under low luminance conditions, we need to measure the VA using test charts with low background luminance. It is well known that VA is affected by the degree of ambient luminance and Shaler[4] reported that the VA of normal eyes decreased under low luminance conditions. Because patients with good VA can have depressed visual function, for example, decreased contrast sensitivity, poorer colour discrimination, reduced focal macular electroretinogram (ERG), reduced focal retinal sensitivity and visual field defects,[5–12] it might be expected that patients with central serous chorioretinopathy would also have decreased VA under low luminance. There have been no studies focusing on low luminance VA in patients with central serous chorioretinopathy.

The purpose of this study was to determine the VA of patients with central serous chorioretinopathy under low luminance conditions. To accomplish this, we made a computer program to create low luminance visual acuity charts and determined the VA under six different background luminance levels in seven patients with central serous chorioretinopathy.

METHODS

Seven eyes of seven patients with central serous chorioretinopathy and six eyes of six age-matched healthy control subjects were tested. The inclusion criteria were:

1. presence of subretinal fluid (serous retinal detachment: SRD) involving the fovea in the optical coherence tomographic (OCT) images
2. unilateral central serous chorioretinopathy with the fellow eye normal and
3. visual acuity of 0 logMAR or better in both eyes.

The exclusion criteria were:

1. evidence of choroidal neovascularisation in the fluorescein angiographic (FA) and indocyanine green angiographic images and
2. the presence of other ocular or macular diseases. Patients with central serous chorioretinopathy, who had received laser photocoagulation were also excluded.

The diagnosis of central serous chorioretinopathy was based on the presence of a serous retinal detachment documented by leakage from the retinal pigment epithelium in the fluorescein angiographic images. The VA was measured with a Landolt C chart using standard retroillumination with a luminance of 220 cd/m^2. We also examined six eyes of six normal volunteers with the same testing protocol. The OCT examination was carried out with either a Heidelberg Spectralis OCT (Heidelberg Engineering, Heidelberg, Germany) or with a Stratus OCT 3000 (Carl Zeiss Meditec, Inc, Dublin, CA, USA). The height of the serous retinal detachment (SRDH), the width of the serous retinal detachment (SRDW) and the thickness of sensory retina (foveal thickness: FT) were manually measured in the horizontal cross-sectional OCT images, which included the fovea (Figure 1). These measurements were made by one of the authors (KS), who had no information about the patients. The values of these parameters were used for statistical analyses.

The procedures used in this study conformed to the tenets of the Declaration of Helsinki. An informed consent was obtained from all subjects. Approval to conduct this study was obtained from the Institutional Review Board of Surugadai Nihon University Hospital, Tokyo, Japan.

Low luminance visual acuity charts and procedures

Low luminance VA charts were created with an Apple PowerMac G5 computer and displayed on a monitor (SONY GDM-F500). Landolt Cs were used for the characters and they followed the design rule of the Early Treatment Diabetic Retinopathy Study charts (Figure 2). Six levels of background luminance were used, namely, 78.20 cd/m^2, 31.87 cd/m^2, 11.37 cd/m^2, 4.14 cd/m^2, 1.30 cd/m^2 and 0.37 cd/m^2. The luminance of the Landolt C rings was kept as close to zero cd/m^2 as possible and the contrast for all conditions approached 100 per cent.

Identification of the largest Landolt C at the distance of 308 cm represented a VA of 0.7 logMAR units. The ring size was reduced in steps of 0.1 to -0.4 logMAR units. The tests were conducted from the lowest luminance level in a dark room after waiting seven minutes for dark adaptation.

Analyses

We compared the VA of the eyes with central serous chorioretinopathy with that of the fellow eyes and that of normal eyes at each luminance level. To determine the statistical significance of any differences, Student's *t*-tests were used. The VA in logMAR units was plotted on the ordinate for the different luminance levels on the abscissa. The data were fit to a linear equation as:

$$y = a * x + b,$$

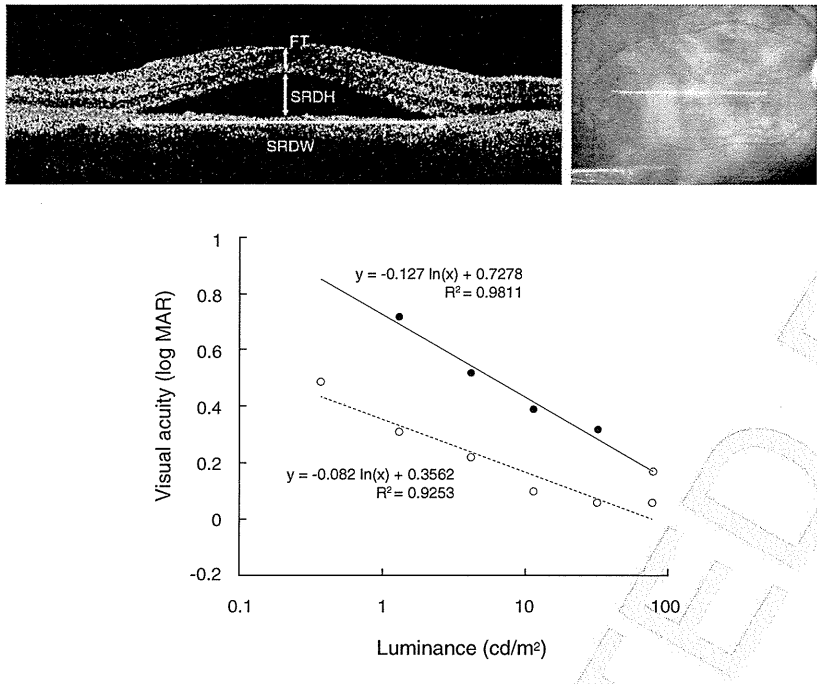
where 'y' is the logMAR VA and 'x' is the luminance expressed in logarithmic units. 'a' is the steepness of the best-fitted line and represents how much the VA is altered by a step change in the background luminance.

Thus, a large 'a' value means that the VA would be greatly changed by a step change in the background luminance. 'b' is the logMAR VA at very low or no background luminance, that is, when 'x' is zero. This is the point where the regression line intersects the ordinate of the logMAR VA line (Figure 1). The difference in the slopes for central serous chorioretinopathy, fellow and normal eyes were tested for significance by assessing the interaction term between background luminance and eye type using an analysis of covariance (ANCOVA) technique.

The correlations between the parameters of the OCT images and the constants 'a' and 'b' were determined by the Spearmann coefficients of correlation. The Bonferroni correlation was used to avoid type I error. The statistical significance was set at 0.01 for the *t*-tests because there were five comparisons and at 0.17 for the ANCOVA because there were three comparisons.

RESULTS

The patients with central serous chorioretinopathy included five men and two women and the mean and standard deviation of their ages was 41.3 ± 3.9 years (range 39–50 years). The duration of the



Colour

Figure 1. Optical coherence tomographic (OCT) image and infrared fundus photograph; also shown in a graph relating the visual acuity in logMAR units to the background luminance in eyes with central serous chorioretinopathy (CSC). The serous retinal detachment height (SRDH) was taken to be the distance between the outer segment/inner segment (IS/OS) line of the photoreceptors and the anterior surface of the retinal pigment epithelium/Bruch membrane. The width of the serous retinal detachment (SRDW) was taken to be the width of the serous retinal detachment in the OCT images and the foveal thickness was the distance between the internal limiting membrane (ILM) and IS/OS line. In cases where the IS/OS line was not clear, the basal edge of the hyper-reflective band representing the detached sensory retina was used.
Top left: Horizontal cross-sectional optical coherence tomographic (OCT) image including the fovea in an eye with central serous chorioretinopathy (Case 5). The cross-section corresponds to the horizontal line indicated in the right side of the fundus photograph. The serous retinal detachment height (SRDH), width of the serous retinal detachment (SRDW) and the foveal thickness (FT) are shown.
Top right: Infrared fundus photograph indicating the cross line of the left-side OCT image.
Bottom: Relationship between logMAR visual acuity (VA) and background luminance in Case 5. The logMAR VA was linearly correlated with the luminance. The logMAR VA of the central serous chorioretinopathy-affected eye was higher than that of the healthy fellow eye at each luminance level. ●: affected eye, ○: healthy fellow eye. The fitted line and the formula are shown as well.

symptoms was 1.0–1.5 months (Table 1). The mean ages of the normal volunteers was 38 ± 9 years (range 22–47 years). The mean VAs of the central serous chorioretinopathy and fellow eyes at each luminance are shown in Table 1. At the lowest luminance level of 0.37 cd/m^2, five of seven patients could not correctly identify any of the targets using the eye with central serous chorioretinopathy. The mean VAs of the normal volunteers were 0 ± 0.05, 0.03 ± 0.04, 0.07 ± 0.06, 0.14 ± 0.06, 0.23 ± 0.11 and 0.38 ± 0.11 logMAR units, respectively.

The VA in logMAR units is plotted against the background log luminance in Figure 3. The VA of the eyes with central serous chorioretinopathy was significantly poorer than that of normal eyes at all luminances except 0.37 cd/m^2 and 78.20 cd/m^2 ($p < 0.01$ for all). The VA of the eyes with central serous chorioretinopathy was significantly poorer than that of fellow eyes at all luminances except 0.37 cd/m^2 and 78.20 cd/m^2 ($p < 0.01$ for all). No significant differences were found among the central serous chorioretinopathy, fellow and volunteer eyes in the slopes of the fitted linear function by ANCOVA.

The constants, 'a' and 'b' and the coefficient of regression (R^2) are shown in Table 2. There was no significant correlation between any OCT parameters and 'a' (slope) or 'b' (intercept).

DISCUSSION

Patients with central serous chorioretinopathy have a relatively central scotoma, metamorphopsia, micropsia, colour vision abnormalities, and visual disturbances under low luminance despite the relatively good standard VA. Studies on the relationship between the luminance of the VA charts and VA in eyes with central serous chorioretinopathy have not been reported. Patients with central serous chorioretinopathy often complain of difficulty in reading during the evening and night, that is, at low luminance levels. The VA obtained by conventional acuity charts is not a good measure for predicting how these patients will perform in low luminance environments.

Patient no.	Age (years)	Gender	Affected eye						Fellow eye					
			78.20 cd/m²	31.87 cd/m²	11.37 cd/m²	4.14 cd/m²	1.30 cd/m²	0.37 cd/m²	78.20 cd/m²	31.87 cd/m²	11.37 cd/m²	4.14 cd/m²	1.30 cd/m²	0.37 cd/m²
1	39	M	0.01	0.12	0.15	0.27	0.55	N.R.	-0.04	0	0	0.03	0.13	0.35
2	41	F	0.16	0.16	0.24	0.3	0.46	0.64	0.03	0.06	0.12	0.17	0.34	0.45
3	50	F	0.16	0.28	0.31	0.5	0.65	N.R.	0.1	0.22	0.31	0.4	0.42	0.55
4	41	M	0.13	0.29	0.3	0.41	0.58	0.76	0.03	0.02	0.07	0.17	0.18	0.45
5	40	M	0.17	0.32	0.39	0.52	0.72	N.R.	0.06	0.06	0.1	0.22	0.31	0.49
6	39	M	0.15	0.23	0.26	0.37	0.59	N.R.	0.04	0.07	0.1	0.24	0.35	0.5
7	39	M	0.1	0.22	0.36	0.6	0.76	N.R.	0.01	0	0.1	0.2	0.29	0.36

Visual acuities are shown as logMAR. M = male, F = female, N.R. = not recordable

Table 1. Visual acuities under different background luminances in patients with central serous chorioretinopaty.

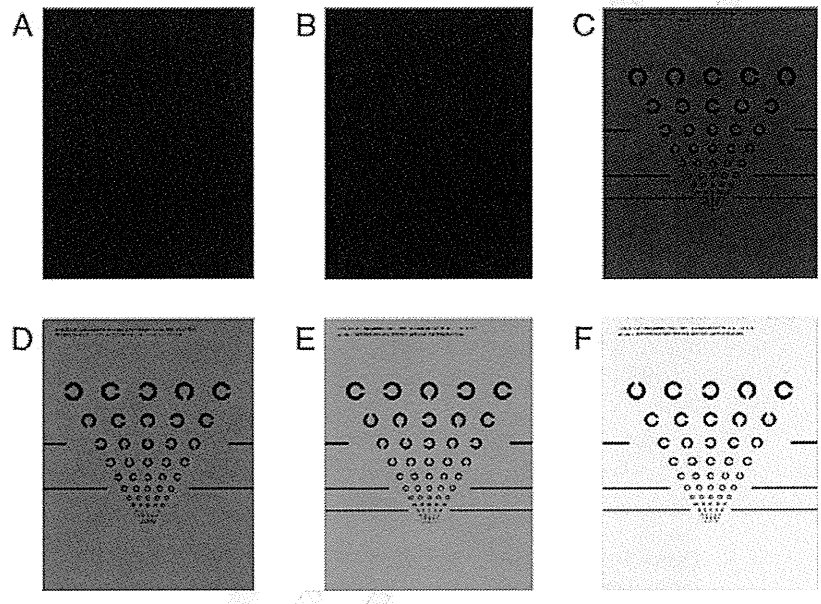


Figure 2. Low luminance visual acuity charts. The background luminance values were (A) 0.37 cd/m², (B) 1.30 cd/m², (C) 4.14 cd/m², (D) 11.37 cd/m², (E) 31.87 cd/m² and (F) 78.20 cd/m².

Case	Age	Gender	OCT parameter (μm)			Low luminance visual acuity			
			FT	SRDH	SRDW	a	b	R^2	p
1	39	M	183.3	275.0	2703.1	-0.121	0.5098	0.9079	0.0122
2	41	F	216.7	141.7	1171.9	-0.091	0.4932	0.9292	0.0193
3	50	F	244.1	141.1	2458.2	-0.118	0.6607	0.9636	0.0030
4	41	M	180.7	231.4	3004.7	-0.111	0.6143	0.9648	0.0005
5	40	M	191.7	308.3	2745.0	-0.127	0.7278	0.9811	0.0011
6	39	M	183.1	404.3	4086.0	-0.101	0.5603	0.9171	0.0104
7	39	M	181.2	322.1	3239.9	-0.166	0.8049	0.9894	0.0005

M = male, F = female, OCT = optical coherence tomography, these parameters are indicated in Figure 1.
FT = foveal thickness, SRDH = height of the serous retinal detachment, SRDW = width of serous retinal detachment. When low luminance visual acuity was plotted against background luminance as shown in Figure 1, the following formula was fitted: $y = a * X + b$, when y indicates log MAR and x indicates log (luminance), R^2: coefficient of regression

Table 2. Parameters of the optical coherence tomographic image and fitting of low luminance visual acuity in eyes with central serous chorioretinopathy

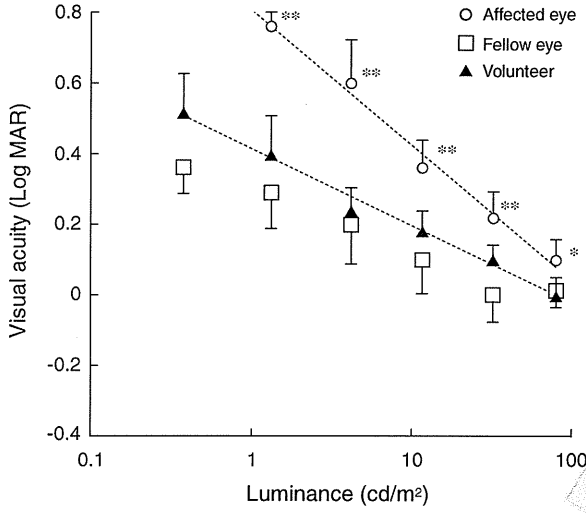


Figure 3. Relationship between logMAR visual acuity (VA) and the log background luminance. The data were fitted by the least square method and a linear equation between the logMAR VA and log luminance for the three groups. The logMAR VA is linearly correlated with the luminance. The logMAR VA of the eye with central serous chorioretinopathy is significantly higher than that of the fellow eye at each luminance level. Visual acuities at all levels of luminance except 0.37cd/m^2 are significantly different between central serous chorioretinopathy and the eyes of normal volunteers (*$p < 0.05$, **$p < 0.01$). ○: affected eye, □: fellow eye, △: normal eye of control participants, Error bars indicate standard deviation.

Thus, we developed a computer program which allowed us to create Landolt Cs on a computer monitor screen with different background luminances. With these targets and background luminances, we were able to evaluate how luminance levels affected the VA in central serous chorioretinopathy patients.

Shlaer[4] reported that lower background luminances led to lower VA in normal eyes and we obtained similar results in our normal eyes. The VA of eyes with central serous chorioretinopathy also decreased according to the decrease in background luminance but the deterioration was more severe than that of normal eyes at all background luminance levels. We found that VA in logMAR units was linearly correlated with the logarithm of the background luminance. The logMAR VA in eyes with central serous chorioretinopathy was significantly higher, that is, poorer VA, than that in normal control eyes.

Hypotheses have been presented to explain the decreased VA under low luminance in normal eyes.[13,14] Thus, Hecht[13] suggested that the number of cone photoreceptors activated is decreased at low luminances. Our subjects were dark-adapted for seven minutes before testing and the cone system was expected to be functioning during this period in a healthy retina, and all of the normal fellow eyes could see at the lowest background luminance. Five of seven eyes with central serous chorioretinopathy could not identify even one Landolt C at the lowest luminance level, although the VA measured under standard conditions was at least 0 logMAR units in all eyes. These findings suggest that the foveal cones are not functioning normally in low light conditions in eyes with central serous chorioretinopathy.

Chuang and colleagues[15] reported that the rods were more affected than cones in eyes with central serous chorioretinopathy; however, they did not evaluate the rods selectively to determine whether the cones were indeed normal. The decreased VA measured under mesopic conditions in our study is probably due to impairments of both cone and rod function. This is consistent with the results of the Humphrey perimetric retinal sensitivity decrease in the detached area in eyes with central serous chorioretinopathy.[9]

Recent advances in OCT have provided some correlations of the foveal microstructure with visual function in several retinal diseases.[9,16–19] Sekine, Imasawa and Iijima[9] reported that the thickness of the serous retinal detachment and not neurosensory retinal thickness, was significantly correlated with visual sensitivity measured by automated static perimetry in eyes with central serous chorioretinopathy. It was also reported that the initial VA was significantly worse in eyes with a higher serous retinal detachment in Vogt-Koyanagi-Harada disease but it was not significantly correlated with foveal thickness.[17] Therefore, we anticipated the possibility that some morphological parameters might be correlated with low luminance VA but this was not the case. Many factors such as the patient's age, duration of central serous chorioretinopathy, size of the detached area, central cone function and arrangement of cone and rod cells, may have influenced the low luminance VA.

There are some limitations of this study. The small sample might have limited the statistical power of our anlayses. Further investigation on the relationship between microstructural changes and low luminance VA would be helpful for understanding the pathologic mechanism of patients' complaints under reduced luminance conditions.

Studies of cases of unilateral central serous chorioretinopathy have shown that

the fellow eyes can have subclinical central serous chorioretinopathy. The studies of Maaranen, Tuppurainan and Mäntyjärvi[20] and Baran, Gürlü and Esgin[21] support this suggestion because they found a high percentage of colour deficiency in the fellow eyes of patients with central serous chorioretinopathy. Baran, Gürlü and Esgin[21] also observed that contrast sensitivity was reduced in the fellow eyes of patients with unilateral central serous chorioretinopathy. Iida and colleagues[22] reported choroidal vascular abnormalities in indocyanine green angiographic images in the unaffected fellow eye. In our study, the VA of fellow eyes was not significantly different from that of age-matched normal eyes. Further studies are needed to assess the visual status of fellow eyes.

In conclusion, the VA of eyes with central serous chorioretinopathy was significantly more depressed at low background luminances than normal eyes. Low background luminance VA testing is useful for evaluating visual disturbances at low ambient luminance experienced by patients with central serous chorioretinopathy. There is a potential use here as one of the functional parameters in evaluating and flagging of central serous chorioretinopathy or therapeutic effect of new therapies such as photodynamic therapy.

ACKNOWLEDGEMENT

Support of this study was provided by Researches on Sensory and Communicative Disorders from the Ministry of Health, Labor, and Welfare, Japan.

REFERENCES

1. Spaide RF, Campeas L, Haas A, Yannuzzi LA, Fisher YL, Guyer DR, Slakter JS et al. Central serous chorioretinopathy in younger and older adults. *Ophthalmology* 1996; 103: 2070–2079.
2. Gilbert CM, Owens SL, Smith PD, Fine SL. Long-term follow-up of central serous chorioretinopathy. *Br J Ophthalmol* 1984; 68: 815–820.
3. Norholm I. Central serous retinitis. A follow-up study. *Acta Ophthalmol* 1969; 47: 890–899.
4. Shlaer S. The relation between visual acuity and illumination. *J Gen Physiol* 1937; 21: 165–188.
5. Plainis S, Anastasakis AG, Tsilimbaris MK. The value of contrast sensitivity in diagnosing central serous chorioretinopathy. *Clin Exp Optom* 2007; 90: 296–298.
6. Marmor MF, Tan F. Central serous chorioretinopathy: bilateral multifocal electroretinographic abnormalities. *Arch Ophthalmol* 1999; 117: 184–188.
7. Miyake Y, Shiroyama N, Ota I, Horiguchi M. Local macular electroretinographic responses in idiopathic central serous chorioretinopathy. *Am J Ophthalmol* 1988; 106: 546–550.
8. Senturk F, Ozdemir H, Karacorlu M, Karacorlu SA, Uysal O. Microperimetric changes after intravitreal triamcinolone acetonide injection for macular edema due to central retinal vein occlusion. *Retina* 2010; 30: 1254–1261.
9. Sekine A, Imasawa M, Iijima H. Retinal thickness and perimetric sensitivity in central serous chorioretinopathy. *Jpn J Ophthalmol* 2010; 54: 578–583.
10. Kim SW, Oh J, Huh K. Correlations among various functional and morphological tests in resolved central serous chorioretinopathy. *Br J Ophthalmol* 2012; 96: 350–355.
11. Ojima Y, Tsujikawa A, Hangai M, Nakanishi H, Inoue R, Sakamoto A, Yoshimura N. Retinal sensitivity measured with the micro perimeter 1 after resolution of central serous chorioretinopathy. *Am J Ophthalmol* 2008; 146: 77–84.
12. Ozdemir H, Karacorlu SA, Senturk F, Karacorlu M, Uysal O. Assessment of macular function by microperimetry in unilateral resolved central serous chorioretinopathy. *Eye* 2008; 22: 204–208.
13. Hecht S. The resolution between visual acuity and illumination. *J Gen Physiol* 1928; 11: 255–281.
14. Chen B, MacLeod DI, Stockman A. Improvement in human vision under bright light: Grain or gain? *J Physiol* 1987; 394: 41–66.
15. Chuang EL, Sharp DM, Fitzke FW, Kemp CM, Holden AL, Bird AC. Retinal dysfunction in central serous retinopathy. *Eye* 1987; 1: 120–125.
16. Forte R, Cennamo G, Finelli M, Cesarano I, D'Amico G, De Crecchio G, Cennamo G. Intravitreal triamcinolone, bevacizumab and pegaptanib for occult choroidal neovascularization. *Acta Ophthalmol* 2010; 88: e305–e310.
17. Ikewaki J, Kimoto K, Choshi T, Nagata M, Motomura Y, Tamura K, Shinoda K et al. Optical coherence tomographic assessment of dynamic macular changes in patients with Vogt-Koyanagi-Harada disease. *Int Ophthalmol* 2010; 31: 9–13.
18. Geitzenauer W, Hitzenberger CK, Schmidt-Erfurth UM. Retinal optical coherence tomography: past, present and future perspectives. *Br J Ophthalmol* 2011; 95: 171–177.
19. Lim JW, Kang SW, Kim YT, Chung SE, Lee SW. Comparative study of patients with central serous chorioretinopathy undergoing focal laser photocoagulation or photodynamic therapy. *Br J Ophthalmol* 2011; 95: 514–517.
20. Maaranen TH, Tuppurainen KT, Mäntyjärvi MI. Color vision defects after central serous chorioretinopathy. *Retina* 2000; 20: 633–637.
21. Baran NV, Gürlü VP, Esgin H. Long-term macular function in eyes with central serous chorioretinopathy. *Clin Experiment Ophthalmol* 2005; 33: 369–372.
22. Iida T, Kishi S, Hagimura N, Shimizu K. Persistent and bilateral choroidal vascular abnormalities in central serous chorioretinopathy. *Retina* 2007; 19: 508–512.

Clinical Ophthalmology

Dovepress
open access to scientific and medical research

Open Access Full Text Article

ORIGINAL RESEARCH

Microperimetric evaluation of chronic central serous chorioretinopathy after half-dose photodynamic therapy

Kyoko Fujita[1]
Kei Shinoda[1,2]
Celso Soiti Matsumoto[2]
Yutaka Imamura[3]
Etsuko Tanaka[4]
Yoshihiro Mizutani[1]
Atsushi Mizota[2]
Mitsuko Yuzawa[1]

[1]Department of Ophthalmology, Surugadai Nihon University Hospital, Tokyo, [2]Teikyo University School of Medicine, University Hospital Itabashi, Tokyo, [3]Teikyo University School of Medicine, University Hospital Mizonokuchi, Kanagawa, [4]Kyorin University School of Medicine, Mitaka, Japan

Background: The purpose of this study was to determine baseline clinical factors to correlate the outcome of half-dose verteporfin photodynamic therapy (PDT) in eyes with chronic central serous chorioretinopathy (CSC).

Methods: In this prospective, non-comparative, interventional case series, 14 eyes of 14 patients with chronic CSC who received half-dose verteporfin PDT were examined. The best-corrected visual acuity (BCVA), macular sensitivity in the central 4, 8, and 12 degrees, and fixation stability were evaluated at baseline and at months 1, 3, 6, and 12 after half-dose verteporfin PDT. Macular sensitivity and fixation stability were determined by MP-1 microperimetry.

Results: Mean retinal sensitivity in the central 4 and 8 degrees was significantly better at 1, 3, 6, and 12 months after half-dose verteporfin PDT than at baseline. BCVA was significantly better after half-dose verteporfin PDT but only after 3 months. Fixation was relatively unstable in three eyes at baseline, but became stable at 12 months. BCVA at 12 months was significantly correlated with pre-PDT fixation stability ($r = 0.7120$, $P = 0.0038$).

Conclusion: Half-dose verteporfin PDT results in a significant increase in mean central retinal sensitivity for at least 12 months. Our findings indicate that microperimetry is a useful method for evaluating the functional benefits of half-dose verteporfin PDT in eyes with chronic CSC.

Keywords: microperimetry, fixation point, retinal sensitivity, photodynamic therapy, chronic central serous chorioretinopathy

Introduction

Central serous chorioretinopathy (CSC) is characterized by a serous retinal detachment in the macular area. Patients complain of a blurred area in the central or paracentral visual field.[1] In the majority of patients, CSC is self-limiting, and their visual acuity recovers fully after resolution of the serous retinal detachment.[1] However, visual acuity only reflects foveal function, and patients, even those with good visual acuity, can have a reduction in other visual functions, eg, contrast sensitivity, color discrimination, dark-adaptation, focal macular electroretinograms, and macular sensitivity.[2–7]

The MP-1 microperimeter (Nidek, Vigonza, Italy) is a relatively new instrument that couples digital fundus imaging with automated microperimetry.[8] Recent MP-1 studies have clearly shown that eyes with resolved CSC can have significantly lower central retinal sensitivity, even after good central visual acuity had been obtained.[9,10]

Photodynamic therapy (PDT) with verteporfin has been used to treat CSC, and positive visual outcomes have been reported in most patients.[11–13] The good results have been attributed to short-term choriocapillaris hypoperfusion and long-term choroidal vascular remodeling, which leads to a reduction in choroidal congestion, vascular hyperperme-

Correspondence: Kei Shinoda
Department of Ophthalmology, Teikyo University School of Medicine, Kaga 2-11-1, Itabashi-ku Tokyo, 173-8606, Japan
Tel +813 3964 1225
Fax +813 3964 1402
Email shinodak@med.teikyo-u.ac.jp

submit your manuscript | www.dovepress.com
Dovepress
http://dx.doi.org/10.2147/OPTH.S33338

ability, and extravascular leakage.[13–16] Because conventional PDT can also result in complications, such as retinal pigment epithelium atrophy, choroidal ischemia, and secondary choroidal neovascularization,[12,13] several authors have used safety-enhanced PDT with half the conventional dose of verteporfin (3 mg/m^2)[17–19] or with reduced fluence of 25 J/cm^2 for 83 seconds, ie, 300 mW/cm^2, in eyes with chronic CSC.[20–22] They found sufficient photodynamic effects on the choroidal vasculature and a good visual outcome with minimal retinal damage. Improvement of macular sensitivity using MP-1 before and after half-dose verteporfin PDT in eyes with chronic CSC has recently been reported.[19,22] We have also reported on the effectiveness and safety of half-dose verteporfin PDT improvements of retinal sensitivity for at least 3 months in patients with chronic chorioretinopathy.[23] The purpose of this study was to evaluate the effectiveness of half-dose verteporfin PDT on macular sensitivity in eyes with chronic CSC after 1 year. In addition, we determined the correlations between visual acuity, retinal sensitivity, and fixation stability.

Materials and methods

This was a prospective, consecutive, open-label, noncomparative, interventional study conducted at the Surugadai Nihon University Hospital. Sixteen eyes from 16 patients with chronic CSC were examined in a prospective manner.[23] Among these, a complete set of data was obtained for 14 patients over a follow-up period of 1 year were included in the study. The demographics of the patients are shown in Table 1. Inclusion criteria were the presence of subretinal fluid involving the fovea in optical coherence tomographic (OCT) images and a serous retinal detachment of at least 6 months in duration. Patients who had evidence of choroidal neovascularization, polypoidal choroidal vasculopathy, or other maculopathy documented by fluorescein angiography or indocyanine green angiography were excluded. Patients who had had treatments such as focal laser coagulation or intravitreal injection of anti-vascular endothelial growth factor agents were also excluded.

Diagnosis of CSC was based on the presence of serous macular detachment with leakage from the retinal pigment epithelium in the fluorescein angiography images. A medical and ocular history was obtained from each patient, and a complete ophthalmic examination, including determination of best-corrected visual acuity (BCVA), slit-lamp biomicroscopy, OCT, fluorescein angiography, and indocyanine green angiography was performed. All OCT examinations were carried out using the Heidelberg Spectralis OCT instrument (Heidelberg Engineering, Heidelberg, Germany) at baseline, and 1, 3, 6, and 12 months after PDT. The procedures used conformed to the guidelines of the Declaration of Helsinki. Informed consent was obtained from all subjects after a complete explanation of the procedures to be used.

Photodynamic therapy

PDT was performed using a 3 mg/m^2 body surface area of verteporfin (Visudyne, Novartis AG, Bülach, Switzerland) which is half the conventional dose of verteporfin.[17–19,23] Verteporfin was infused over a 10-minute period followed by delivery of 50 J/cm^2 from a 689 nm laser system (Carl Zeiss, Dublin, CA) over an 83-second exposure period. The size of

Table 1 Demographics of the patients with central serous chorioretinopathy

Case	Gender	Age (years)	Affected eye	Duration (months)	GLD (μm)	VA (decimal)	LogMAR	Fixation**
1	m	45	R	12	3800	0.9	0.05	S
2	m	64	R	120	5100	0.7	0.15	S
3	m	40	R	48	2700	1.0	0.00	S
4	m	54	R	132	5900	1.5	−0.18	S
5	m	62	L	13	5300	0.7	0.15	S
6	m	57	R	Unknown	4500	0.15	0.82	R
7	m	55	R	12	4500	0.7	0.15	S
8	m	45	R	72	4200	1.2	−0.08	S
9	m	41	R	6	4300	0.5	0.30	S
10	m	44	L	36	3500	0.2	0.70	R
11	m	53	R	39	3100	0.5	0.30	R
12	m	50	L	6	4900	0.7	0.15	S
13	m	46	R	33	4000	0.9	0.05	S
14	m	56	L	60	5400	0.9	0.05	S
Mean		50.9		45.3	4371.4	0.65*	0.19	
SD		7.6		41.5	910.1		0.28	

Notes: *Geometric mean; **S = stable; R = relatively unstable.
Abbreviations: GLD, greatest linear dimension = spot size; VA, visual acuity; m, male; SD, standard deviation.

the laser spot was the diameter of the region of indocyanine green hyperpermeability. After treatment, protective spectacles were given to the patients, and they were instructed to avoid strong light for 5 days.

Assessment of location and stability of fixation by MP-1 microperimetry

Fundus-monitored microperimetry was performed with the MP-1.[8,23] A 4-2 staircase strategy using a Goldmann III size stimulus was used, and 45 stimulus locations covering the central 12 degrees were tested by microperimetry (Figure 1, see the middle row of the center and right columns). The mean retinal sensitivities at 12 locations covering the central 4 degrees (central microperimetry, c4MP-1), 28 locations covering the central 8 degrees (central microperimetry, c8MP-1), and at 45 locations covering the central 12 degrees (central microperimetry, c12MP-1) were determined.

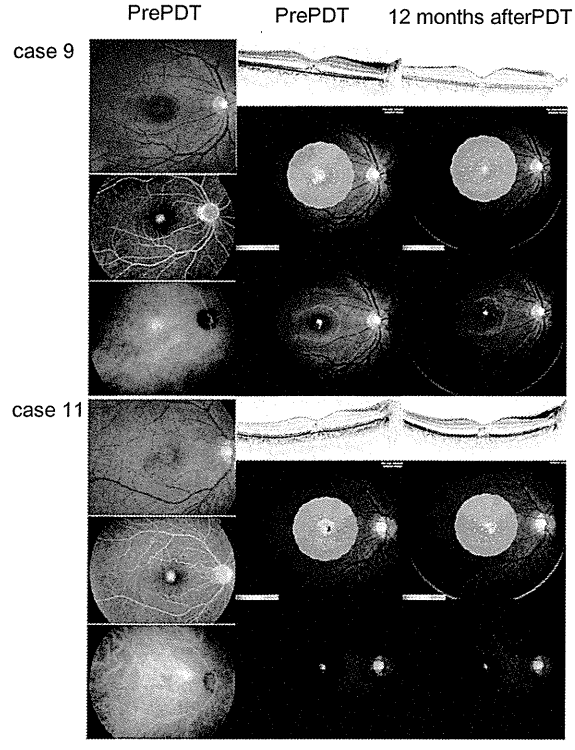


Figure 1 Representative cases with similar pretreatment findings but with different outcomes after half-dose verteporfin PDT.

Notes: The left column shows the fundus photographs (top), fluorescence angiographic images at a late phase (middle), and indocyanine green angiographic images at a late phase (bottom) for each case. The middle column shows a horizontally scanned optical coherence tomographic image (top), macular retinal sensitivity (middle), and fixation stability (bottom) at baseline for each case. The right column shows horizontally scanned optical coherence tomographic image (top), macular retinal sensitivity (middle), and fixation stability (bottom) 12 months after half-dose verteporfin PDT for each case. Fundus photography, fluorescein angiography, indocyanine green angiography, and optical coherence tomographic findings, and macular sensitivity, but not fixation stability, at baseline are similar in the two cases. The visual acuity at baseline was 0.5 in each case. The spot size for PDT was 4300 μm for case 9 and 3100 μm for case 11. Twelve months after half-dose verteporfin PDT, the optical coherence tomographic findings and macular sensitivity was different although fixation stability became similar in both cases. Visual acuity was 0.9 in case 9 and 0.4 in case 11.

Abbreviation: PDT, photodynamic therapy.

A fixation cross was presented at a maximum luminance of MP-1. Subjects were asked to look at the center of the cross and were encouraged to use their peripheral vision if needed. Once the subjects had located the cross, the stability of fixation was measured for a period of 30 seconds. To determine the stability of fixation, movements of the fundus image were tracked while the patient tried to maintain continuous fixation on the target. The autotracking system calculated the horizontal and vertical shifts relative to a reference frame and drew a map of the patient's eye movements at 25 Hz throughout the examination.

The stability of fixation was based on the locations and movements using the MP-1 software, as recommended by Fujii et al.[24] Fixation was defined as being stable when more than 75% of the fixation points were located within a predetermined 2 degree diameter circle centered on the gravitational center of all fixation points, regardless of the position of the foveal center. Location of fixation was classified as "relatively unstable" fixation when less than 75% of fixation points were located within a 2 degree diameter circle, but more than 75% of fixation points were located within a 4 degree diameter circle. The fixation was classified as "unstable fixation" when less than 75% of the fixation points were located within a 4 degree circle. All patients were allowed one preliminary practice of the MP-1 to try to standardize the learning effect.

Statistical analysis

Paired *t*-tests were used to determine whether retinal sensitivity and BCVA in each post-treatment period were significantly different from corresponding values at baseline. Spearman's correlation of coefficient analysis was performed to determine the correlation between mean retinal sensitivity and BCVA. We also performed stepwise multiple regression analyses to determine if any pretreatment factors were significantly associated with post-PDT BCVA. Independent factors investigated in the analysis were age (years), greatest linear diameter of the choroidal hyperpermeability region (microns), fixation stability, baseline BCVA in logarithm of the minimum angle of resolution (logMAR) units, and retinal sensitivity at 4, 8, and 12 degrees. The Bonferroni correlation was used to avoid type I error. Statistical significance was set at $P < 0.0125$ for the *t*-tests because there were four comparisons and at 0.05 for the Spearman's correlation of coefficient analysis.

Results

The CSC patients consisted of 14 men whose mean age was 51 ± 7.6 (range 40–64) years. Duration of symptoms was 6–132 months (Table 1). Serous retinal detachment was resolved 1 month after PDT in 11 eyes, but cases 6 and 11 had a reduction and flatter serous retinal detachment, which was still present 12 months after PDT.

Mean BCVA was 0.19 ± 0.28 logMAR units at baseline, 0.18 ± 0.29 logMAR units at 1 month ($P > 0.05$), 0.11 ± 0.28 logMAR units ($P = 0.01$) at 3 months, 0.04 ± 0.27 logMAR units ($P = 0.0002$) at 6 months, and 0.03 ± 0.26 logMAR units ($P = 0.002$) at 12 months after PDT (Table 2 and Figure 2). At 12 months, all patients reported an improvement in their vision, but only five patients had an improvement of their BCVA by more than 0.2 logMAR units.

Mean retinal sensitivity within the central 4 degrees (12 points) improved significantly from 7.42 ± 4.75 dB at baseline to 11.31 ± 4.51 dB at 1 month, 13.66 ± 4.57 dB at 3 months, 14.39 ± 4.97 dB at 6 months, and 15.19 ± 4.84 dB at 12 months (Figure 3, $P < 0.0125$ for all time points). Mean retinal sensitivity within the central 8 degrees (28 points) improved significantly from 10.03 ± 4.45 dB at baseline to 13.11 ± 3.88 dB at 1 month, 15.15 ± 3.41 dB at 3 months, 15.68 ± 3.84 dB at 6 months, and 16.48 ± 3.49 dB at 12 months (Figure 3, $P < 0.0125$ for all time points).

Mean retinal sensitivity within the central 12 degrees (45 points) improved significantly from 11.84 ± 3.89 dB at baseline to 14.26 ± 3.15 dB at 1 month, 15.95 ± 2.80 dB at 3 months, 16.41 ± 3.11dB at 6 months, and 17.11 ± 2.82 dB at 12 months (Figure 3, $P < 0.0125$ at 3, 6, and 12 months).

Fixation was central in all eyes for all measurements. Fixation was stable in eleven cases at baseline and relatively unstable in the other three cases (6, 10, and 11). Fixation became stable at 1 month after PDT in cases 6 and 10, and at 12 months after PDT in case 11 (Table 2).

Significant correlations were found between the sensitivities of c12MP-1 and BCVA at 6 and 12 months, between the sensitivities of c8MP-1 and BCVA at 3, 6, and 12 months, and between the sensitivities of c4MP-1 and BCVA at 3 and 12 months.

Multiple regression analysis showed that among the independent factors, only fixation stability ($P = 0.0038$, regression coefficient 0.357, adjusted $R^2 = 0.507$) was significantly associated with BCVA at 12 months.

We present two representative cases with different outcomes after half-dose verteporfin PDT, although several pretreatment findings were similar (Figure 1). The fundus appearance, fluorescein angiography and indocyanine green angiography findings, OCT findings, and macular sensitivity, but not fixation properties, in both cases were similar at baseline. However, the response to half-dose verteporfin PDT was very different.

Discussion

Our results showed that mean retinal sensitivity in the central 4 and 8 degrees was significantly better than baseline at 1, 3, 6, and 12 months after half-dose verteporfin PDT in eyes with CSC. BCVA was also significantly better, but only after 3 months. Fixation was relatively unstable in three eyes at baseline but became stable at 12 months after PDT. These findings indicate that half-dose verteporfin PDT is effective

Table 2 Visual acuity in patients with central serous chorioretinopathy before and after half-dose photodynamic therapy

Case	Pretreatment	After treatment				Period of stable fixation*
		1 month	3 months	6 months	12 months	
1	0.9	1.0	1.2	1.5	1.5	Pre
2	0.7	0.6	0.6	0.8	0.7	Pre
3	1.0	1.0	1.5	1.5	1.5	Pre
4	1.5	1.2	1.5	1.5	1.5	Pre
5	0.7	0.7	0.8	1.0	1.0	Pre
6	0.15	0.1	0.15	0.2	0.2	1 month
7	0.7	1.0	1.0	1.5	1.5	Pre
8	1.2	1.2	1.5	1.5	1.5	Pre
9	0.5	0.7	0.8	0.9	0.9	Pre
10	0.2	0.3	0.4	0.4	0.7	1 month
11	0.5	0.5	0.4	0.5	0.4	12 months
12	0.7	0.7	0.9	0.9	0.9	Pre
13	0.9	0.9	1.0	1.0	1.5	Pre
14	0.9	0.7	1.0	1.5	1.2	Pre
Geomean**	0.649	0.657	0.785	0.917	0.942	

Notes: *The point when stable fixation was observed. 'pre' means the stable fixation was first observed already at pre-PDT.
Abbreviations: geomean, geometric mean; PDT, photodynamic therapy.

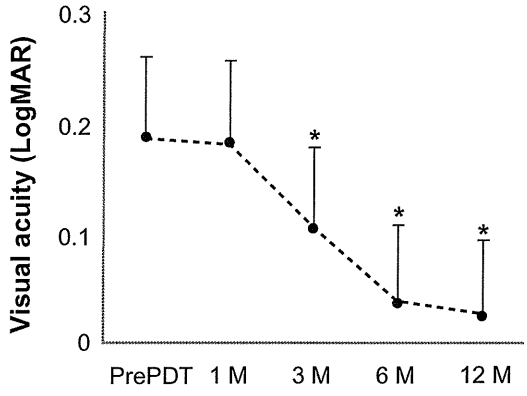


Figure 2 Mean best-corrected visual acuity in logarithm of the minimum angle of resolution units before and after half-dose verteporfin PDT in patients with chronic central serous chorioretinopathy.
Notes: The best-corrected visual acuity is significantly better at 3 months than at baseline. *$P < 0.0125$; Bars are the standard deviations.
Abbreviation: M, months; PDT, photodynamic therapy.

in improving not only sensitivity in the macular region, but also the stability of fixation.

We found that measuring retinal sensitivity and fixation stability by microperimetry was probably more important than determining just the visual acuity when evaluating CSC patients. This was because visual acuity is measured using high contrast letters under bright light conditions and does not represent the visual tasks of CSC patients in their daily lives.

We found that not only BCVA but also retinal sensitivity and fixation stability improved significantly after half-dose verteporfin PDT. In addition, retinal sensitivity improved significantly at just 1 month after PDT, while

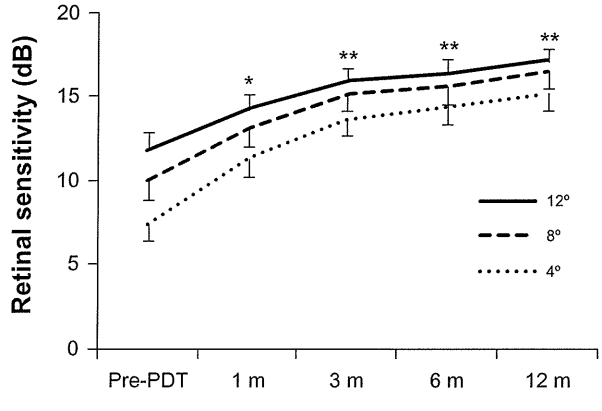


Figure 3 Mean retinal sensitivity in the central retinal areas of 4, 8, and 12 degrees before and after half-dose verteporfin PDT in patients with central serous chorioretinopathy.
Notes: There is significant improvement in sensitivity compared with baseline after 1 month. *$P < 0.0125$ in comparison of mean retinal sensitivity from central 4 and 8 degrees at 1 month after treatment. **$P < 0.0125$ in comparison of mean retinal sensitivity from central 4, 8, and 12 degrees at 3, 6, and 12 months. Bars show standard errors of the means.
Abbreviation: M, months; PDT, photodynamic therapy.

BCVA improved only after 3 months. It is interesting that all of the patients reported an improvement in their vision and symptoms.

Senturk et al[19] reported that both visual acuity and retinal sensitivity significantly improved at 1, 3, and 6 months after PDT in eyes with CSC. Reibaldi et al[22] reported that both visual acuity and retinal sensitivity significantly improved at 3 and 12 months after PDT in eyes with CSC.

Our study had a small sample number, no control subjects, and different durations of symptoms. These factors may partly explain the discrepancies between our results and those of Senturk et al[19] and Reibaldi et al.[22] However, these are quantitative differences and do not invalidate the effectiveness of half-dose verteporfin PDT. Reibaldi et al[22] also reported that retinal sensitivity in the central 12 degrees at 12 months after PDT was significantly higher in low fluence-treated eyes than in standard fluence-treated eyes.

A significant correlation was found between retinal sensitivity and BCVA as early as 6 months after treatment, and the difference decreased with time. Sensitivity in c4MP-1 were significantly correlated with BCVA at 3 months. This was expected because the retinal sensitivity from the smaller central area tends to reflect central foveal function. It was interesting that retinal sensitivity was lowest in the most central area and decreased with increasing eccentricity, ie, c4MP-1 < c8MP-1 < c12MP-1. One explanation for this is that the central retina might be more susceptible to the effects of serous retinal detachment because the mean greatest linear diameter in our cases was approximately 4700 μm, which covered the central retinal area containing the area of MP-1 measurements.

Sekine et al[25] investigated the relationship between retinal sensitivity measured by Humphrey visual field analyzer and morphological changes in eyes with CSC. They found a significant correlation between retinal sensitivity and height of the serous retinal detachment. It was striking that this correlation, like that of c4MP-1 < c8MP-1 < c12MP-1, lasted throughout the follow-up period of 12 months in our study. We suggest that the long-lasting sensitivity reduction was due to PDT. However, Ozdemir et al[9] reported that retinal sensitivity was lower in the central 10 degrees in eyes with resolved CSC than in control eyes. The sensitivity reduction in the central area was present even after spontaneous resolution.

Because visual acuity is good in cases of CSC, it is reasonable that fixation stability would also be good. In other words, unstable fixation might indicate greater impairment of central retinal function. Although our findings should be carefully interpreted because of a small sample size, it is

interesting that fixation stability at baseline was significantly correlated with final visual acuity at 12 months. Two cases with similar visual acuity and OCT appearances at baseline had different courses after PDT.

There are several studies describing the importance of fixation stability in evaluation of macular function after therapeutic intervention in retinal diseases.[21,26,27] Further studies are needed to determine whether fixation stability can be a predictive factor for BCVA after half-dose verteporfin PDT in eyes with CSC.

Our study has several limitations, such as a relatively small sample size and no control group. Further prospective studies with control groups in larger series will be necessary to determine the efficacy of half-dose verteporfin PDT or any other treatment on the retinal sensitivity and fixation stability in eyes with CSC.

In conclusion, retinal sensitivity and BCVA improved or was maintained after half-dose verteporfin PDT. Our findings indicate that it is important to determine retinal sensitivity and fixation stability when evaluating the effect of PDT on eyes with CSC. These parameters may be useful indicators of the effectiveness of treatment.

Acknowledgment

This study was supported by Research on Sensory and Communicative Disorders from the Ministry of Health, Labor, and Welfare, Japan, and is registered at clinicaltrials.gov (NCT01434095).

Disclosure

The authors report no conflicts of interest in this work.

References

1. Spaide RF. Central serous chorioretinopathy. In: Holz FG, Spaide RF, editors. *Medical Retina*. Heidelberg, Germany: Springer Verlag; 2004.
2. Nagata M, Honda Y. Studies on local electric response of the human retina. VI. Macular ERGs of a typical central serous retinopathy. *Nippon Ganka Gakkai Zasshi*. 1970;74:957–964. Japanese.
3. Folk JC, Thompson HS, Han DP, Brown CK. Visual function abnormalities in central serous retinopathy. *Arch Ophthalmol*. 1984;102:1299–1302.
4. Chuang EL, Sharp DM, Fitzke FW, et al. Retinal dysfunction in central serous retinopathy. *Eye (Lond)*. 1987;1:120–125.
5. Miyake Y, Shiroyama N, Ota I, Horiguchi M. Local macular electroretinographic responses in idiopathic central serous chorioretinopathy. *Am J Ophthalmol*. 1988;106:546–550.
6. Marmor MF, Tan F. Central serous chorioretinopathy: bilateral multifocal electroretinographic abnormalities. *Arch Ophthalmol*. 1999;117:184–188.
7. Maaranen TH, Tuppurainen KT, Mäntyjärvi MI. Color vision defects after central serous chorioretinopathy. *Retina*. 2000;20:633–637.
8. Springer C, Bültmann S, Völcker HE, Rohrschneider K. Fundus perimetry with the Micro Perimeter 1 in normal individuals: comparison with conventional threshold perimetry. *Ophthalmology*. 2005;112:848–854.
9. Ozdemir H, Karacorlu SA, Senturk F, Karacorlu M, Uysal O. Assessment of macular function by microperimetry in unilateral resolved central serous chorioretinopathy. *Eye (Lond)*. 2008;22:204–208.
10. Ojima Y, Tsujikawa A, Hangai M, et al. Retinal sensitivity measured with the micro perimeter 1 after resolution of central serous chorioretinopathy. *Am J Ophthalmol*. 2008;146:77–84.
11. Yannuzzi LA, Slakter JS, Gross NE, et al. Indocyanine green angiography-guided photodynamic therapy for treatment of chronic central serous chorioretinopathy: a pilot study. *Retina*. 2003;23:288–298.
12. Cardillo Piccolino F, Eandi CM, Ventre L, Rigault de la Longrais RC, Grignolo FM. Photodynamic therapy for chronic central serous chorioretinopathy. *Retina*. 2003;23:752–763.
13. Chan WM, Lam DS, Tam BS, Liu DT, Chan CK. Choroidal vascular remodeling in central serous chorioretinopathy after indocyanine green guided photodynamic therapy with verteporfin: a novel treatment at the primary disease level. *Br J Ophthalmol*. 2003;87:1453–1458.
14. Schlötzer-Schrehardt U, Viestenz A, Naumann GO, Laqua H, Michels S, Schmidt-Erfurth U. Dose-related structural effects of photodynamic therapy on choroidal and retinal structures of human eyes. *Graefes Arch Clin Exp Ophthalmol*. 2002;240:748–757.
15. Schmidt-Erfurth U, Laqua H, Schlotzer-Schrehard U, Schlötzer-Schrehard U, Viestenz A, Naumann GO. Histopathological changes following photodynamic therapy in human eyes. *Arch Ophthalmol*. 2002;120:835–844.
16. Lee JY, Chae JB, Yang SJ, Kim JG, Yoon YH. Intravitreal bevacizumab versus the conventional protocol of photodynamic therapy for treatment of chronic central serous chorioretinopathy. *Acta Ophthalmol*. 2011;89:e293–e294.
17. Chan WM, Lai TY, Lai RY, Liu DT, Lam DS. Half-dose verteporfin photodynamic therapy for acute central serous chorioretinopathy: one-year results of a randomized controlled trial. *Ophthalmology*. 2008;115:1756–1765.
18. Lim JW, Kang SW, Kim YT, Chung SE, Lee SW. Comparative study of patients with central serous chorioretinopathy undergoing focal laser photocoagulation or photodynamic therapy. *Br J Ophthalmol*. 2011;95:514–517.
19. Senturk F, Karacorlu M, Ozdemir H, Karacorlu SA, Uysal O. Microperimetric changes after photodynamic therapy for central serous chorioretinopathy. *Am J Ophthalmol*. 2011;151:303–309.
20. Reibaldi M, Boscia F, Avitabile T, et al. Low-fluence photodynamic therapy in longstanding chronic central serous chorioretinopathy with foveal and gravitational atrophy. *Eur J Ophthalmol*. 2009;19:154–158.
21. Reibaldi M, Cardascia N, Longo A, et al. Standard-fluence versus low-fluence photodynamic therapy in chronic central serous chorioretinopathy: a nonrandomized clinical trial. *Am J Ophthalmol*. 2010;149:307–315.
22. Reibaldi M, Boscia F, Avitabile T, et al. Functional retinal changes measured by microperimetry in standard-fluence vs low-fluence photodynamic therapy in chronic central serous chorioretinopathy. *Am J Ophthalmol*. 2011;151:953–960.
23. Fujita K, Yuzawa M, Mori R. Retinal sensitivity after photodynamic therapy with half-dose verteporfin for chronic central serous chorioretinopathy: short-term results. *Retina*. 2011;31:772–778.
24. Fujii GY, De Juan E Jr, Humayun MS, Sunness JS, Chang TS, Rossi JV. Characteristics of visual loss by scanning laser ophthalmoscope microperimetry eyes with subfoveal choroidal neovascularization secondary to age-related macular degeneration. *Am J Ophthalmol*. 2003;136:1067–1078.

25. Sekine A, Imasawa M, Iijima H. Retinal thickness and perimetric sensitivity in central serous chorioretinopathy. *Jpn J Ophthalmol*. 2010;54:578–583.
26. Pearce E, Sivaprasad S, Chong NV. Comparing fixation location and stability in patients with neovascular age-related macular degeneration treated with or without ranibizumab. *Eye (Lond)*. 2010;25:149–153.
27. Senturk F, Ozdemir H, Karacorlu M, Karacorlu SA, Uysal O. Microperimetric changes after intravitreal triamcinolone acetonide injection for macular edema due to central retinal vein occlusion. *Retina*. 2010;30:1254–1261.

Case Reports in Ophthalmology

Case Rep Ophthalmol
DOI: 10.1159/000345507

Published online:
■■■, 2012

ISSN 1663–2699
www.karger.com/cop

Acute Visual Field Defect following Vitrectomy Determined to Originate from Optic Nerve by Electrophysiological Tests

Atsuro Uchida[a] Kei Shinoda[a, b] Celso Soiti Matsumoto[b]
Miho Kawai[a] Sayaka Kawai[b] Hisao Ohde[a, d]
Yoko Ozawa[a] Susumu Ishida[e] Makoto Inoue[c]
Atsushi Mizota[b] Kazuo Tsubota[a]

[a]Department of Ophthalmology, Keio University School of Medicine, [b]Department of Ophthalmology, Teikyo University School of Medicine, University Hospital Itabashi, and [c]Department of Ophthalmology, Kyorin Eye Center, Kyorin University School of Medicine, Tokyo, [d]Makuhari Ode Eye Clinic, Chiba, and [e]Department of Ophthalmology, Hokkaido University School of Medicine, Sapporo, Japan

Key Words
Ischemic optic neuropathy · Proliferative diabetic retinopathy · Multifocal electroretinogram · Multifocal visual evoked potentials · Photopic negative response

Abstract
Purpose: To present our findings on the cause of an acute visual field defect (VFD) that developed in a patient on the day after vitrectomy for proliferative diabetic retinopathy.
Case: A 50-year-old man complained of a blind area in the superior visual field that developed one day after vitrectomy. The patient had undergone uncomplicated vitrectomy for a long-duration vitreous hemorrhage associated with proliferative diabetic retinopathy. Residual vitreous hemorrhage hampered a clear view of the fundus. Goldmann perimetry showed a horizontal VFD in the superior field. The area corresponding to the VFD was examined by multifocal electroretinograms (mfERGs) and multifocal visual evoked potentials (mfVEPs). The amplitudes of the mfVEPs were reduced with prolonged implicit times especially when the superior hemifield was stimulated, while the amplitudes and implicit times were within the normal range when other parts of the visual field were stimulated. In addition, the full-field photopic ERGs and photopic negative responses were attenuated in the right eye. These findings suggested that the VFD did not originate from alterations in the retinal inner and middle layer but in the ganglion cells. The visual acuity improved to 1.2 but his optic disc became pale and the VFD remained unchanged more than 12 years after the surgery.

Kei Shinoda, MD

Department of Ophthalmology
Teikyo University School of Medicine
2-11-1 Kaga, Itabashi-ku, Tokyo 173-8605 (Japan)
E-Mail shinodak@med.teikyo-u.ac.jp

Case Rep Ophthalmol
DOI: 10.1159/000345507
Published online:
■■■, 2012

ISSN 1663–2699
www.karger.com/cop

Conclusion: We suggest that vitrectomy can cause ischemic optic neuropathy by interfering with the circulation associated with diabetes mellitus. Evaluations by mfERGs, mfVEPs, and full-field photopic ERGs were helpful in making the diagnosis.

Introduction

The visual function after vitrectomy depends on many factors, e.g., the underlying vitreoretinal disease, surgical procedures, and complications in either the anterior or posterior segments of the eye. Visual field defects (VFDs) are known to be a postsurgical complication, and they can be caused by retinochoroidal circulatory disturbances [1, 2], nerve fiber damage due to excessive exposure to dry air [3–5], optic nerve damage due to retrobulbar anesthesia [6–9], phototoxicity [10], and elevation of the intraocular pressure [11]. We report our findings in a patient who developed a severe VFD on the day following an uncomplicated vitrectomy for a vitreous hemorrhage associated with proliferative diabetic retinopathy [12]. A tentative diagnosis of ischemic optic neuropathy (ION) was made from the acute onset, superior hemianopsia, and the results of electrophysiological tests. We re-examined the patient after 10 years, and the VFD and the electrophysiological results remained unchanged. We conclude that our original diagnosis was correct, and also that the electrophysiological findings were critical in determining the pathological site of the VFD.

Case Report

A 50-year-old man underwent uncomplicated vitrectomy on September 22, 1998 for a vitreous hemorrhage of 2 months duration which was associated with proliferative diabetic retinopathy. His preoperative best-corrected visual acuity (BCVA) was hand movements in the right eye and 1.2 in the left eye. He underwent conventional pars plana vitrectomy, and no complications were encountered during the surgical procedures. His blood pressure increased to 176/107 mm Hg just before the surgery, but it decreased and became stable between 116–140/70–90 mm Hg intra- and postoperatively.

The patient complained of a blind area in the superior visual field of the right eye on the day after the vitrectomy (fig. 1a). His decimal BCVA was 0.02 in the right eye. The residual vitreous hemorrhage hampered a clear view of the fundus. On the second day after surgery, flash visual evoked potentials (VEPs) and full-field single-flash electroretinograms (ERGs) were recorded simultaneously [13]. The recording electrodes for the ERGs were attached to the surface of the lower eyelids to avoid using a contact lens electrode.

The implicit times of the flash VEPs were slightly delayed in both eyes and no difference was found between the eyes (fig. 2). The amplitudes of the a- and b-waves of the full-field ERGs were normal but the oscillatory potentials were slightly reduced in both eyes. However, no differences were found between the eyes (fig. 2). At that time, we did not evaluate the photopic negative response (PhNR) because its origin had not fully been determined.

Blood tests showed no abnormalities in the erythrocyte sedimentation rate, blood coagulation factor, C-reactive protein, and complete blood count. The results for antinuclear antibody were negative. ION was suspected because of the acute onset, horizontal hemianopsia, normal full-field ERGs, and diabetes.

Oral carbazochrome and kallidinogenase were started. The fundus became more visible one week after the surgery, and the BCVA improved to 0.7. Ophthalmoscopy showed localized edema adjacent

Case Rep Ophthalmol
DOI: 10.1159/000345507
Published online:
■■■, 2012

ISSN 1663–2699
www.karger.com/cop

to the optic disc (fig. 3a). The arm-to-retina time of the fluorescein angiography (fig. 3b) was delayed, and an island-like hypofluorescence surrounded by a hyperfluorescent region was present inferior to the optic disc.

Multifocal ERGs (mfERGs) and multifocal VEPs (mfVEPs) were recorded approximately two weeks after the surgery according to the ISCEV standard [14, 15]. The amplitudes of the mfERGs (fig. 4a) were within the normal range over the central retinal area, while the amplitudes of the mfVEPs (fig. 4b) were reduced and the implicit times prolonged especially those elicited by stimulating the superior hemifield of the right eye. These findings suggested that the VFD did not originate in the retinal inner and middle layer but was of ganglion cell origin.

The visual acuity improved to 1.2 in one month and has been stable for 12 years in the right eye, but the optic disc gradually became paler especially in the inferior region (fig. 3c). Fluorescein angiography (fig. 3d) showed a delayed arm-to-retina time and a semicircular hypofluorescent region inferior to the optic disc. The VFD remained unchanged for more than 12 years after the surgery (fig. 1b). Optical coherence tomography (Spectralis OCT, Heidelberg Engineering, Germany) performed 12 years after the vitrectomy demonstrated a selective atrophy of the nerve fiber layer inferior to the optic disc in the right eye (fig. 3e).

A re-examination of the PhNR of the photopic ERGs recorded at the initial examination showed that it was selectively reduced in the right eye (table 1 and table 2). These findings strongly supported our initial diagnosis of ION.

Discussion

Several mechanisms have been reported to explain the VFDs after vitreous surgery: phototoxicity due to the bright light from the operating microscope or endoillumination [16, 17], intra- or postoperative fluctuations of the intraocular pressure and/or systemic blood pressure [18–20], mechanical stress on the optic nerve during the creation of a posterior vitreous detachment [21], chemicophysical stress on the retina by dry air during fluid-air exchange [3], retinal damage due to panretinal photocoagulation [22], optic nerve damage due to retrobulbar anesthesia [6–9], and damage to the optic nerve because of the compromised circulation associated with diabetes mellitus [23–25].

Our case was initially diagnosed with ION because of the acute superior horizontal VFD. The attenuated mfVEPs corresponding to the VFD and normal mfERGs suggested that the pathological site was not in the outer and middle layers of the retina but the ganglion cells and/or optic nerve. This supported our initial diagnosis.

Little information is available of cases that developed ION after vitrectomy [18, 26]. Pendergast et al. [18] reported on a 73-year-old woman with coronary artery disease who developed ION 4 months after vitrectomy. Taban et al. [26] reported on two cases, a 65-year-old woman with hypertension and diabetes mellitus who developed ION at 3.5 weeks after vitrectomy, and a 94-year-old man with hypertension whose visual acuity was found to be reduced on postoperative day 34. Both were diagnosed with ION but the etiology of the ION was not determined. Taban et al. [26] also found 190 cases that developed a VFD after vitrectomy, and approximately 20% of these had evidence of optic nerve damage, relative afferent pupillary defect, or optic nerve pallor. They stated that in spite of the fact that the etiology of the VFD remains undetermined, VFD as a complication of vitreous surgery is relatively common. We suggest that circulatory disturbances associated with diabetes mellitus might have played some part in our case.

Case Rep Ophthalmol
DOI: 10.1159/000345507
Published online:
■■■, 2012

ISSN 1663–2699
www.karger.com/cop

No obvious difference was found between the mfERGs from the superior and inferior retina which also supports our suggestion that the VFD did not originate in the inner and middle retinal layer but was of ganglion cell and/or optic nerve origin. Furthermore, the selectively reduced PhNR in the right eye strongly supported this idea, although we did not use this test in 1998. The PhNR has been reported to be a sensitive test to determine functional alterations of ganglion cells, and its clinical application has been extended [28–30]. Our case highlights the importance of the PhNR in differentiating ganglion cell damage in patients with VFD after surgery. It is, however, difficult to determine whether the ganglion cells or optic nerve was the exact origin in the present case. We believe that it is more likely that the ganglion cell damage was related to ION.

In summary, electrophysiological evaluations were helpful in making a diagnosis in our case. The mfERGs, mfVEPs, and PhNR were useful in determining the pathological site of the VFD that occurred after vitrectomy.

Acknowledgements

Support of this study was provided by Research Grants on Sensory and Communicative Disorders from the Ministry of Health, Labor, and Welfare, Japan.

Disclosure Statement

No author has a financial or proprietary interest in any material or method mentioned.

Table 1. Amplitude and implicit time of the P-100 in flash VEPs

Stimulus intensity	Right		Left		R-L	
	Amp., μV	Imp.T., ms	Amp., μV	Imp.T., ms	Amp., μV	Imp.T., ms
0.3 J						
ND-3	3.4	130	2.4	138	1.00	−8.00
ND-2	5.4	117.5	5	130	0.40	−12.50
ND-1	6.3	127.5	11.6	130	−5.30	−2.50
ND-0	9.9	126.3	8.9	125	1.00	1.30
2.0 J	4.9	105	5.6	105	−0.70	0.00

Amp. = Amplitude; Imp.T. = implicit time.

Case Rep Ophthalmol
DOI: 10.1159/000345507
Published online:
■■■, 2012

ISSN 1663–2699
www.karger.com/cop

Table 2. Amplitude and implicit time of the a- and b-waves and PhNR in each eye

Stimulus intensity	Right					Left					R-L				
	Amp., μV			Imp.T., ms		Amp., μV			Imp.T., ms		Amp., μV			Imp.T., ms	
	a-wave	b-wave	PhNR	a-wave	b-wave	a-wave	b-wave	PhNR	a-wave	b-wave	a-wave	b-wave	PhNR	a-wave	b-wave
0.3 J															
ND-3	0	2.24	2.24	45	82.5	0.56	2.24	1.4	60	80	−0.56	0.00	0.84	−15.00	2.50
ND-2	0.56	0.84	2.8	80	90	1.68	3.36	1.96	47.5	90	−1.12	−2.52	0.84	32.50	0.00
ND-1	0	5.32	7.84	40	65	0.84	5.32	10.08	42.5	65	−0.84	0.00	−2.24	−2.50	0.00
ND-0	1	8.4	8.4	42.5	70	6.16	17.08	13.16	45	70	−5.16	−8.68	−4.76	−2.50	0.00
2.0 J	6.16	14.56	12.04	37.5	60	7.28	17.08	23.8	45	67.5	−1.12	−2.52	−11.76	−7.50	−7.50

Amp. = Amplitude; Imp.T. = implicit time.

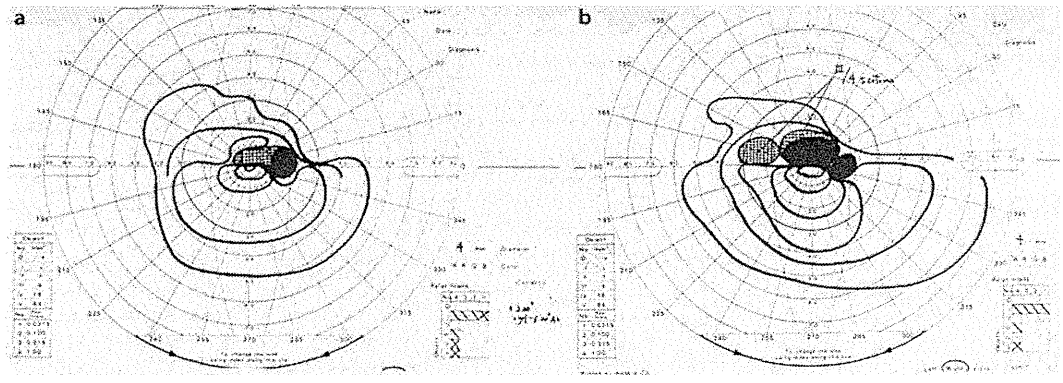


Fig. 1. Goldmann perimetry performed on the day after vitrectomy and again more than one year after surgery. The V-4 isoptor is constricted in the superior and temporal-superior visual field, and the internal isoptor shows a superior hemianopsia on the following day (**a**). The superior hemianopsia remained unchanged (**b**).

Case Rep Ophthalmol
DOI: 10.1159/000345507

Published online:
■■■, 2012

ISSN 1663–2699
www.karger.com/cop

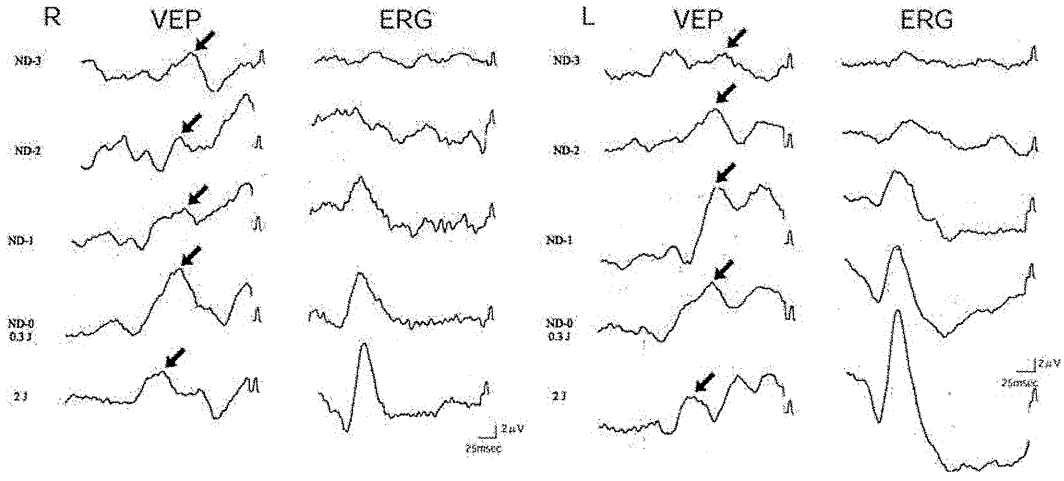


Fig. 2. Simultaneously recorded flash VEPs and full-field single-flash ERGs. No significant differences were found between the two eyes in the amplitude and implicit times of N-70 and P-100 in the flash VEPs. The photopic ERGs recorded with skin electrodes showed no obvious differences between the eyes in the amplitude and implicit times of the a- and b-waves, but the amplitudes of the PhNR were reduced in the right eye. The arrow points to P-100. The values of the amplitudes and implicit times are shown in table 1 and 2.

Case Rep Ophthalmol
DOI: 10.1159/000345507
Published online:
■■■, 2012
© 2012 S. Karger AG, Basel
ISSN 1663–2699
www.karger.com/cop

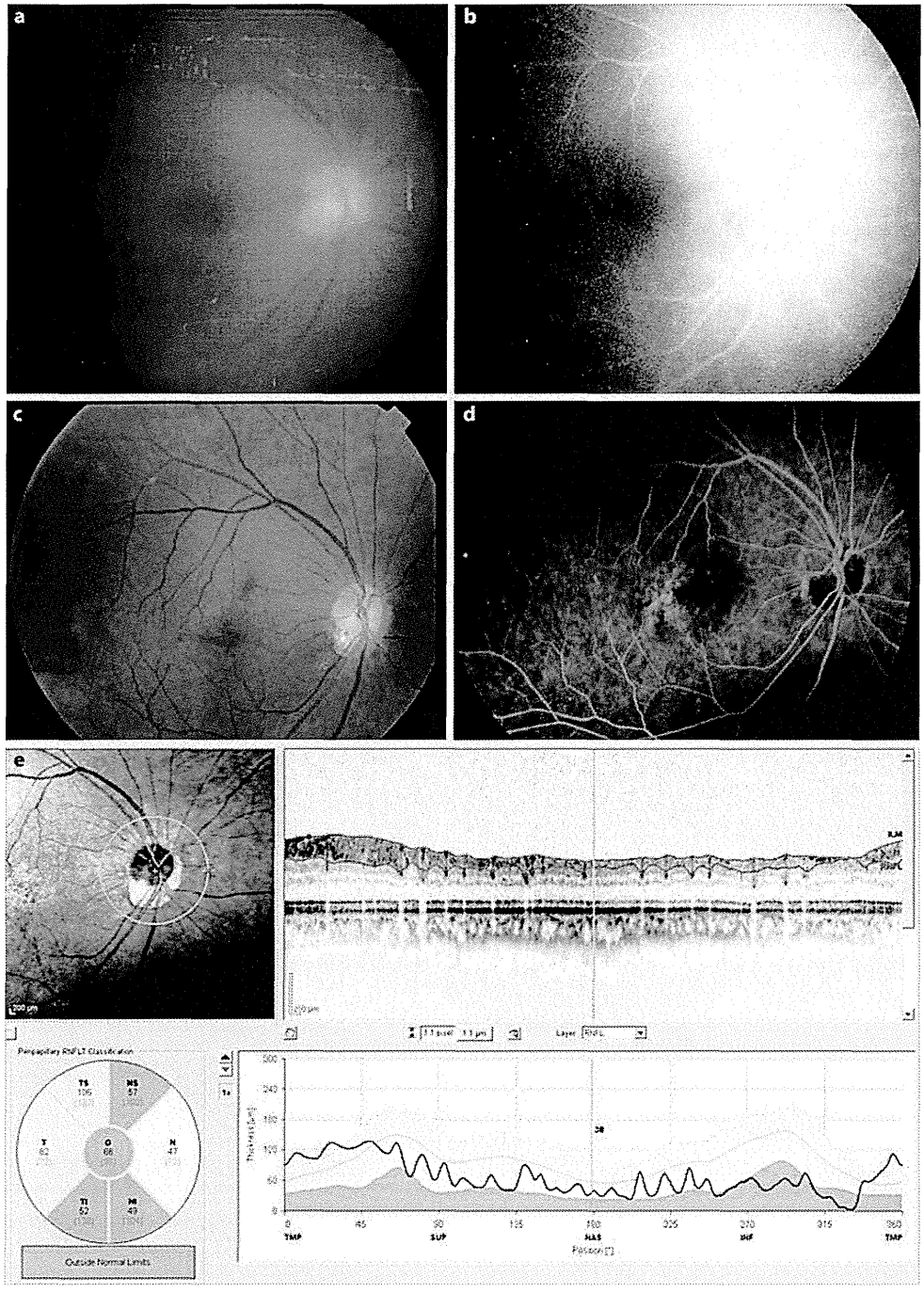


Fig. 3. Fundus photograph, fluorescein angiogram, and optical coherence tomographic images. **a** Fundus photograph taken one week after surgery showed localized edema adjacent to the optic disc. **b** Fluorescein angiogram obtained on the same day as that in **a** shows a delayed arm-to-retina time and island-like hypofluorescence surrounded by a hyperfluorescent region inferior to the optic disc. **c** Fundus photograph taken 10 years after surgery shows a pale optic disc especially in the inferior region. Visual acuity was 1.2. **d** Fluorescein angiogram obtained on the same day as **c** shows a delay in the arm-to-retina time and semicircular hypofluorescent region inferior to the optic disc. **e** The optic nerve fiber layer thickness analysis using optical coherence tomography (Spectralis OCT, Heidelberg Engineering, Germany) performed 12 years after vitrectomy showing selective atrophy of inferior nerve fiber layer around optic disc in the right eye.

Case Rep Ophthalmol
DOI: 10.1159/000345507

Published online:
■■■, 2012

ISSN 1663–2699
www.karger.com/cop

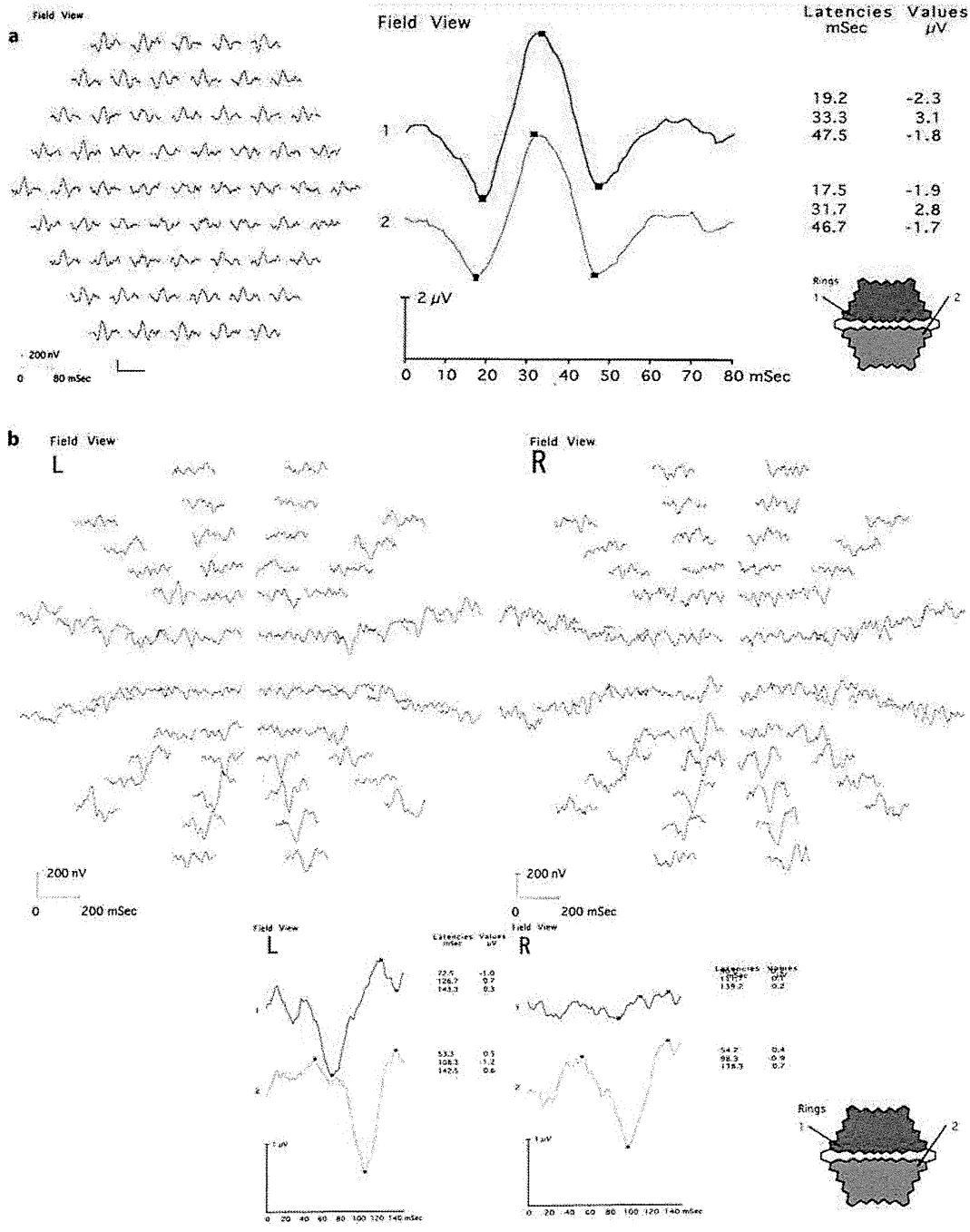


Fig. 4. Multifocal ERGs and VEPs recorded one week after the vitreous surgery. **a** The amplitudes and the implicit times of the mfERGs from the right eye are within the normal range. **b** The mfVEP showed amplitude reduction and delayed implicit time especially from superior hemifield in the right eye.