Central serous chorioretinopathy (CSC) is a common idiopathic retinal disease characterized by central vision loss from serous detachment of the neurosensory retina, serous pigment epithelial detachments and leakage of fluid through the retinal pigment epithelium into the subretinal space. The concept of an association between CSC and exogenous glucocorticoid use is widely accepted among ophthalmologists.

Sophie J. Bakri, M.D., and researchers with Ophthalmology at Mayo Clinic's campus in Rochester, Minnesota, analyzed the evidence for and against an association between glucocorticoids and CSC. Results of their study were published in *Survey of Ophthalmology* in 2017.

"CSC has been associated with several risk factors, including male sex, hypertension, alcohol use, gastroesophageal reflux disease, pregnancy and use of psychotropic medications. It is also traditionally and controversially associated with psychological stress and the Type A personality," says Dr. Bakri. "Perhaps the most widely accepted association, however, is that with use of corticosteroid medication. We wanted to determine whether that assumption was accurate."

The researchers conducted a systematic review of the literature using PubMed databases (search terms: *central serous chorioretinopathy, central serous retinopathy and central serous*) to identify studies for evaluation. Articles with data on steroids were identified via reviews of PubMed abstracts and citations in previous work on the subject. The researchers included case reports only if they contributed original information about steroid and CSC.

"Although our study also documents evidence related to other specific risk factors, we ultimately identified two large, case-control studies that found strong associations and a smaller, population-based study that found no association between CSC and corticosteroid medication," notes Dr. Bakri.

Research published in *American Journal of Ophthalmology* in 1999 studied systemic factors associated with CSC. The study included a total of 230 patients with CSC and 230 age- and sex-matched controls. Steroid use was defined as treatment for any medical condition with corticosteroids via parenteral, inhalational or topical steroid, excluding those who were treated with steroid for CSC itself. At presentation, 21 patients with CSC were using corticosteroid medications, whereas seven controls were using corticosteroids. This difference yielded an odds ratio of 3.2. Asthma and renal transplantation were the most frequent reasons for steroid treatment.

"The numbers were not sufficient for statistical analysis of route of administration, although three cases of CSC were associated with inhalational steroid use," says Dr. Bakri. Other statistically significant associations were identified, including hypertension and psychopharmacological medication use.

The second large case-control study, published in *Ophthalmology* in 2004, was a multicenter, retrospective study with 312 cases of both acute CSC and chronic CSC. Cases were compared to 312 age- and sex-matched controls. Only systemic steroid use was considered.

Forty-five cases and just five controls were using steroid medication at presentation, for an odds ratio of 10.3. Bivariate logistic regression analysis showed that steroid
use remained a risk factor when corrected for autoimmune diseases. There were several additional statistically significant associations with CSC shown in this study, including alcohol use, antibiotic treatment, pregnancy, uncontrolled hypertension and allergic respiratory disease.

In contrast to these studies, a retrospective, population-based study from Olmsted County, Minnesota, failed to identify an association between CSC and steroid medication. This study, published in *Ophthalmology* in 2008, included 74 cases of CSC over a 22-year period that ended in 2002. Six (8 percent) patients with CSC were using corticosteroids at the time of diagnosis, and six of 74 controls were taking corticosteroids at the time of the study visit.

“This is the only major study that does not support an association between corticosteroid use and CSC, and the results of a long-term population-based study cannot be ignored,” says Dr. Bakri. “Nonetheless, the sample size is small, and the retrospective design is a limitation.”

**Significant association**

Dr. Bakri notes: “The preponderance of the literature on CSC and steroid medication suggests a significant association. Both exogenous and endogenous glucocorticoids have been implicated, and CSC has been associated with most routes of steroid administration. The association offers a potential target for treatment trials, although the mechanism of association remains to be established.

“The association deserves broader recognition among physicians who prescribe glucocorticoids. Also, CSC is uncommonly mentioned as a side effect of steroid use by nonophthalmologists. Patients would likely benefit from a broader understanding of this disease.”

**For more information**


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**Psychological Factors May Impact Quality of Life After Strabismus Surgery**

For most patients, health-related quality of life (HRQOL) improves dramatically following strabismus surgery. For some patients, however, HRQOL does not improve. Jonathan M. Holmes, M.D., and fellow researchers in Ophthalmology at Mayo Clinic’s campus in Rochester, Minnesota, conducted a retrospective study between July 2012 and August 2016 to identify why.

“Previously, we have studied the associations with decreased HRQOL as measured at a single time point. We found depressive symptoms associated with reduced HRQOL, in addition to clinical factors such as worse diplopia and greater magnitude of deviation,” says Dr. Holmes. “In this study we asked, “What factors are associated with failure of the AS-20 scores to improve after eye muscle surgery?”

The researchers enrolled 276 consecutive adult patients with strabismus undergoing strabismus surgery in the observational case series. Patients with all types of diplopic and nondiplopic strabismus were included, and previous strabismus surgery was allowed.

Participants completed the following four questionnaires, both preoperatively and six weeks postoperatively:

- **Adult Strabismus-20 (AS-20) HRQOL questionnaire**, which measures HRQOL in four domains: Self-Perception, Interactions, Reading Function, General Function
- **Diplopia questionnaire**, which allows patient reporting of diplopia severity in seven gaze positions
- **The Center for Epidemiologic Studies Depression Scale Revised (CESD-R)**, which measures current depressive symptoms
- **Type-D Scale 14 questionnaire**, which assesses for type distressed (type-D) personality

Researchers then performed univariate and multiple logistic regression analyses to assess factors associated with failure of HRQOL to improve (no change in score or a decrease in score) in each of the four AS-20 domains. Analysis included only patients able to improve at least by the magnitude of previously defined 95 percent limits of agreement. Factors assessed include:

- **Age at onset and at surgery**
- **Sex**
- **Number of previous surgeries**
- **Presence of visually obtrusive facial anomaly**
• Visual acuity
• Preoperative and postoperative diplopia questionnaire scores
• Magnitude of ocular misalignment (as a vector)
• Presence of esotropia
• Presence of a vertical deviation
• CESD-R scores
• Type-D personality

“We found that poorer postoperative improvement in AS-20 scores is associated with depressive symptoms,” says Dr. Holmes. “The finding that nonstrabismus factors, such as depressive symptoms, may also be associated with failure of AS-20 scores to improve postoperatively has important clinical implications, because there is increasing emphasis on using patient-reported outcomes for evaluating treatment effectiveness, and we need to understand the factors that might be influencing the patient’s responses on these questionnaires.”

Double vision
The researchers found that persistent double vision or new-onset double vision after surgery was also strongly associated with failure to improve AS-20 scores, both in functional vision domains such as Reading Function and General Function and in the Self-Perception domain. “Our results indicate that residual or new-onset double vision should be addressed by every means possible, such as providing prism in spectacles, or serious consideration of additional surgery,” says Dr. Holmes.

Psychological factors
Researchers also found that psychological and personality factors were associated with failure of AS-20 scores to improve. Dr. Holmes notes: “Specifically, type-D personality was associated with failure to improve in the Self-Perception domain, and postoperative depressive symptoms were associated with failure to improve in the Interactions domain.”

Facial anomalies
The presence of a coexistent noticeable anomaly affecting the face, such as a drooping eyelid (ptosis) was also associated with failure of AS-20 scores to improve on the AS-20 Interactions domain. “We still see that the vast majority of adult patients with strabismus still have measurable improvement in HRQOL and functional vision following strabismus surgery,” says Dr. Holmes. “However, our study highlights the need to consider psychological factors and personality parameters when interpreting patient-reported outcome measures such as HRQOL. The treating strabismus specialist should provide appropriate referral to psychiatry colleagues if the patient expresses depressive symptoms. These symptoms may coexist with strabismus, and although they may affect the patient’s strabismus-related HRQOL and functional vision, they should be addressed directly, because they often have profound effects on the patient’s well-being.”

Study results were published in JAMA Ophthalmology in 2018.

For more information


Research Confirms the Clinical Characteristics of Ocular Sarcoidosis

The reported incidence of sarcoidosis — a chronic granulomatous disease of unknown etiology characterized by the presence of nonnecrotizing granulomata — varies from 6 to 70 per 100,000 people per year. Sarcoidosis typically affects the lungs and hilar lymph nodes, although any organ system may be affected, which may pose a diagnostic challenge.

Ocular involvement is a well-recognized extrathoracic complication of systemic sarcoidosis. The reported prevalence of ocular disease among patients with systemic sarcoidosis varies from 12 to 50 percent. Uveitis is the most common ocular disease, although any eye structure may be affected.

Wendy M. Smith, M.D., and a research team with Ophthalmology and Rheumatology at Mayo Clinic’s campus in Rochester, Minnesota, studied a population-based cohort to develop comprehensive data on the clinical characteristics of ocular involvement of sarcoidosis. “Most of the available studies are referral based, which may potentially capture only more-severe cases and not represent the true spectrum of the disease in the community,” says Dr. Smith. “The objective of this study...
was to describe the epidemiology of ocular sarcoidosis, with an emphasis on clinical characteristics, in a geographically well-defined population of patients.” Study findings were published in Ocular Immunology and Inflammation in 2017.

Rochester Epidemiology Project

The population of Olmsted County, Minnesota, as documented in the Rochester Epidemiology Project, allowed a virtually complete ascertainment of all clinically recognized cases of ocular sarcoidosis among the residents of Olmsted County, Minnesota. The population is predominantly Northern European, although it has become increasingly more diverse.

The researchers used Rochester Epidemiology Project data to identify an inception cohort of patients with systemic sarcoidosis from 1976 to 2013, based on comprehensive individual medical records review. They then reviewed those medical records for ocular involvement, using a standardized data extraction form to record the following information:

• Age at diagnosis
• Sex
• Ethnicity
• Duration of follow-up
• Type of ocular involvement, which included scleritis, episcleritis, conjunctivitis, conjunctival nodule, uveitis, optic neuritis, orbital pseudotumor, eyelid lesion and lacrimal gland disease
• Ophthalmological presentations
• Laterality
• Visual acuity at diagnosis and at last follow-up
• Angiotensin-converting enzyme (ACE) level and serum calcium level at diagnosis
• Treatment and response to treatment

Researchers identified a total of 345 patients with incident cases of systemic sarcoidosis. Ocular involvement occurred in 23 of those patients (7 percent). The most common ocular disease was uveitis (61 percent), followed by dry eye disease, conjunctival nodule, episcleritis, anterior scleritis and conjunctivitis. Anterior uveitis was the most common type of uveitis (71 percent). The visual outcome of uveitis was favorable: Only one patient lost three or more lines of visual acuity during follow-up and had visual acuity of less than 20/200 at last visit.

Only 151 (44 percent) of the 345 patients with systemic sarcoidosis had at least one ophthalmic examination. Ocular involvement was identified in 15 percent of those patients. Dr. Smith notes: “It is possible there was a selection bias, since patients with eye complaints are more likely to be referred for ophthalmic evaluation and probably more likely to have ocular involvement. The true frequency of ocular involvement is probably somewhere between 7 and 15 percent.”

Among this predominantly Caucasian cohort of patients with sarcoidosis, eye symptoms were the first presentation that led to the diagnosis of systemic sarcoidosis in more than half of the patients with uveitis. “This finding highlights the importance of the ophthalmological assessment in the diagnosis of this systemic disorder,” says Dr. Smith.

For more information
