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Central serous chorioretinopathy and *Helicobacter pylori*

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PURPOSE. *This study was designed to evaluate the prevalence of* Helicobacter pylori *infection in patients with central serous chorioretinopathy (CSC).*
METHODS. *Retrospective observational case series. A group of 23 patients (22 men and 1 woman, age range 34–62 years, median age 47 years) with diagnosis of CSC, confirmed by fluorescein angiogram, and a control group of 23 consecutive patients (22 men and 1 woman, age range 41–69 years, median age 50 years) referred to our Department for retinal disease other than CSC were studied. Each patient provided peripheral venous blood samples and a stool specimen, which were analyzed at the Department of Gastroenterology and Microbiology at the same university.* H. pylori *infection was determined by measurement of IgG antibodies to* H. pylori *and by determination of* H. pylori *antigens in the stool specimens by enzyme-linked immunosorbent assay technique. Patients were defined as* H. pylori *infected if both tests were positive.*
RESULTS. *The prevalence of* H. pylori *infection was 78.2% (95% CI, 56%–92%) in CSC patients and 43.5% (95% CI, 23%–65%) in control subjects ($p<0.03$ by two-tailed Fisher exact test). The odds ratio for CSC associated with* H. pylori *infection was 4.6 (95% CI 1.28–16.9).*
CONCLUSIONS. *The results of this study show that the prevalence of* H. pylori *infection seems to be significantly higher in patients with CSC than in controls.* H. pylori *infection may represent a risk factor in patients with CSC. (Eur J Ophthalmol 2006; 16: 274-8)*

KEY WORDS. Helicobacter pylori, *Central serous chorioretinopathy*

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INTRODUCTION

Central serous chorioretinopathy (CSC) is an ocular pathology characterized by serous detachment of the sensory retina at the posterior pole demonstrated by fluorescein and indocyanine green angiography (1, 2). CSC pathogenesis is poorly understood but possible risk factors have been described, such as type A personality (3), psychological stress (2), pregnancy (4), and increased level of endogenous and exogenous corticosteroid (5-7). CSC seems to affect mainly young men between 20 and 45 years of age (2); after 50 years of age, the male:female ratio decreases from 10:1 to 2:1 as women seem to develop the disease later in life (8).

Patients with CSC often complain of central scotomas, decrease of visual acuity, micropsia, metamorphopsia, and dyschromatopsia. Although the symptoms usually recover spontaneously within a maximum of 4 months, patients still refer visual symptoms such as metamorphopsia and reduced contrast sensitivity due to permanent damage of the retinal pigment epithelium (3).

Recently a study on optical coherence tomography

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findings in unilateral resolved CSC demonstrated a decrease in the central foveal thickness in the involved eye and a statistically significant correlation between the foveal thickness and visual acuity even in those eyes where the vision is relatively preserved; the detachment caused by the CSC may be responsible of a varying amounts of photoreceptor loss, atrophy, and shortening of the photoreceptor outer segment (9). It has also been proposed that Helicobacter pylori may play a role in the development of pigment epithelium and choriocapillaris defects responsible for the clinical manifestation of CSC (10, 11).

TABLE I - OCULAR INVOLVEMENT IN 23 PATIENTS WITH CENTRAL SEROUS CHORIORETINOPATHY AND SYMPTOMS REFERRED

Characteristic	**N (%)**
Eye involved	
Right	7/23 (30)
Left	8/23 (35)
Right and left	8/23 (35)
Reactivation episodes	
1	12 /23 (52.17)
2–3	6/23 (26)
4–6	1/23 (4.3)
Never got better	4/23 (17.53)
Symptoms referred in the acute phase	
Visus loss	14/23 (60.9)
Central scotoma	3/23 (13)
Metamorphopsia	6/23 (26)
No symptoms	2/23 (8.7)
Visual acuity at the interview of the affected eye	
9–10/10	4/23 (17.53)
7–8/10	7/23 (30)
5–6/10	10/23 (43.77)
3–4/10	2/23 (8.7)

No patient was interviewed in the acute phase of the disease

TABLE II - PREVALENCE OF *H. PYLORI* INFECTION IN PATIENTS WITH CENTRAL SEROUS CHORIORETINOPATHY (CSC) AND CONTROLS

Group *H. pylori*	**Positive**
CSC 18/23; 78.2%*	(95% CI 56%–92%)
Controls 10/23; 43.5%	(95% CI 23%–65%)

* p<0.03 By two-tailed Fisher exact test vs controls

It has long been known that some infectious agents that affect specific areas of the body may also have systemic sequelae. *H. pylori* is one of the most frequent causes of gastrointestinal infections worldwide and represents the major causative agent of chronic gastritis and peptic ulcer disease in humans (12). Mounting evidence suggests that *H. pylori* infection might also be involved in the pathogenesis of a number of extraintestinal diseases (13); in particular, *H. pylori* has been implicated in the pathogenesis of a number of vascular diseases including ischemic heart disease, ischemic cerebrovascular disorders, focal occlusive arterial diseases in young people, and vascular functional disorders (13). This study was designed to evaluate the prevalence of *H. pylori* infection in subjects with CSC.

PATIENTS AND METHODS

The files of 23 patients with diagnosis of CSC were reviewed between January 2001 and March 2003 at the Department of Ophthalmology of the Seconda Università degli Studi di Napoli. Fluorescein angiogram demonstrated a small leak from a retinal pigment epithelial (RPE) defect early in the transit phase which increased in size and intensity over the course of the examination. Less frequently, characteristic smokestack hyperfluorescence due to pooling of fluorescein dye in the subretinal space in the late phase was observed. None of the patients enrolled in this group was in the acute phase of the disease at the time of our study.

A control group of 23 consecutive patients was also identified and consisted of subjects referred to our Department for retinal disease other than CSC. For each patient, chorioretinal inflammatory or infiltrative exudation as well as neovascularization was excluded. Informed consent to enter the study was obtained from each patient. The prevalence of *H. pylori* infection observed in CSC patients was also compared with that observed in 460 age- and sex-matched subjects who underwent endoscopy at the Gastroenterology Unit of the Seconda Università degli Studi di Napoli because of dyspeptic symptoms over the same period of time.

All patients, both from the CSC group and from the control group, provided peripheral venous blood samples and a stool specimen, which were analyzed at the Department of Gastroenterology and Microbiology of the same university. *H. pylori* infection was determined by measurement of IgG antibodies to *H. pylori* (GAP IgG *H. pylori*, BIO-RAD,

Milan, Italy) and by determination of *H. pylori* antigens in the stool specimens using the enzyme-linked immunosorbent assay technique (Premiere Platinum HpSA, Meridian Bioscience, Cincinnati, OH, USA). Patients were defined as *H. pylori* infected if both tests were positive. In the group of 460 dyspeptic patients *H. pylori* infection was defined by positive rapid urease test and histology.

For all participants a completed medical history was taken with special care for the presence of upper gastrointestinal symptoms, history of peptic ulcer disease, drinking habits, and use of nonsteroidal anti-inflammatory drugs or of antisecretory agents. Patients belonging to the CSC group underwent full ocular examination; the eyes affected were carefully examined and the duration of the acute phase investigated; symptoms referred in the acute phase as well as at the moment of the interview were recorded. Best-corrected visual acuity was measured at the time of the interview (Tab. I).

RESULTS

Between January 2001 and March 2003, 46 patients were enrolled in this study. Twenty-three patients (22 men and 1 woman, age range 34–62 years, median age 47 years) with diagnosis of CSC, confirmed by fluorescein angiogram, but in remission at the time of the study, and 23 randomly selected patients (22 men and 1 woman, age range 41–69 years, median age 50 years) referred to our Department for retinal disease other than CSC were included.

In the CSC group the eye involvement was equally distributed between the right and the left eye (30% right eye, 35% left eye, 35% both eyes); in the acute phase of the disease, 60.9% (14/23) of the patients referred visual loss, 26% (6/23) metamorphopsia, 13% (3/23) central scotoma, and 8.7% (2/23) of the patients described no symptoms. According to the data collected, 52.17% of the patients reported only one episode of CSC; two to three episodes of reactivation were reported in 26% (6/23) of the cases; four to six episodes were reported in 4.3% (1/23) of the cases; 17.53% (4/23) of the patients examined reported no improvement of their visual condition after the first episode.

At the time of the interview the majority of the patients presented a best-corrected visual acuity of 5–6/10 (43.77%), 30% of the patients showed best corrected visual acuity of 7–8/10, in 4/23 patients (17.53%) the visual acuity was 9–10/10, while 8.7% of the patients examined had a visual acuity of 3–4/10.

Twelve of 23 (52%) CSC patients referred dyspeptic symptoms whereas upper gastrointestinal symptoms were present in 5/23 (21.7%) of control subjects. All dyspeptic control subjects had functional (i.e., non-ulcer) dyspepsia while 2/12 dyspeptic CSC patients had duodenal ulcer at endoscopy. In the 23 patients with CSC the prevalence of *H. pylori* infection was 78.2% (18/23) (95% CI 56–92%), whereas in the control group the prevalence of *H. pylori* infection was 43.5% (10/23) (95% CI 23%–65%), $p<0.03$ by two-tailed Fisher exact test, with a D value of 34.8% (95% CI 4.1%–65.5%) (Tab. II). The odds ratio for CSC associated with *H. pylori* infection was 4.6 (95% CI 1.28–16.9) as assessed by Woolf approximation.

We also compared the prevalence of *H. pylori* infection in CSC patients with that observed in a larger control group of 460 subjects undergoing endoscopy because of dyspepsia.. In this group the prevalence of infection was 41.3% (95% CI 36.7–45.9) and this was significantly lower than the prevalence observed in the CSC patient group ($p<0.001$) (data not shown).

DISCUSSION

This study was designed to evaluate the prevalence of *H. pylori* infection in patients with CSC. We compared 23 patients with diagnosis of CSC, confirmed by fluorescein angiogram, and a control group of 23 consecutive patients referred to our Department for retinal disease other than CSC. The prevalence of *H. pylori* infection appeared to be significantly higher in CSC patients than in the patients belonging to the control group with an odds ratio of approximately 4.6. This result strongly indicates that *H. pylori* may play a role in the pathogenesis of CSC. To further strengthen our finding, the prevalence of *H. pylori* infection in CSC patients was also significantly higher than that observed in a larger group of 460 control subjects with dyspepsia. Our data are in agreement with a recent report by Mauget-Faÿsse et al, who found a significantly higher prevalence of *H. pylori* infection in 16 patients with active long lasting CSC/diffuse retinal epitheliopathy compared with a control population (10).

Our series consisted almost exclusively of male patients (M/F ratio = 22/1). This is consistent with the observation of Ahnoux-Zabsonre et al, who found that the prevalence of CSC is tenfold higher in men than in women when con-

sidering patients younger than 50 years (8), as is the case with our patients. Moreover, our finding, suggesting a causative role for *H. pylori* infection in the development of CSC, is in agreement with Mauget-Faÿsse et al, who found that the association between *H. pylori* infection and CSC was more evident in men than in women (10).

The mechanism by which *H. pylori* is associated with the development of CSC remains speculative. However, it is possible to hypothesize that *H. pylori* interferes with the choroidal vascular functions. In partial support of this hypothesis, *H. pylori* has been postulated to be directly or indirectly involved in the pathogenesis of a number of cardiovascular diseases (14-16). In particular, *H. pylori* infection has been suggested to play a role in the development of arteriosclerosis (17) and might increase cardiovascular risk (18) by lowering plasma levels of B12 vitamin and folic acid, thereby increasing homocysteine levels. Moreover, significantly lower levels of high density lipoproteins have been found in *H. pylori* infected individuals (14). Finally, *H. pylori* increases blood vessel permeability, leucocytes adhesion, and platelets reactivity, and induces changes in the gastric mucosal microcirculation in rats (19); also, *H. pylori* may activate coagulation due to an increased level of mononuclear leucocytes in humans (20).

Our results seem to confirm the importance of *H. pylori* infection in CSC pathogenesis. We hypothesize that *H. pylori* infection in susceptible subjects may cause a chronic local release of cytokines or vasoactive or procoagulant substances that in turn might be responsible for alterations of the endothelial cells of the choriocapillaris under the macula, thus leading to the clinical form of CSC. Based on this study, we suggest investigating for *H. pylori* infection in patients with CSC in order to provide new therapeutic option (i.e., eradication of *H. pylori* infection). However, further studies in larger series of patients are needed to establish whether *H. pylori* infection plays a pathogenic role in CSC and whether *H. pylori* eradication affects the severity and likelihood of CSC recurrences.

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