

The effect of allergic rhinitis with positive skin prick test on choroidal thickness

Alper Yenigun¹ · Ahmet Elbay² · Remzi Dogan¹ · Orhan Ozturan¹ · Mehmet Hakan Ozdemir²

Received: 26 November 2016 / Accepted: 17 February 2017
© Springer-Verlag Berlin Heidelberg 2017

Abstract Allergic rhinitis is an inflammatory disease that develops through immunoglobulin E in the rhino-ocular mucosa due to allergy. The main symptoms are runny nose, nasal congestion, sneezing and itchy nose. This study was designed to investigate the effect of allergic rhinitis on choroidal thickness. This study was planned as a case-control study. This study performed in a tertiary referral center. The study included 61 patients with allergic rhinitis and 35 healthy subjects. Patients in both groups underwent skin prick test. In allergic rhinitis patients and healthy persons; subfoveal, temporal and nasal choroidal thickness measurement was performed. The choroidal thicknesses were measured without pupil dilation using the Spectralis Optical Coherence Tomography. In the subfoveal and temporal region, choroidal tissue was followed up significantly thicker in allergic rhinitis patients statistically compared to healthy persons ($p=0.031$, $p=0.049$). However, no significant difference was followed up between the nasal choroidal thickness measurements statistically ($p=0.54$). Runny nose (67.2%), sneeze (65.5%), stuffiness (62.2%), itching of the nose (40.9%), and nasal discharge (21.3%) complaints were observed significantly higher in the group having allergic rhinitis. The effect of allergic rhinitis on choroidal thickness were assessed and compared with the control group. Our study revealed that there was significant association between increased choroidal thickness and allergic

rhinitis. Allergic sensitivity may play an important role in increased choroidal thickness.

Keywords Choroid · Allergy · Allergic reaction · Allergic rhinitis · Skin tests · Prevalence · Immunoglobulin E · Optical coherence tomography

Abbreviations

AR	Allergic rhinitis
EDI-OCT	Enhanced depth imaging optical coherence tomography
GAG	Glycosaminoglycan
IgE	Immunoglobulin E
NCSS	Number Cruncher Statistical System
OCT	Optical Coherence Tomography
PASS	Power Analysis and Sample Size
VKH	Vogt-Koyanagi-Harada

Introduction

Allergic rhinitis (AR) is the type 1 hypersensitivity reaction of the nasal mucosa and it impairs the quality of person's life [1]. AR is characterized by rhinorrhea, nasal obstruction or blockage, nasal itching, sneezing, and postnasal drip, due to inflammation of the nasal mucosa [2]. The prevalence of AR in the general population of Europe has been reported to be around 10–30% [3, 4]. AR is an inflammatory disease that develops through immunoglobulin E (IgE) in the rhino-ocular mucosa [4]. AR is a chronic upper respiratory tract disease and diagnosis is determined based on the history and physical examination [5]. Although clinical findings are essential for diagnosis, skin prick test is the most common method used to determine allergy and

✉ Alper Yenigun
alperyenigun@gmail.com

¹ Bezmialem Vakif University, Faculty of Medicine,
Department of Otorhinolaryngology, Adnan Menderes
Boulevard, Vatan Street, Fatih, 34093 Istanbul, Turkey

² Bezmialem Vakif University, Faculty of Medicine,
Department of Ophthalmology, Fatih, Istanbul, Turkey

identify the responsible allergen, and has become the gold standard for diagnosis [6].

Choroid is one of the most vascularized tissues in the human body and assumes important roles in oxygenation and nutrition of outer retina, temperature regulation of retina, positional condition of retina and secretion of growth factors [8].

With the development of optical coherence tomography (OCT) in recent years, it has become possible to display in vivo cross sectional images of the technical choroid, which is enhanced depth imaging optical coherence tomography, EDI-OCT [7]. The first study in which choroidal thickness was measured by OCT was performed by Spaide et al. in 2008 [7]. Likewise in Vogt-Koyanagi-Harada (VKH) [8], Behçet's disease [9], sarcoidosis [10], sympathetic ophthalmia [11], toxoplasma chorioretinitis [12], posterior scleritis [13], ankylosing spondylitis [14] and hypothyroid [15]; it was revealed in the studies that there was an increase in subfoveal choroidal thickness in autoimmune and inflammatory diseases.

Since AR is a disease of the immunological base and a chronic upper respiratory tract disease, we aimed to investigate the effect of allergic rhinitis on choroidal thickness and compare with normal subjects.

Material and method

This is a prospective study, the approval dated 30/12/2015 and decision number 24/19 was received by the local Clinical Research Ethics Committee. Written informed consents of all patients were obtained. The study included a total of 96 consecutive patients (61 patients with allergic rhinitis and 35 control subjects); who applied to the Otorhinolaryngology and Ophthalmology Outpatient Clinics during January and February 2016.

Exclusion criteria included the presence of systemic diseases, myopia or hypermetropia of more than 3 diopters (D), glaucoma, retinal diseases, uveitis, other ocular disturbances like cataract that prevents a detailed fundus examination or ocular tests, medical history of ocular surgery, injection or laser treatment, poor image quality due to unstable fixation. Patients under corticosteroids treatment were excluded from the study.

Cases were divided into two different groups: allergic rhinitis group and healthy subjects (control group). Allergic rhinitis group: 61 allergic rhinitis patients (20 male, 41 female, age range between 18 and 38 years, average age 33.4 ± 14.6). Patients were accepted as symptomatic when their clinic symptoms include itchy and stuffy nose, sneezing, runny nose and aqueous nasal discharge. The patients who had an allergy against at least one active agent at skin prick test were accepted as sensitized. Allergic rhinitis

group in our study was formed with symptomatic and sensitized patients. AR symptom frequency has been divided into intermittent (<4 days per week or <4 weeks per year) and persistent (>4 days per week and >4 weeks per year). In our study, allergic rhinitis group included patients who had mild and moderate rhinitis and did not have any treatment before, and the symptom frequency was persistent.

The control group consisted of 35 healthy people of similar age and gender (9 male, 26 female, ages between 18 and 43, average age 30.9 ± 10.7) who have normal ocular examination except refractive disorders, without any history of allergic disorders, systemic diseases or drug consumption and with negative skin prick test results.

Ophthalmic examinations

The choroidal thickness were measured without pupil dilation using the Spectralis OCT (software version 5.3, Heidelberg Engineering, Heidelberg, Germany). OCT scans were acquired with the 30° line scan enhanced depth imaging mode. The images were averaged over 100 scans using an automatic real-time imaging value of 100 and active eye-tracking features. The choroidal thickness was defined as the distance between the hyper scattering line of the retinal pigment epithelial cells and that of the inner surface of the sclera. All OCT scans were performed by the same operator. Measurements were made of the central foveal segment and at segments that were 1500 µm temporal and 1500 µm nasal from the center of the fovea. Measurements taken at the same time every day.

Skin-prick test

Standard allergen extracts of the brand Alyostal ST-IR (Staller genes S.A., France) were used for skin prick tests. Allergen extracts were drawn into Quick test applicators with 8 heads, and were applied to the skin at the ventral side of the forearm, after the testing site was cleaned with alcohol. We used histamine (1 mg/ml) as a positive control and isotonic NaCl as a negative control. The results were read at the 15th minute after application. Test validity criteria were set as >3 mm for positive controls and <3 mm for negative controls. A skin reaction with an induration of 3 mm or more was accepted as positive [16]. Fourteen common allergens (D. pteronyssinus, D. farina, Cockroach, Trees mix, Grasses mix, Pine, Cat feather, Nuts, Penicillium mix, Cladosporium, Cacao, Egg, Wheat, Alterina) plus a negative and a positive control were applied to the skin of the forearm with two 8-headed applicators.

Table 1 Demographic data of the groups

Variables	Allergic rhinitis group	Control group	<i>p</i>
Sex			
Male	20	9	(0.473)
Female	41	26	
Age; (median)	33.4 ± 14.6	30.9 ± 10.7	(0.384)
Age; (range)	18–38	18–43	

Independent-samples test * $p < 0.05$, ** $p < 0.001$

Table 2 Allergic rhinitis symptoms of the allergic rhinitis group

Symptoms	Allergic rhinitis group
Runny nose	67.2% (41/61)
Sneeze	65.5% (40/61)
Stiffness	62.2% (38/61)
Itching of the nose	40.9% (25/61)
Nasal discharge	21.3% (13/61)

Statistical analysis

The NCSS (Number Cruncher Statistical System) 2007 & PASS (Power Analysis and Sample Size) 2008 Statistical Software (Utah, USA) program was employed for evaluating the data gathered in the study. Besides using descriptive statistics (mean, standard deviation) in evaluating the data, the One-Sample Kolmogorov–Smirnov Test was used for comparing the quantitative data and for comparing the normally distributed parameters in between groups. The significance level was set at $p < 0.001$ and $p < 0.05$.

Results

The study included 96 patients [67 females (69.8%), 29 males (30.2%)] who were examined in our clinic. The patients were assigned into 2 groups: Group 1 included 61 allergic rhinitis patients; Group 2 included 35 healthy people. Independent-Samples test results comparing the mean ages and sex of the two groups did not reveal any statistically significant differences ($p = 0.384$ and $p = 0.473$, respectively) (Table 1).

Table 3 Mean of choroidal thickness of the groups

Variables	Allergic rhinitis group	Control group	<i>p</i>
Mean of subfoveal choroidal thickness	367.49 ± 92.73 µm	327.62 ± 72.39 µm	0.031*
Mean of temporal choroidal thickness	306.52 ± 85.19 µm	272.45 ± 77.52 µm	0.049*
Mean of nasal choroidal thickness	286.87 ± 91.94 µm	275.49 ± 80.80 µm	0.54

One-Sample Kolmogorov–Smirnov Test * $p < 0.05$, ** $p < 0.001$

The study included 61 patients with allergic rhinitis (20 male, 41 female, age range between 18 and 38 years, average age 33.4 ± 14.6) and a control group of 35 healthy people (9 male, 26 female, ages between 18 and 43, average age 30.9 ± 10.7). Correlation was compared with allergic symptoms and skin test results.

In our cases, symptoms of patients with allergic rhinitis were listed as runny nose (67.2%), sneeze (65.5%), stuffiness (62.2%), itching of the nose (40.9%), and nasal discharge (21.3%) (Table 2).

The average subfoveal choroidal thickness was identified as 327.62 ± 72.39 µm in the control group of healthy subjects whereas average subfoveal choroidal thickness was 367.49 ± 92.73 µm in allergic rhinitis patients. Statistically significant difference was tracked between allergic rhinitis group and the control group ($p = 0.031$) (Table 3).

The average temporal choroidal thickness was identified as 272.45 ± 77.52 µm in the control group of healthy subjects whereas the average temporal choroidal thickness was 306.52 ± 85.19 µm in allergic rhinitis patients. Statistically significant difference was tracked between allergic rhinitis group and the control group ($p = 0.049$) (Table 3).

The average nasal choroidal thickness was identified as 275.49 ± 80.80 µm in the control group of healthy subjects whereas the average nasal choroidal thickness was 286.87 ± 91.94 µm in allergic rhinitis patients. Statistically significant difference was tracked between allergic rhinitis group and the control group ($p = 0.54$) (Table 3).

Discussion

In our study, we attempted to investigate the underlying allergic rhinitis together with the pathogenesis of an increase in choroidal thickness. We tracked the choroidal thickness of symptomatic patients in whom allergy was identified against at least one factor in the skin prick test and observed significantly thicker choroidal when compared to healthy individuals in temporal and subfoveal regions ($p = 0.031$, $p = 0.049$).

Choroid is the vascular tissue layers formed by cavernous spaces. Choroid has an important role in pathogenesis of the physiology of the healthy eye and various ocular diseases [17, 18]. It was revealed in the studies that there was an increase in choroidal thickness in most inflammatory

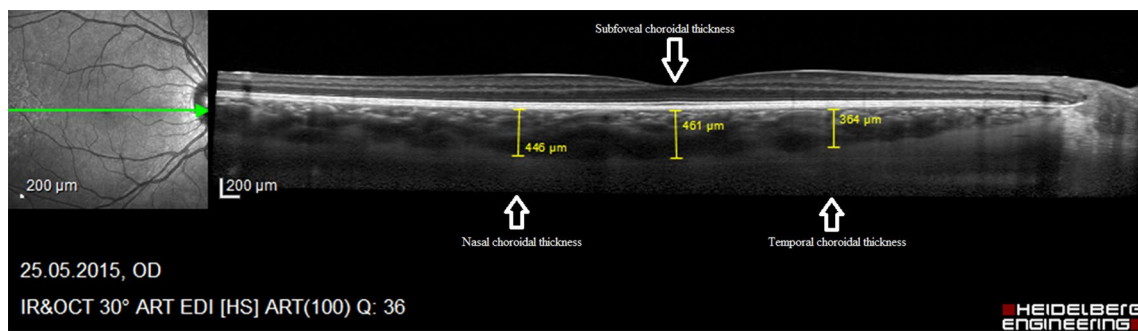


Fig. 1 Measurement of choroidal thickness

diseases [9–16]. In a study conducted by Read et al. on 8 patients having VKH disease, they revealed that a significant difference in subfoveal choroidal thickness in the acute phase of the disease and after inflammation control by systemic steroid treatment, that subfoveal choroidal thickness was lowered in 14 days. They asserted that this increase in the acute period was probably associated with the increased inflammatory infiltration and increased exudation. After systemic steroid treatment, choroidal thickness and exudative retinal detachment showed a rapid decrease [8].

Kim et al. compared the subfoveal choroidal thickness of 30 subjects in active and passive periods who had an average age of 47 and had posterior uveitis based on Behçet's disease. They showed that subfoveal thickness was greater during the acute phase of the disease compared to its passive phase. This situation was linked to choroidal infiltration of inflammatory cells. Patients in active phases were given systemic steroid treatment to help them achieve a passive phase [9].

It was revealed that in a patient diagnosed with sarcoidosis by biopsy and having unilateral, multifocal choroidal granuloma, choroidal thickness regressed by steroid treatment [10]. Fleishman et al. found the subfoveal choroidal thickness was 500 µm in a 39-year-old patient in the acute period who had sympathetic ophthalmic diagnosis. They identified that after 60 mg prednisolone treatment, that the subfoveal choroidal thickness was lowered to 237 µm [11]. Goldenberg et al. compared the region where the lesion took place and the subfoveal choroidal thickness of 15 patients having toxoplasma chorioretinitis in active and passive periods. They reported that during the active period of the disease, the choroidal thickness of the region where the lesion took place was thicker compared to the post treatment passive period [12]. Hirukawa et al. found the subfoveal choroidal thickness of a 58-year-old patient who had posterior scleritis diagnosis of 548 µm in the active period, 308 µm 2 weeks after the

systemic steroid treatment and 226 µm 6 months later [13]. Kola et al. compared the subfoveal choroidal thickness of 84 patients with ankylosing spondylitis and 63 healthy individuals, and found that subfoveal choroidal thickness was significantly thicker in subjects with ankylosing spondylitis compared to healthy individuals [14]. Ulas et al. compared the subfoveal, nasal and temporal choroidal thickness of 71 patients with hypothyroidism diagnosis and 22 healthy individuals (Fig. 1). They found the choroidal thickness greater in the group with hypothyroidism compared to normal individuals. They stated that glycosaminoglycan (GAG) production and accumulation in connective tissue caused the increase in choroidal thickness [15].

As is seen, it was revealed in the conducted studies that choroidal thickness became normal again with corticosteroid treatment in inflammatory diseases where choroidal thickness increases [9–12, 14]. Allergic rhinitis starts the inflammatory process by stimulating the mast cells and releasing vasoactive substances during the first stage and by causing immunocomplex increase in serum during the second stage [19]. Corticosteroids are also among the most potent drugs in the treatment of allergic diseases [20]. The apparent role of corticosteroids in the treatment of both conditions implies a common pathogenic mechanism in increased choroidal thickness disease and allergic rhinitis. There is also evidence of large diurnal choroidal thickness variation. For this reason, we took measurements at the same time every day.

Ours is a preliminary study describing the probable relationship between increased choroidal thickness and allergic rhinitis. In this study, the sample size was small, so studies with larger numbers of patients are needed to confirm our findings. This is the first investigation to point out the association of increased choroidal thickness and allergic rhinitis in adults. Further studies are necessary to explore the mechanism of this association.

Conclusion

In our study, it was revealed that choroid was significantly thicker with allergic rhinitis. To the best of our knowledge, this is the first study demonstrating the relationship between increased choroidal thickness and allergic rhinitis. In addition, more advanced studies are necessary to fully clarify the mechanism of increased choroidal thickness with allergic rhinitis. To track allergic rhinitis activity and evaluate the effectiveness of the treatment, choroidal thickness measure can be utilized.

Compliance with ethical standards

This article does not contain any studies with human participants or animals performed by any of the authors.

Informed consent Written informed consents of all patients were obtained.

Conflict of interest All authors declare that they have no conflict of interest.

References

- Woods L, Craig TJ (2006) The importance of rhinitis on sleep, daytime somnolence, productivity and fatigue. *Curr Opin Pulm Med* 12:390–396. doi:[10.1097/01.mcp.0000245710.43891.5f](https://doi.org/10.1097/01.mcp.0000245710.43891.5f)
- Bellanti JA, Wallerstedt DB. Allergic rhinitis update: Epidemiology and natural history. *Allergy Asthma Proc* 21:367–70
- Bauchau V, Durham SR (2005) Epidemiological characterization of the intermittent and persistent types of allergic rhinitis. *Allergy* 60:350–353. doi:[10.1111/j.1398-9995.2005.00751.x](https://doi.org/10.1111/j.1398-9995.2005.00751.x)
- Bousquet J, Van Cauwenberge P, Khaltaev N (2001) Allergic rhinitis and its impact on asthma. *J Allergy Clin Immunol* 108:S147–S334
- Yasui K, Asanuma F, Arimura A (2001) Inhibitory effect of a TP-receptor antagonist, S-1452, on antigen-induced nasal plasma exudation in guinea pig model for allergic rhinitis. *Pharmacology* 63:65–70. doi:[10.1159/000056114](https://doi.org/10.1159/000056114)
- Li JT, Andrist D, Bamlet WR, Wolter TD (2000) Accuracy of patient prediction of allergy skin test results. *Ann Allergy Asthma Immunol* 85:382–384. doi:[10.1016/S1081-1206\(10\)62550-1](https://doi.org/10.1016/S1081-1206(10)62550-1)
- Spaide RF, Koizumi H, Pozzoni MC, Pozzoni MC (2008) Enhanced depth imaging spectral-domain optical coherence tomography. *Am J Ophthalmol* 146:496–500. doi:[10.1016/j.ajo.2008.05.032](https://doi.org/10.1016/j.ajo.2008.05.032)
- Maruko I, Iida T, Sugano Y, Oyamada H, Sekiryu T, Fujiwara T et al (2011) Subfoveal choroidal thickness after treatment of Vogt-Koyanagi-Harada disease. *Retina* 31:510–517. doi:[10.1097/IAE.0b013e3181eef053](https://doi.org/10.1097/IAE.0b013e3181eef053)
- Kim M, Kim H, Kwon HJ, Kim SS, Koh HJ, Lee SC (2013) Choroidal thickness in Behcet's uveitis: an enhanced depth imaging-optical coherence tomography and its association with angiographic changes. *Invest Ophthalmol Vis Sci* 54:6033–6039. doi:[10.1167/iovs.13-12231](https://doi.org/10.1167/iovs.13-12231)
- Modi YS, Epstein A, Bhaleeya S, Harbour JW, Albin T (2013) Multimodal imaging of sarcoid choroidal granulomas. *J Ophthalmic Inflamm Infect* 3:58. doi:[10.1186/1869-5760-3-58](https://doi.org/10.1186/1869-5760-3-58)
- Fleischman D, Say EAT, Wright JD, Landers MB (2012) Multimodality diagnostic imaging in a case of sympathetic ophthalmia. *Ocul Immunol Inflamm* 20:300–302. doi:[10.3109/09273948.2012.682637](https://doi.org/10.3109/09273948.2012.682637)
- Goldenberg D, Goldstein M, Loewenstein A, Habot-Wilner Z (2013) Vitreal, retinal, and choroidal findings in active and scarred toxoplasmosis lesions: a prospective study by spectral-domain optical coherence tomography. *Graefes Arch Clin Exp Ophthalmol Albr von Graefes Arch Für Klin Und Exp Ophthalmol* 251:2037–45. doi:[10.1007/s00417-013-2334-3](https://doi.org/10.1007/s00417-013-2334-3)
- Hirukawa K, Keino H, Watanabe T, Okada AA (2013) Enhanced depth imaging optical coherence tomography of the choroid in new-onset acute posterior scleritis. *Graefes Arch Clin Exp Ophthalmol Albr von Graefes Arch Für Klin Und Exp Ophthalmol* 251:2273–5. doi:[10.1007/s00417-013-2265-z](https://doi.org/10.1007/s00417-013-2265-z)
- Kola M, Kalkisim A, Karkucak M, Turk A, Capkin E, Can I et al (2014) Evaluation of choroidal thickness in ankylosing spondylitis using optical coherence tomography. *Ocul Immunol Inflamm* 22:434–438. doi:[10.3109/09273948.2014.928734](https://doi.org/10.3109/09273948.2014.928734)
- Ulas F, Dogan Ü, Dikbas O, Celebi S, Keles A (2015) Investigation of the choroidal thickness in patients with hypothyroidism. *Indian J Ophthalmol* 63:244–249. doi:[10.4103/0301-4738.156976](https://doi.org/10.4103/0301-4738.156976)
- Eriksson NE, Holmen A (1996) Skin prick tests with standardized extracts of inhalant allergens in 7099 adult patients with asthma or rhinitis: cross-sensitizations and relationships to age, sex, month of birth and year of testing. *J Investig Allergol Clin Immunol* 6(1):36–46
- Maruko I, Iida T, Sugano Y, Ojima A, Sekiryu T (2011) Subfoveal choroidal thickness in fellow eyes of patients with central serous chorioretinopathy. *Retina* 31:1603–1608. doi:[10.1097/IAE.0b013e31820f4b39](https://doi.org/10.1097/IAE.0b013e31820f4b39)
- Nakayama M, Keino H, Okada AA, Watanabe T, Taki W, Inoue M et al. Enhanced depth imaging optical coherence tomography of the choroid in Vogt-Koyanagi-Harada disease. *Retina* 32:2061–9. doi:[10.1097/IAE.0b013e318256205a](https://doi.org/10.1097/IAE.0b013e318256205a)
- Abdel Fattah M, El Baz M, Sherif A, Adel A (2010) Complement components (C3, C4) as inflammatory markers in asthma. *Indian J Pediatr* 77:771–773. doi:[10.1007/s12098-010-0117-y](https://doi.org/10.1007/s12098-010-0117-y)
- Abelson MB, Smith L, Chapin M (2003) Ocular allergic disease: mechanisms, disease sub-types, treatment. *Ocul Surf* 1:127–149