterioration of VA was the irreversible damage of anterior and posterior segment of their eyes.

In our study, we made follow-ups by basic ophthalmic examinations and OCT as a modern ophthalmic imaging procedure to follow the third-line therapy in both paediatric and adult uveitic patients. At the beginning of the therapy we diagnosed CME in 2 children (18%). After initiating the adalimumab, CME disappeared in both cases. In adult uveitic patients, at the start of our study, we detected CME in a total of 16 (8 right, 8 left) eyes. At the end of the follow-up period, only 4 eyes (1 right, 3 left) were affected by CME thanks to the adalimumab therapy.

6.3. Examination of MEWDS patient

The lesions found at our patient support the hypothesis that a herpes infection can manifest after SARS CoV-2 infection. MEWDS is an acute, multifocal, and rarely bilateral retinopathy. The multiple white infiltrations or foci could be seen at the level of the outer retina. In our case, SARS-CoV-2 could trigger the inactive herpes simplex infection that caused MEWDS. We could make the prompt diagnosis and follow-ups by using OCT as a non-contact diagnostic tool, that was very important during SARS-2 Covid pandemic. OCT showed inflammatory lesions in the level of the outer retina. The disruption of the ellipsoid zone could produce granular foveal area. OCT images showed swelling of the outer retinal layers and granules at the level of RPE. We detected discontinuities in inner segment - outer segment junction and mild attenuation of external limiting membrane in acute phase that disappeared a few weeks later.

Early and late hyperfluorescence of the white spots could be seen on the UWFI FLAG picture. We also performed Optos FLAG in order to get more information about the periphery of the

eyes. No vasculitis could be detected. The UWFI FAF images showed hyperautofluorescence corresponding to the white dots in the acut phase.
As retinal imaging technic continues to improve, the understanding of eye disease processes continues getting better and better. Newer technologies helps ophthalmologists to achieve appropriate diagnosis and treatment of disease entities.

7. Summary

1. To the best of our knowledge, we reported first the investigation of macula with OCT in anterior scleritic patients. The changes seen on OCT pictures correlated well with the severity of the ophthalmic disease.

2. We classified ME into three subgroups: cystoid macular edema (CME), diffuse macular edema (DME) and serosus retinal detachment (SRD). ME and ERM could work as biomarkers in chronic scleritis cases, since their presence helps evaluating the course of the disease. These changes affect the treatment of scleritis.

3. As a result of our research work, we were the first to publish in the Hungarian literature the ophthalmic examinations of paediatric uveitic patients treated with adalimumab in Hungary. The most common cause of uveitis in children is JIA. In 73% of these cases, uveitis occured within the first year of the onset of arthritis and could be the first sign of JIA.

The data of adult uveitic patients treated at our Department were also analyzed. We provided real-world clinical data supporting the treatment efficacy and safety of adalimumab for the patients with vision-threatening uveitis in Hungary. We found improved or stable vision and decreased need to use additional therapy like prednisolone, immunosuppressive drugs, or local dexamethason therapy.

4. We found that macular complications affect the prognosis and the treatment in uveitis independently on the etiology of the uveitis.

5. SARS-CoV-2 would trigger the inactive herpes simplex infection to cause MEWDS. We were the first who presented a bilateral MEDWS case caused by SARS CoV2. We showed the usefulness of modern non-contact imaging procedures (like OCT, OCTA and Optos) in time of SARS-CoV-2 pandemic.

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