Osmangazi Tıp Dergisi
Osmangazi Journal of Medicine 2022;

Research Article / Araştırma Makalesi

An Evaluation of the Autofluorescence Changes with Wide-Angle Digital Fundus Camera in Chronic Central Serous Chorioretinopathy Patients

Kronik Santral Seröz Koryoretinopati Hastalarında Geniş Açılı Dijital Fundus Kamera ile Otofloresan Değişikliklerinin Değerlendirilmesi

[1]Mustafa Değer Bilgec, [2]Erdoğan Yaşar, [1]Nazmiye Erol

[1]Eskisehir Osmangazi Faculty of Medicine, Department of Ophthalmology, Eskisehir, Turkey

[2]Aksaray Faculty of Medicine, Department of Ophthalmology, Aksaray, Turkey

Correspondence:
Erdoğan YAŞAR
Aksaray Medicine Faculty, Department of Ophthalmology, Aksaray, Turkey
e-mail: dr.e.yasar@gmail.com

Abstract

To evaluate the autofluorescence variations and localisation in wide-angle digital fundus camera images of patients with chronic central serous chorioretinopathy (CSCR). A retrospective scan was made of the images of patients diagnosed with chronic CSCR with wide-angle digital fundus angiography and applied at the same time with autofluorescence imaging. The ultra wide area autofluorescence images of 46 patients were examined. The retina was separated as zone 1, zone 2, and zone 3 in respect of disease involvement, and zone 3 represented the peripheral retina. The images of the patients were recorded as hyperautofluorescence (punctate, diffuse) or hypo-autofluorescence (granular, confluent) in respect of the type of autofluorescence involvement. After the exclusion of 2 patients because peripheral images could not be clearly selected, the study evaluations were made of 44 eyes of 44 patients. The mean duration of the disease was found to be 2.7 years. In the result of the examination with wide-angle digital fundus autofluorescence imaging, there was seen to be zone 2 involvement in the 4 quadrants of inferior, nasal, temporal and superior. Peripheral retinal involvement in zone 3 was seen in a total of 7 (15.9%) patients in the form of inferior gravitational defect, in 6 (13.6%) patients together with zones 1 and 2, and in 1 (2.3%) patient together with zone 2. Hyperautofluorescence was determined in 39 (88.6%) patients and hypo-autofluorescence in 5 (11.4%). The involvement frequency was determined as zone 1+2 in 19 (43.2%) patients, followed by zone 1 involvement alone in 16 (36.4%) patients. Common autofluorescence type was detected as hyperautofluorescence in chronic CSCR patients with a high rate of approximately 90%. It has also been shown that in some patients, the disease may also affect the inferior peripheral retina due to the effect of gravity.

Keywords: central serous chorioretinopathy, wide-angle digital fundus autofluorescence, peripheral retina, hyperautofluorescence, hypo-autofluorescence

Özet

Kronik santral seröz koryoretinopatili (CSCR) hastaların geniş açılı dijital fundus kamera görüntülerinde otofloresan değişiklikleri ve lokalizasyonunu değerlendirmek. Geniş açılı dijital fundus anjiyografi ile kronik CSCR tanısı konulan hastaların görüntüleri retrospektif olarak tarandı ve aynı zamanda otofloresan görüntüleme ile uygulandı. 46 hastanın ultra geniş alan otofloresan görüntüleri incelendi. Retina hastalık tutulumuna göre zon 1, zon 2 ve zon 3 olarak ayrıldı ve zon 3 periferik retinayı temsil etti. Hastaların görüntüleri otofloresan tutulum tipine göre hiperotofloresan (punktat, yaygın) veya hipo-otofloresan (granüler, konfluent) olarak kaydedildi. Periferik görüntüler net seçilemediği için 2 hasta dışlandıktan sonra 44 hastanın 44 gözü ile çalışma değerlendirmeleri yapıldı. Ortalama hastalık süresi 2,7 yıl olarak bulundu. Geniş açılı dijital fundus otofloresan görüntüleme ile yapılan inceleme sonucunda alt, nazal, temporal ve üst olmak üzere 4 kadranda zon 2 tutulum olduğu görüldü. Zon 3'te periferik retina tutulumu inferior gravitasyonel defekt şeklinde toplam 7 (%15.9) hastada, zon 1 ve 2 ile birlikte 6 (%13.6) ve 1 (%2.3) hastada ise zon 2 ile birlikte görüldü. Hiperotofloresan 39 (%88.6) hastada ve hipo-otofloresan 5 (%11.4) hastada saptandı. Tutulum sıklığı en fazla 19 (%43.2) hastada zon 1+2, ardından 16 (%36.4) hastada tek başına zon 1 tutulum olarak belirlendi. Kronik SSR hastalarında yaygın otofloresans tipi hiperotofloresans şeklinde ve yaklaşık %90 gibi yüksek bir oranda tespit edilmiştir. Ayrıca bazı hastalarda hastalığın yerçekimi etkisi nedeniyle inferior periferik retinayı da etkileyebileceği gösterilmiştir. Anahtar
Kelimeler: santral seröz koryoretinopati, geniş açılı dijital fundus otofloresansı, periferik retina, hiperotofloresan, hipo-otofloresan

Received 30.03.2022 Accepted 27.04.2022 Online published 09.04.2022

Bilgec MD, Yasar E, Erol N, An Evaluation of the Autofluorescence Changes with Wide-Angle Digital Fundus Camera in Chronic Central Serous Chorioretinopathy Patients, Osmangazi Journal of Medicine, 2022;44(6):755-760
Doi: 10.20515/otd.1092900

1. Introduction

Central serous chorioretinopathy (CSCR) is a disease characterised by serous fluid accumulation below the sensory retina in the macular region, which generally resolves spontaneously within 1-6 months, and causes a moderate degree of loss of vision. It is generally seen in males and in the 20-50 years age group (1). In addition, there are also patients who present with persistence of neurosensorial retina detachment or recurrence and chronic CSCR (longer than 4 months) which leads to widespread changes in photoreceptors and the retina pigment epithelium (RPE) with subsequent vision loss (2). The pathophysiology of CSCR has not yet been fully understood and among the theories proposed are choroidal vascular hyperpermeability (3,4), RPE dysfunction(5), and the combination of these two theories(6). Risk factors have been reported to include stress and Type A personality (7), increased sympathetic system activation and the use of sympathomimetic agents (8), the use of glucocorticoids and endogenous hypercortisolism (9). The majority of patients have complaints of clouded vision, metamorphopsia, micropsia, and scotoma in the visual field (10). Optic coherence tomography (OCT), which is used in the diagnosis of CSCR, is useful in the determination of subretinal fluid accumulation, pigment epithelial detachment and retinal atrophy (11, 12).

Although CSCR can be diagnosed from typical clinical findings and the observation of retinal elevation in ophthalmoscopic examination, and subretinal fluid on OCT, or PED, it can be confirmed with the observation of a typical leakage pattern (hyperfluorescence) on fluorescein angiography. Fundus autofluorescence (FAF) is used in the evaluation of some retina diseases, including CSCR. The source of autofluorescence to a large degree is lipofuscin formed with the accumulation in lysosomes of fatty acids with phagocytosis of damaged photoreceptor outer segments and the oxidative destructive products of retinoid and proteins (13,14). This non-invasive method is used as an additional diagnostic tool in CSCR, showing changes in the distribution and density of autofluorescence in the acute and chronic phases of the disease (15). In studies made related to FAF in CSCR, just as hypo-autofluorescence may be seen in acute CSCR patients because oedema blocks the autofluorescence on FAF images of the serous retina detachment area (16,17), hyperautofluorescence may also be seen associated with accumulated photoreceptor chromophores with insufficient phagocytosis made due to the separation of the retina outer segments and RPE (18, 19). In chronic CSCR, hypo-autofluoresence representing RPE damage or subretinal deposit accumulation, and hyperautofluorescence may be observed (19, 20).

Classic fundus imaging systems can visualise the fundus up to 50 degrees. A non-midriatic camera (Optos Tx-200), is a device which can acquire images reaching the ora serrata by retinal scanning of an ultra wide area up to 200 degrees. Similar to the current study, a previous autofluorescence study of CSCR patients made with an ultra wide imaging system (Optos) determined more peripheral retinal findings at the rate of 57% than could be determined with a standard FAF system (21). The aim of this study was to evaluate the types of autofluorescence involvement and localisation in detail up to the periphery in chronic CSCR patients using an ultra wide-angle imaging system.

2. Methods

In this retrospective study was conducted according to the principles of the Declaration of Helsinki and ethics committee approval was obtained from Local Ethics Committee. A retrospective scan was made of the images of patients diagnosed with chronic CSCR (Presence of subretinal fluid for more than 4 months) with wide-angle digital fundus angiography and applied at the same time with autofluorescence imaging. The ultra wide area autofluorescence images of 46 patients were examined.

Patients were excluded from the study if they had another eye disease accompanying CSCR (age-related macular degeneration, diabetic retinopathy, any other macular or retinal

disease), if they had received treatment for CSCR (photodynamic therapy, micropulse laser, anti-VEGF treatment) or if the peripheral retina image could not be evaluated in detail.

Disease involvement on the images was classified in 3 groups as zone 1, zone 2, and zone 3. Zone 1 was defined as a round region 5.4mm in diameter, in the central fovea including the nasal edge of the optic disc and the macular temporal area. Zone 2 was defined as a round region, 16.2 mm in diameter equivalent to 9 optic disc diameters, starting from the inner border of zone 1 and the outer border coinciding with vortex veins. Zone 3 was defined as the region formed of the peripheral retina remaining outside zone 2 (Figure 1) (22). Patients were grouped as those with involvement in zones 1+2, zones 2+3, and zones 1+2+3. Of the patients with involvement in both eyes, the eye with more severe involvement was included in the study. The auto-fluorescence appearance was separated into 4 groups as punctate or diffuse involvement showing hyperautofluorescence and granular or confluent showing hypo-autofluorescence.

Data obtained in the study were analysed statistically using IBM SPSS for Windows vn. 22.0 software. Continuous variables were stated as mean±standard deviation (SD) values and categorical variables as number (n) and percentage (%). A value of $p<0.05$ was accepted as statistically significant.

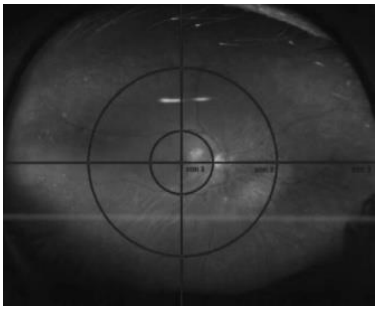

Figure 1. Separation of the retina according to zones

3. Results

The ultra wide area autofluorescence images of 46 patients were examined, and after the exclusion of 2 patients because peripheral images could not be clearly selected, the study evaluations were made of 44 eyes of 44 patients.

The 44 patients comprised 27 (61.4%) males and 17 (38.6%) females with a mean age of 40.4±6.4 years (range, 25-57 years) Table 1. In 7 patients with involvement of both eyes, the eye with more severe involvement was evaluated in the study. The autofluorescence images of 24 right eyes and 20 left eyes were evaluated. The mean duration of the disease was found to be 2.7 years.

The results of the examinations of the ultra wide area autofluorescence images with evaluations of zones 1, 2 and 3 are shown in Table 2.

Table 1. Demographic data of patients

	Age	Gender
Male	43	17
Female	39	27
Total	40.6	44

Table 2. The staging according to autofluorescense

	n	%
Zone 1	16	36,4
Zone 2	2	4,5
Zone 1+2	19	43,2
Zone 2+3	1	2,3
Zone 1+2+3	6	13,6
Total	44	100,0

According to the results, the most involvement was determined in zone 1+2 or in zone 1 only. There was seen to be zone 2 involvement in the 4 quadrants of inferior, nasal, temporal and superior. Zone 3 involvement was seen in the form of inferior gravitational defect only in the inferior quadrant.

Zone 3 involvement of peripheral retina involvement alone was not determined in any patient. Involvement in zone 3 was seen in a total of 7 (15.9%) patients, in 6 (13.6%) patients together with zones 1 and 2, and in 1 (2.3%) patient together with zone 2. The ultra wide area autofluorescence images of the retinal involvements of patients according to zone are shown in Figures 2a-b-c.

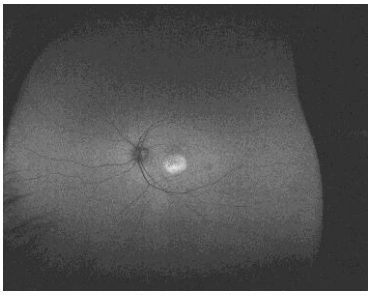

Figure 2a: Involvement of zone 1

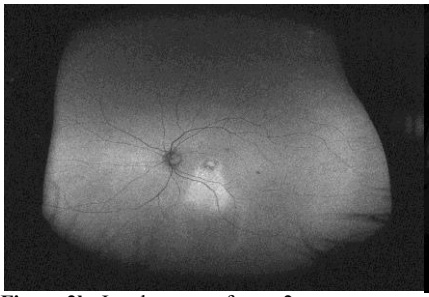

Figure 2b: Involvement of zone 2

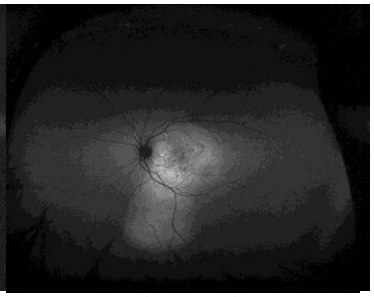

Figure 2c: Involvement of zone 3

Figure 2a-b-c. The retinal autofluorescense according to the zones

Hyperautofluorescence was determined in 39 (88.6%) patients and hypo-autofluorescence in 5 (11.4%). The details of involvement are shown in Table 3.

Table 3. Types of autofluorescense

Tutulum		**n**	**%**	**Total n%**
Hyperautofluorescense	**Punctate**	19	43.2	
	Diffuse	16	36.4	39(%88.6)
	Punctate + Diffuse	4	9.1	
Hypoautofluorescense	**Granular**	4	9.1	5(11.4)
	Confluent	1	2.3	
Total		44	100	44(%100)

As a result of binomial logistic regression performed between the presence of hyperautofluorescence and the duration of the disease, no significant relationship was found($p>0.05$).

4. Discussion

CSCR causes choroidal vascular hyperpermeability and is characterised by focal leakage at the RP level and serous separation of the neurosensorial retina which can be seen on fundus fluorescein

angiography (1,23-25). The source of FAF used in the evaluation of CSCR is to a great degree, lipofuscin, which is formed with the accumulation of the oxidative destructive products of retinoid and proteins in lysosomes and fatty acid with phagocytosis of damaged photoreceptor outer segments (13, 14).

Previous studies have determined CSCR more in males than females (1, 19). Consistent with these findings in literature, 27 (61.4%) of the 44 patients in the current study were male. CSCR has been reported to be seen in the 20-50 years age group (1), and similarly in the current study, the mean age was 40.4±6.4 years, with a range of 25-57 years.

Accumulations showing hyperautofluorescence on blue light autofluorescence imaging in CSCR have been previously reported and have been stated to be due to photoreceptor outer segments that have elongated and fallen (19,26). In recent studies of chronic CSCR, hyperautofluorescence and hypo-autofluorescence involvement types have been examined. In a study by Lee et al, hyperautofluorescence was determined in 63.3% of CSCR patients and minimal changes in 36.4% (18). Zola et al determined 31.25 hyperautofluorescence (19.7% punctate, 11.5% diffuse), 59.9% hypo-autofluorescence (51.0% granular, 8.9% confluent) and mixed patterns in 8.3% of chronic CSCR patients, showing a much higher rate of hypo-autofluorescence (27). Similar to the current study, in a study performed with ultra wide area autofluorescence of 65 eyes with CSCR, Pang et al. (21) reported hyperautofluorescence with subretinal fluid in 19 (29.2%) eyes, hyperautofluorescence with normal RPE and photoreceptors without subretinal fluid in 44 (70%) patients, and hypo-autofluorescence with RPE atrophy and photoreceptor loss in 5 (0.8%) patients. As a result of the study it was said that there could be hyperautofluorescence or a mixed fluorescence image in regions with subretinal fluid, and even if the fluid disappeared, hyperautofluorescence could continue or could change to hypo-autofluorescence together with RPE atrophy. It was also reported in that study that hyperautofluorescence in the periphery could be a useful finding of disease activation. Consistent with the studies of Pang et al and Lee et al, hyperautofluorescence was seen in the majority of the current study patients (39/44, 88.6%) and hypo-autofluorescence in a much smaller proportion (5/44, 11.4%). In the evaluation of the types of autofluorescence, hyperautofluorescence was determined at the higher rate of 43.2% punctate compared to 36.4% diffuse and 9.1% punctate+diffuse, and in the hypo-autofluorescence type, granular involvement was higher at 9.1% than confluent at 2.3%.

The much higher rate of hyperautofluorescence determined in the chronic CSCR patients in the current study was thought to have formed associated with accumulated photoreceptor chromophores as a result of sufficient phagocytosis with separation of retina outer segments and RPE, and the low rate of hypo-autofluorescence was thought to be related to damaged photoreceptors and RPE (18-20). That autofluorescence types in zone 2 were seen in 4 quadrants suggests that the leakage in the disease is not only in the macular region, but can include all the quadrants contained in zone 2. As peripheral retina involvement was determined only in the form of gravitational defect in the inferior, this shows that basically the disease does not involve the periphery, but the inferior quadrant is affected associated with gravity.

This study had some limitations, primarily the low number of patients and that the autofluorescence regions corresponding to hyperautofluorescence or hypo-autofluorescence could not be compared with the areas of subretinal fluid in those regions because the OCT results could not be evaluated. In addition, the duration of the disease, and whether it was chronic active or chronic recurrent type was not reported.

In conclusion, the results of this study, in which the autofluorescence images taken with a wide angle digital fundus camera system of chronic CSCR patients were evaluated, showed that the vast majority of involvement was determined as hyperautofluorescence, peripheral retina involvement was only seen in the inferior quadrant in the form of gravitational defect, and zone 2 involvement

was seen in 4 quadrants. These findings can be considered important in respect of being of guidance for further studies of disease activation and progression.

Ethical approval

All procedures performed in studies involving human participants were under the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. This article does not contain any studies with animals performed by any of the authors. The institutional review board/Ethics Committee has approved the study from Eskisehir Osmangazi University with number of 2018-200.

REFERENCES

1. Wang M, Munch IC, Hasler PW, et al. Central serous chorioretinopathy. *Acta Ophthalmol* 2008;86:126-145.
2. Nicholson B, Noble J, Forooghian F, Meyerle C. Central serous chorioretinopathy: update on pathophysiology and treatment. *Surv Ophthalmol*. 2013;58:103-126.
3. Spaide RF, Goldbaum M,Wong DWK et al. Serous Detachment of the retina. *Retina* 2003;23: 820-846
4. Ciardella AP, Borodoker N, Costa DLL et al. The expanding clinical spectrum of central serous choriorethinopathy. *Comp Ophthalmol Update* 2003;4: 71-84
5. Ko HU: An experimental study of the nature of Masuda's chorioretinitis: III. A study of the relationship existing between chorioretinitis centralis photodynamica and the function of the kidney. *Acta Soc Ophthalmol Jpn* 1934; 38: 1060-1073.
6. Ryan SJ. Central serous chorioretinopathy. *Retina 3rd edn*. 2001;2:1153- 1181
7. Tittl MK, Spaide RF, Wong D.: Systemic findings associated with central serous chorioretinopathy. *Am J Opthalmol*. 1999; 128: 63- 68.
8. Michael JC1, Pak J, Pulido J, de Venecia G.Central serous chorioretinopathy associated with administration of sympathomimetic agents. *Am J Ophthalmol*. 2003;136:182-5.
9. Haimovici R, Rumelt S, Melby J. Endocrine abnormalities in patients with central serous chorioretinopathy. *Ophthalmology* 2003;110: 698–703
10. Gass JDM. Pathogenesis of disciform detachment of the neuroepithelium, idiopathic central serous choroidopathy. *Am J Ophthalmol*. 1967;63:587-615.
11. Hee MR, Puliafito CA, Wong C et al. Optical coherence tomography of central serous chorioretinopathy. *Am J Ophthalmol*. 1995;120:65-74.
12. Wang M, Sander B, Lund-Andersen H and Larsen M. Detection of shallow detachments in central serous chorioretinopathy. *Acta Ophthalmologica Scandinavica.* 1999;77:402-5.
13. Delori FC, Dorey CK, Staurenghi G, Arend O, Goger DG and Weiter JJ. In vivo fluorescence of the ocular fundus exhibits retinal pigment epithelium lipofuscin characteristics. *Invest Ophtolmol Vis Sci*. 1995;36:718–29.
14. Von Rückmann A, Fitzke FW, Bird AC. Distribution of fundus autofluorescence with a scanning laser ophthalmoscope. *Br J Ophthalmol*. 1995;79:407-12.
15. Dinc UA, Tatlipinar S, Yenerel M, Görgün E, Ciftci F. Fundus autofluorescence in acute and chronic central serous chorioretinopathy. *Clin Exp Optom*. 2011;94:452-7
16. Eandi CM, Ober M, Iranmanesh R, Peiretti R, Yanuzzi LA. Acute central serous retinopathy and fundus autofluorescent. *Retina.* 2005;25:989–93.
17. Yaylacıoğlu FT, Gürelik G. Santral seröz koryoretinopati. *Ret-Vit*. 2010;2:85-111.
18. Lee WJ, Lee JH, Lee BR. Fundus autofluorescence imaging patterns in central serous chorioretinopathy according to chronicity. *Eye (Lond)*. 201610:1336-42.
19. Spaide R.: Autofluorescence from the outer retina and subretinal space: hypothesis and review. *Retina.* 2008;28:5-35.
20. Ayata, Ali, et al. "Kronik santral seröz koriyoretinopatide optik koherens tomografi ve otofloresans bulguları." *Ret-Vit* 17 2009: 9-13.
21. Pang CE, Shah VP, Sarraf D, & Freund KB. Ultra-widefield imaging with autofluorescence and indocyanine green angiography in central serous chorioretinopathy. *American journal of ophthalmology.* 2014;158:362-71.
22. Küçükiba, K., Erol, N., & Bilgin, M. (2020). Evaluation of Peripheral Retinal Changes on Ultra-widefield Fundus Autofluorescence Images of Patients with Age-related Macular Degeneration. *Turk J Ophthalmol*.2020; 50: 6-14.
23. Aggio FB, Roisman L, Melo GB, Lavinsky D, Cardillo JA, Farah ME. Clinical factors related to visual outcome in central serous chorioretinopathy. *Retina* 2010; 30: 1128–34.
24. Chen SN, Hwang JF, Tseng LF, Lin CJ. Subthreshold diode micropulse photocoagulation for the treatment of chronic central serous chorioretinopathy with juxtafoveal leakage. *Ophthalmology* 2008; 115: 2229–34.
25. Spaide RF, Campeas L, Haas A, Yannuzzi LA, Fisher YL, Guyer DR et al. Central serous chorioretinopathy in younger and older adults. *Ophthalmology* 1996; 103: 2070–79
26. Framme C, Walter A, Gabler B, et al.: Fundus autofluorescence in acute and chronic-recurrent central serous chorioretinopathy. *Acta Ophthalmol Scand.* 2005;83:161-67.