RHEOHEMAPHERESIS IN THE TREATMENT OF DRY FORM OF AMD. A CASE REPORT

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The authors of the article declare that no conflict of interests exists in the compilation, theme and subsequent publication of this professional communication, and that it is not supported by any pharmaceuticals company. The study has not been submitted to any other journal or printed elsewhere.

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Received: 16 August 2022
Accepted: 15 November 2022
Available on-line: 20 February 2023

SUMMARY

Aim: We present a case report of a patient with dry form of age-related macular degeneration (AMD) in whom we monitored the effect of rheohemapheresis (RhF) treatment over 6 years.

Methods: A 67-year-old man was examined in April 2014 at the Department of Ophthalmology at the University Hospital in Hradec Králové for metamorphopsia and decreased visual acuity of the left eye. The patient received general treatment for hypercholesterolemia with Lipfix 10 mg once a day (atorvastatin 10 mg). The cholesterol level in the blood was 3.41 mmol/l, the lipid profile was normal. The patient's previous ocular medical history was unremarkable.

The patient reported ocular complaints over the course of the last year, the main symptom of which was image distortion on the Amsler grid on the left eye. Baseline best corrected visual acuity of the left eye was 6/10. Visual acuity in the right eye was 6/6. In both eyes, the findings on the anterior segment corresponded to the patient's age, with the exception of incipient cortical cataract. On the fundus of both eyes, the border of the optic nerve was demarcated, in the macula of the left eye there were a number of soft confluent drusen, in the central periphery there were no pathological changes. On the fundus of the right eye the finding was similar, but to a lesser degree. Optical coherence tomography on the macula of the left eye showed drusoid ablation of the retinal pigment epithelium (RPE), with accumulation of hyperreflectivities below the RPE. Pattern-reversal electroretinography (pERG): showed a slightly prolonged retention of the activity of the central region of the retina (p50 wave) and ganglion cells (N95 wave). Multifocal electroretinography (mfERG) in the central 30° of the retina was within normal limits. Electroretinography (ERG) demonstrated physiological photopic and scotopic rod activity. The patient was treated with 8 RhF procedures, two per week, with a 2-week interval, and the pulse was repeated 4 times.

Results: We noted a gradual resorption of soft drusen in the patient, with attachment to the RPE line according to OCT examination at the following six-monthly check-ups over the next 6 years. Visual acuity of both eyes was maintained at the baseline values at the last check-up in April 2020, the area of soft drusen was significantly reduced. The function of the rod, cone system and the central region of the retina mfERG fluctuated only to an insignificant degree during the entire follow-up period, with a tendency towards a slight increase in activity after RhF treatment.

Conclusion: We noted an improvement of the anatomical and functional findings in a patient with dry form of AMD during a 6-year follow-up period after RhF treatment. The visual acuity of the affected eye remained at the baseline values.

Key words: age-related macular degeneration, rheohemapheresis, soft drusen, electroretinography, blood viscosity

Čes. a slov. Oftal., 79, 2023, No. 1, p. 42–46

INTRODUCTION

Medical history and subjective complaints of patient

In April 2014 a 67-year-old man was examined at the Department of Ophthalmology at the University Hospital in Hradec Králové for metamorphopsia and a deterioration of visual acuity (VA) in the left eye. The patient was receiving general therapy for hypercholesterolemia, regularly taking Lipfix 10 mg 1x per day (atorvastatin 10 mg). The patient's blood cholesterol level was 3.41 mmol/l, his lipid profile was within the norm. His previous ocular medical history was unremarkable. He had experienced ocular complaints over the course of 1 year, at the examination he stated distortion of the image in front of the left eye on an Amsler grid.

Objective status

Baseline VA in the left eye was 6/10, not improved by correction. VA in the right eye was 6/6. In both eyes the finding on the anterior segment was commensurate to age, with the exception of an incipient cortical cataract. On the ocular fundus bilaterally the optic nerve disc was bordered, in the macular region there were a number of soft confluent drusen (Fig. 1), in the central periphery the finding was without pathological changes. Optical coherence tomography (OCT, Zeiss Cirrus 4000) of the central landscape of both eyes showed drusoid ablation of the retinal pigment epithelium (RPE), with an accumulation of hyperreflectivities beneath the RPE (Fig. 2). The area of drusoid ablation of the RPE in the macula of the right eye measured 3.8 mm2, in the left eye 5.2 mm2 (Fig. 3). Patter-n-reversal electroretinography (pERG) showed a slightly prolonged retention of the activity of the central region of the retina (p50 wave) and ganglion cells (N95 wave). Multifocal electroretinography (mfERG) in the central 30° of the retina was within normal limits. Electroretinography (ERG) demonstrated physiological photopic and scotopic rod activity. The baseline values of the electrophysiological methods of examination are presented in Table 1.

Development following treatment with rheohemapheresis

The patient was diagnosed with dry form of age-related macular degeneration (AMD) bilaterally, and treatment was commenced consisting of 8 rheohemapheresis (RhF) procedures, twice per week followed by a 2-week break, and the pulse was repeated 4x. During the subsequent 6-month follow-up examinations over the course of 6 years, we observed a gradual resorption of the soft drusen in the macula of both eyes (Fig. 1), with attachment of the

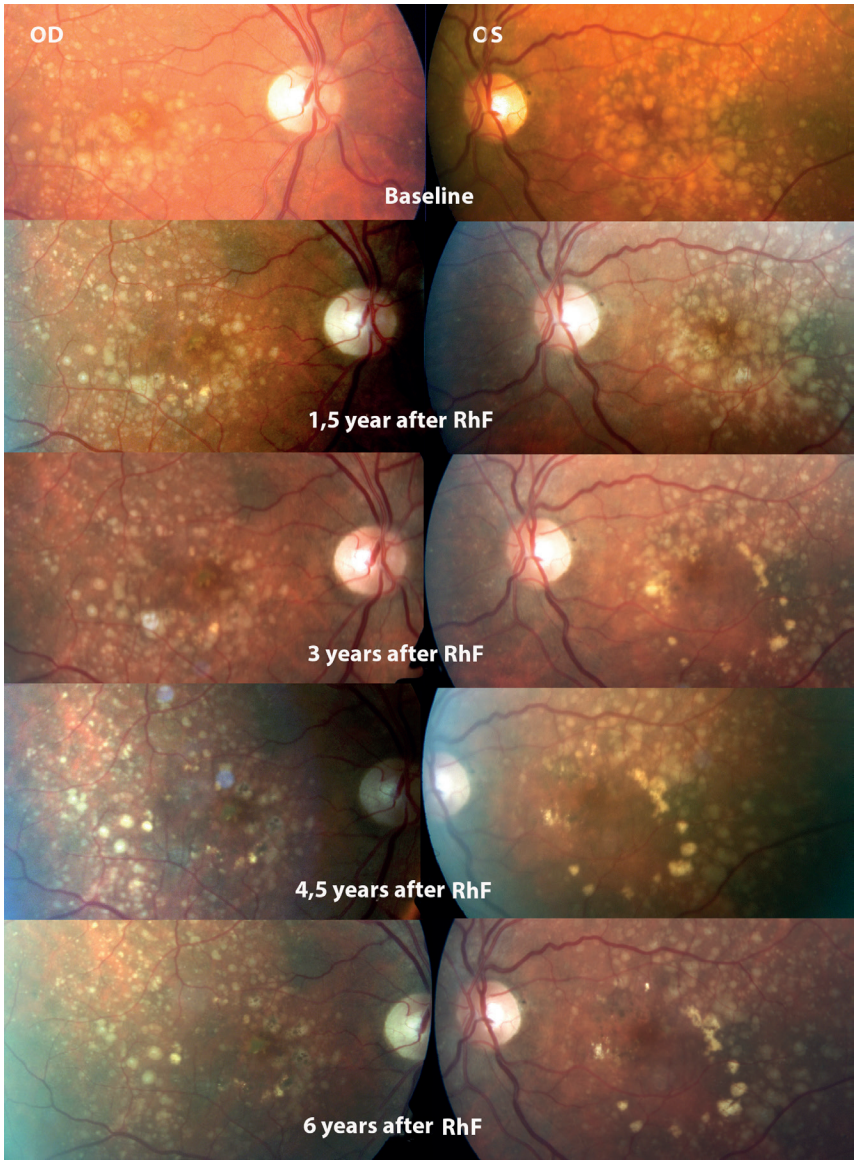


Figure 1. Development of the fundus findings of both eyes after rheohemapheresis treatment during a 6-year follow-up. Gradual resorption of soft drusen is evident

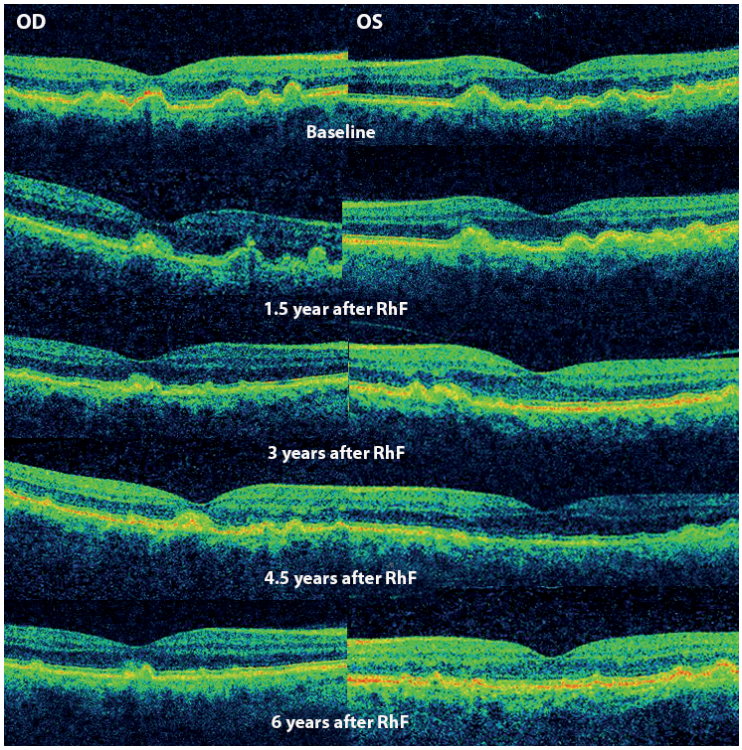
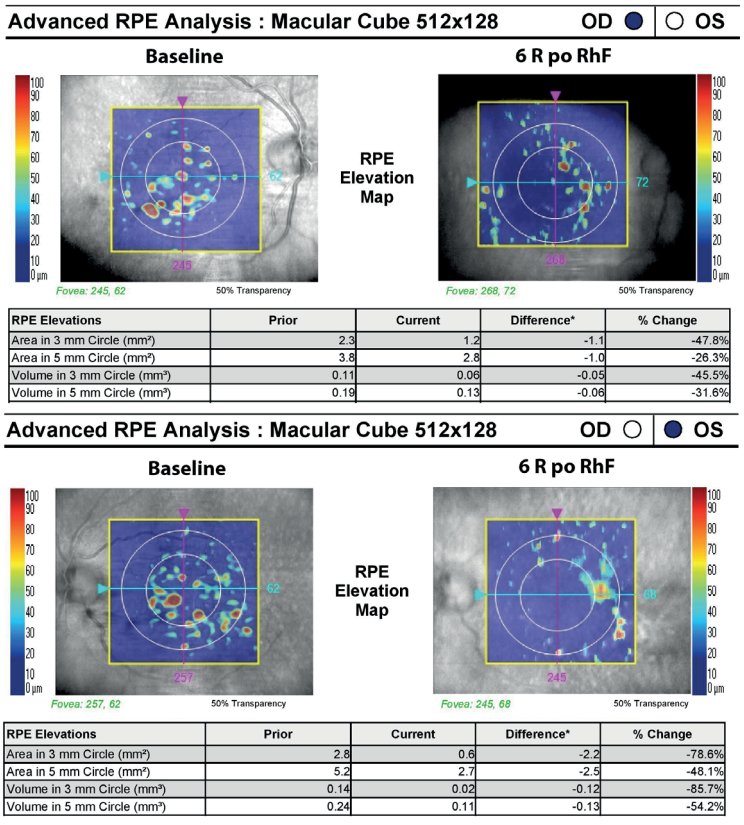


Figure 2. Development of OCT findings in both eyes after rheohemapheresis treatment during the 6-year follow-up. Gradual restoration of the retinal pigment epithelium line



RPE Elevations	Prior	Current	Difference*	% Change
Area in 3 mm Circle (mm²)	2.3	1.2	-1.1	-47.8%
Area in 5 mm Circle (mm²)	3.8	2.8	-1.0	-26.3%
Volume in 3 mm Circle (mm³)	0.11	0.06	-0.05	-45.5%
Volume in 5 mm Circle (mm³)	0.19	0.13	-0.06	-31.6%

RPE Elevations	Prior	Current	Difference*	% Change
Area in 3 mm Circle (mm²)	2.8	0.6	-2.2	-78.6%
Area in 5 mm Circle (mm²)	5.2	2.7	-2.5	-48.1%
Volume in 3 mm Circle (mm³)	0.14	0.02	-0.12	-85.7%
Volume in 5 mm Circle (mm³)	0.24	0.11	-0.13	-54.2%

Figure 3. Reduction of the area of drusoid ablation of retinal pigment epithelium in the macula of both eyes, retinal pigment epithelium analysis 6 years after rheohemapheresistreatment

line of the RPE according to the OCT examination (Fig. 2). At a follow-up examination in April 2020, VA in both eyes was preserved at the baseline values. The surface area of drusoid ablation of the RPE in the macula of the right eye was significantly reduced to a value of 2.8 mm2 (reduction by 26.3%), and in the macula of the left eye to 2.7 mm2 (reduction by 48.1%) – Fig. 3.

The latency of both waves (P50 and N95) was slightly prolonged according to the pERG examination. The function of the rod and cone system and the central region of the retina mfERG fluctuated only to an insignificant degree during the entire follow-up period, with a tendency towards a slight increase in activity after RhF treatment (Table 1).

The fundamental haematological and biochemical parameters (haemoglobin, haematocrit, leukocytes, parameters of laminae, glycaemia, minerals, renal and liver functions) were not significantly clinically affected by RhF. Nevertheless, we recorded a reduction of the spectrum of high molecular weight substances (Table 2). The decrease in the above factors had an influence on rheological parameters: whole blood viscosity decreased by 9.2% and plasma viscosity by 10.2%. The result was an improvement of the flow in the microcirculation of the macular region.

DISCUSSION

According to the ASFA (American Society for Hemapheresis), RhF is recommended as the treatment of first choice for AMD [6]. The aim of the therapy is to stabilise or improve visual functions, prevent transition to neovascular form of AMD and prevent the progression of geographical atrophy in the macula [7]. The series of therapeutic RhF pulses leads to a reduction of the barrier of diffusion from the Bruch's membrane and normalises metabolic exchange between the RPE and the choriocapillaris. It improves the nutrition of the cells of the RPE and neuroepithelium. By reducing ischaemia, it brings about a reduction in the production of VEGF (vascular endothelial growth factor) by the RPE cells. Modification of the parameters on a molecular level and activation of the functional reserves of the retina may prevent the progression of the process leading to loss of sight. An improvement of blood flow through the choroid, which is markedly altered in dry form of AMD, is also expected [8]. Lower whole blood and plasma viscosity is demonstrated, as well as reduced aggregation of erythrocytes [9].

There are published case reports or series of patients, two controlled trials and eight randomised controlled trials [6] which attest to the success of rheopheresis in dry from AMD. Of course, rheopheresis cannot cure AMD, but the aforementioned studies document the

Table 1. Results of electrophysiological examination methods during the 6-year follow-up)

Amplitude	Baseline	1.5 year after RhF	3 years after RhF	4.5 years after RhF	6 years after RhF
pERG: wave p50 µV OD/OS wave N95 µV OD/OS	 5.42/5.58 4.71/6.99	 5.7/8.75 5.38/9.97	 5.42/8.2 5.2/8.76	 4.64/6.39 6.48/6.31	 4.43/6.45 4.53/5.33
ERG: **Photopic conditions** a wave µV OD/OS b wave µV OD/OS **Scotopic conditions** b wave µV OD/OS	 21.8/39.9 112/145 109/102	 60.3/34.2 103/159 115/117	 32.5/49.1 143/165 137/170	 35.6/35.3 146/159 120/127	 26.6/35.6 97.2/143 114/118
mfERG (Ring 1): P1 µV OP/OL	 220.3/192.4	 181.8/254.6	 147.6/198.8	 224.9/127.2	 113.0/144.6

ERG – electroretinography, pERG – pattern-reversal electroretinography, mfERG – multifocal electroretinography, RhF – rheohemapheresis, OD – right eye, OS – left eye

Table 2. Indicators of the effectiveness of rheohemapheresis on the spectrum of high molecular weight substances

Parameter	Before RhF (average)	After RhF (average)	Decrease (%)
Total cholesterol	3.84	1.94	49.5
LDL cholesterol	1.95	0.7	64.1
Lp(a)	2.47	1.44	41.7
Apolipoprotein B	0.71	0.24	66.2
Immunoglobulin M	0.3	0.14	53.3
Fibrinogen	2.78	1.3	53.2
Plasma viscosity	1.97	1.77	10.2
Blood viscosity	7.27	6.6	9.2

RhF – rheohemapheresis, LDL – low-density lipoprotein, Lp(a) – lipoprotein (a)

possibility of halting its progression or even improving the condition of the patients for a long period of time. In the presented case report, we achieved stabilisation of dry form of AMD over the course of a 6-year observation period, furthermore with gradual resorption of soft drusen in the macula of both eyes, and attachment of the line of the RPE following RhF treatment.

The development of VA in patients with dry form of AMD following RhF treatment over the course of a one-year observation period was evaluated by the multicentric randomised double-blind trial MIRA-1 [10]. The trial included a total of 216 patients, of whom 104 treated patients and 63 patients in a control group receiving a placebo were assessed at the end of one year of observation. The treated patients showed an improvement of VA by 0.02 ±0.213 logMAR, and the patients with a placebo by 0.02 ±0.20 ($p = 0.977$). In the case of our patient, during the 6-year observation period we recorded a stabilisation of visual functions, which we consider a success. It is not always possible to expect a statistically significant improvement of VA following treatment of dry form of AMD by RhF. This can be achieved only in the case of resorption of soft drusen localised directly in the central foveola, furthermore upon an absence of degenerative changes such as RPE defects, pigmentation and atrophy of the photoreceptor layer.

The results of the examination of rheologically significant factors document that RhF procedures are rheologically highly effective, achieving a more than 50% reduction of rheologically effective parameters, which is a fundamental precondition for increasing flow in microcirculation [9]. In the case of our patient also we achieved a reduction of the spectrum of high molecular weight substances, with a subsequent positive influence on rheological parameters.

CONCLUSION

In the case of our patient with dry form of AMD, RhF treatment led to an anatomical improvement and a stabilisation of the functional finding in both eyes over the course of a 6-year observation period.

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