Commentary: Our understanding of central serous chorioretinopathy—coming a full circle?

Central serous chorioretinopathy was first described by Von Graefe in 1866 as "Ueber centrale recidivirende retinitis".[1] The usage of the term "retinitis" suggests that initially it was believed to be an inflammatory condition. Later it was described as an idiopathic serous detachment of the macula caused by focal leakage of choroidal interstitial fluid through the retinal pigment epithelium.[2] The exact molecular mechanisms though remain uncertain.[3] High levels of endogenous (i.e., in Cushing's syndrome or in pregnancy) or exogenous (i.e., intra-articular, intranasal, systemic, or topical) corticosteroids, type A personality, abnormal coagulation and platelet aggregation, male gender, smoking, hypertension, and oxidative stress have been considered to be significant risk factors for the development of CSCR.[4]

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, however, 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. 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.[3] It is thus interesting that an article in this issue comes a full circle and attempts to re-establish CSCR as an inflammatory condition.[5]

The article in the current issue explores the theory of oxidative stress and inflammation resulting in higher levels of nitric oxide, prostaglandins and reactive oxygen species that result in choroidal vascular hyperpermeability and abnormal leakage. This is intriguing as it can be argued that corticosteroids can theoretically counter these pathways. However, glucocorticoids cause an increased expression of ocular mineralocorticoid receptors (MR)[6] and act by binding both to the receptor for glucocorticoid and that for mineralocorticoid with equally high affinity.[4] Over activation of the MR in the choroidal endothelial cells induces upregulation of vasodilator potassium channels which modulates smooth muscle cells relaxation in the choroidal vasculature causing choroidal vasodilation and fluid accumulation in the retina. MR antagonists like spironolactone and eplerenone have been successfully used in the treatment of CSCR.[4] Thus we may agree that there are at least two pathways that lead to CSCR–one driven by inflammation and the other driven by MR agonism.

Currently the standard of care is observation as a large proportion of acute presentations are self-resolving. Treatment like focal laser, subthreshold laser, and photodynamic therapy are reserved for the chronic cases.[7] A literature search for the treatment of systemic steroid induced CSCR with MR antagonists without the discontinuation of the offending agent yielded no results. This would have been interesting as not only could the systemic and the ocular disease have been treated

effectively, it would also have given us a proof of concept for the combined use of glucocorticoids and MR antagonists. It will be interesting to have a prospective study that attempts to target both the pathways mentioned above, possibly by the combined use of systemic corticosteroids and MR antagonists hypothesized to use the anti-inflammatory effect of corticosteroids without their effects on the mineralocorticoid receptors.

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