Microstructural Changes in Central Serous Chorioretinopathy
Documented by Spectral-domain Optical Coherence Tomography

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Abstract
Central serous chorioretinopathy (CSC) was first described more than 140 years ago. Due to the rapid development in modern imaging methods, better understanding of changes occurring in the retina in CSC is possible. Spectral-domain optical coherence tomography (SD-OCT) has increased our ability to study this disease, especially microstructural changes during active phase and after resolution of CSC. SD-OCT enables a highly detailed in vivo evaluation of the individual retinal layers especially external limiting membrane (ELM), the inner and outer segments of photoreceptors and changes in retinal pigment epithelium (RPE), which are the most essential and important in described disease. It allows us better understand pathogenesis of CSC.

Keywords
Spectral-domain optical coherence tomography, central serous chorioretinopathy, photoreceptor inner and outer segments, retinal pigment epithelium, visual acuity

Central serous chorioretinopathy (CSC) is a disease characterised by idiopathic serous neurosensory retinal detachment secondary to leakage from retinal pigment epithelium (RPE). This disease was first recognised in 1866 by Albrecht von Graefe. 

Due to the rapid development of modern imaging methods, better understanding of changes occurring in the retina in CSC is possible. Also, their influence on functional results in active CSC and after resolution of subretinal fluid in CSC can be presented. Stratus optical coherence tomography (OCT) (Carl Zeiss Meditec, Inc., Dublin, California, US) shows many changes appearing in retinal layers, especially in the photoreceptor layer in the area of the serous detachments in CSC. However, the details of the retinal layers are unclear because of the 10 µm axial resolution limitation.

Spectral-domain OCT (SD-OCT) instruments offer two main advantages compared with the previous traditional time-domain (TD) OCT: higher speed and improved resolution (~3–7 µm). Multiple B-scan averaging technology permits the production of detailed, speckle-noise-reduced images of all the retinal layers. SD-OCT’s superior resolution allows highly detailed in vivo evaluation of the individual retinal layers, especially the external limiting membrane (ELM), the inner and outer segments (IS/OS) of photoreceptors and changes in RPE. 

Several papers describing OCT findings in eyes with CSC have been published. Various abnormalities were described. OCT presents foveal distoration, cystic and macular changes, RPE detachment (PED) and small bulges protruding from RPE. Some of the authors thought that part of these abnormalities can be artefacts due to the limited axial resolution of the OCT.

Retinal Thickness
Using TD-OCT, it was difficult to measure each retinal layer in acute phase of CSC, thus these studies provided total retinal thickness.

Different thickening of the retina during the active phase of CSC has been presented by various authors. Some claim that the thickness of the retina in CSC is thinner than in healthy eyes. In our patients [unpublished data], mean foveal retinal thickness during the acute phase of CSC was similar to that of healthy eyes, and the results were similar among other authors. In patients with chronic CSC the thickness of the retina is slightly reduced in comparison with healthy eyes [unpublished data]. Some authors thought that part of these abnormalities can be artefacts, because of the limited axial resolution of the OCT. Sun et al. also stated that the height of the detached retina at the fovea was similar to that of RRD.

High-speed, high-resolution OCT has expanded our ability to study these diseases, especially microstructural changes during the active phase and after the resolution of CSC.

Photoreceptors Changes
Changes in photoreceptors and RPE layers are the most essential and important changes in described disease. Matsumoto et al. analysed morphological changes in the photoreceptor segment of the detached retina in CSC. The authors showed that outer nuclear layer (ONL) thickness (the measurement between the internal limiting membrane [ILM] and the ELM) in the central fovea was approximately 75 µm in CSC, and was statistically significant shorter than the average thickness of 135 µm in healthy eyes. ONL thickness correlated weakly with age, best corrected visual acuity (BCVA) and the duration of symptoms. Matsumoto also presented the elongation of photoreceptor OS. The average thickness of the longest outer photoreceptor segment was
90 µm in CSC and was significantly longer than that of healthy subjects with a typical value of 60 µm. OS was not at all or was weakly correlated with age, BCVA and duration of symptoms. Similar to Matsumoto et al., we stated that during the active process extension of the photoreceptor OS was taking place (see Figure 1) [unpublished data]. These results are in opposition to the studies of Yu et al.17 The ONL thickness in CSC is not different from that of healthy eyes and measures 97 µm on average. The authors also did not find the difference between the length of photoreceptors in patients with CSC and in healthy eyes.

Another interesting publication concerning ONL is one by Maruko et al.14 The authors compared changes in the outer layer of the detached retina in patients with rhegmatogenous retinal detachment (RRO) and CSC. According to their study, ONL was significantly thicker in patients with retinal detachment than in patients with CSC. Moreover, the authors noticed that BCVA after reattachment was correlated with the thickness of the ONL in patients with detachment of the retina. These results stood in opposition to those of the CSC group where no correlation was noted between retinal morphological changes and visual function.

The development of SD-OCT technology in recent years resulted in the observation that persistent leakage and subretinal fluid may cause RPE alterations and photoreceptor changes, which may correlate with a worsening of VA.9,16 Ooto et al. compared pathological changes in photoreceptors in eyes with resolved CSC seen on high-resolution images obtained from adaptive optics scanning laser ophthalmoscopy (AO SLO) with VA and findings on SD-OCT.11 The study included 54 eyes of 38 patients with resolved CSC and 20 healthy eyes. In eyes with disruption in the photoreceptor IS/OS visible in SD-OCT, the mean cone density was significantly lower than in eyes with intact IS/OS or the intermediate line. These findings correlate with VA loss. Ojima et al. also analysed OS of foveal photoreceptors after resolution of CSC. They showed in 71.6% of eyes that IS/OS were clearly detectable in SD-OCT with good VA. In 12 % of the eyes, they noted recovery of the IS/OS foveal line, which was connected with VA recovery. In some eyes no restoration of outer segments of foveal photoreceptors was detected and the prognosis of visual recovery remained poor. In conclusion of the cited examinations we can state that defects in the photoreceptor layer correlated with VA (see Figure 2). Analysis of these results is supported by other authors, who state that if subfoveal fluid persisted more than 4 months foveal atrophy may occur anytime,9 and degenerative changes often develop in the macula in CSC cases lasting longer than 6 months.10 These changes correlate with the changes in VA.

SD-OCT reveals also that ONL and photoreceptor inner segments were thicker in healthy eyes than in eyes with CSC and polypoidal choroidal vasculopathy (PCV).17 However, Ooto stated that the photoreceptor OS were thinner in eyes with PCV than in healthy eyes or in eyes with CSC. These findings make SD-OCT helpful in differentiating PCV from CSC. Another option available in SD-OCT is autofluorescence examination. It is helpful in the evaluation of changes occurring in the retina during the active phase of CSC (see Figure 3). It can give us additional answers about the progression and lifetime of the active process. In the authors’ opinion it was not possible to evaluate any irreversible changes that had already occurred in the photoreceptor layer during active phase of CSC [unpublished data]. Elongation of the outer segments of photoreceptors, which is observed in CSC, may be due to a lack of photoreceptor phagocytosis by the RPE.18 The duration of the elongation of this layer may affect the simultaneous initiation of photoreceptor apoptosis. The results are also supported by Spaide,19 who analysed the autofluorescence of CSC. Spaide hypothesised that...
Figure 4: Two Different Leakage Sites Visible in the Fluorescein Angiography and Spectral-domain Optical Coherence Tomography

Top and bottom left: Leakage site in fluorescein angiography. Top right: Spectral-domain optical coherence tomography (SD-OCT) shows protruding retinal pigment epithelium (RPE) layer (blue arrow) at the leakage site. Bottom right: SD-OCT shows pigment epithelium detachment at the leakage site (red arrow).

an increased autofluorescence may represent photoreceptor outer segments phagocytised by the RPE.

Retinal Pigment Epithelium Changes

Various abnormalities in RPE have been described in eyes with CSC. Gup et al. proved the presence of PED in nearly 11.8% of eyes with idiopathic CSC and PED. Yu et al. showed PED in 72.2% of eyes and a small bulge of RPE in only 34.5% of eyes. Yu et al. showed that mean choroidal thickness was significantly greater in areas with leakage visible on FA and in areas with choroidal vascular hyperpermeability on IA. These findings strongly support that changes in the choroid may give us an answer about the pathogenesis of the disease.

In conclusion, the latest publication gives us more information about microstructural changes in the retina occurring in CSC, especially in the IS/OS of photoreceptors and RPE. It allows us to better understand the pathogenesis of this disease. The development of OCT technology in recent years has resulted in various authors noting that persistent leakage and subretinal fluid may cause RPE alterations and photoreceptor changes, which may correlate with a worsening of VA. Despite the significant progress that has been made in the last few years in OCT technology, we still do not have sufficient knowledge about the pathogenesis of CSC.