Progress in Retinal and Eye Research 48 (2015) 82–118

Contents lists available at ScienceDirect

Progress in Retinal and Eye Research

journal homepage: www.elsevier.com/locate/prer

Central serous chorioretinopathy: Recent findings and new physiopathology hypothesis

Alejandra Daruich [a, 1], Alexandre Matet [a, 1], Ali Dirani [a], Elodie Bousquet [b, c, d, e], Min Zhao [b, c, d], Nicolette Farman [b, c, d], Frédéric Jaisser [b, c, d], Francine Behar-Cohen [a, b, c, d, *]

[a] Department of Ophthalmology, University of Lausanne, Jules-Gonin Eye Hospital, Fondation Asile des Aveugles, Lausanne, Switzerland
[b] Sorbonne Universités, UPMC Université Paris 06, UMR 1138, Centre de Recherche des Cordeliers, Team 1 and 17, Paris, France
[c] INSERM, UMR 1138, Centre de Recherche des Cordeliers, Paris, France
[d] Université Paris Descartes, Sorbonne Paris Cité, UMR 1138, Centre de Recherche des Cordeliers, Paris, France
[e] AP-HP, Hôpital Hôtel-Dieu, Service d'ophtalmologie, Paris, France

ARTICLE INFO

Article history:
Received 12 February 2015
Received in revised form
10 May 2015
Accepted 14 May 2015
Available online 27 May 2015

Keywords:
Central serous chorioretinopathy
Mineralocorticoid receptor
Retina
Physiopathology
Mineralocorticoid receptor antagonists
Glucocorticoids
Corticosteroids

ABSTRACT

Central serous chorioretinopathy (CSCR) is a major cause of vision threat among middle-aged male individuals. Multimodal imaging led to the description of a wide range of CSCR manifestations, and highlighted the contribution of the choroid and pigment epithelium in CSCR pathogenesis. However, the exact molecular mechanisms of CSCR have remained uncertain. The aim of this review is to recapitulate the clinical understanding of CSCR, with an emphasis on the most recent findings on epidemiology, risk factors, clinical and imaging diagnosis, and treatments options. It also gives an overview of the novel mineralocorticoid pathway hypothesis, from animal data to clinical evidences of the biological efficacy of oral mineralocorticoid antagonists in acute and chronic CSCR patients. In rodents, activation of the mineralocorticoid pathway in ocular cells either by intravitreous injection of its specific ligand, aldosterone, or by over-expression of the receptor specifically in the vascular endothelium, induced ocular phenotypes carrying many features of acute CSCR. Molecular mechanisms include expression of the calcium-dependent potassium channel (KCa2.3) in the endothelium of choroidal vessels, inducing subsequent vasodilation. Inappropriate or over-activation of the mineralocorticoid receptor in ocular cells and other tissues (such as brain, vessels) could link CSCR with the known co-morbidities observed in CSCR patients, including hypertension, coronary disease and psychological stress.

Contents

* Corresponding author. Hôpital Ophtalmique Jules-Gonin, Avenue de France 15, CP 133, 1000 Lausanne 7, Switzerland.
E-mail address: francine.behar@gmail.com (F. Behar-Cohen).
[1] Both authors have contributed equally to this work.

http://dx.doi.org/10.1016/j.preteyeres.2015.05.003

1. Introduction

Central serous chorioretinopathy (CSCR or CSC) is a posterior segment disease characterized by localized and limited serous detachments of the neurosensory retina often associated with focal detachments of an altered retinal pigment epithelium. The term "central" refers to the form of the disease causing visual symptoms due to the presence of serous detachments in the macular area. But asymptomatic subjects may have presented one or multiple episodes of extra macular serous detachments, as often observed in the contralateral eye of an active CSCR patient or when systematically examining relatives of CSCR patients (Lehmann et al., 2015; Weenink et al., 2001) (Figs. 1 and 5D). The prevalence of CSCR is therefore likely to have been underestimated.

Whilst the acute CSCR form is clinically obvious especially in middle-aged men, the clinical diagnosis in older patients is more challenging, as chronic CSCR often resembles age-related macular degeneration (AMD) or can be complicated by choroidal neovascularization (CNV) (Fung et al., 2012; Inhoffen et al., 2012; Pang and Freund, 2015; Schatz et al., 1992). CSCR diagnosis is also difficult when occurring secondarily to steroid treatments administered for other retinal diseases (Khairallah et al., 2012). Recently, enhanced visualization of the choroid with spectral-domain optical coherence tomography (SD-OCT) has facilitated a more robust assessment of the role played by the choroid in CSCR, which in the past five years has resulted in more than 100 publications (Mrejen and Spaide, 2013). Based on these observations, it was recently proposed that "pachychoroid pigment epitheliopathy" could be a subclinical phenotype potentially complicated by serous detachments and/or choroidal vasculopathy, including type 1 CNV and polypoidal vasculopathy (Pang and Freund, 2015; Warrow et al., 2013). The segregation of the CSCR phenotypes becomes unclear. In particular, whether there is a continuum between acute simple CSCR associated or not with pachychoroid (Fig. 2), and the chronic variants of the disease (referred to as Diffuse Retinal Pigment Epitheliopathy, DRPE) is yet to be prospectively investigated. Sparse or unique acute episodes of CSCR have a favorable visual prognosis but DRPE is associated with progressive and bilateral vision impairment, and has been estimated as the fourth most frequent non-surgical retinopathy (Wang et al., 2008). To date, the genetic, environmental, biological or clinical factors that favor one or the other form of this disease have not been established.

The relation between CSCR and corticoids is probably one of the most intriguing aspects of the disease. Glucocorticoids efficiently reduce macular edema of many origins, even when associated with subretinal fluid (Noma et al., 2012; Ossewaarde-van Norel et al., 2011), but glucocorticoids can aggravate subretinal fluid accumulation in CSCR patients. Even exposure to low-dose non-ocular corticosteroids has been associated with the occurrence of CSCR (Bouzas et al., 2002; Thinda et al., 2015). But high-dose intraocular injection of glucocorticoids, routinely administered for the treatment of macular edema, has not been associated with increased incidence of CSCR. Such discrepancies reflect the still non-elucidated complexity of steroids regulation on ocular physiopathology.

Since glucocorticoids aggravate rather than improve CSCR, inflammation was disregarded among potential disease mechanisms. This should be re-examined from the time when inflammation is recognized as a key player in the pathogenesis of AMD, in which unexpectedly glucocorticoid treatments did not show any major benefit (Geltzer et al., 2013).

Specific psychological and personality profiles have been associated with CSCR (Piskunowicz et al., 2014; Yannuzzi, 1986) but the