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RETINAL DISORDERS

Obstructive sleep apnea in patients with central serous chorioretinopathy

Patrik Kloos · Irene Laube · Adelheid Thoelen

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Abstract
Background Patients with central serous chorioretinopathy (CSC) show an increased sympathetic activity compared to controls. Additionally, there are several reports of increased corticosteroid and catecholamine levels in these patients. Obstructive sleep apnea syndrome (OSAS) has been shown to enhance sympathetic activity depending on severity. Respiratory disturbance increases urinary catecholamine secretion and is associated with the occurance of hypertension in a dose dependent manner. Therefore we hypothesize that OSAS may act as a risk factor for the development of CSC.
Methods Patients with active CSC or with pigment epithelial disturbances after CSC were contacted to answer a questionnaire about general health, drugs and sleeping habits and to complete the Epworth Sleepiness Scale (ESS) score, a widely used subjective measure of daytime sleepiness. Patients with an ESS score of >10 were referred to our department of pulmonary medicine for evaluating of respiratory disturbance in sleep.
Results We identified 56 consecutive patients with angiographic criteria for acute CSC or pigment epithelial defects after CSC, seven (12.5%) of whom were excluded because of a history of systemic or topic corticosteroid use. Thirty-six (73.5%) of the remaining 49 patients returned the questionnaire. Fourteen (38.8%) had an ESS score of >10. They were referred to the Department of Pulmonary Medicine. In eight (22.2%) of these patients, a diagnosis of obstructive sleep apnea syndrome was confirmed.
Conclusions We found that 22% of the patients with acute or chronic CSC in this case series also suffered from OSAS, whereas in the general population OSAS is considerably less frequently reported (2–4%). OSAS therefore may act as a risk factor for the development of CSC. However, prospective controlled data is needed to definitely evaluate the possible association between CSC and OSAS. Also the clinical course of CSC during treatment of OSAS would be of particular interest.

Keywords Central serous chorioretinopathy · CSC · Obstructive sleep apnea · OSAS

The authors have full control of all primary data, and they agree to allow Graefe's Archive for Clinical and Experimental Ophthalmology to review their data upon request.

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P. Kloos · A. Thoelen
Department of Ophthalmology, Stadtspital Triemli, Zürich, Switzerland

I. Laube
Department of Pulmonary Medicine, Stadtspital Triemli, Zürich, Switzerland

P. Kloos (✉)
Department of Ophthalmology, Kantonsspital St. Gallen, 9007 St. Gallen, Switzerland
e-mail: patrik.kloos@kssg.ch

Introduction

Central serous chorioretinopathy (CSC) is characterized by an idiopathic serous detachment of the neurosensory retina. It mainly affects young adults. The etiology and pathogenesis of this disorder are still unknown. Maumenee described the concept of a leakage site within the retinal pigment epithelial layer, visible on fluorescein angiography in patients with CSC [1]. Recent studies have indicated that the possible site of primary pathology is the choroidal vessels [2], and that the involvement of the retinal pigment epithelium may play a pathogenetic role. Risk factors

including psychological stress and type-A behaviour [3], corticosteroids [4] and sympathomimetic use [5] have been reported to induce or exacerbate CSC. Patients with CSC demonstrated increased heart-rate variability as a marker of sympathetic activity compared to controls [6]. Additionally, there are several reports of increased corticosteroid and catecholamine levels in these patients [7]. All these observations suggest that increased sympathetic activity may be of importance in the pathogenesis of CSC.

Obstructive sleep apnea syndrome (OSAS) is characterized by repeated episodes of sleep-disruptive upper airway closure, leading to motor restlessness, lack of refreshing sleep and excessive daytime sleepiness [8]. OSAS has been shown to affect catecholamine excretion levels [9] and to enhance sympathetic activity and blood pressure, with a clear dose effect [10].

Due to these possible common pathophysiological factors, we hypothesize that OSAS may act as a risk factor for the development of CSC.

Material and methods

In 2006, all 56 patients with angiographic findings of CSC (e.g., active site of leakage and/or disturbances of the retinal pigment epithelium on fluorescein angiography) were contacted to answer a questionnaire about general health, drugs and sleeping habits and the Epworth Sleepiness Scale (ESS). When returning the completed questionnaire, the patients also provided their informed consent to the evaluation of their data for scientific purposes and for further investigations. In the case of further examinations, again they had to provide their informed consent. All investigations and related work adhered to the tenets of the declaration of Helsinki. The Epworth Sleepiness Scale (ESS) is widely used as a subjective measure of daytime sleepiness. The test measures the probability of falling asleep in eight daily situations (scores 0–3; total possible score of 24). ESS scores in healthy subjects differ from those in patients with obstructive sleep apnea syndrome. The clinically normal range is 2 to 10, and ESS scores increase with the severity of OSAS [11]. An ESS score of >5 identifies a respiratory disturbance index (RDI) of >5/hour with a sensitivity of 95% and a specificity of 9%. To diagnose OSAS, a threshold disturbance index or apnea-hypopnea index (AHI) of 5 or more in connection with daytime hypersomnolence was used. Cut-off points of 5, 15 and 30 events/hour were used to indicate mild, moderate and severe levels of OSAS [12]. The ESS score in the ESS validation study for German-speaking people without OSAS ranged from 0 to 15, with 93% of the subjects having a score of 10 or less [13]. Patients with an ESS score of >10 were referred to our department of pulmonary medicine for further investigations. Generally, the condition of OSAS is diagnosed with an overnight polysomnography, including cardiorespiratory parameters, oxygen saturation

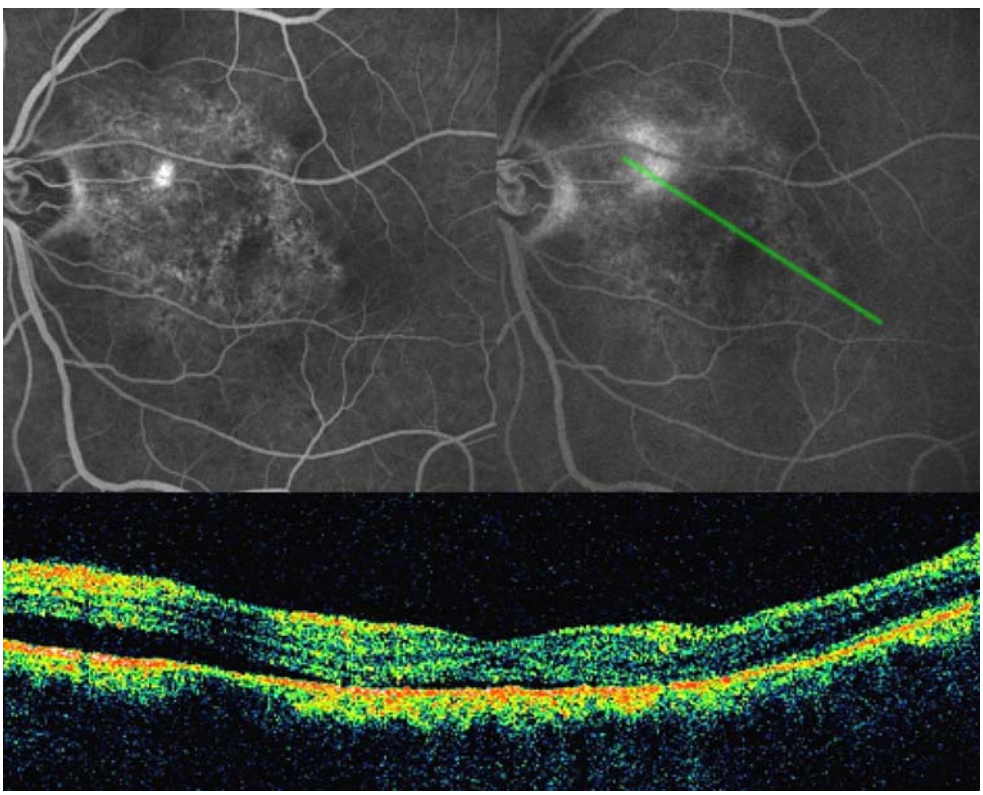
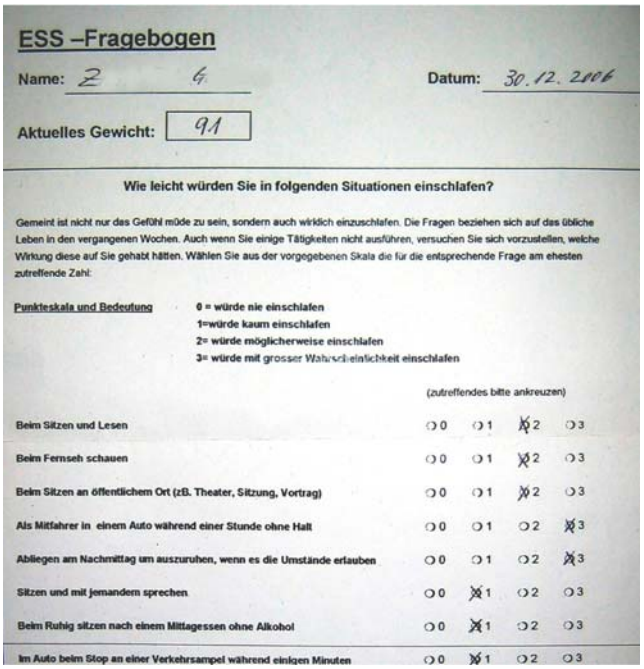


Fig. 1 Chronic alteration of the pigment epithelium and an active site of leakage on the fluorescein angiography (mid and late phase) with the corresponding detachment of the neurosensory retina on the OCT (6-mm horizontal scan nasal to temporal) in a patient with CSC and OSAS



ESS –Fragebogen

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Wie leicht würden Sie in folgenden Situationen einschlafen?

Gemeint ist nicht nur das Gefühl müde zu sein, sondern auch wirklich einzuschlafen. Die Fragen beziehen sich auf das übliche Leben in den vergangenen Wochen. Auch wenn Sie einige Tätigkeiten nicht ausführen, versuchen Sie sich vorzustellen, welche Wirkung diese auf Sie gehabt hätten. Wählen Sie aus der vorgegebenen Skala die für die entsprechende Frage am ehesten zutreffende Zahl:

Punkteskala und Bedeutung
0 = würde nie einschlafen
1=würde kaum einschlafen
2= würde möglicherweise einschlafen
3= würde mit grosser Wahrscheinlichkeit einschlafen

(zutreffendes bitte ankreuzen)

Beim Sitzen und Lesen	○0	○1	X2	○3
Beim Fernseh schauen	○0	○1	X2	○3
Beim Sitzen an öffentlichem Ort (zB. Theater, Sitzung, Vortrag)	○0	○1	X2	○3
Als Mitfahrer in einem Auto während einer Stunde ohne Halt	○0	○1	○2	X3
Abliegen am Nachmittag um auszuruhen, wenn es die Umstände erlauben	○0	○1	○2	X3
Sitzen und mit jemandem sprechen	○0	X1	○2	○3
Beim Ruhig sitzen nach einem Mittagessen ohne Alkohol	○0	X1	○2	○3
Im Auto beim Stop an einer Verkehrsampel während einigen Minuten	○0	X1	○2	○3

Fig. 2 German ESS questionnaire of a CSC patient (his fluorescein angiography and OCT scans are shown in Fig. 1) with an ESS score of 15 and diagnosed OSAS

and electroencephalography. Patients with a history of topical (eye and skin) inhaled or systemic corticosteroid use, or having any endocrine disorders, were not included.

Results

Of the 56 consecutive patients with acute or chronic CSC (diagnosed by fluorescein angiography and OCT scans), seven (12.5%) patients were excluded because of a history of systemic corticosteroid use. Thirty-six (73.5%) of the remaining 49 patients returned the questionnaire, of whom 30 patients (83.3%) were men. The mean age of our patients was 56.7 years (range 31 – 76 years). Fourteen patients demonstrated an ESS score of >10 and were therefore referred to the Department of Pulmonary Medicine for further examinations. Eight (22.2%) of these were diagnosed as having obstructive sleep apnea (five patients with mild OSAS, three with moderate to severe OSAS).

Four of the eight patients with OSAS suffered from chronic CSC with longstanding alterations of the pigment epithelium, and the remaining four showed acute CSC with an active site of leakage in the retinal pigment epithelium and a detachment of the neurosensory retina. Figure 1 shows a typical case of chronic alteration of the pigment epithelium, and Fig. 2 a questionnaire for a patient with an ESS score >10. All the patients suffering from OSAS and CSC were men. The body mass index (BMI) was similar in the two groups with or without OSAS (25.8 vs 24.9, p= 0.47). Four (50%) of the eight patients with OSAS and 11 (39%) of the 28 patients without OSAS were under treatment for arterial hypertension (Table 1).

Discussion

Previous studies have shown an association between CSC and increased sympathetic activity [6], higher levels of catecholamine [7] and high blood pressure [6]. Since OSAS causes an increase in sympathetic activity and may increase cortisol levels [9, 14], it can be speculated that patients with OSAS are at higher risk of developing CSC than the general population. We found that 22% of our patients with CSC also suffered from OSAS, whereas OSAS is less frequently reported (2–4%) in the general population [15].

OSAS may therefore play a role in the pathogenesis of CSC. We were able to quite reliably exclude BMI as a risk factor for CSC, as our OSAS patients had a mean BMI close to normal, whereas a typical OSAS cohort has a BMI over 30 kg/m2. BMI in non-OSAS and OSAS patients with CSC did not differ. With the exception of a 35-year-old patient, all patients with CSC and OSAS were older (55–75 years) than the population that is usually affected by CSC [16]. OSAS frequently occurs in middle or advanced age, and both diseases show several common pathophysiological pathways as mentioned. These facts are consistent with the suggestion that OSAS might be another independent risk factor for CSC in higher age. All factors that are known to be associated with OSAS, such as raised sympathetic

Table 1 Patient demographics

	All patients with CSC	Patients with CSC without OSAS	Patients with CSC and OSAS
Number of patients	36	28 (77.8%)	8 (22.2%)
Male	30 (83.3%)	22 (78.5%)	8 (100%)
Female	6 (16.7%)	6 (21.5%)	0 (0%)
Mean age (range)	56.7 years (31–76)	59.8 years (31–73)	53.6 years (35–76)
Mean ESS	8.1	7.0	12.0
Mean BMI (range)	25.3 (18.9–28.7)	24.9 (18.9–28.4)	25.8 (22.7–28.7)

activity and increased catecholamine and corticosteroid levels, might be risk factors for CSC in elderly people.

In a recent study, Leveque et al. [17] also postulated a possible association between CSC and OSAS. This study was, however, based exclusively on the Berlin Questionnaire to predict OSAS. To our knowledge, this is the first report about patients with CSC and OSAS diagnosed by polysomnography and pulse oximetry.

Respiratory disturbance could compromise choriocapillary perfusion by sympathetic activation, as well as by inflammatory and procoagulant mechanisms [18, 19]. Also, OSAS may cause systemic hypertension [10], while CSC too has been found to be associated with hypertension [20, 21].

CSC mainly affects male patients [16]. All our patients with CSC and OSAS were men. For OSAS too, most population-based studies have reported about two- to three-fold higher risk for men compared to women [22].

Our report needs consideration of relevant bias. Not only due to the questionnaires that were not returned but also due to patients who were excluded because of the use of corticosteroids, of 56 patients identified with CSC, only 36 were included in the final analysis. However, if all of the non-included patients were free of OSAS, the prevalence of OSAS would still be clearly higher than exspected. Moreover, due to the retrospective observational design, important physiological parameters such as surrogates of sympathetic activity and blood pressure, but also endogeneous corticosteroid activity and procoagulant factors, were not assessed for. To support the hypothesis of a common pathophysiological pathway, the metabolic risk factors like catecholamine and cortisol levels should be analyzed in further studies. In addition the course of CSC under treatment would be of particular interest.

We conclude that, in this limited retrospective case series, an overrepresentation of OSAS in patients with CSC was found. CSC and OSAS share common risk factors. Therefore, OSAS might indicate patients at risk for CSC, possibly by affecting sympathetic activity, procoagulant factors, cortisol levels or yet undetermined factors. Prospective studies are needed to confirm this concept.

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