Research Article

Pamukkale Medical Journal
doi:https://dx.doi.org/10.31362/patd.1483135

Choroidal and retinal changes in patients with allergic rhinoconjunctivitis

Alerjik rinokonjonktivitli hastalarda koroid ve retina değişiklikleri

Ömer Akçal, Matin Suleymanzade, Burcu Işık, Mehmet Giray Ersöz

Posted date:14.05.2024 Acceptance date:29.07.2024

Abstract

Purpose: Allergic rhinoconjunctivitis (ARC) is an allergic upper respiratory tract disease characterized by sneezing, runny nose, nasal congestion and ocular and nasal itching due to inflammation of the nasal and conjunctival mucosa. There are no studies evaluating both the choroidal and retinal areas in ARC patients. Our objective was to evaluate patients with ARC at the time of diagnosis and before initiating treatment using Optical Coherence Tomography (OCT).

Material and methods: This prospective cross-sectional study included 30 patients with ARC who presented to the Pediatric Allergy & Immunology Outpatient Clinic and 30 healthy control individuals. OCT scans were captured with Cirrus HD OCT-5000 (Carl Zeiss, Jena, Germany) in the enhanced depth imaging (EDI) mode.

Results: Of the study population, 66.7% (n=20) of patient group and 56.6% (n=17) of control group were female. The mean age was 13±2.3 and 13.9±1.8 years in the patient and control groups, respectively. The temporal subfoveal choroidal thickness was statistically significantly thinner in ARC patients with asthma (p=0.032). A robust negative correlation was found between minimum ganglion cell-inner plexiform layer (GCIPL) thickness and absolute eosinophil count (AEC) in patients with ARC (r:-0.551, p<0.0001).

Conclusion: In our study, the GCIPL thickness was lower in ARC patients. Similarly, although it did not reach statistical significance, the minimum GCIPL thickness was lower in our patient group with asthma compared to those without asthma. Our results suggest that multiple allergen sensitization and elevated eosinophils may influence GCIP thickness. However, both choroidal and retinal tissue might be impacted during chronic follow-up. Further studies are needed to support these findings.

Keywords: Retina, allergy, rinitis, choroid.

Akcal O, Suleymanzade M, Isik B, Ersoz MG. Choroidal and retinal changes in patients with allergic rhinoconjunctivitis. Pam Med J 2024;17:734-744.

Öz

Amaç: Alerjik rinokonjonktivit (ARK), burun ve konjonktival mukozanın iltihaplanmasına bağlı olarak hapşırma, burun akıntısı, burun tıkanıklığı ve gözde ve burunda kaşıntı ile karakterize alerjik bir üst solunum yolu hastalığıdır. ARK hastalarında hem koroid hem de retina bölgelerini değerlendiren çalışma bulunmamaktadır. Amacımız ARK'lı hastaları tanı anında ve tedaviye başlamadan önce Optik Koherens Tomografi (OKT) kullanarak değerlendirmektir.

Gereç ve yöntem: Bu prospektif kesitsel çalışmaya Çocuk Alerji ve İmmünoloji Polikliniği'ne başvuran 30 ARK hastası ve 30 sağlıklı kontrol dahil edildi. OKT taramaları, gelişmiş derinlik görüntüleme (EDI) modunda Cirrus HD OCT-5000 (Carl Zeiss, Jena, Almanya) ile ölçüldü.

Bulgular: Çalışma popülasyonunun hasta grubunun %66,7'si (n=20), kontrol grubunun %56,6'sı (n=17) kadındı. Ortalama yaş hasta ve kontrol gruplarında sırasıyla 13±2,3 ve 13,9±1,8 yıldı. Astımlı ARK hastalarında temporal subfoveal koroid kalınlığı istatistiksel olarak anlamlı derecede daha inceydi (p=0,032). ARK'lı hastalarda minimum ganglion hücre-iç pleksiform tabaka (GCIPL) kalınlığı ile mutlak eozinofil sayısı arasında güçlü bir negatif korelasyon bulundu (r:-0,551, p<0,0001).

Sonuç: Çalışmamızda ARK hastalarında GCIPL kalınlığı daha düşüktü. Benzer şekilde astımlı hasta grubumuzda da minimum GCIPL kalınlığı istatistiksel anlamlı bulunmasa da astımı olmayanlara göre daha düşüktü. Sonuçlarımız çoklu alerjen duyarlılığının ve yüksek eozinofillerin GCIPL kalınlığını etkileyebileceğini göstermektedir. Ancak kronik takip sırasında hem koroid hem de retina dokusu etkilenebilir. Bu bulguları desteklemek için daha ileri çalışmalara ihtiyaç vardır.

Anahtar kelimeler: Retina, alerji, rinit, koroid.

Akçal Ö, Suleymanzade M, Işık B, Ersöz MG. Alerjik rinokonjonktivitli hastalarda koroid ve retina değişiklikleri. Pam Tıp Derg 2024;17:734-744.

Ömer Akçal, Asst. Prof. Department of Pediatrics, Division of Immunology and Allergy Clinic, Biruni Univesity Medicine Faculty Hospital, Istanbul, Türkiye, e-mail: omerakcal@hotmail.com (https://orcid.org/0000-0002-3046-7133) (Corresponding Author)

Matin Suleymanzade, Specialist, Department of Ophthalmology, Biruni Univesity Medicine Faculty Hospital, Istanbul, Türkiye, e-mail: msuleymanzade@biruni.edu.tr (https://orcid.org/0000-0002-6500-4091)

Burcu Işık, Asst. Prof. Department of Ophthalmology, Atlas University Medicine Faculty Hospital, Istanbul, Türkiye, e-mail: burcuisik0@gmail.com (https://orcid.org/0000-0002-7853-522X)

Mehmet Giray Ersöz, Assoc. Prof. Department of Ophthalmology, Biruni Univesity Medicine Faculty Hospital, Istanbul, Türkiye, e-mail: mersoz@biruni.edu.tr (https://orcid.org/0000-0002-2336-0696)

Introduction

Allergic rhinitis (AR) is an upper respiratory system disorder associated with inflammation of nasal mucosa, and characterized by sneezing, nasal itching, runny nose and nasal congestion. It is a chronic allergic disease commonly seen in both children and adults [1]. It develops on the basis of type 1 hypersensitivity reaction in an early phase where mediators released upon mast cell degranulation, including histamine, prostaglandins, leukotrienes, quinines, and platelet-activating factor, play a major role. In the late phase, eosinophil-mediated inflammation is predominant in the nasal mucosa [2]. Inflammation leads to increased vascular permeability, mucosal edema and impaired mucociliary clearance [1]. It predisposes to respiratory problems such as severe nasal congestion, impaired sleep quality and sinusitis [3]. Recent studies suggest an estimated prevalence of 10% to 40% for AR [1, 2]. Clinical manifestation accompanied by ocular involvement with symptoms such as ocular itching, watering and redness are called allergic rhinoconjunctivitis (ARC) [4]. ARC can be triggered by many external factors such as air pollution, seasonal change, cigarette smoke, and viral infections. However, the most common triggering agents are aeroallergens such as tree or grass pollens, mold fungi, house dust mites and animal dander [2, 5]. These allergens are also involved in the etiology of allergic asthma (AA) in addition to AR and ARC [6].

The choroid is a posterior eye tissue with a dense vascular network that nourishes the outer layers of the retina. Figure 1 schematically illustrates layers of the retina and the choroid [7]. Clinical studies have shown that both the stromal and vascular structures of the choroid are impacted by various systemic diseases [8-11]. New imaging methods that measure choroidal thickness (ChT) and choroidal vascularity index (CVI) have spurred research on the correlation between the choroid and numerous diseases. In the literature, there are studies investigating choroidal parameters in diseases involving the respiratory tract such as asthma bronchiale, chronic obstructive lung disease, and sleep apnea syndrome [12-15]. The Ganglion Cell-Inner Plexiform Layer (GCIPL) complex comprises ganglion cell nuclei and dendrites in the retina. GCIPL thickness has been evaluated in various autoimmune and autoinflammatory disease groups [16]. Moreover, noteworthy findings have been shown in different systemic conditions including sleep apnea syndrome, Parkinson's disease, and Alzheimer's disease [17-19]. However, there has been no evaluation of both the choroid and retinal ganglion area in patients with ARC. In our study, we aimed

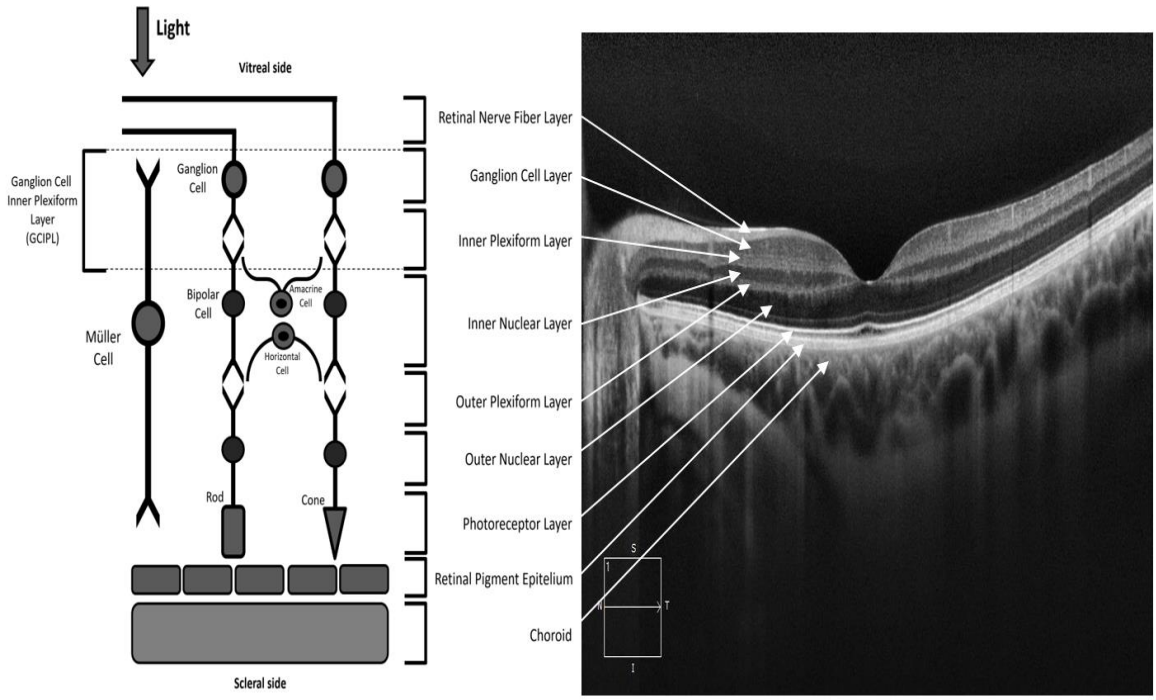

Figure 1. Layers of retina and choroid

to evaluate patients with ARC at the time of diagnosis and before initiating treatment using *Optical Coherence Tomography (*OCT).

Material and methods

This prospective cross-sectional study included 30 patients with ARC who presented to the pediatric allergy & immunology outpatient clinic and 30 healthy control individuals. The study was approved by the local Ethics Committee and conducted according to the Declaration of Helsinki Ethical Principles.

Power analysis

The sample size was determined based on previous studies with similar designs and objectives. Although there is limited literature evaluating both choroidal and retinal changes in patients with allergic rhinoconjunctivitis (ARC), an estimated effect size (Cohen's d ≈ 0.75) was used to calculate the required sample size. Using a significance level (alpha) of 0.05 and a desired statistical power of 80% (beta = 0.20), it was determined that a minimum of 30 patients and 30 controls would provide adequate power to detect meaningful differences between groups. This sample size is consistent with other ophthalmologic and immunologic studies that employed Optical Coherence Tomography (OCT) to assess retinal and choroidal parameters.

Patient group

The study included patients with newly diagnosed and treatment-naive ARC who presented to our hospital between July 2022 and September 2023. Patients who received any prior treatment, who were previously diagnosed with ARC and under follow-up and who had concomitant infections were excluded. A skin prick test (SPT) was performed to determine aeroallergen sensitization in patients with ARC. Following a thorough assessment involving detailed medical history, physical examination and allergy tests to confirm the diagnosis, the patients were referred to our ophthalmology outpatient clinic and they underwent OCT. Thirty patients with ARC included in the study.

Control group

Thirty healthy children of equivalent age and gender were selected as the control group. They were not receiving any medical treatment and had no chronic disease. They also underwent OCT in our ophthalmology outpatient clinic. Afterwards, the same parameters were compared between the patient and control groups.

Skin prick test

SPT was applied to the volar aspect or dorsum of the forearm. Patients were instructed to refrain from any antihistaminic agents at least one week prior to test. Histamine served as the positive control, and physiologic saline was the negative control during SPT. Reactions were assessed 15 minutes after administration. Allergens that produced an induration at least 3 mm greater than that of the negative control (excluding erythema) were deemed positive, while those producing a reaction less than 3 mm were considered negative.

Choroidal measurements

OCT scans were performed in Enhanced Depth Imaging (EDI) mode using a Cirrus HD OCT-5000 device (Carl Zeiss, Jena, Germany). Measurements were performed early in the morning to avoid interference with the diurnal rhythm. The fovea was evaluated through a single 30° horizontal Spectral Domain EDI OCT scan comprising an average of 100 images. ChT and CVI were also quantified. CVI was assessed using the open-source software ImageJ Fiji (//fiji.sc./Fiji) as described by Agrawal et al. [20]. The images transferred to ImageJ were rescaled by set scaling. The choroidal area to be measured was marked using polygon selection tool. Choroidal boundaries were marked as the outer border of the retinal pigment epithelium/ Bruch's membrane complex anteriorly and the inner border of the sclera posteriorly. For each of the subfoveal 1500 µm, temporal 1500 µm and nasal 1500 µm choroidal areas, CVI was calculated using the following steps. After selecting the region of interest, it was added to the ROI manager tool to calculate its total area. The image was converted to 8 bits and binarized using autolocal threshold (Niblack). Then the image was converted back to red-green-blue (RGB) and added to the ROI manager tool using color threshold. The two images in the ROI manager were merged and the resulting image was saved and the marked area was calculated. The first measurement indicated the total choroidal area (TCA), and the last

measurement provided stromal area (SA). The luminal area (LA) was obtained by subtracting the stromal area from the total choroidal area. CVI was computed by expressing the ratio of LA to TCA as a percentage (CVI=[LA/TCA]X100). Subfoveal ChT was measured manually from the outer edge of the retinal pigment epithelium at the fovea to the sclerochoroidal interface. Figure 2 illustrates the measured areas of the retina and choroidal tissue.

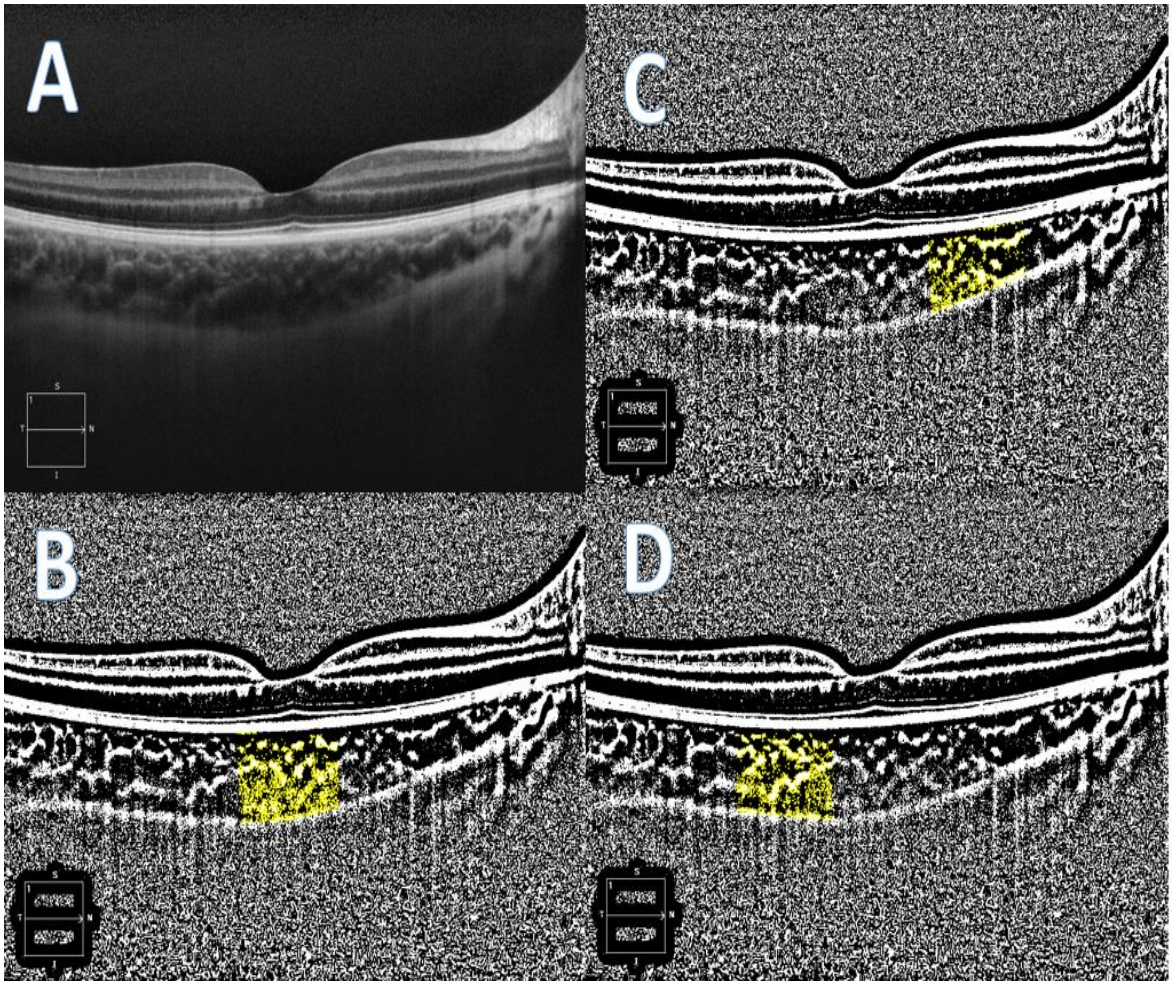

Figure 2. OCT images and binarized images taken in enhanced depth of imaging (EDI) mode of a 15-year-old allergic rhinitis patient; Black pixels in the marked area in the choroid indicate stroma, and white pixels indicate vascular lumen areas

Original OCT image (A), subfoveal 1500 µm (B), nasal 1500 µm (C), temporal 1500 µm (D)

Retinal measurements

The minimum and mean thickness of the GCIPL layers, macular volume (MV) and central subfield thickness (CST) were measured automatically using the Cirrus HD OCT-5000 device during OCT scans of patient and control groups. Cirrus HD OCT-5000 measures GCIPL thickness within annulus area of the fovea with an inner ring vertical diameter of 1 mm, and outer ring vertical diameter of 4 mm. Horizontal diameters are 20% wider. In this elliptical annulus area, the minimum and mean value of GCIPL thickness are automatically measured and reported [21]. CST is reported as the mean thickness of the retina within a 1 mm diameter circle centered at the fovea. Macular volume refers to the retinal volume within a 6x6 mm cube centered at the fovea [22].

Data evaluation

Demographic data, patient gender, patient age, blood tests, total IgE levels, skin prick test results and presence of concomitant asthma were analyzed from the patient files. OCT outcomes obtained in the opthtalmologic outpatient clinic in both the patient and control groups were evaluated. Based on the SPT results, the patients were divided into three groups as “those without allergen sensitization”, “those with single allergen sensitization”, and “those with multiple allergen sensitization”. The patient group was divided into two subgroups as those with and without concomitant asthma. Thus, the patient group was compared both with the control group and within the subgroups.

Statistical analysis

Data were analyzed using SPSS statistical software, version 22 (SPSS Inc, Chicago, IL). Continuous variables were expressed as mean ± SD and categorical variables as number (%). Normality testing was conducted to determine if the data followed a normal distribution. For this purpose, histograms and Q-Q plots were generated in SPSS to visually inspect the shape of the distribution. The Shapiro-Wilk test was used due to the sample size of 30, which is considered suitable for this test. A p-value greater than 0.05 from the Shapiro-Wilk test indicated that the data were normally distributed. Additionally, skewness and kurtosis values were calculated to assess the normality of the data further. For comparing continuous variables, independent t-tests and One-Way ANOVA were used for normally distributed data. In contrast, Mann-Whitney U test was employed for data not meeting the normality assumption.Categorical variables were analyzed using Chi-square tests. This comprehensive approach ensured the appropriate use of statistical methods and the reliability of the results.

Results

Of the study population, 66.7% (n=20) of patient group and 56.6% (n=17) of control group were female. The mean age was 13±2.3 and 13.9±1.8 years in the patient and control groups, respectively. There was no significant difference in age and gender between the two groups. A comparison of demographic data and parameters measured by OCT are shown in Table 1. No significant difference was found in choroidal tissue measurements between the patient and control groups. An evaluation of the patient group by allergen sensitization showed that absolute eosinophil count (AEC) was statistically significantly higher in patients with multiple allergen sensitization (p=0.002). Similarly, GCIPL thickness was lower in this group compared to those with monoallergen sensitization and non-sensitization, but the difference did not reach statistical significance (p=0.054). Table 2 shows a detailed comparison between the patient groups according their allergen sensitization status. The comorbidity rate in ARC cases was as follows: 36.6% (n=11) had asthma, 10% (n=3) had atopic dermatitis, and 10% (n=3) had food allergy to which tolerance developed. The patient group was also evaluated as those with and without asthma (Table 3). The temporal SA value of ARC patients with asthma was statistically significantly thinner (p=0.032).

We found a strong negative correlation between GCIPL thickness and AEC in patients with ARC (r:-0.551, p<0.0001).

Table 1. Comparison of study groups

		Patients (n=30)	Control (n=30)	*p* value	t or z value
Gender					
Female (n, %)		10 (33.3%)	13 (43.4%)	0.426	0.635[k]
Male (n, %)		20 (66.7%)	17 (56.6%)		
Age (years, mean±SD)		13±2.3	13.9±1.8	0.085	1.752[z]
ChT (µm, mean±SD)		353.9±61.6	353.5±74.5	0.985	-0.019[z]
Total TCA (µm, mean±SD)		1255306.2±2.3	1243306.4±2.3	0.844	-0.197[t]
Total SA (µm, mean±SD)		414441.1±85493.9	416809.4±85250.1	0.915	0.107[t]
Total LA (µm, mean±SD)		840871.1±1.5	826493.1±1.5	0.723	-0.356[t]
Total CVI (%, mean±SD)		67.02±2.1	66.5±1.9	0.346	-0.951[t]
Subfoveal TCA 1500 (µm, mean±SD)		439510.3±80467.7	446803±86456.9	0.736	0.338[t]
Subfoveal SA 1500 (µm, mean±SD)		142171.4±30948.4	146658±33018.5	0.589	0.543[t]
Subfoveal LA 1500 (µm, mean±SD)		297338.9±52224.2	300144.6±55820.4	0.841	0.201[t]
Subfoveal CVI 1500 (%, mean±SD)		67.7±2.5	67.3±2.5	0.483	-0.706[t]
Temporal TCA 1500 (µm, mean±SD)		441002.3±73861.9	424704.8±77193.8	0.407	-0.836[t]
Temporal SA 1500 (µm, mean±SD)		146785.8±27013.7	144597.6±27933.1	0.759	-0.308[t]
Temporal LA 1500 (µm, mean±SD)		294216.5±49806.7	280107.2±50593.7	0.281	-1.089[t]
Temporal CVI 1500 (%, mean±SD)		66.7±2.3	65.9±1.7	0.163	-1.412[t]
Nasal TCA 1500 (µm, mean±SD)		374799.6±114201	371794.7±94319.,4	0.907	-0.117[t]
Nasal SA 1500 (µm, mean±SD)		125483.9±37295.2	125553.4±31683.3	0.994	-0.212[t]
Nasal LA 1500 (µm, mean±SD)		249315.6±69300.2	246241.3±66084.1	0.861	-0.176[t]
Nasal CVI 1500 (%, mean±SD)		66.4±3.2	66.05±3.2	0.596	-0.533[t]
GCIPL	**Mean** (µm, mean±SD)	83.7±4.7	84.8±4.8	0.405	0.838[t]
	Minimum (µm, mean±SD)	78.6±14.5	83.7±4.2	0.068	1.858[t]
CST (µm, mean±SD)		249.8±19.4	249.6±18.6	0.962	1.858[t]
MV (µm, mean±SD)		10.2±0.4	10.2±0.3	0.975	-0.031[t]

ChT: choroidal thicknes, TCA: total choroidal area, SA: stromal area, LA: luminal area, CVI: choroid vascularity index, MV: macular volume GCIPL: ganglion cell inner plexiform layer, CST: central subfield thickness, SD: standart deviation, k: chi-square; t: t value ; z: z value

Table 2. Comparison of patient groups according to allergen sensitization

		Non-sensitized patients (n=12)	Monosensitized patients (n=13)	Multiple sensitization patients (n=5)	*p* value	f value
Age (years, mean±SD)		12.3±2.5	13.5±2.1	13.2±2.3	0.455	0.812
Eosinophil (count /mm^3, mean±SD)		245.5±252.1	424.4±361.2	1206.1±496.4	**0.002**	9.217
Total IgE (kU/l, mean±SD)		145.3±122.5	418.6±753.9	1277.5±392.4	0.100	2.6
ChT (µm, mean±SD)		344.1±70.5	350±33.6	392±88.7	0.310	1.225
Total TCA (µm, mean±SD)		1199806±2191985	1247716±1791845	1409806±3716325	0.253	1.447
Total SA (µm, mean±SD)		393243.6±71582.7	409972.7±72417.1	476933±1298985	0.181	1.82
Total LA (µm, mean±SD)		806595.3±1555125	837120.7±1139695	932883.8±2451975	0.330	1.154
Total CVI (%, mean±SD)		67.1±2.5	67.2±2.1	66.2±1.36	0.673	0.402
Subfoveal TCA 1500 (µm, mean±SD)		415916±78886.9	446137.3±66550.1	478906.4±1130975	0.325	1.173
Subfoveal SA 1500 (µm, mean±SD)		132496±28028.6	145548.3±28570.1	156612.4±41908.8	0.309	1.227
Subfoveal LA 1500 (µm, mean±SD)		283420±55404.1	300589.1±39664.4	322294±52224.2	0.373	1.024
Subfoveal CVI 1500 (%, mean±SD)		68.1±3.3	67.5±2	67.5±1.7	0.839	0.176
Temporal TCA 1500 (µm, mean±SD)		447090±64014.7	414709±50808.1	494754.4±1207050	0.110	2.4
Temporal SA 1500 (µm, mean±SD)		148491±23678.1	136798.3±18826.4	168660.8±41886.5	0.073	2.883
Temporal LA 1500 (µm, mean±SD)		298599±43646.3	277910.7±36778.2	326093.6±80601.1	0.173	1.874
Temporal CVI 1500 (%, mean±SD)		66.7±2.3	67±2.5	65.8±1.6	0.666	0.412
Nasal TCA 1500 (µm, mean±SD)		336833±94515.3	386247±89539.7	436156±1436820	0.178	1.843
Nasal SA 1500 (µm, mean±SD)		112256.6±29500.4	127626.1±36201	151659.8±48613.1	0.134	2.17
Nasal LA 1500 (µm, mean±SD)		224576.3±67144.5	258620.9±56059.2	284496.2±96579.9	0.223	1.588
Nasal CVI 1500 (%, mean±SD)		66.3±3.4	67.1±3.4	65±2.1	0.473	0.77
GCIPL	**Mean** (µm, mean±SD)	83.2±4	84.9±5.3	82.6±4.8	0.637	0.459
	Minimum (µm, mean±SD)	81±4.1	82±5.5	64.6±33	0.054	3.251
CST (µm, mean±SD)		242.8±13.8	252.3±21.2	257±26.4	0.260	1.416
MV (µm, mean±SD)		10±0.3	10.3±0.5	10.2±0.2	0.209	1.662

ChT: choroidal thicknes, TCA: total choroidal area, SA: stromal area, LA: luminal area, CVI: choroid vascularity index, GCIPL: ganglion cell inner plexiform layer, CMT: central subfield thickness, MV: macular volume
SD: standart deviation, One-way ANOVA test: f value
*Post Hoc analized with tukey test: For eosinophil: non-sensitized versus multiple sensitization p=0.001, monosensitized versus multiple sensitization p=0.007; non-sensitized versus monosensitized p=0.511

Table 3. Comparison of patients with and without asthma

		With asthma (n=11)	Without asthma (n=19)	*p* value	t or z value
Gender					
Female (n, %)		4 (36.4%)	6 (31.5%)	0.789	0.072[k]
Male (n, %)		7 (63.6%)	13 (68.5%)		
Age (years, mean±SD)		12.6±2.6	13.2±2.2	0.533	0.631[z]
Eosinophil (count /mm^3, mean±SD)		587.5±518.8	363.3±396.4	0.275	-1.125[z]
Total IgE (kU/l, mean±SD)		401.2±499.3	363.3±396.4	0.904	0.122[z]
ChT (µm, mean±SD)		347.5±45.9	357.5±70.1	0.675	0.423[z]
Total TCA (µm, mean±SD)		1166306±1063905	1306800.6±2761490.5	0.119	1.61[t]
Total SA (µm, mean±SD)		376668.7±45357.7	436309.4±96209.6	0.064	1.925[t]
Total LA (µm, mean±SD)		789643.8±73639.9	870529±1854690.5	0.180	1.377[t]
Total CVI (%, mean±SD)		67.7±2.1	66.6±2.1	0.186	-1.356[t]
Subfoveal TCA 1500 (µm, mean±SD)		416949.8±40127.3	452571.6±95112.3	0.249	1.176[t]
Subfoveal SA 1500 (µm, mean±SD)		131843.1±16541.8	148150.9±35891.2	0.168	1.415[t]
Subfoveal LA 1500 (µm, mean±SD)		285106.7±26765.7	304420.7±62062.2	0.338	0.975[t]
Subfoveal CVI 1500 (%, mean±SD)		68.4±1.8	67.3±2.8	0.301	-1.504[t]
Temporal TCA 1500 (µm, mean±SD)		406804.3±51763.1	460801.1±78565.5	0.052	2.031[t]
Temporal SA 1500 (µm, mean±SD)		133059.8±19075.4	154732.4±28138.1	**0.032**	2.263[t]
Temporal LA 1500 (µm, mean±SD)		273744.5±37498.1	306068.7±53020.1	0.087	1.775[t]
Temporal CVI 1500 (%, mean±SD)		67.2±2.5	66.4±2.1	0.328	-0.995[t]
Nasal TCA 1500 (µm, mean±SD)		342558.3±42826.9	393465.5±1243830	0.203	1.305[t]
Nasal SA 1500 (µm, mean±SD)		111765.8±21393.3	133426.1±42486.5	0.127	1.571[t]
Nasal LA 1500 (µm, mean±SD)		230792.5±27723.1	260039.5±83542.4	0.273	1.119[t]
Nasal CVI 1500 (%, mean±SD)		67.4±3.6	65.9±2.9	0.219	-1.257[t]
GCIPL	**Mean** (µm, mean±SD)	84±5.4	83.6±4.3	0.841	-0.203[t]
	Minimum (µm, mean±SD)	74.8±23.4	80.8±4.3	0.281	1.809[t]
CST (µm, mean±SD)		251.4±25.2	248.9±15.8	0.740	-0.336[t]
MV (µm, mean±SD)		10.3±0.4	10.1±0.4	0.429	-0.803[t]

ChT: choroidal thicknes, TCA: total choroidal area, SA: stromal area, LA: luminal area, CVI: choroid vascularity index, MV: macular volume GCIPL: ganglion cell inner plexiform layer, CST: central subfield thickness, SD: standart deviation, k: chi-square; t: t value ; z: z value

Discussion

The choroid is one of the vascular tissues with the highest blood supply. Its blood supply is affected by local or systemic inflammatory factors. Recently, the choroid has become a focal point of research in numerous systemic diseases, with promising findings indicating its potential as a biomarker. Various studies across diverse disease groups with systemic inflammation have demonstrated significant reductions in CVI and ChT [23].

Studies related with diseases involving the upper and lower respiratory tract are gaining momentum in the literature. A study in patients with nasal septal deviation showed no significant differences in subfoveal, temporal and nasal ChT measurements compared to a control group [24]. Another study by Savran Elibol et al. [25] evaluated patients with nasal polyps using OCT and suggested that increased inflammation in the nasal region might contribute to an increase in choroidal blood supply in the anatomically adjacent area. Inflammation and obstruction in the upper respiratory system may influence the sympathetic and parasympathetic balance, potentially resulting in changes in the choroidal tissue thickness. However, both studies found no significant differences compared to the control group. In our study, we observed no significant difference in choroidal measurements among patients with ARC (Table 1). Decreased CVI and ChT levels have been reported in various clinical studies, particularly in respiratory conditions such as sarcoidosis, asthma and sleep apnea syndrome [26-28]. We also examined patients with and without asthma. Many studies have shown an increased prevalence of allergic conditions such as atopic dermatitis (AD), food allergy (FA), AR, and AA within specific age groups, following a sequential pattern with increasing age. AD and FA are more prevalent in infancy while AR and AA commonly manifest in childhood [29]. This progressive nature of allergic conditions is referred to as “atopic march”. Accordingly, there is a risk of development of AA in cases with AR. Atopic inflammation in nasal mucosa may induce changes in the lower respiratory tract through three fundamental mechanisms: nasal-tracheal reflex, cytokines and secretions [29]. A study by Yılmaz et al. [12] reported statistically significant reductions in CVI and subfoveal ChT in asthma patients. In our study, when comparing our ARC patients with and without asthma, we observed a lower ChT in asthmatic patients, although the difference was not statistically significant. Across all three areas (subfoveal 1500μm, temporal 1500μm, and nasal 1500μm), TCA, SA and LA were lower in ACR patients with asthma than those without asthma. Notably, the decrease in temporal 1500μm SA was statistically significant. On the other hand, CVI ratio was higher, albeit not statistically significant, in ARC patients with asthma. We attribute this finding to the fact that the decrease in SA was more pronounced compared to LA.

It could be proposed that CVI and ChT ratios of ACR patients may be influenced by the subsequent development of AA in the context of atopic march in the coming years. Considering that we conducted the measurements in our ARC patients prior to the initiation of treatment, we have shown that choroidal tissue was not significantly affected in allergic patients with upper respiratory tract involvement. However, in the light of recent studies, it has been substantiated that alterations in choroidal tissue occur in conditions associated with lower respiratory tract such as asthma [12, 26, 27].

Chen et al. [30] reported a thinner retinal nerve fiber layer (RNFL) in patients with allergic conjunctivitis (AC). The same study showed no significant difference in macular thickness measurements among AC patients compared to the control group. Similarly, in our study, we observed no statistically significant differences in macular measurements between the patient and control groups. Nevertheless, there is no study evaluating the GCIPL thickness in patients with ARC. Although the minimum GCIPL thickness in our patient group was lower compared to the control group, the difference did not reach statistical significance. Notably, in the group with multiple sensitizations, the minimum GICPL thickness was significantly lower compared to the other two groups (monoallergen sensitization group and non-sensitization group) (Table 2). The macular thickness was similar in these groups. Additionally, the minimum GCIPL thickness was lower in our patient group with asthma than those without asthma (Table 3). In the literature, there are studies evaluating both retina and choroid in various autoimmune and autoinflammatory disease groups, revealing

that inflammation may lead to thinning, especially in the choroid and retina [16]. Clinical studies suggest that assessing choroidal measurements provide more informative insights than retinal measurements. Despite the abundance of clinical studies evaluating ChT and CVI measurements, research on GCIPL is very limited. Notably, some findings suggest the potential benefit of retinal measurements in conditions such as psoriasis, metabolic syndrome and Behcet's disease, offering promise for future studies [16]. Our study also emphasized the significance of choroidal and retinal measurements in chronic respiratory allergies such as AR, ARC and AA as we observed a robust negative correlation between the minimum GCIPL thickness and AEC. Patients with predominant eosinophil exhibited multiple sensitizations, and AEC was statistically significantly higher in ARC patients with multiple allergen sensitization. Our results suggest that multiple allergen sensitization and elevated eosinophil levels contribute to GCIPL thickness. The findings also suggest choroidal and retinal tissue measurements are promising indicators in ARC patients with multiple sensitization and elevated AEC, possibly serving as biomarkers in the future. However, further evidence-based studies are required to support these findings.

In conclusion, our study did not find any significant impact on choroidal tissue in patients with ARC. However, we observed that ChT was thinner in patients with concomitant asthma. On the other hand, GCIPL thickness was lower in patients with ARC. Although not reaching statistical significance, the minimum GCIPL thickness was also lower in our asthmatic patients compared to those without asthma. These findings suggest that both choroidal and retinal tissues may be affected in the chronic follow-up. Additional studies are necessary to provide robust support for these observations.

Conflict of interest: No conflict of interest was declared by the authors.

References

1. Eifan AO, Durham SR. Pathogenesis of rhinitis. Clin Exp Allergy 2016;46:1139-1151. https://doi.org/10.1111/cea.12780
2. Okano M, Fujieda S, Gotoh M, et al. Executive summary: Japanese guidelines for allergic rhinitis 2020. Allergol Int 2023;72:41-53. https://doi.org/10.1016/j.alit.2022.11.003
3. Blaiss MS. Pediatric allergic rhinitis: physical and mental complications. Allergy Asthma Proc 2008;29:1-6. https://doi.org/10.2500/aap2008.29.3072
4. Phipatanakul W. Allergic rhinoconjunctivitis: epidemiology. Immunol Allergy Clin North Am 2005;25:263-281. https://doi.org/10.1016/j.iac.2005.03.001
5. Yorgancıoğlu AA, Gemicioğlu B, Cingi C, et al. ARIA 2019, Allerjik rinite tedavi yaklaşımı-Türkiye. Turk Thorac J 2020;21:122-133. https://doi.org/10.5152/TurkThoracJ.2019.19084
6. Tsuge M, Ikeda M, Matsumoto N, Yorifuji T, Tsukahara H. Current ınsights into atopic march. Children (Basel) 2021;8:1067. https://doi.org/10.3390/children8111067
7. Joyce C, Le PH, Sadiq NM. Histology, Retina. 2023 Aug 8. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2023 Jan
8. Nickla DL, Wallman J. The multifunctional choroid. Prog Retin Eye Res 2010;29:144-168. https://doi.org/10.1016/j.preteyeres.2009.12.002
9. Wei WB, Xu L, Jonas JB, et al. Subfoveal choroidal thickness: the Beijing Eye Study. Ophthalmology 2013;120:175-180. https://doi.org/10.1016/j.ophtha.2012.07.048
10. Aksoy M, Asena L, Tekindal MA, Ayvazoğlu Soy EH, Yılmaz G, Haberal M. Choroidal vascularity ındex and choroidal thickness changes following renal transplantation. Turk J Ophthalmol 2023;53:97-104. https://doi.org/10.4274/tjo.galenos.2022.02489
11. Seo WW, Yoo HS, Kim YD, Park SP, Kim YK. Choroidal vascularity index of patients with coronary artery disease. Sci Rep 2022;12:3036. https://doi.org/10.1038/s41598-022-07120-8
12. Yılmaz M, Polat OA, Karayiğit DZ, Ayyıldız T. Choroidal vascularity index and choroidal thickness changes in patients with allergic asthma. Photodiagnosis Photodyn Ther 2021;36:102494. https://doi.org/10.1016/j.pdpdt.2021.102494
13. Kocamış O, Zorlu D. Choroid and retinal nerve fiber layer thickness in patients with chronic obstructive pulmonary disease exacerbation. J Ophthalmol 2018;2018:1201976. https://doi.org/10.1155/2018/1201976
14. Xin C, Wang J, Zhang W, Wang L, Peng X. Retinal and choroidal thickness evaluation by SDOCT in adults with obstructive sleep apnea-hypopnea syndrome (OSAS). Eye (Lond) 2014;28:415-421. https://doi.org/10.1038/eye.2013.307
15. Yakut ZI, Karadag R, Ozol D, Senturk A. Evaluation of arterial blood flow changes by orbital Doppler in chronic obstructive pulmonary disease and asthma. J Investig Med 2015;63:12-16. https://doi.org/10.1097/jim.0000000000000118

16. Steiner M, Esteban Ortega MDM, Muñoz Fernández S. Choroidal and retinal thickness in systemic autoimmune and inflammatory diseases: a review. Surv Ophthalmol 2019;64:757-769. https://doi.org/10.1016/j.survophthal.2019.04.007
17. Sundaram V, Haridas S, Dhar M, Harikrishnan CP. Evaluation of retinal nerve fiber layer, ganglion cell layer, and optic nerve head morphological parameters in patients with obstructive sleep apnea and comparison with normal population. Indian J Ophthalmol 2022;70:453-457. https://doi.org/10.4103/ijo.IJO_985_21
18. Živković M, Dayanir V, Stamenović J, et al. Retinal ganglion cell/inner plexiform layer thickness in patients with Parkinson›s disease. Folia Neuropathol 2017;55:168-173. https://doi.org/10.5114/fn.2017.68584
19. López de Eguileta A, Cerveró A, Ruiz de Sabando AR, Sánchez Juan P, Casado A. Ganglion cell layer thinning in alzheimer's disease. Medicina (Kaunas) 2020;56:553. https://doi.org/10.3390/medicina56100553
20. Agrawal R, Salman M, Tan KA, et al. Choroidal vascularity index (CVI)–a novel optical coherence tomography parameter for monitoring patients with panuveitis? PLoS One 2016;11:e0146344 https://doi.org/10.1371/journal.pone.0146344
21. Mwanza JC, Durbin MK, Budenz DL, et al. Cirrus OCT Normative Database Study Group. Profile and predictors of normal ganglion cell–ınner plexiform layer thickness measured with frequency-domain optical coherence tomography. Invest Ophthalmol Vis Sci 2011;52:7872-7879. https://doi.org/10.1167/iovs.11-7896
22. Saxena S, Caprnda M, Ruia S, et al. Spectral domain optical coherence tomography based imaging biomarkers for diabetic retinopathy. Endocrine 2019;66:509-516. https://doi.org/10.1007/s12020-019-02093-7
23. Ataş F, Kaya M, Ayhan Z, Ozkan O, Birlik M. Evaluation of choroidal vascularity index in systemic sclerosis patients. Photodiagnosis Photodyn Ther 2023;41:103297. https://doi.org/10.1016/j.pdpdt.2023.103297
24. Üstün Bezgin S, Çakabay T, Bayramoğlu SE, Sayın N, Koçyiğit M. Evaluation of choroidal thickness measurements in patients with marked nasal septal deviation. Braz J Otorhinolaryngol 2020;86:242-246. https://doi.org/10.1016/j.bjorl.2018.11.009
25. Savran Elibol E, Doğan R, Elbay A, Cırık AA, Aykut V, Yenigün A. Evaluation of coroid thickness of patients with nazal polype. J Ear Nose Throat and Head Neck Surgery 2020;28:216-221. https://doi.org/10.24179/kbbbbc.2020-75404
26. Ugurlu E, Pekel G, Akbulut S, Cetin N, Durmus S, Altinisik G. Choroidal vascularity index and thickness in sarcoidosis. Medicine (Baltimore) 2022;101:e28519. https://doi.org/10.1097/MD.0000000000028519
27. Özcan G, Temel E, Örnek K, et al. Choroidal vascularity index in obstructive sleep apnea syndrome. Sleep Breath 2022;26:1655-1659. https://doi.org/10.1007/s11325-021-02538-2
28. Yang L, Fu J, Zhou Y. Research progress in atopic march. Front Immunol 2020;11:1907. https://doi.org/10.3389/fimmu.2020.01907
29. Leynaert B, Neukirch C, Kony S, et al. Association between asthma and rhinitis according to atopic sensitization in a population-based study. J Allergy Clin Immunol 2004;113:86-93. https://doi.org/10.1016/j.jaci.2003.10.010
30. Chen D, Li R, Huang D, et al. Altered retinal nerve fiber layer thickness in children with allergic conjunctivitis: the Nanjing eye study. BMC Ophthalmol 2022;22:183. https://doi.org/10.1186/s12886-022-02399-7

Ethics committee approval: This study was approved by the Biruni University Non-Interventional Clinical Research Ethics Committee (date: 24/05/2022 and number: 2022/71-31).

Author contributions

O.A. is the first author of this article. Designed the study: O.A., M.S., M.G.E. Preparation of ethics forms and apply: O.A. Manuscript preparation, analysis interpretation of data: O.A., B.I., M.G.E. Contributed reagents/materials/analysis tools: O.A., M.S., B.I. Wrote the paper: O.A., M.G.E. Collected and entered the data: O.A., M.S., B.I., M.G.E. All authors read and approved the final manuscript.