Original article

Role of intravitreal ranibizumab for rapid recovery of central serous chorioretinopathy

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ABSTRACT

Background: Central serous chorioretinopathy (CSCR) is an idiopathic disorder in which there is leakage of fluid from hyper permeable choriocapillaris and the collection of fluid between neurosensory and neuropigmentry retina in the macular area that is responsible for decrease visual acuity. CSCR may be acute or chronic. Various treatment options include simple observation, argon laser photocoagulation of the leaking spot, photodynamic therapy (PDT), oral ketoconazole and oral rifampicin are available. Ranibizumab is a monoclonal antibody fragment that act as vascular endothelial growth factor inhibitor, stabilize blood retinal barrier and decrease leakage from choriocapillaris. This study aims to evaluate the role of intravitreal ranibizumab for rapid recovery in central serous chorioretinopathy.

Patients and methods: This descriptive case series was carried out at Department of Ophthalmology, Nishtar Medical University Multan, Pakistan from 01-10-2019 till 30-04-2020. The study included twelve eyes of twelve patients suffering from acute CSCR. All patients were given a single injection of intravitreal ranibizumab (0.5mg/0.05ml) as a primary treatment and followed for two months after injection at one week, one month and two months interval to document efficacy of intravitreal ranibizumab. At each baseline and follow up visits, dilated fundus examination was carried out, ending up with patients' best corrected visual acuity. Central retinal thickness (CRT) was also recorded and results were compared with prior visit results of patients. Major outcomes were the improvement in visual acuity and decrease in CRT. Baseline CRT values were also compared with post injection CRT values at one week, one month and two months intervals using paired sample t-test and best corrected visual acuity (BCVA) was compared using chi–square test.

Results: Mean age of the patients was 39.6 years with a male to female ratio of 9:1. Best corrected visual acuity was 6/60 on Snellen chart at baseline. All patients exhibited mean improvement of best corrected visual acuity of three Snellen lines after one week. Eleven patients were back to best corrected visual acuity of 6/6 after one month. Remaining one patient gained best corrected visual acuity of 6/6 after two months of post injection. The mean CRT at presentation was 500 ± 80U (range; 386–580) which reduced significantly to 272 ± 52 U (range 220–338) from baseline after one month showing significant reduction ($p<0.001$). At the last follow-up visit, the CRT was measured 230 ± 20 U (range 220—250) which shows complete resolution of sub-retinal fluid.

Conclusion: Intravitreal ranibizumab can be used for rapid absorption of sub-retinal fluid in acute CSCR and significant reduction in CRT along with improvement in BCVA indicate that it may be safely employed in CSCR to achieve better clinical outcomes.

Keywords:
Intravitreal ranibizumab, Central serous chorioretinopathy, Central retinal thickness

INTRODUCTION

Central serous chorioretinopathy (CSCR) is a rare disorder of young adults. Its prevalence is more common in males between the ages of 20 to 50 years.[1] Women with CSCR tend to be older. The disease is idiopathic characterized by collection of sub–retinal fluid and detachment of the sensory retina in macular area due to leakage from the choriocapillaris.[2] Patients with CSCR usually present with the symptoms of reduced visual acuity, metamorphopsia, color vision changes, micropsia and a positive scotoma caused detachment in macular area. The disease may be acute or chronic. Exact pathophysiology is not well understood but there are some risk factors associated with CSCR including pregnancy, *Helicobacter pylori* infection, steroid administration, psychological stress and sleeping apnea syndrome. Patients with CSCR shows impaired auto-regulation of choroidal circulation, increase sympathetic and decrease parasympathetic activity and up regulation adrenergic receptors.[3] All these effects are believed to be the reason of increased levels of serum cortisol and epinephrine.[4] Different treatment modalities include; simple observation, administration of pharmacological agents (oral adrenergic blockers, rifampicin, corticosteroids like ketoconazole), photocoagulation of extrafoveal leaking

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spot, micro-pulse diode laser, intravitreal anti-VEGF (an anti-vascular endothelial growth factor) agents (bevacizumab) and photodynamic therapy with vertaporin. However, none of these have proven to be curative.[6-8] Indocyanine green (ICG) angiography demonstrated choroidal vascular hyper permeability and hence leakage and accumulation of subretinal fluid which can leads to RPE decompensation in pathogenesis of CSCR.[9] Therefore, it seems logical to treat CSCR with agents which have ability to decrease choroidal vascular hyper permeability and stabilize blood retinal barrier.[10] Ranibizumab, a humanized IgG1 monoclonal antibody fragment that lack Fc portion of antibody, is an anti-VEGF agent that is manufactured with recombination technology. In the eye, ranibizumab binds to VEGF-A receptors and blocks the interaction of VEGF with its receptors thereby preventing the formation of new blood vessels. Ranibizumab stabilizes the blood retinal barrier and decreases choroidal vascular permeability.[10,11] Its use has been proven in many ocular pathologies for example, wet form of age related macular degeneration, macular oedema secondary to central retinal vein occlusion and branch retinal vein occlusion and diabetic macular edema. Therefore, current study aims to evaluate the efficacy of ranibizumab in rapid recovery of CSCR patients.

PATIENTS AND METHODS

This descriptive case series was carried out at Department of Ophthalmology, Nishter Medical University Multan from 01-10-2019 to 30-04-2020 including twelve eyes of twelve patients with acute CSCR diagnosed by fundus examination and optical coherence tomography (OCT). Patients with no secondary cause of reduced vision, sensory macular detachment, presence of sub-retinal fluid and increased central retinal thickness evident on OCT were included. Patients with less capability to follow or comply with study-related procedures, history of treatment with photodynamic therapy, history of cerebrovascular accident in last six months, history of transient ischemic attacks and history of treatment of leaking spot with argon laser were excluded from the study. All study participants were informed about the nature of the disease, different available treatment options, benefits and drawbacks of each treatment. They were also informed about the different procedural steps, benefits and possible complications. Topical anesthetic drops instilled into the corresponding eye for two minutes before procedure. The eye was draped as for cataract surgery, with insertion of a speculum and cleaning with 5% povidone-iodine. Inferotemporal quadrant was marked and measured with caliper (4 mm from the limbus in phakic eyes and 3.5 mm from limbus in pseudophakic eyes). All CSCR patients were given single injection of intravitreal ranibizumab (0.5mg/0.05ml) as primary treatment. Patients were followed for two months after injection at one week, one month and two months interval to document efficacy of intravitreal ranibizumab. At baseline and each follow up visits dilated fundus examination were carried out, patients best corrected visual acuity, central retinal thickness were recorded and compared with previous visits. Post injection oral and topical antibiotic was given for 3 days to all patients.

All findings at baseline and at each follow up visit were recorded and compared with previous results. Baseline CRT values were compared with post injection CRT values at one week, one month and two months intervals using paired sample t-test and BCVA was compared using chi–square test analyzed on SPSS version 23. A p-value of ≤ 0.05 was considered as significant.

RESULTS

Mean age of the participants was 39.6 ± 8.69 years (range 20-51 years). The male to female ratio was 9:1. The mean BCVA at presentation was 6/36. All the patients after receiving intravitreal ranibizumab presented mean improvement of best corrected visual acuity of 3 Snellen's line after one weak and 98% of patients were back to best corrected visual acuity of 6/6 after one month. The remaining 2% improved to BCVA of 6/6 after 2 months of injection. Mean CRT was decreased significantly from 500 ± 80U (range; 386–580) to 330 ± 60U (range; 276-360) ($p=0.02$) at first follow up visit after one week. Furthermore, the mean CRT at one month was 272 ± 52 U (range 220–338) showing significant reduction ($p<0.001$) from baseline values. At last follow up visit, the CRT was 230 ± 20 U (range 220—250) which shows complete resolution of sub-retinal fluid. Significant reduction of central retinal thickness in OCT these patients is shown in Figures 1-8 which was correlated with the improvement in BCVA (Table 1).

DISCUSSION

Indocyanine angiography (ICG) revealed that in CSCR basic defect is choroidal vascular hyper permeability which leads to leakage of fluid in sub-retinal space and retinal pigment epithelial dysfunction in both acute and

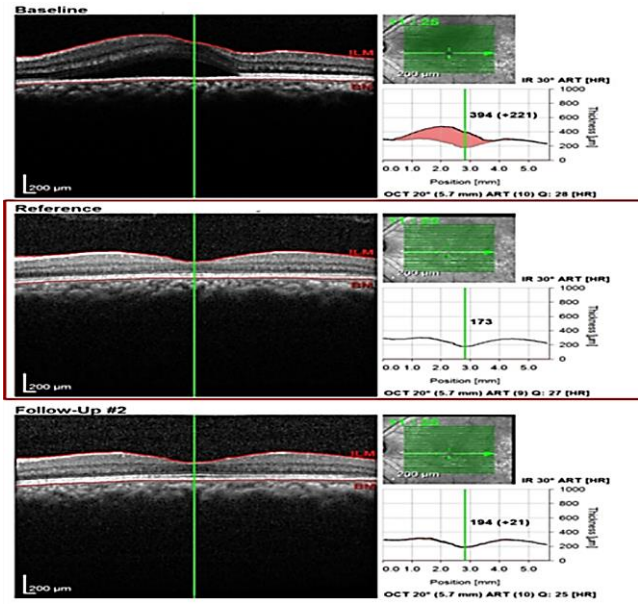

Figure 1. OCT of the patient showing retinal thickness at presentation 1st and 2nd post injection follow up

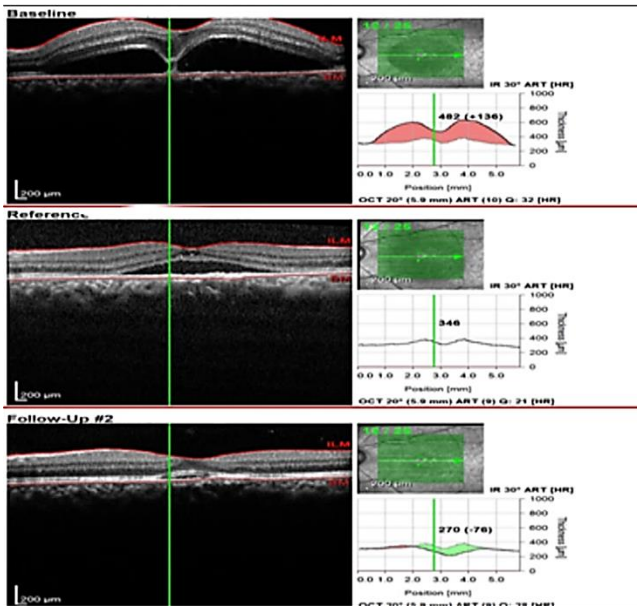

Figure 3. OCT of the patient showing central central retinal thickness at baseline 1st and 2nd post injection follow up

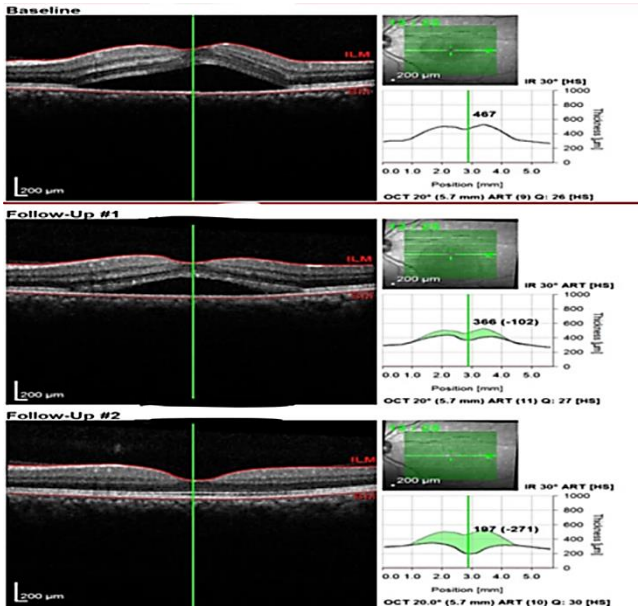

Figure 2. OCT of the patient showing central retinal thickness at baseline 1st and 2nd post injection follow up

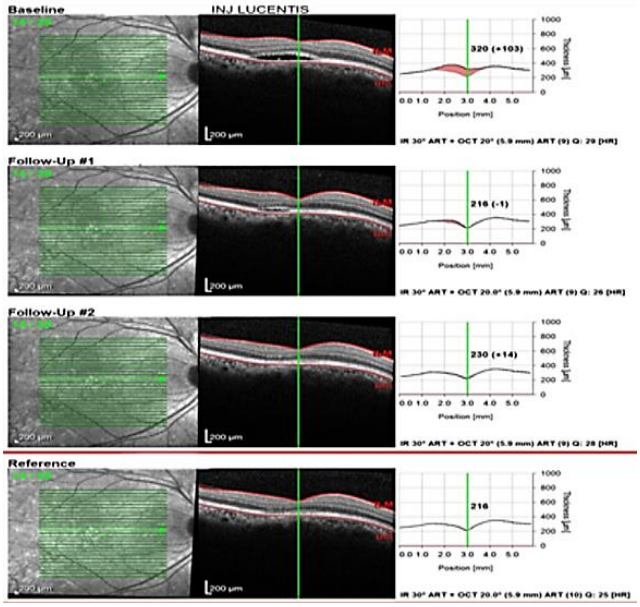

Figure 4. OCT of the patient showing central retinal thickness at baseline 1st and 2nd post injection follow up

chronic CSCR.[12] Wang and colleagues reported that prolonged detachment of sensory retina at the macular area may lead to retinal pigment epithelial (RPE) cell decompensation and atrophy of photoreceptors.[13] So resorption of fluid and reattachment of sensory retina should occur within four months to avoid complications. Hence observation for more than four months is not a therapeutic option. Argon laser can only be applied to extrafoveal leaking spot not the juxta or sub foveal leaking spot. Stewart and coworkers reported that argon laser can damage the RPE which can lead to choroidal neo vascularization (CNV) which may later lead to scarring on macular area.[14] Hence new treatment options are needed that are more effective with no side effects. Piccolino and associates reported that with photodynamic therapy (PDT) there is rapid resorption

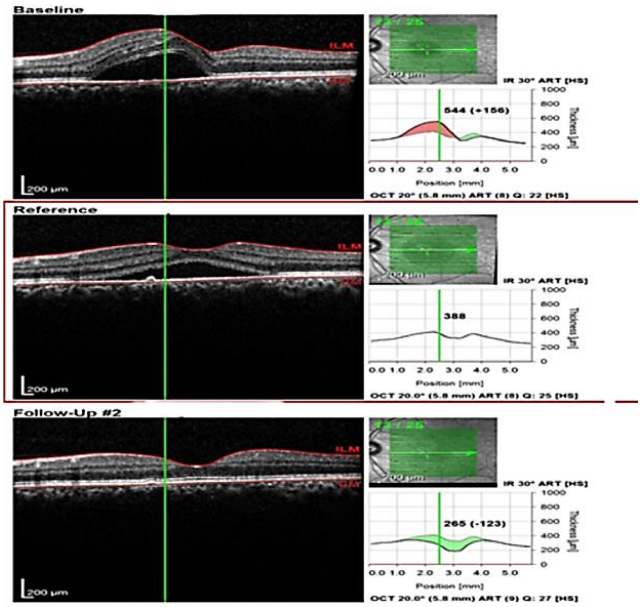

Figure 5. OCT of the patient showing central retinal thickness at baseline 1st and 2nd post injection follow up

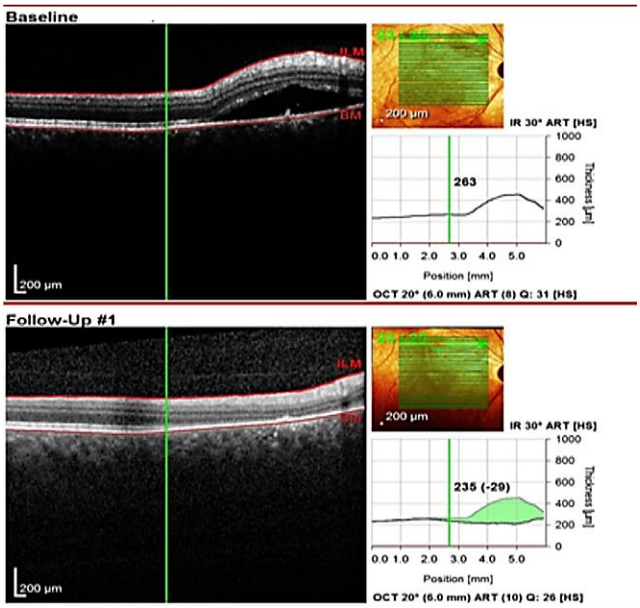

Figure 7. OCT of the patient showing central retinal thickness at baseline 1st and 2nd post injection follow up

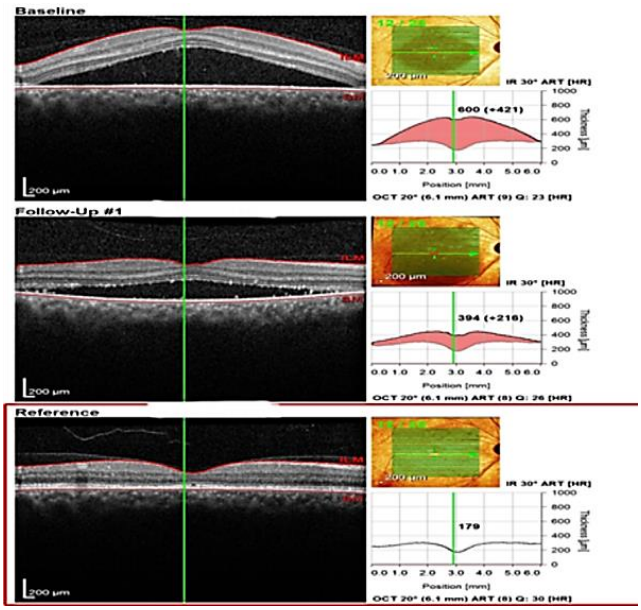

Figure 6. OCT of the patient showing central retinal thickness at baseline 1st and 2nd post injection follow up

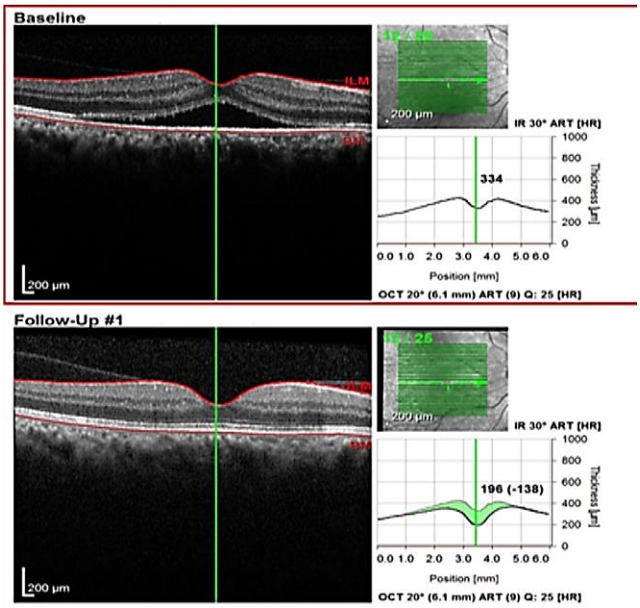

Figure 8. OCT of the patient showing central retinal thickness at baseline 1st and 2nd post injection follow up

Table 1. Improvement in BCVA and decrease in CRT data

Timing	Mean (±SD) range CRT (U)	Dif.CRT (U)	p-value	Mean BCVA	p-value
Baseline	500 ± 80U (range; 386–580)			6/36	
1 week	330 ± 60U (range , 276-360)	170	<0.02	6/18	<0.01
1 month	272 ± 52 U (range 220–338)	228	<0.02	6/6	<0.01
2 month	230 ± 20 U (range 220—250)	270	<0.001	6/6	<0.003

of sub-retinal fluid and decrease in CRT for CSCR patients.[15] However PDT may lead to pigmentary mottling and choroidal neovessels formation in the macular area due to ischemia of choriocapillaris in treatment zone which may lead to permanently reduced vision.

In this study, inravitreal ranibizumab was used for treatment of patients with acute CSCR for rapid recovery as most patients with acute CSCR are young and need to resume daily life activities as early as possible. Excellent results were observed despite no direct proven role of vascular endothelial growth factor (VEGF) in CSCR. If increased choroidal hyper permeability thought to be the main cause of CSCR, it seemed reasonable to treat CSCR with anti-VEGF agent such as ranibizumab. Prognosis depends depend on severity of photoreceptor damage at the time injection. Results of this study are in agreement with Kim and colleagues who reported the role of Intravitreal injection of ranibizumab for acute CSCR on twenty patients (0.5 mg/0.05 ml).[16] All the patients were followed for six months. The results when compared with observation group, it was reported that long time needed for complete recovery in the observation group if compared with the intravitreal injection of ranibizumab group.

CONCLUSIONS

Intravitreal ranibizumab can be used for rapid absorption of sub-retinal fluid in acute CSCR. Significant reduction in CRT along with improvement of best corrected visual acuity (BCVA) was noted in this study. Intravitreal Ranizbizumab can be safely employed for rapid resolution of CSCR to gain desired CRT and BCVA for better clinical outcomes. However, to confirm the safety, efficacy and ideal protocol for this treatment, further studies with large number of patients and longer follow up are recommended.

REFERENCES

1. Daruich A, Matet A, Behar-Cohen F. Central serous chorioretinopathy. Dev Ophthalmol. 2017; 58:27-38. DOI: 10.1159/000455267
2. Chhablani J, Anantharaman G, Behar-Cohen F, Boon C, Manayath G, Singh R. Management of central serous chorioretinopathy: Expert panel discussion. Indian J Ophthalmol. 2018 Dec; 66(12): 1700-3. DOI: 10.4103/ijo.IJO_1411-18
3. Lajmi H, Hmaied W, Ben Jalel W, Akremi A, El Fekih L. Central serous chorioretinopathy: Professional repercussions among agents of the internal security forces. J Fr Ophtalmol. 2018; 41(8):739-43. DOI: 10.1016/j.jfo.2017.12.012
4. Demirok G, Kocamaz F, Topalak Y, Altay Y, Sengun A. Macular ganglion cell complex thickness in acute and chronic central serous chorioretinopathy. Int Ophthalmol. 2017; 37(2): 409-16. DOI: 10.1007/s10792-016-0278-4
5. Gawęcki M, Jaszczuk-Maciejewska A, Jurska-Jaśko A, Kneba M, Grzybowski A. Impairment of visual acuity and retinal morphology following resolved chronic central serous chorioretinopathy. BMC Ophthalmol. 2019; 19(1): 160. DOI: 10.1186/s12886-019-1171-5
6. Sulzbacher F, Schütze C, Burgmüller M, Vécsei-Marlovits PV, Weingessel B. Clinical evaluation of neovascular and non-neovascular chronic central serous chorioretinopathy (CSC) diagnosed by swept source optical coherence tomography angiography (SS OCTA). Graefes Arch Clin Exp Ophthalmol. 2019; 257(8): 1581-90. DOI: 10.1007/s00417-019-04297-z
7. Xu Y, Su Y, Li L, Qi H, Zheng H, Chen C. Effect of photodynamic therapy on optical coherence tomography angiography in eyes with chronic central serous chorioretinopathy. Ophthalmologica. 2017; 237(3): 167-72. DOI: 10.1159/000456676
8. Fujita K, Kawamura A, Yuzawa M. Choriocapillaris changes imaged by OCT angiography after half-dose photodynamic therapy for chronic central serous chorioretinopathy. Ophthalmic Surg Lasers Imaging Retina. 2017; 48(4): 302-10. DOI: 10.3928/23258160-20170329-04.
9. Cardillo Piccolino F, Borgia L, Zinicola E. indocyanine green angiographic findings in central serous chorio – retinopathy. Eye. 1995; 9: 324-332.
10. Yumusak E, Gokcinar NB, Ornek K. Choroidal thickness changes in non-treated acute and ranibizumab-treated chronic central serous chorioretinopathy. Medicine (Baltimore). 2018; 97(43): e12885. DOI: 10.1097/MD.0000000000012885
11. Tekin K, Sekeroglu MA, Cankaya AsB, Teke MY, Doguizi S, Yilmazbas P. Intravitreal bevacizumab and ranibizumab in the treatment of acute central serous chorioretihopathy: A single center retrospective study. Semin Ophthalmol. 2018; 33(2): 265-70. DOI: 10.1080/08820538.2016.1228985
12. Sahoo NK, Singh SR, Rajendran A, Shukla D, Chhablani J. Masqueraders of central serous chorioretinopathy. Surv Ophthalmol. 2019; 64(1): 30-44. DOI: 10.1016/j.survophthal.2018.09.001
13. Wang M, Sander B, Larsen M. Retinal atrophy in idiopathic central serous chorioretinopathy. Am J Ophthalmol. 2002; 133: 787-93.
14. Stewart JM. Central serous chorioretinopathy half dose verteporfin PDT for central serious chorioretinopathy. Br J Ophthalmol. 2006; 90: 805-6.
15. Cardillo Piccolino F, Eandi CM, Ventre L, Rigaultde de la Longrais RC, Grignolo FM. Photodynamic therapy for chronic central serous chorioretinopathy. Retina. 2003; 23: 752-63.
16. Kim M, Lee SC, Lee SJ. Intravitreal ranibizumab for acute central serous retinopathy. Ophthalmologica. 2013; 229: 152-7.