Endogenous cortisol profile in patients with central serous chorioretinopathy

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Abstract

***Aim*—To study the endogenous cortisol levels in patients with central serous chorioretinopathy (CSCR).**

***Methods*—Endogenous cortisol levels in urine and plasma were determined in 30 patients with acute CSCR and compared with 30 age and sex matched controls.**

***Results*—The mean values of the 8 am plasma cortisol (29.97 µg/dl *v* 18.76 µg/dl), 11 pm plasma cortisol (22.03 µg/dl *v* 13.06 µg/dl), and 24 hour urine cortisol (11.01 mg/24 h *v* 7.39 mg/24 h) revealed significantly higher values in the patient group ($p<0.001$).**

***Conclusions*—Increased levels of endogenous cortisol are present in patients with CSCR.**

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Central serous chorioretinopathy (CSCR) is a localised serous detachment of the posterior pole of the retina, occurring as a result of a focal defect in the retinal pigment epithelium (RPE), which leads to fluid of choroidal origin leaking into the subretinal space, causing a detachment of the neurosensory retina from the RPE in the macular area. The typical clinical picture is that of a male aged 20–50 years, presenting with an acute onset of blurring of vision associated with metamorphopsia, micropsia, and a central scotoma.[1] Fundus examination reveals a transparent blister at the posterior pole with a ring reflex marking the limits of the elevated area.[1] The diagnosis is confirmed by fluorescein angiography which reveals one or more leakage points at the level of the RPE. Various studies have implicated infective,[2] vascular,[3 4] toxic, immunological,[5 6] allergic,[7 8] mechanical,[9] psychological,[10 11] and endocrinological[12–16] factors in the pathogenesis of this disease. However the exact cause remains obscure.

Many conditions including emotional stress, type A personality, pregnancy, and Cushing's syndrome have been associated with an increased incidence of CSCR.[2 17–20] An analysis of the pathophysiology of these states reveals a strong association in each, with endogenous hypercortisolism.[21–26] Furthermore, anecdotal reports exist in the literature, of the worsening or precipitation of CSCR in patients started on systemic steroid therapy,[13–15 27] thus supporting the association between steroids and CSCR. Since there are no studies in western literature which have evaluated the endogenous cortisol (glucocorticoid) levels in CSCR patients, it was decided to evaluate the same in patients with this disorder.

Methodology

Thirty patients with CSCR who presented to the medical ophthalmology clinic of Dr R P Centre for Ophthalmic Sciences, All India Institute of Medical Sciences, New Delhi were included in the study. The criteria for inclusion into the study were: males between 20–40 years of age, first attack of CSCR, documentation of a single leak on fluorescein angiography, and presentation within 2 weeks of onset of symptoms. Patients with any other ocular or systemic disease, any surgery or trauma within 2 weeks of presentation, receiving any form of local or systemic steroids, obesity with a body mass index of more than 30, alcohol abuse or dependence, and major depression (DSM III R criteria) were excluded from our study, since all these conditions can independently alter the endogenous cortisol levels.[25] Thirty age and sex matched patients with an acute unilateral retinal detachment were used as controls. The rationale for having retinal detachment patients as controls was to have a comparison group with a history of sudden visual loss, with no known systemic association with hypercortisolism. Since sudden vision loss is a stressful event, its occurrence could result in elevated cortisol levels in any subject. The use of patients with retinal detachment as controls obviated the possibility of bias on this account.

At the time of inclusion into our study, all the subjects underwent a systemic evaluation, comprising a complete medical history, general physical examination, erythrocyte sedimentation rate, liver and kidney function tests. The ocular evaluation comprised visual acuity testing, slit lamp biomicroscopy of the anterior and posterior segment (with a +90 D lens), indirect ophthalmoscopy, and fluorescein angiography.

Cortisol sampling was done one day after admission, in order to give the patients time to get acclimatised to the hospital environment. For plasma cortisol estimation, 10 ml of venous blood was taken at 8 am (when endogenous cortisol levels are at their maximum) and at 11 pm (when endogenous cortisol is at its minimum). In addition, 24 hour urine collection was done to measure the 17-hydroxysteroids (the major metabolite of cortisol metabolism). Cortisol analysis was done on the spectrophotometer based on the Porter–Silber reaction, in which cortisol was made to react with phenylhydrazine in alcoholic sulphuric acid to yield a yellow phenylhydrazone

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compound with maximum absorbence at 410 nm.[25] For the urine analysis, the cortisol conjugates were first hydrolysed with the enzyme β glucuronidase to liberate the steroid, which was then similarly measured.

Results

There was no significant difference in the age and duration of symptoms in the two groups. The mean age (SD) of the patients and controls was 28.6 (5.59) years (range 20–36 years) and 29.27 (5.07) years (range 22–36 years) respectively. The mean duration of symptoms before inclusion in the study was 8.56 (4.19) days in the patients and 6.93 (4.40) days in the controls, with a similar range (1–14 days) in both groups. In 18 patients, the right eye was involved, while 12 had CSCR in the left eye. In the control group, the right eye was involved in 22 cases, while the left was affected in nine cases.

The best corrected Snellen visual acuities in the patient group varied from 6/6 to 6/12 in 24 cases and 6/18 to 6/36 in six cases, while in the control group 25 patients had a visual acuity of less than 6/60, three cases had a visual acuity of 6/18 to 6/36, and two cases had a visual acuity of 6/6 to 6/12. The difference was statistically significant (χ^2 test $p < 0.001$). The means (SD) of the 8 am and 11 pm plasma cortisol values in the patients and controls were 29.97 (12.44) μg/dl *v* 18.76 (8.26) μg/dl and 22.03 (11.54) μg/dl *v* 13.06 (6.9) μg/dl, revealing significantly higher cortisol values in CSCR patients (*t* test $p<0.001$). The means (SD) of the 24 hour urine cortisol values (which gives a better idea of the existence of a state of endogenous hypercortisolism) also showed that patients with CSCR had significantly higher values (11.01 (4.14) mg/day in patients *v* 7.39 (2.47) mg/day in controls, *t* test $p < 0.001$).

Discussion

The exact aetiology of CSCR remains controversial. Various studies have documented raised levels of endogenous steroids in states associated with an increased incidence of CSCR, such as pregnancy[18 28] stress,[10 11 17 19] type A personality,[20] and Cushing's syndrome.[12] CSCR has also been shown to have been precipitated by systemic steroid therapy,[6 14 15 27] indirectly implicating steroids in the pathogenesis of CSCR. Recently Bouzas *et al* [12] reported the development of CSCR in three out of 60 (5%) patients with confirmed Cushing's syndrome, during a period of active untreated disease while plasma cortisol levels were high. Since both CSCR and endogenous Cushing's syndrome are rare diseases, their coincidental association would be highly improbable, especially as Cushing's syndrome affects women more frequently while CSCR is seen predominantly in men. Our study has convincingly shown the positive association between endogenous glucocorticoids (cortisol) and CSCR. We documented the presence of high endogenous cortisol levels in CSCR patients, with significantly higher levels of urine and plasma cortisol compared with the control group ($p<0.001$). In view of the fact that the control group had significantly worse visual acuity, and was likely to have had more stress and consequent endogenous cortisol rise, the higher values of cortisol detected in CSCR patients are even more significant. It is hypothesised that increased endogenous glucocorticoids may act as the inciting or precipitating factor for the development of CSCR by their effect on the RPE and the choroidal vasculature.

Cortisol, by suppressing synthesis of extracellular matrix components[29] and inhibiting fibroblastic activity,[30 31] may cause direct damage to the RPE cells or their tight junctions and may even inhibit any reparative activity in the RPE after damage by another aetiological agent. Secondly, cortisol excess may cause increased capillary fragility[32] and hyperpermeability, leading to choroidal circulation decompensation and leakage of fluid into the subretinal space. Furthermore, endogenous hypercortisolism, by inhibiting proliferation of T and B lymphocytes[33 34] and the migration of leucocytes and macrophages[35] may induce a state of immunosuppression, which may increase the proneness to a subclinical acquired infection or reactivation of a latent infection, which may then damage the RPE barrier. Finally, cortisol by its direct effect on ion transport[36–38] may be responsible for the reversal of polarity of the RPE cells, causing them to secrete ions into the subretinal space, leading on to osmotic fluid attraction and the serous macular detachment.

It is our belief that raised levels of endogenous steroids could set off a chain of events, which could result in damage to the RPE barrier and the choroidal vasculature, consequently precipitating CSCR. We, therefore feel that CSCR may be a multifactorial disorder, with increased levels of endogenous steroids playing a pivotal role in the pathogenesis of the disease.

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