RESEARCH ARTICLE / Araştırma Makalesi

The Investigation of the Relationship Between Retinal and Choroidal Thickness by Sedimentation Rate for Patients with Ankylosing Spondylitis

Ankilozan Spondilitli Hastalarda Retina ve Koroid Kalınlığının Sedimantasyon Hızı ile İlişkisi

İsa Yuvacı[1], Mahmut Atum[1], Emine Pangal[2], Nurettin Bayram[2], Emel Güler[2], Fatmagül Ülkü Demir[2]

[1] Department of Ophthalmology, Sakarya University Training and Research Hospital, Sakarya, Turkey
[2] Department of Ophthalmology, Kayseri Training and Research Hospital, Kocasinan, Kayseri, Turkey

Yazışma Adresi / Correspondence:
Mahmut Atum

Sakarya University Training and Research Hospital, Sakarya, Turkey
Sakarya Training and Research Hospital Eye Clinic, Adnan Menderes St. Sağlık Sok. No: 195 Adapazarı Sakarya, Turkey
T: **+90 555 809 62 75** E-mail: **mahmutatum@gmail.com**

Geliş Tarihi / Received : **15.10.2018** Kabul Tarihi / Accepted : **03.12.2018**

Abstract

Objective The investigation of the relationship between retinal and choroidal thickness with Erythrocyte Sedimentation Rate (ESR) for systematically active ankylosing spondylitis (AS) patients without ocular involvement. **(Sakarya Med J 2018, 8(4):775-781)**

Materials and Methods Among the patients being followed-up with a diagnosis of AS in the rheumatology clinic, those with proper conditions who required eye consultation and normal subjects demographically similar to these patients being inspected in the eye section were included in the study. After blood test, eye examination and optic coherence tomography (OCT) measurements were performed within one hour. Central macular thickness (CMT), central subfoveal choroidal thickness (CSCT), and retinal nerve fiber layer (RNFL) thickness were measured with OCT. Results were obtained with SPSS evaluated for patients with AS compared to normal people and within the group with AS according to ESR levels.

Results The mean age of participating patients was 35.8, mean of disease duration was 6.38 years and average ESR level was 18.2 mm/H. Average CSCT thickness of patients with AS was 321.00 µm, average CMT thickness was 255.56 µm and average RNFL thickness was 99.87 µm. CSCT, CMT and RNFL thickness of control group participants were as follows: 317.21 µm, 259.02 µm and 100.98 µm. No significant difference was observed with regard to CSCT, CMT and RNFL thickness values between patients with AS and the control group. When patients with AS were evaluated among themselves, a connection between ESR level and CSCT, CMT and RNFL thickness could not be established.

Conclusion In our study, we could not establish a connection between ESR level and CSCT, CMT, and RNFL.

Keywords blood sedimentation; ankylosing; spondylitis; retina; choroid

Öz

Amaç Aktif göz tutulumu bulunmayan Ankilozan Spondilitli (AS) hastalarda eritrosit sedimantasyon hızı (ESR) ile retina ve kororidal kalınlık bağlantısının araştırılması **(Sakarya Tıp Dergisi 2018, 8(4):775-781).**

Gereç ve Yöntem Romatoloji kliniğinde AS tanısı ile takip edilen, göz bölümüne konsülte edilen, göz tutulumu bulunmayan kişiler ile demografik olarak benzer göz kliniğinde takip edilen normal kişiler kontrol grubu olarak çalışmaya alındı. Kan testi sonrası göz muayenesi ve optik koherens tomografi (OKT) ölçümü 1 saat içerisinde yapıldı. Merkezi makula kalınlığı (MMK), merkezi subfoveal koroid kalınlığı (MSKK), retina sinir lifi kalınlığı (RSLK), OKT cihazı ile ölçüldü. Çıkan sonuçlar, SPSS programı ile kontrol grubu ve AS'liler arasında ve AS'liler de kendi içinde, sedimantasyon hızına göre değerlendirildi.

Bulgular AS'li hastaların ortalama yaşı 35.8 ve ortalama hastalık süreleri 6.38 yıl idi. Ortalama ESR seviyesi 18.2 mm/H idi. Sırasıyla ortalama olarak MSKK 321.00 µm, MMK 255.56 µm ve RSLK 99.87 µm kalınlığında idiler. Kontrol grubunda ise sırasıyla bu değerler 317.21 µm, 259.02 µm ve 100.98 µm kalınlığında idi. MSKK, MMK ve RSLK kalınlıkları bakımından AS'liler ve normal grup arasında fark izlenmedi. AS'li hastalar ESR seviyesine göre kendi aralarında kıyaslandığında ise bu verilerin hiçbirinin ESR ile bağlantısı kurulamadı.

Sonuç Çalışmamızda göz tutulumu olmayan, sistemik olarak aktif AS'lilerde ESR seviyesi ile retina ve koroid kalınlık bağlantısı araştırıldı ve herhangi bir bağlantı kurulamadı.

Anahtar Kelimeler sedimantasyon; ankilozan; spondilit; retina; koroid

Introduction

Erythrocyte Sedimentation Rate (ESR) is defined as fall speed of erythrocytes in an hour's drive. Factors augmenting fibrinogen and acute phase reactants increase ESR level as well. Inflammations are the main causes of this condition.[1,2] ESR is a sensitive test used for the diagnosis of disease, activation tracking and the monitoring of response to treatment. Ankylosing spondylitis (AS) is a chronic inflammatory disorder that affects the spinal joints. In connection with B27 '+', Human Leukocyte Antigens (HLA) is a disease from the seronegative spondyloarthropathies group. Anterior uveitis (AU) is the most common extra-articular finding and its incidence has been reported between 20-40% in different series.[3-5]

Although disease most frequently causes acute AU, as it goes into a chronic phase it leads to complications affecting visual prognosis poorly such as cataract, glaucoma, vitritis, cystoid macular edema (CME), macular hole, papillitis, retinal vasculitis and epiretinal membrane. In the literature, there is various information related to the involvement of eye tissues of AS patients.[6,7] There are also studies where these are evaluated by OCT as well.[8,9] However, there is no study about the evaluation of the retina and choroid structure with ESR level for an active period without ocular involvement. The most important ESR-enhancing plasma protein is fibrinogen.[1,2] Fibrinogen level rises due to various causes creating vascular damage. The choroid structure, which is rich in the vascular network with extremely high blood flow, is very likely to be affected by this condition. Therefore, the presence of subclinical amendments in posterior tissue for cases with active disease statement and high ESR level but without ocular involvement and the relation of these amendments to ESR were investigated.

The aim of this study is to investigate the relationship between retinal and choroidal thickness with erythrocyte sedimentation rate (ESR) for systematically active ankylosing spondylitis (AS) patients without ocular involvement.

Materials and Methods

Our study was conducted in the Kayseri Training and Research Hospital Eye Clinic between February 2014 and January 2015. All research was performed according to the Helsinki declaration and approval for the study was received from the ethics committee. Verbal and written consent was obtained from study participants.

This case-control study was performed on 69 patients, 35 of them were AS and 34 of them were controls. Participants in the study were selected from patients with AS diagnosis and non-ocular involvement being admitted to the rheumatology clinic of our hospital and with eye consultation requested during routine follow-up. Normal subjects had 10/10 best corrected visual acuity (Snellen) with a refractive error level below +3.0 or -3.0 diopters, and they did not have any ocular pathology or any ophthalmic surgery in the history. The criteria to be involved in this study were the absence of ocular involvement, best corrected visual acuity of 0.8 and above, axial length (AL) level below 25 mm, spherical equivalent (SE) values in the range of ±4, and lack of evidence of previous ocular inflammation, intravitreal injection or intraocular surgery. Only one eye of the patients meeting these criteria was included in the study.

Patients diagnosed with AS in the rheumatology department were sent to the eye department after

blood test. Visual acuity, biomicroscopy with slit lamp, intraocular pressure (IOP) measurement by tonometry and fundus examination after dilatation were performed on all patients. Biometry was performed by Zeiss® IOL Master device (Carl Zeiss Meditec, Dublin, CA, USA). Thereafter, macula, choroid and retinal nerve fiber layer (RNFL) analyses were performed by spectral-domain OCT (Spectralis®, wave-length: 870 nm; Heidelberg Engineering Heidelberg, Germany) on each patient with the appropriate conditions. All these processes were performed with in one hour after blood test.

Procedure of Image Acquisition

RNFL, the central macular thickness (CMT), and the central subfoveal choroidal thickness (CSCT) measurements were obtained through the Spectralis OCT. The procedure of obtaining EDI-OCT has previously been described.[10] CSCT were measured using spectral-domain OCT (Spectralis, wave-length: 870 nm, Heidelberg Engineering, Heidelberg, Germany) with EDI modality. CSCT were defined as the vertical distance from the hyper-reflective line of Bruch's membrane to the hyper-reflective line of the inner surface of the sclera. All subjects were imaged by the same experienced technician. Two independent clinicians measured CSCT and the average of these measurements was used in the analysis. The peripapillary RNFL thickness parameters that were automatically calculated by the SD-OCT device and divided in to regions included average (G) thickness (360 degrees), temporal (T) quadrant thickness (90 degrees), temporal superior (Ts) quadrant thickness (45 degrees), nasal superior (Ns) quadrant thickness (45 degrees), nasal (N) quadrant thickness (90 degrees), nasal inferior (Ni) quadrant thickness (45 degrees), and temporal inferior (Ti) quadrant thickness (45 degrees).

Statiscal Analysis

All statistical analyses were performed using SPSS for Windows version 22.0 (SPSS Inc, Chicago, IL, USA). Continuous variables were presented as mean ± standard deviation. The Pearson chi-square test was used to evaluate qualitative variables. Normal distribution was evaluated using the Kolmogorov-Smirnov test. Homogeneity of variances was tested using Levene's test. The independent samples t-test was used to evaluate parametric data analysis. For non-parametric statistics, data were analyzed using Mann–Whitney U test. P value less than 0.05 was considered as statistically significant.

Results

The 35 patients with AS participating in the study were composed of 19 females and 16 males. The average age was 37.5. Average AL was 23.63 and the average SE was -0.15 D. Average IOP was 15, 40 mm Hg. The median of overall RNFL thickness was 99.70 µm, average CSCT value was 320.71 ± 81.6 µm, average CMT value was 275.4 ± 23.9 µm and average ESR value was 13.5 ± 12.4 mm/h(range: 2-58). The measurements of the posterior structures in AS group can be seen in table 1.

Table 1: Posterior ocular measurements and sedimentation rates in patients with AS (n=35)

	Mean	SD
CMT	275.40 µm	23,9
CSCT	320.71 µm	81,6
RNFL	99.70 µm	12,7
Ns	112.70 µm	13,4
N	74.3 µm	12,2
Ni	112.5 µm	15,8
Ti	142.8 µm	18,2
T	74.4 µm	11,4
Ts	138.8 µm	15,4
CMV	0.21 mm3	0,04
TMV	8.70 mm3	0,8
ESR	13.5 mm/h	1,2

CMT; central macular thickness, CSCT; central subfoveal choroidal thickness, RNFL; median retinal nerve fiber layer, Ns; nasal superior, Ni; nasal inferior, N; nasal, T; temporal, Ti; temporal inferior, Ts; temporal superior, CMV; central macular volume, TMV; total macular volume, ESR; Erythrocyte Sedimentation Rate, SD; Standard Deviation

In the control group consisting of 34 patients, 17 were male and 17 were female. The average age was 36.3, average AL 23:59 mm, average IOP 15,48 mmHg, average SE value 0.06 D, average CSCT value 318.10± 74.2 µm, average CMT value 265.3 ± 16.6 µm, and average RNFL value 99.63 µm. Values of all AS patients and normal people can be seen in table 2.

Table 2: Comparison of ocular parameters of AS group and control group

	Age (Year)	İOP (mm Hg)	SE (D)	AL (mm)	CMT (µm)	CSCT (µm)	RNFL (µm)
AS Group (n=35)	37.50 ±13.4	15.40 ±2.65	-0.15 ±1.16	23.63 ±0.82	275.40 ±23.9	320.71 ±81.6	99.70 ± 12.7
Control group (n=34)	36.30 ±12.3	15.48 ±2,74	0.06 ±1.02	23.59 ±0.79	265.30 ±16.6	318.10 ±74.2	99.63 ±10.2
p value	0.52	0.37	0.27	0.19	0.04	0.89	0.49

IOP; intraocular pressure, SE; spherical equivalent, AL; axial length, CMT; central macular thickness, CSCT; central subfoveal choroidal thickness, RNFL; median retinal nerve fiber layer, D; diopter

In the analysis, no statistical difference was found between the group of patients with AS and the control group in terms of CMT, CSCT and RNFL. When AS patients were compared among themselves, no statistically significant relationship between ESR level and CMT, CSCT, and RNFL thickness was found.

Discussion

OCT, a non-invasive, simple and reproducible test, is widely used to diagnose clinically, monitor disease and evaluate the efficacy of treatment. It can evaluate anterior segment and posterior segment structures at micron level with precision. In clinical practice, OCT is one of the frequently used tests for retinal thickness analysis, volume analysis, RNFL analysis and choroidal thickness analysis for the posterior ocular structures.[11]

Although the most frequent form of ocular involvement is AAU for AS patients, the disease occasionally affects posterior tissues. In the studies, while clinical examination findings for AU were normal, macular edema was identified by OCT.[12,13] There are some studies indicating the presence of various degrees of macular edema in moderate AU cases.[12] Szeppessy et al. found thickening in spondyloarthropathies with AAU and indicated that this thickening rises with AAU levels.[14]

In the study that Tuzcu et al. made on AS patients without AAU, a meaningful difference could not be found in terms of CMT and RNFL thickness level[9]. In a similar study, while retina and RNFL measurements were not different from normal people, only the CT level was found to be thicker.[8] In another study made on AS patients with AAU but without posterior involvement, thinning in the retina was observed.[15] This result suggests the presence of a subclinical answer in the posterior tissues owing to possible inflammation. In our study, the eyes of patients with AS were found to be thicker compared to normal ones in terms of CMT. However, no evidence explaining this in a clinical sense was found. Either possible previous mild or subclinical AAU's might cause this result or the difference may be normal. The main aim of this study was to investigate the relationship between ESR level and retinal and chorodial thickness but no link between ESR level and CMT could be established.

After the development of EDI-OCT mode, choroid tissue began to be evaluated with more precision. For some diseases and conditions, the thickness of the choroid with functions such as feeding the various retinal layers, oxygenation and adjusting temperature were investigated and the results were published. For example, age related maculopathy, myopia, diseases such as central serous retinopathy and influences such as smoking, coffee intake and diurnal variation during the day were investigated.[16-21]

There is evidence of CT thickening in the acute phase in studies into the investigation of choroidal changes in posterior uveitis.[22-27] However, there is not enough research regarding other types. In the study of Gehl et al, where they investigated choroidal thickness alteration for AU and inter mediate uveitis (IMU), while the CT level was not found different compared to normal people, it was found thicker for IMU.[28] In our study, no difference in terms of CT was observed between normal people and patients with AS but the people in our study had no acute uveitis table. No connection between the main item, ESR level, which we aimed to observe, and choroidal thickness was detected.

In a study measuring the thickness of the choroid for patients with AS, there is a finding that CT is thicker than that in healthy controls.8 In our study, no statistical difference was found between

choroidal thickness of ankylosing spondylitis and normal control test subjects. This result was already expected for people without ocular involvement. When the patients of our study were examined, no link could be established between ESR level and choroidal thickness.

There was no significant difference between the ankylosing spondylitis group and normal groups in terms of generalized RNFL thickness. For the group with AS, a statistical link could not be established between ESR level and RNFL thickness. Tuzcu et al. could not find a meaningful difference between the group with AS and the normal one in terms of RNFL thickness.[9] In the same study, it was reported that a negative relation between disease duration and temporal quadrant thickness was detected. The author stressed that this might be related tothe duration and severity of the disease.[9] In our study we could not establish a link. In both studies there is no known AAU story. The differences may be due to mild or previous subclinical attacks. This topic requires longer term studies, which can be monitored more carefully.

In our study, for patients with AS and without ocular involvement, the relation between ESR levels and retinal and especially choroidal thickness variation was investigated. No statistical connection was detected. Either these results are completely normal or the non-ocular involvement of the disease in the selected group and the fact that this disease causes AU more frequently lead to this result. Comparison with diseases with ocular involvement and causing posterior uveitis more may be more enlightening.

Conflict of Interests

None of the authors has conflict of interests with the submission of this paper.

1. Bridgen ML. Clinical utility of the eryhrocyte sedimentation rate. Am. Fam Phisician. 1999;60:1443-50.
2. Sox HC Jr, Liang MH. The erythrocyte sedimentation rate guidelines for rational use. Annals of Internal Medicine. 1986;104:515-23.
3. Ji SX, Yin XL, Yuan RD, Zheng Z, Huo Y, Zou H. Clinical features of ankylosing spondylitis associated with acute anterior uveitis in Chinese patients. Int J Ophthalmol. 2012;5:164-6.
4. Chan CC, Inrig T, Molloy CB, Stone MA, Derzko-Dzulynsky L. Prevalence of inflammatory back pain in a cohort of patients with anterior uveitis. Am J Ophthalmol. 2012;153:1025-30.
5. Chang JH, Mc Cluskey PJ, Wakefield D. Acute anterior uveitis and HLA-B27. Surv Ophthalmol. 2005;50(4):364-88.
6. Brophy S, Pavy S, Lewis P, et al. Inflammatory eye, skin and bowel disease in spondyloarthritis: Genetic, phenotypic and environmental factors. J Rheumatol. 2001;28:2667-73.
7. Fernández-Melón J, Muñoz-Fernández S, Hidalgo V, et al. Uveitis in the initial clinical manifestation in patients with spondyloartropathies. J Rheumatol. 2004;31:524-7.
8. Kola M, Kalkisim A, Karkucak M, et al. Evaluation of choroidal thickness in ankylosing spondylitis using optical coherence tomography. Ocul Immunol Inflamm. 2014;22(6):434-8.
9. Tuzcu E, Ustun N, Ilhan N, et al. Peripapillary retinal nerve fiber layer and ganglion cell-inner plexiform layers thickness in ankylosing spondylitis. Ocul Immunol Inflamm. 2014;22(6):429-33.
10. Spaide RF, Koizumi H, Pozzoni MC. Enhanced depth imaging spectral-domain optical coherence tomography. Am J Ophthalmol. 2008;146:496–500.
11. Chakraborty R, Read SA, Collins MJ. Diurnal variations in axial length, choroidal thickness, intraocular pressure, and ocular biometrics. Investigative Ophthalmology and Visual Science. 2011;52(8):5121–5129.
12. Shulman S, Goldenberg D, Habot-Wilner Z, et al. Optical coherence tomography characteristics of eyes with acute anterior uveitis. Isr Med Assoc J. 2012;14:543–546.
13. Traill A, Stawell R, Hall A, Zamir E. Macular thickening in acute anterior uveitis. Ophthalmology. 2007;114:402.
14. Szepessy Z, Barsi Á, Németh J. Macular Changes Correlate with the Degree of Acute Anterior Uveitis in Patients with Spondyloarthropathy. Ocul Immunol Inflamm. 2015;24:1-6.
15. Buttanrı İB, Kurtuluş D, Serin D. Eye Involvement in Patients with Ankylosing Spondylitis. Glo-Kat 2014;9:267-269
16. Fujiwara T, Imamura Y, Margolis R, Slakter JS, Spaide RF. Enhanced depth imaging optical coherence tomography of the choroid in highly myopic eyes. American Journal of Ophthalmology. 2009;148(3):445–450.
17. Imamura Y, Fujiwara T, Margolis R, Spaide RF. Enhanced depth imaging optical coherence tomography of the choroid in central serous chorioretinopathy. Retina. 2009;29(10)1469–1473
18. Spaide R. F. Age-related choroidal atrophy. American Journal of Ophthalmology. 2009;147(5) 801–810.
19. Usui S, Ikuno Y, Akiba M, et al. Circadian changes in subfoveal choroidal thickness and the relationship with circulatory factors in healthy subjects. Invest Ophthalmol Vis Sci. 2012;53(4):2300–7.
20. Dervişoğulları MS, Totan Y, Tenlik A, Yuce A. Effects of cigarette smoking on choroidal and retinal thickness and ocular pulse amplitude. Cutan Ocul Toxicol. 2015;34(3):217-21.
21. Vural AD, Kara N, Sayin N, Pirhan D, Ersan HBA. Choroidal thickness change safter a single administration of coffee in healthy subjects. Retina, 2014;34(6):1223–1228.
22. Fong AHC, Li KKW, Wong D. Choroidal evaluation using enhanced depth imaging spectral domain optical coherence tomography in Vogt-Koyanagi-Harada disease. Retina, 2011;31:502–509.
23. Nakayama M, Keino H, Okada AA, et al. Enhanced depth imaging optical coherence tomography of the choroid in Vogt-Koyanagi-Harada disease. Retina. 2012;32(10):2061–2069.
24. Maruko I, Lida T, Sugano Y, et al. Subfoveal choroidal thickness after treatment of Vogt-Koyanagi-Harada disease. Retina. 2011;31(3):510–517.
25. Aoyagi R, Hayashi T, Masai A, et al. Subfoveal choroidal thickness in multiple evanescent white dot syndrome. Clin Exp Optom. 2012;95:212–217.
26. Kim M, Kim H, Kwon HJ, Kim SS, Koh HJ, Lee SC. Choroidal thickness in Behcet's uveitis: an enhanced depth imaging-optical coherence tomography and its association with angiographic changes. Invest Ophthalmol Vis Sci. 2013;54:6033–6039.
27. Karampelas M, Sim DA, Keane PA, et al. Choroidal assessment in idiopathic panuveitis using optical coherence tomography. Graefes Arch Clin Exp Ophthalmol . 2013;251(8):2029–2036.
28. Géhl Z, Kulcsár K, Kiss HJ, Németh J, Maneschg OA, Resch MD. Retinal and choroidal thickness measurements using spectral domain optical coherence tomography in anterior and intermediate uveitis. BMC Ophthalmol. 2014;14:103.