Central Serous Chorioretinopathy/ Pachychoroid Eye Diseases

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Abbreviations

AMD	Age-related macular degeneration
CNV	Choroidal neovascularization
CSC	Central serous chorioretinopathy
FA	Fluorescein angiography
FAF	Fundus autofluorescence
ICGA	Indocyanine green angiography
OCT	Optical coherence tomography
PDT	Photodynamic therapy
PED	Pigment epithelial detachment
PPE	Pachychoroid pigment epitheliopathy
PPS	"Peripapillary pachychoroid syndrome"
RPE	Retinal pigment epithelial
VEGF	Vascular endothelial growth factor

Central Serous Chorioretinopathy

Introduction

Central serous chorioretinopathy (CSC) is a chorioretinal disorder characterized by serous detachment of the neurosensory retina, associated with serous retinal pigment epithelial (RPE) detachment, angiographic leakage at the level of the RPE, and choriodal hyperpermeability (Nicholson et al. 2013). It is usually idiopathic but might also be secondary to high levels of endogenous or exogenous corticosteroids. CSC typically affects young to middle-aged men, and the lesion is usually located at the posterior pole (Kitzmann et al. 2008). CSC can be classified according to its clinical course: acute or chronic (persisting for more than 3–6 months). Acute CSC usually resolves spontaneously within 2–3 months with good visual prognosis. However, some patients with chronic CSC may suffer from persistent or recurrent serous macular detachment with subsequent progressive visual loss (Gilbert et al. 1984).

Pathogenesis

The pathophysiology of CSC is poorly understood. It was initially suggested that CSC results from the dysfunction of RPE ion pumping, with a reverse in fluid movement in a chorioretinal direction (Spitznas 1986). Later, the pathogenesis of CSC was proposed to be choroidal vascular hyperpermeability, with and without associated active pigment epithelial leaks or pigment epithelial detachment (PED) (Guyer et al. 1994). It has been widely accepted that choroidal hyperpermeability causes serous detachments of the RPE, which can induce a rip or decompensation of the RPE. This subsequently causes RPE leakage, leading to diffusion of water, electrolytes, and proteins to neurosensory retinal space. The cause of the choroidal abnormality is still unknown, and changes of the autoregulation in the choroidal blood flow or localized lobular choroidal ischemia have been suggested as a possible cause (Tittl et al. 2005; Prunte and Flammer 1996).

The risk factors for CSC include the use of corticosteroid medication, psychological stress and type A personality, hypertension, gastroesophageal reflux disease, pregnancy, and the use of psychotropic medication (Yannuzzi 1987; Tittl et al. 1999; Liew et al. 2013). The use of corticosteroid medication is the most widely accepted risk factor, and the use of both systemic and local glucocorticoids has been implicated in CSC (Carvalho-Recchia et al. 2002). The proposed mechanisms to explain this association are induction of choroidal vasoconstriction by reducing nitric oxide production, direct increase in the permeability of the blood vessels, and RPE cell tight junction damage (Smith 1984; Liew et al. 2013). Corticosteroids can

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also reverse the polarity of RPE cells, which causes them to pump ions into the subretinal space (Bastl 1987; Sandle and McGlone 1987).

Clinical Features

On fundus examination, acute CSC typically shows a well-demarcated oval-shaped area of neurosensory retinal detachment in the posterior pole (Fig. 4.1). Serous PED can also occur together or independently. In chronic recurrent cases, RPE changes and atrophy may develop and an atrophic RPE tract connecting the macula to the inferior detachment might be seen. Bullous neurosensory detachments can be noted in atypical CSC cases, which are usually located inferiorly as the subretinal fluid drains down from the macula by gravity (Yannuzzi et al. 1984; Gass and Little 1995) (Fig. 4.2).

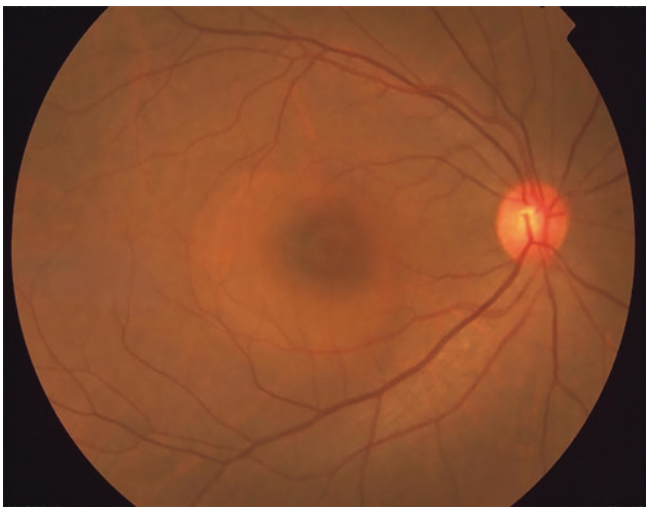

Fig. 4.1 Color fundus photograph shows round neurosensory retinal detachment at the posterior pole

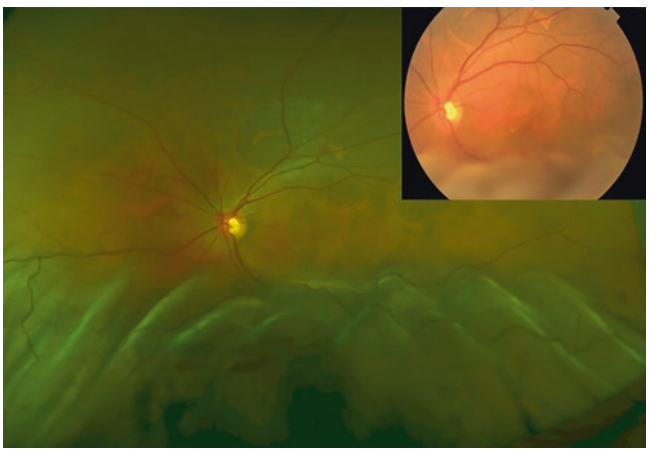

Fig. 4.2 Wide color fundus photograph shows serous pigment epithelial detachment at the posterior pole and bullous neurosensory detachment involving the inferior half of the retina

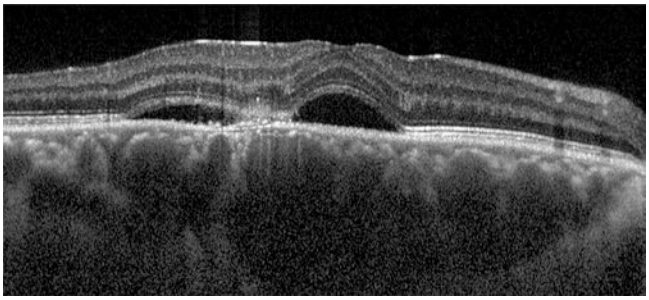

Fig. 4.3 Enhanced-depth imaging optical coherence tomography shows increased choroidal thickness (measured subfoveally at 650 μm), a retinal pigment epithelial elevation, and a hyper-reflective flow within the subretinal fluid. Beneath the retinal pigment epithelial elevation, the choroidal vessels are more dilated, and the choriocapillaris is thinner than in the adjacent area

Optical coherence tomography (OCT) is the primary modality for the diagnosis and follow-up of CSC. Recently, enhanced-depth imaging and swept-source technologies have allowed full-depth visualization of the choroid, improving the morphological analysis of choroidal vessels. Compared to healthy subjects, increased choroidal thickness has been reported in both affected and fellow eyes of CSC patients (Kuroda et al. 2013; Maruko et al. 2011). Increased choroidal thickness can result from focal or diffuse dilatation of large choroidal vessels, which are commonly co-localized within areas of choroidal vascular hyperpermeability on indocyanine green angiography (ICGA) (Jirarattanasopa et al. 2012; Yang et al. 2013). Attenuation of the inner choroidal layer or RPE elevations are also frequently observed above dilated choroidal vessels (Fig. 4.3). Elongation of photoreceptor outer segments in the area of serous retinal detachment, which is attributable to the lack of phagocytosis by the RPE, is a frequent OCT finding in CSC (Matsumoto et al. 2008).

Fluorescein angiography (FA) in acute CSC typically shows one of the two different types of leakage patterns: ink blot or smoke stack (Fig. 4.4). Smoke stack appearance is less common and only appears in about 10–15% of patients with acute CSC (Bujarborua et al. 2010). PED manifests on FA as the pooling of dye in the sub-RPE space. Chronic CSC may show an RPE window defect due to RPE atrophy. In atypical CSC cases, multiple sites of leakage can be noted (Fig. 4.5).

In CSC, ICGA provides an insight into choroidal changes contributing to the disease process and essential data to distinguish complex chronic cases with accompanying choroidal neovascularization (CNV). ICGA typically exhibits abnormally dilated choroidal vasculature in the early phase and choroidal hyperpermeability in the mid- to late phase (Spaide et al. 1996) (Fig. 4.6). Delayed initial filling of arteries and choriocapillaris in the early phase and hypofluorescent areas persisting in mid- and late phases can also be seen, which

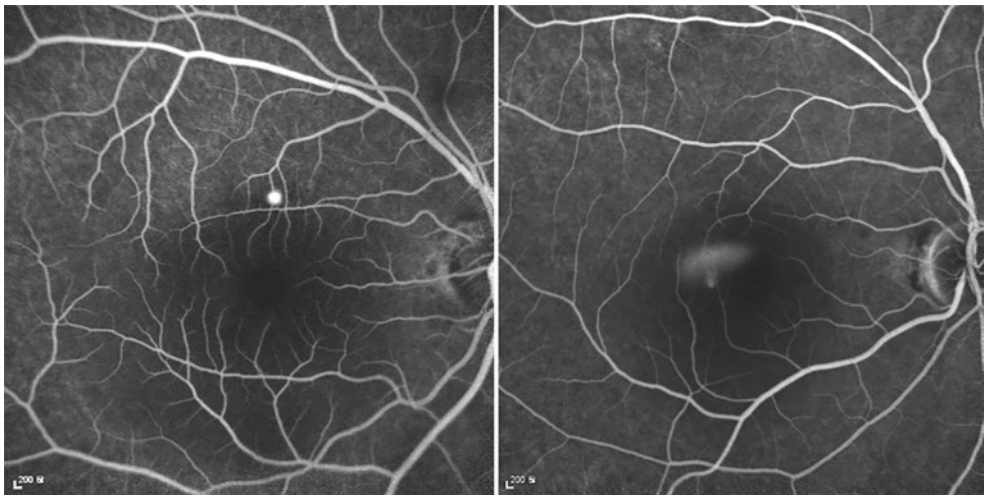

Fig. 4.4 Fundus fluorescein angiography of acute central serous chorioretinopathy shows leakage with an ink blot appearance (left) and a smoke stack appearance (right)

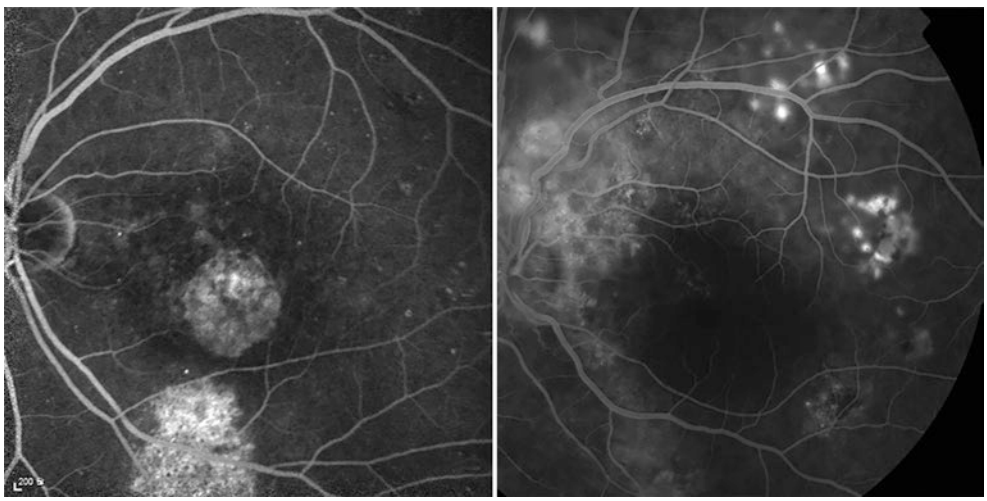

Fig. 4.5 Fundus fluorescein angiography of chronic central serous chorioretinopathy shows a window defect due to retinal pigment epithelial atrophy (left) and multiple pin-point leakages (right)

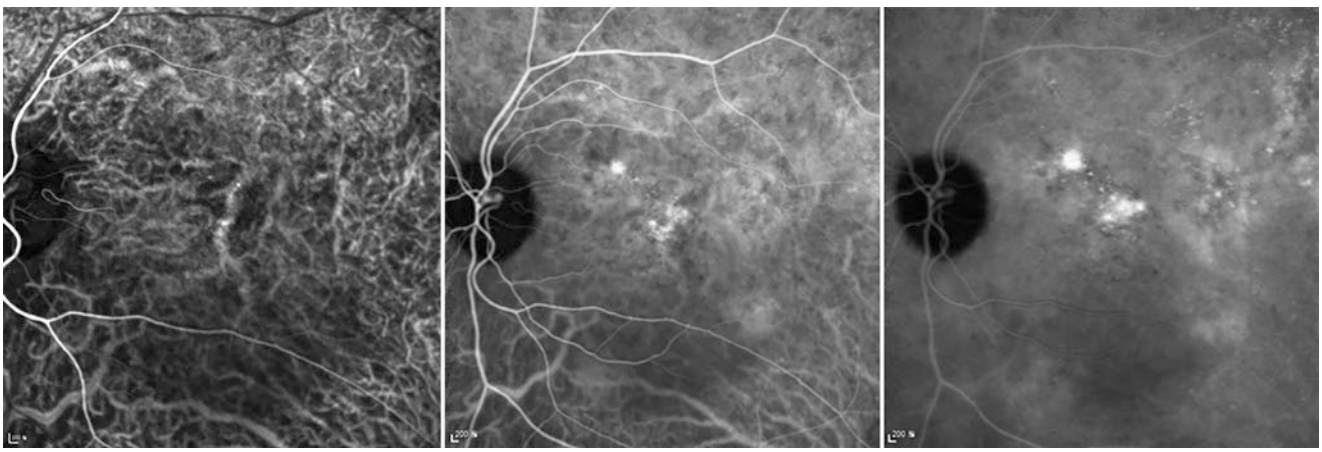

Fig. 4.6 Indocyanine green angiography shows delayed initial filling of arteries and choriocapillaris in the early phase (left), and areas of hyperfluorescence in the mid-phase (middle) which persist through the lase phase (right)

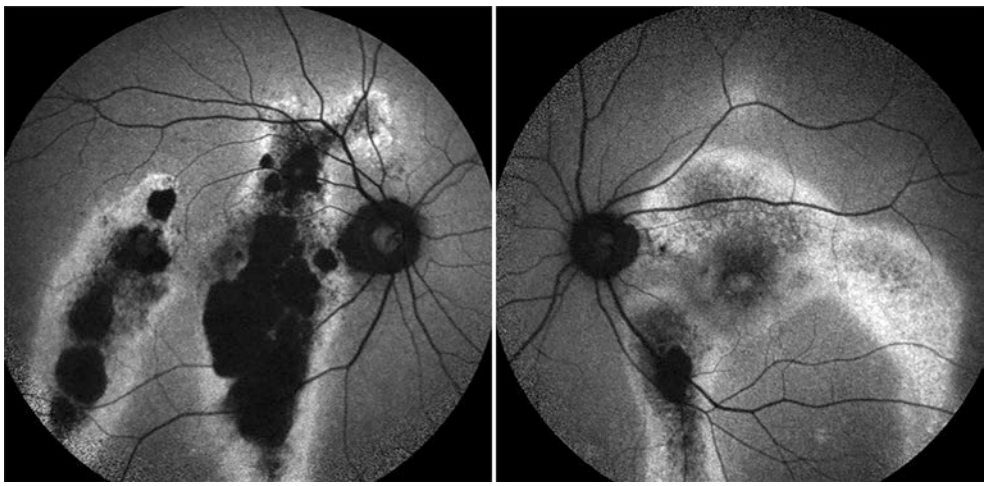

Fig. 4.7 Fundus autofluorescence imaging of chronic central serous chorioretinopathy shows hypo-autofluorescent gravitational tracks in both eyes, and areas of hyperfluorescence in the left eye

may be one of the mechanisms that lead to choroidal venous dilation and congestion (Prunte and Flammer 1996; Kitaya et al. 2003). In more than half of the asymptomatic fellow eyes, choroidal changes similar to those of affected eyes were observed on ICGA (Iida et al. 1999).

During the acute phase of the disease, fundus autofluorescence (FAF) typically shows hypofluorescence over the area of neurosensory detachment due to blockage by subretinal fluid. It may either return to normal, or be progressively replaced by hyperfluorescence (Framme et al. 2005). The accumulation of non-shed fluorophore in elongated outer segments or the loss of photoreceptor outer segments may explain the subsequent increase in FAF (Iacono et al. 2015; Matsumoto et al. 2011). In chronic CSC, multiple oblong descending tracks of decreased FAF surrounded by a thin contour of increased FAF can be noted, often originating from the optic disc and the macula (Fig. 4.7).

Management

There is no consensus about the most suitable treatment and the optimal timing for intervention in CSC. Regarding the favorable natural course of the disease, observation can be the appropriate first-line approach in acute CSC. However, intervention can be considered in the following indications: persistent submacular fluid for over 4–6 months, history of multiple recurrences, diffuse RPE atrophy, reduced visual acuity, and cases requiring rapid recovery (Nicholson et al. 2013).

Medical Therapy: Mineralocorticoid Receptor Antagonists

The association between CSC and elevated systemic cortisol level has been well documented, and steroid antagonists have been investigated as treatments for CSC. The mineralocorticoid antagonists, spironolactone and eplerenone, have been introduced as a systemic treatment option for CSC by reducing steroid levels. Although short-term anatomical and visual benefits were demonstrated in several retrospective and a few prospective studies (Daruich et al. 2016; Bousquet et al. 2015), most were limited by their retrospective and non-randomized designs, small sample sizes, and relatively short follow-up periods. Ongoing and future studies are needed to elucidate the role of mineralocorticoid antagonists in the treatment of CSC.

Medical Therapy: Anti-vascular Endothelial Growth Factor Agents

Although CSC is not associated with increased vascular endothelial growth factor (VEGF) ocular levels (Shin and Lim 2011), anti-VEGF therapy has been used based on the expectation of reducing the choroidal hyperpermeability (Chung et al. 2013). A few case series reported beneficial effects of anti-VEGF treatment in chronic or recurrent cases (Artunay et al. 2010; Pitcher et al. 2015). However, based on the meta-analysis of comparative studies including acute and chronic CSC, no significant difference was observed between anti-VEGF treatment and observation in visual and anatomical outcomes (Ji et al. 2017; Chung et al. 2013).

Conventional Laser Photocoagulation

Traditionally, the use of thermal laser photocoagulation has been attempted to seal the RPE leakage points, although it is not expected to act on choroidal congestion and hyperpermeability. Several studies have compared laser photocoagulation to observation and reported that it may not affect the final functional outcomes or the rate of recurrence (Burumcek et al. 1997). Also, significant adverse effects such as permanent scotoma, enlargement of RPE scarring, and secondary laser-induced CNV formation have been reported (Robertson and Ilstrup 1983). However, laser photocoagulation may still have a role in the management of CSC with a discrete, solitary extrafoveal leaking point.

Subthreshold Laser Therapy

In subthreshold laser therapy, RPE cells are selectively destroyed by exploding melanosomes with microsecond or nanosecond pulses, while photoreceptors and Bruch membrane are spared (Roider et al. 1993). The RPE cells in the surrounding areas then stretch, migrate, and proliferate to refill the damage zone. It is assumed that this process improves the cellular tight junctions and pumping functions of RPE cells (Flaxel et al. 2007; Paulus et al. 2011). This may theoretically reduce the risk of structural and functional retinal damage while retaining the therapeutic efficacy of conventional laser treatment. Several retrospective, prospective case series and small randomized clinical trials have demonstrated the safety and short-term efficacy of subthreshold laser therapy in patients with chronic and possibly acute CSC (Scholz et al. 2015; Kretz et al. 2015). Because of wide variations in study designs and laser protocols, further prospective, randomized, and controlled studies should be performed to fully substantiate the observed treatment efficacy and safety of subthreshold laser therapy.

Photodynamic Therapy

Photodynamic therapy (PDT) is proposed to work through vascular remodeling of the choroid which leads to decreased choroidal volume, permeability, and leakage of fluid. At the beginning, several studies reported that ICGA-guided PDT with standard parameters and standard dose of verteporfin led to anatomic and functional improvement in CSC (Yannuzzi et al. 2003; Battaglia Parodi et al. 2003). However, complications appeared in some cases subsequently, including RPE atrophy, choriocapillaris ischemia, and secondary CNV (Chan et al. 2003). In an attempt to enhance the efficacy of PDT in treating CSC while minimizing its side effects, distinct strategies modifying the route of administration, timing of laser exposure, and reduction in fluence and verteporfin dose have been tried. Both half-dose verteporfin (3.0 mg/m^2) and half-fluence (25 J/cm^2) PDT achieved resolution of subretinal fluid and visual improvement. Also, these safety-enhanced PDT protocols could significantly decrease the hypoxic damage to physiologic choroid caused by conventional PDT (Reibaldi et al. 2010; Shin et al. 2011). In several meta-analyses, PDT was superior with respect to absorption of subretinal fluid compared to laser photocoagulation and intravitreal injection of anti-VEGF drugs (Ma et al. 2014; Lu et al. 2016). Also, a randomized, controlled trial demonstrated the superiority of half-fluence PDT compared with intravitreal ranibizumab in the treatment of chronic CSC (Bae et al. 2014). Therefore, based on the evidence to date, PDT stands out as the most promising therapy among all treatment options in treating both acute and chronic CSC patients.

Pachychoroid Eye Diseases

The term pachychoroid was initially introduced into the literature in 2013 to describe retinal pigment epitheliopathy in patients with choroidal findings resembling those of central serous chorioretinopathy (Warrow et al. 2013). It was originally conceived to reflect choroidal congestion and choroidal hyperpermeability manifested by choroidal thickening on OCT. However, there is no consensus on the definition of thick choroid. Subfoveal choroidal thickness can be influenced by physiologic and ocular factors including age, sex, and axial length, and the normative value has not been determined (Barteselli et al. 2012). Also, it is possible for an eye with normal choroidal thickness to be defined as pachychoroid when the increased luminal volume secondary to choroidal vessel dilation is offset by the reduction in tissue volume from the stroma. Indeed, further investigations have broadened its original description to emphasize additional qualitative features. These features include diffuse or focal choroidal thickening that is localized within the disease focus and attributable to pathologically dilated Haller's veins (termed "pachyvessels") (Lee et al. 2016a, b; Balaratnasingam et al. 2016). Choriocapillaris and Sattler layers overlying pachyvessels become attenuated focally, and close approximation of pachyvessels and the Bruch-RPE complex may lead to pathologic pachychoroid-driven process. Currently, the concept of pachychoroid includes not only the anatomical increase of choroidal thickness, but has evolved into structural and functional changes of the choroid.

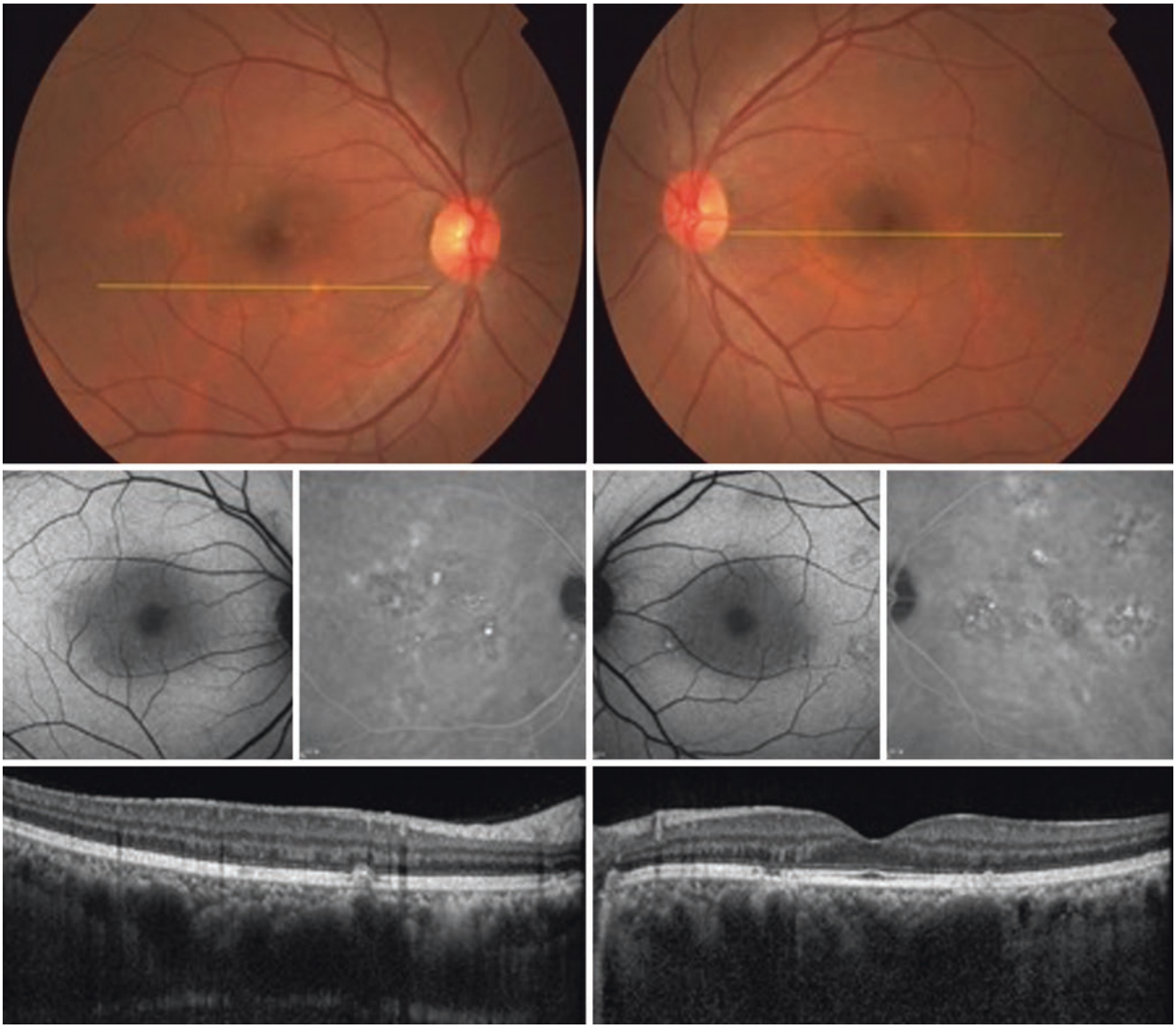

Fig. 4.8 Multimodal imaging of pachychoroid pigment epitheliopathy. Color fundus photographs of both eyes show pigmentary changes without drusen. Fundus autofluorescence imaging reveal hyper- and hypoautofluorescent changes in the posterior poles, and indocyanine green angiography in the mid- to late phase shows choroidal hyperpermeability. Enhanced depth imaging optical coherence tomography reveals retinal pigment epithelial elevation inferonasal to the fovea in the right eye. Disruption of ellipsoid zone and shallow pigment epithelial detachment temporal are seen in the left eye. Note the thickened choroid with dilated choroidal vessels under the RPE changes

Pachychoroid Pigment Epitheliopathy

Pachychoroid pigment epitheliopathy (PPE) is a novel clinical entity first described in 2013 that is characterized by a range of RPE abnormalities and pigmentary changes overlying the areas of choroidal thickening (Warrow et al. 2013). These patients exhibit reduced fundus tessellation at the posterior pole on ophthalmoscopy, choroidal hyperpermeability on ICGA, and relatively thick subfoveal choroid and Haller's layer vessel dilation on enhanced depth imaging OCT, particularly at the sites of RPE abnormalities (Fig. 4.8). FAF abnormalities are also noted at the sites corresponding to RPE disturbances. Although these features are similar to that of CSC, these patients had no findings or history indicative of subretinal fluid. Therefore, PPE was described as a possible precursor, or forme fruste, of CSC. Since none of the patients developed clinically evident subretinal fluid, choroidal vascular hyperpermeability and/or choroidal thickening alone may be the cause of pigment epitheliopathy.

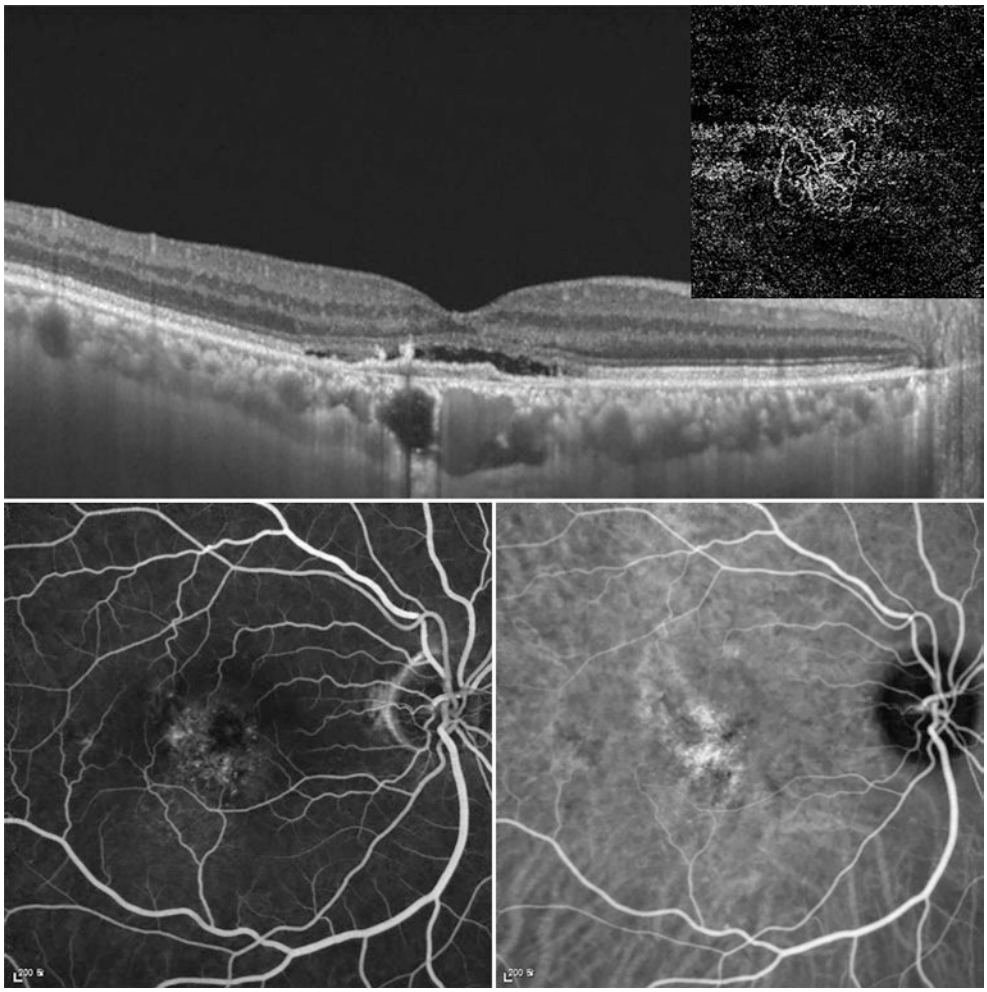

Fig. 4.9 Multimodal imaging of pachychoroid neovasculopathy. Swept-source optical coherence tomography and optical coherence tomography angiography show type 1 neovascularization above the dilated Haller's vessels. Fluorescein angiography shows occult choroidal neovascularization with diffuse leakage, and indocyanine green angiography in the early to mid-phase reveals hyperfluorescent plaque without polypoidal lesions

Pachychoroid Neovasculopathy

The term "pachychoroid neovasculopathy" has been introduced to describe type 1 neovascularization associated with choroidal thickening and/or dilated Haller's vessels in the absence of characteristic age-related macular degeneration features such as drusen (Pang and Freund 2015) (Fig. 4.9). The proposed mechanism for the development of pachychoroid neovasculopathy is the mechanical stress and/or ischemic insult induced by dilated Haller vessels to the overlying RPE-Bruch membrane-choriocapillaris complex, leading to the expression of angiogenic factors. It can develop after long-standing CSC, but it can also develop without antecedent neurosensory detachment attributable to CSC (Fung et al. 2012). It was hypothesized that pachychoroid neovasculopathy is associated with PCV and that pachychoroid neovasculopathy can ultimately progress to the development of polypoidal lesions. Eventually, a pachychoroid-related spectrum of diseases including PPE-CSC-pachychoroid neovasculopathy-PCV has been proposed. The frequency of pachychoroid neovasculopathy among neovascular age-related macular degeneration (AMD) is not reported yet, but it is considered to comprise a significant portion of lesions which were classified as exudative AMD in Asians previously (Wong et al. 2016). OCT angiography can be useful in detecting the CNV complex within irregular PEDs in chronic CSC, particularly where FA, ICGA, and OCT reveal inconclusive results (Hage et al. 2015). The treatment response to anti-VEGF injection is not fully understood in pachychoroid neovasculopathy. Since aflibercept showed greater effects on the choroid and was superior to ranibizumab in achieving remission of exudation in eyes with choroidal hyperpermeability (Hata et al. 2014; Koizumi et al. 2015), it may also have advantages in treating pachychoroid neovasculopathy. In cases refractory to anti-VEGF injection, adjunctive PDT was reported to be effective in the resolution of the exudation and stabilization/improvement of vision (Lee and Lee 2016).

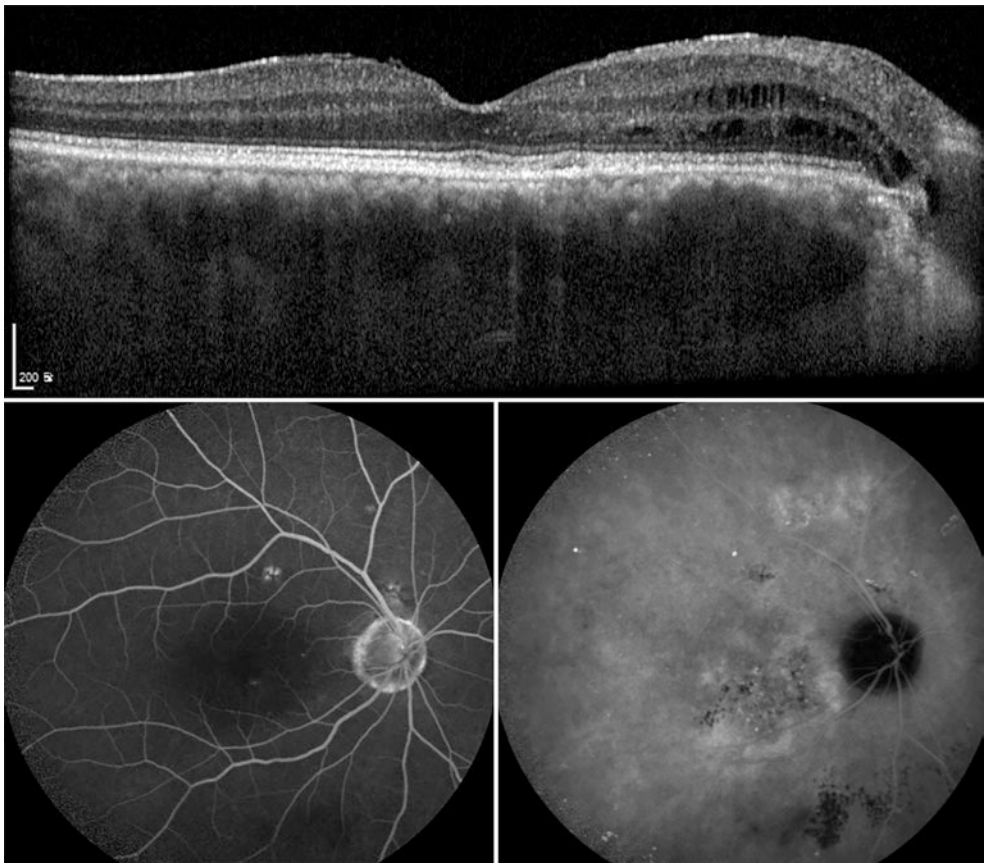

Fig. 4.10 Multimodal imaging of peripapillary pachychoroid syndrome. Enhanced-depth imaging optical coherence tomography shows intraretinal fluid in the nasal macula extending from the temporal optic disc margin in which atrophy of the retinal pigment epithelium, ellipsoid zone, and external limiting membrane is noted. Fluorescein angiography demonstrates the peripapillary hyperfluorescent ring without significant leakage. Indocyanine green angiography exhibits choroidal hyperpermeability at the papillomacular area

Peripapillary Pachychoroid Syndrome

The term "peripapillary pachychoroid syndrome" (PPS) has been suggested to describe eyes that exhibit peripapillary choroidal thickening and intraretinal and/or subretinal fluid in the nasal macular region extending from the temporal margin of the optic disc (Phasukkijwatana et al. 2018). The nasal macular choroid tends to be thicker than the temporal macular choroid, and dilated large choroidal vessels are more prominent in the nasal areas versus the temporal areas (Fig. 4.10). Intraretinal and/or subretinal fluid can also be seen on the nasal side of the nerve. FA usually illustrates minimal or no leakage, and mild late fluorescein disc leakage can be identified in some cases. Dilated Haller's vessels on OCT and choroidal hyperpermeability are frequently noted, and eyes with PPS can exhibit overlapping findings with CSC, such as serous PED and gravitational tracks. The reason why the choroid is congested preferentially in the peripapillary region and the mechanism of intraretinal fluid extension from the disc margin are unclear. Acquired lamina cribrosa defects or disinsertion have been noted in a certain portion of PPS eyes and have been suggested as a potential source of fluid entrance (Lee et al. 2016a, b). Alternatively, atrophy of RPE and external limiting membrane in the peripapillary region may allow fluid from congested choroid to enter the retina (Pautler and Browning 2015).

References

Artunay O, Yuzbasioglu E, Rasier R, et al. Intravitreal bevacizumab in treatment of idiopathic persistent central serous chorioretinopathy: a prospective, controlled clinical study. Curr Eye Res. 2010;35:91–8.

Bae SH, Heo J, Kim C, et al. Low-fluence photodynamic therapy versus ranibizumab for chronic central serous chorioretinopathy: one-year results of a randomized trial. Ophthalmology. 2014;121:558–65.

Balaratnasingam C, Lee WK, Koizumi H, et al. Polypoidal choroidal vasculopathy: a distinct disease or manifestation of many? Retina. 2016;36:1–8.

Barteselli G, Chhablani J, El-Emam S, et al. Choroidal volume variations with age, axial length, and sex in healthy subjects: a three-dimensional analysis. Ophthalmology. 2012;119:2572–8.

Bastl CP. Regulation of cation transport by low doses of glucocorticoids in in vivo adrenalectomized rat colon. J Clin Invest. 1987;80:348–56.

Battaglia Parodi M, Da Pozzo S, Ravalico G. Photodynamic therapy in chronic central serous chorioretinopathy. Retina. 2003;23:235–7.

Bousquet E, Beydoun T, Rothschild PR, et al. Spironolactone for non-resolving central serous chorioretinopathy: a randomized controlled crossover study. Retina. 2015;35:2505–15.

Bujarborua D, Nagpal PN, Deka M. Smokestack leak in central serous chorioretinopathy. Graefes Arch Clin Exp Ophthalmol. 2010;248:339–51.

Burumcek E, Mudun A, Karacorlu S, Arslan MO. Laser photocoagulation for persistent central serous retinopathy: results of long-term follow-up. Ophthalmology. 1997;104:616–22.

Carvalho-Recchia CA, Yannuzzi LA, Negrao S, et al. Corticosteroids and central serous chorioretinopathy. Ophthalmology. 2002;109:1834–7.

Chan WM, Lam DS, Lai TY, et al. Choroidal vascular remodelling in central serous chorioretinopathy after indocyanine green guided

photodynamic therapy with verteporfin: a novel treatment at the primary disease level. Br J Ophthalmol. 2003;87:1453–8.
Chung YR, Seo EJ, Lew HM, Lee KH. Lack of positive effect of intravitreal bevacizumab in central serous chorioretinopathy: meta-analysis and review. Eye (Lond). 2013;27:1339–46.
Daruich A, Matet A, Dirani A, et al. Oral mineralocorticoid-receptor antagonists: real-life experience in clinical subtypes of nonresolving central serous chorioretinopathy with chronic epitheliopathy. Transl Vis Sci Technol. 2016;5:2.
Flaxel C, Bradle J, Acott T, Samples JR. Retinal pigment epithelium produces matrix metalloproteinases after laser treatment. Retina. 2007;27:629–34.
Framme C, Walter A, Gabler B, et al. Fundus autofluorescence in acute and chronic-recurrent central serous chorioretinopathy. Acta Ophthalmol Scand. 2005;83:161–7.
Fung AT, Yannuzzi LA, Freund KB. Type 1 (sub-retinal pigment epithelial) neovascularization in central serous chorioretinopathy masquerading as neovascular age-related macular degeneration. Retina. 2012;32:1829–37.
Gass JD, Little H. Bilateral bullous exudative retinal detachment complicating idiopathic central serous chorioretinopathy during systemic corticosteroid therapy. Ophthalmology. 1995;102:737–47.
Gilbert CM, Owens SL, Smith PD, Fine SL. Long-term follow-up of central serous chorioretinopathy. Br J Ophthalmol. 1984;68:815–20.
Guyer DR, Yannuzzi LA, Slakter JS, et al. Digital indocyanine green videoangiography of central serous chorioretinopathy. Arch Ophthalmol. 1994;112:1057–62.
Hage R, Mrejen S, Krivosic V, et al. Flat irregular retinal pigment epithelium detachments in chronic central serous chorioretinopathy and choroidal neovascularization. Am J Ophthalmol. 2015;159:890–903.
Hata M, Oishi A, Tsujikawa A, et al. Efficacy of intravitreal injection of aflibercept in neovascular age-related macular degeneration with or without choroidal vascular hyperpermeability. Invest Ophthalmol Vis Sci. 2014;55:7874–80.
Iacono P, Battaglia PM, Papayannis A, et al. Acute central serous chorioretinopathy: a correlation study between fundus autofluorescence and spectral-domain OCT. Graefes Arch Clin Exp Ophthalmol. 2015;253:1889–97.
Iida T, Kishi S, Hagimura N, Shimizu K. Persistent and bilateral choroidal vascular abnormalities in central serous chorioretinopathy. Retina. 1999;19:508–12.
Ji S, Wei Y, Chen J, Tang S. Clinical efficacy of anti-VEGF medications for central serous chorioretinopathy: a meta-analysis. Int J Clin Pharm. 2017;39:514–21.
Jirarattanasopa P, Ooto S, Tsujikawa A, et al. Assessment of macular choroidal thickness by optical coherence tomography and angiographic changes in central serous chorioretinopathy. Ophthalmology. 2012;119:1666–78.
Kitaya N, Nagaoka T, Hikichi T, et al. Features of abnormal choroidal circulation in central serous chorioretinopathy. Br J Ophthalmol. 2003;87:709–12.
Kitzmann AS, Pulido JS, Diehl NN, et al. The incidence of central serous chorioretinopathy in Olmsted County, Minnesota, 1980-2002. Ophthalmology. 2008;115:169–73.
Koizumi H, Kano M, Yamamoto A, et al. Short-term changes in choroidal thickness after aflibercept therapy for neovascular age-related macular degeneration. Am J Ophthalmol. 2015;159:627–33.
Kretz FT, Beger I, Koch F, et al. Randomized clinical trial to compare micropulse photocoagulation versus half-dose verteporfin photodynamic therapy in the treatment of central serous chorioretinopathy. Ophthalmic Surg Lasers Imaging Retina. 2015;46:837–43.
Kuroda S, Ikuno Y, Yasuno Y, et al. Choroidal thickness in central serous chorioretinopathy. Retina. 2013;33:302–8.
Lee JH, Lee WK. One-year results of adjunctive photodynamic therapy for type 1 neovascularization associated with thickened choroid. Retina. 2016;36:889–95.
Lee WK, Baek J, Dansingani KK, et al. Choroidal morphology in eyes with polypoidal choroidal vasculopathy and normal or subnormal subfoveal choroidal thickness. Retina. 2016a;36(Suppl 1): S73–s82.
Lee JH, Park HY, Baek J, Lee WK. Alterations of the lamina cribrosa are associated with peripapillary retinoschisis in glaucoma and pachychoroid spectrum disease. Ophthalmology. 2016b;123: 2066–76.
Liew G, Quin G, Gillies M, Fraser-Bell S. Central serous chorioretinopathy: a review of epidemiology and pathophysiology. Clin Exp Ophthalmol. 2013;41:201–14.
Lu HQ, Wang EQ, Zhang T, Chen YX. Photodynamic therapy and anti-vascular endothelial growth factor for acute central serous chorioretinopathy: a systematic review and meta-analysis. Eye (Lond). 2016;30:15–22.
Ma J, Meng N, Xu X, et al. System review and meta-analysis on photodynamic therapy in central serous chorioretinopathy. Acta Ophthalmol. 2014;92:e594–601.
Maruko I, Iida T, Sugano Y, et al. Subfoveal choroidal thickness in fellow eyes of patients with central serous chorioretinopathy. Retina. 2011;31:1603–8.
Matsumoto H, Kishi S, Otani T, Sato T. Elongation of photoreceptor outer segment in central serous chorioretinopathy. Am J Ophthalmol. 2008;145:162–8.
Matsumoto H, Kishi S, Sato T, Mukai R. Fundus autofluorescence of elongated photoreceptor outer segments in central serous chorioretinopathy. Am J Ophthalmol. 2011;151:617–23.
Nicholson B, Noble J, Forooghian F, Meyerle C. Central serous chorioretinopathy: update on pathophysiology and treatment. Surv Ophthalmol. 2013;58:103–26.
Pang CE, Freund KB. Pachychoroid neovasculopathy. Retina. 2015;35:1–9.
Paulus YM, Jain A, Nomoto H, et al. Selective retinal therapy with microsecond exposures using a continuous line scanning laser. Retina. 2011;31:380–8.
Pautler SE, Browning DJ. Isolated posterior uveal effusion: expanding the spectrum of the uveal effusion syndrome. Clin Ophthalmol. 2015;9:3–49.
Phasukkijwatana N, Freund KB, Dolz-Marco R, et al. Peripapillary pachychoroid syndrome. Retina. 2018;38:1652–67.
Pitcher JD 3rd, Witkin AJ, DeCroos FC, Ho AC. A prospective pilot study of intravitreal aflibercept for the treatment of chronic central serous chorioretinopathy: the CONTAIN study. Br J Ophthalmol. 2015;99:848–52.
Prunte C, Flammer J. Choroidal capillary and venous congestion in central serous chorioretinopathy. Am J Ophthalmol. 1996;121:26–34.
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;149:307–15.
Robertson DM, Ilstrup D. Direct, indirect, and sham laser photocoagulation in the management of central serous chorioretinopathy. Am J Ophthalmol. 1983;95:457–66.
Roider J, Hillenkamp F, Flotte T, Birngruber R. Microphotocoagulation: selective effects of repetitive short laser pulses. Proc Natl Acad Sci U S A. 1993;90:8643–7.
Sandle GI, McGlone F. Acute effects of dexamethasone on cation transport in colonic epithelium. Gut. 1987;28:701–6.
Scholz P, Ersoy L, Boon CJ, Fauser S. Subthreshold micropulse laser (577 nm) treatment in chronic central serous chorioretinopathy. Ophthalmologica. 2015;234:189–94.
Shin MC, Lim JW. Concentration of cytokines in the aqueous humor of patients with central serous chorioretinopathy. Retina. 2011;31:1937–43.
Shin JY, Woo SJ, Yu HG, Park KH. Comparison of efficacy and safety between half-fluence and full-fluence photodynamic therapy for chronic central serous chorioretinopathy. Retina. 2011;31:119–26.

Smith TJ. Dexamethasone regulation of glycosaminoglycan synthesis in cultured human skin fibroblasts. Similar effects of glucocorticoid and thyroid hormones. J Clin Invest. 1984;74:2157–63.

Spaide RF, Hall L, Haas A, et al. Indocyanine green videoangiography of older patients with central serous chorioretinopathy. Retina. 1996;16:203–13.

Spitznas M. Pathogenesis of central serous retinopathy: a new working hypothesis. Graefes Arch Clin Exp Ophthalmol. 1986;224:321–4.

Tittl MK, Spaide RF, Wong D, et al. Systemic findings associated with central serous chorioretinopathy. Am J Ophthalmol. 1999;128:63–8.

Tittl M, Maar N, Polska E, et al. Choroidal hemodynamic changes during isometric exercise in patients with inactive central serous chorioretinopathy. Invest Ophthalmol Vis Sci. 2005;46:4717–21.

Warrow DJ, Hoang QV, Freund KB. Pachychoroid pigment epitheliopathy. Retina. 2013;33:1659–72.

Wong CW, Yanagi Y, Lee WK, et al. Age-related macular degeneration and polypoidal choroidal vasculopathy in Asians. Prog Retin Eye Res. 2016;53:107–39.

Yang L, Jonas JB, Wei W. Optical coherence tomography-assisted enhanced depth imaging of central serous chorioretinopathy. Invest Ophthalmol Vis Sci. 2013;54:4659–65.

Yannuzzi LA. Type-A behavior and central serous chorioretinopathy. Retina. 1987;7:11–131.

Yannuzzi LA, Shakin JL, Fisher YL, Altomonte MA. Peripheral retinal detachments and retinal pigment epithelial atrophic tracts secondary to central serous pigment epitheliopathy. Ophthalmology. 1984;91:1554–72.

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;23:288–98.