Incidence of *Helicobacter pylori* in central serous chorioretinopathy: a case control study

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Abstract
***Helicobacter pylori* infection is one of the most common infections worldwide. Central serous chorioretinopathy (CSCR) is a serous macular detachment that usually affects young people. The aetiopathogenesis of the disease is still not completely understood. Recently, an interesting association has been observed between this disease and the *H. pylori* infection. This study was conducted to investigate a possible association between *H. pylori* infection and CSCR. A prospective study was performed and we evaluated a total of 54 CSCR patients (48 males and 6 females, median age 35.7 years), and a control group of 59 patients (25 women, 34 males; mean age 42.6±11 years) who referred to gastroenterology department of Imam Hospital, Ahvaz Jundishapur University of Medical Sciences, were studied. Central serous chorioretinopathy was diagnosed on the basis of findings in ophthalmic examinations and confirmed by fluorescein angiogram. All patients underwent a ^{13}C-urea breath test (UBT) and serum IgG anti-bodies to *H. pylori* by enzyme-linked immunosorbent assay technique to detect *H. pylori* infection. Patients were defined as *H. pylori* infected if both tests were positive. The mean duration of symptoms before diagnosis was 10.5±4.5 days. Overall no statistically significant difference was found between left and right eyes, bilaterally was in 5 patients (9.2%). The incidence of *H. pylori* infection was 68.5% in CSCR patients and 65% in control subjects (p=0.64). These results indicate that the prevalence of *H. pylori* infection is not higher in patients with CSCR than in controls. Further large studies will be required to determine the role of *H. pylori* infection in patients with CSCR.**

Keywords: Central serous chorioretinopathy, *Helicobacter pylori*, Macula, Retina

Introduction

There is increasing evidence that *H. pylori* as an important pathogen in human infections. It is confined to the stomach, if induces a strong systemic immune host responses. It is therefore plausible that untoward effects of these responses may contribute to development of disease in areas other than the gastrointestinal tract. Unfortunately, demonstration of a causal relationship is rather difficult, since the etiology of most of the disorders in which this organism might be involved is multifactorial, *H. pylori* being, at best, one of the causative factors.

Helicobacter pylori has been implicated in focal occlusive arterial diseases in young people [1]. CSCR being suspected vascular occlusive disease of choriocapillaris, but precise pathophysiology of CSCR is still poorly understood. CSCR is a disease that typically described as a condition with an acute presentation, characterized by a serious detachment of the neurosensory retina in the macular region, preferentially affecting young men (85%) between 25 and 45 years of age [2]. Patients usually have visual loss and one eye is predominantly affected and recurrences have been documented in 50% or more of cases [2]. Additional retinal findings include Retinal Pigment Epithelium (RPE) detachment, RPE atrophic tracks, capillary teleangiectasis, retinal or choroidal neovascularisatious and intraretinal or subretinal depositions [2-5].

Most cases (80-90%) of CSCR spontaneously resolve with recovery of visual function within one to six months of the onset of symptoms [6] but in some cases a chronic or progressive disease with widespread decomposition of the RPE and severe vision loss may develop [3, 6]. The precise pathophysiology of CSCR is still poorly understood [7]. A possible correlation between CSCR and the *H. pylori* infection has recently been hypothesized [8, 9]. The purpose of this study is to determine the prevalence of *H. pylori* infection in patients with CSCR.

Patients and Materials

Study Population

From 2004 to 2006, during a two year period we have set up a clinical program to evaluate a total of 54 CSCR patients 48 males and six females subjects, median age 35.7 years who referred and were observed in our Center. All patients underwent a complete ophthalmic examination and fluorecein angiography to confirm the diagnosis of acute CSCR. Classic CSCR was defined as a localized neurosensory retinal detachment associated with a focal leak or leaks at the level of the RPE by fluorescein angiography in the absence of associated uveitis, optic disc edema, choroial infiltrates.

Alterations in color vision are detectable on standard testing (e.g. Ishihara plates, Lanthony 15-Hue Desaturated Test) and the central visual defect may be demonstrated by using an Amsler grid test or a microperimetric examination [2]. Demographic data, medical history, past history of previous peptic ulcer were recorded. We examined serum samples from all of the cases for screening. Sera were examined for *H. pylori* specific antibodies by an Ig G enzyme-linked immunosorbent assay [10, 11]. *H. pylori* infection was confirmed by ^{13}C-urea breath test (C13 UBT Test, Cortex Italia, Milan, Italy). Patients were defined as *H. pylori* infected if both tests were positive.

A control group of 59 patients without CSCR (25 women, 34 men; mean age 42.6 ±11 years) who came to the gastroenterology outpatient clinic with different complains, without previous history of known *H. pylori* infection, and also had normal laboratory results (blood sugar, liver and renal functions, whole blood count, sedimentation rate) were considered as the control group.

Ethics

The institutional Ethics Review Committee approved the study protocol and consent for an interview was taken from each participant.

Statistical analysis

Collected data were coded, analyzed and computed using Microsoft Access 2000 database software was used (Microsoft Corp., Redmond, WA, USA). Basic descriptive statistics were performed using SPSS for Windows (version 11.0; SPSS Inc., Chicago, IL, USA) software. Simple statistics such as frequency, and standard deviation were also used. Differences between the two groups were evaluated using the Mann Whitney U-test, and chi-square analysis for categorical values. Kaplan Meier plots were used to calculate

patient survival and differences were compared using the log-rank test. The criterion for statistical significance was $p<0.05$.

Results

During the study period, 54 patients with CSCR were enrolled to this study. Forty eight patients (88.8%) of them were males and others were females. Their mean age was 35.7±10.1 years (range 25-45 years). Clinical characteristics of the study and control groups are summarized in table 1. The mean duration of symptoms before diagnosis was 10.5±4.5 days. Overall no statistically significant difference were found between left and rights eyes, bilaterally was in 5 patients (9.2%). 20.3% of patients had experienced recurrence. Initial visual acuity was 20/100-20/50 in 22 patients (40.6%) and ≥20/40 in 32 patients (59.2%). The incidence of *H. pylori* infection was 68.5% in CSCR patients and 65% in control subjects (p=0.64).

Table 1: Clinical characteristic of the case study and control groups

	Cases		Control
	Patients with CSCR and *H. pylori* (n=37)	Patients without CSCR and *H. pylori* (n=17)	Patients without CSCR (n=59)
Mean age (years)	35.7 ± 10.1	34.4±9.2	42.6 ±11
M/F ratio	33/4	15/2	25/34

Discussion

A correlation between CSCR and the *H. pylori* infection has recently been hypothesized [1, 7-9]. A case report of CSCR in a 43 years old man, documented that recurrences of the disease were always associated with the presence of *H. pylori* [9]. Resolution of CSCR and recovery of visual acuity were correlated significantly with successful eradication of the bacterium utilizing the conventional antimicrobial therapy. However, although indicative of an association, it should be emphasized that in this patient other factors (e.g. stress) may have been involved in the resolution of CSCR independently of any contribution made by the bacterial infection [9].

In a prospective pilot study of sixteen subject's affected either by active long-lasting CSCR or by diffuse retinal epithelopatly, the prevalence of *H. pylori* infection was found to be significantly higher in subjects with CSCR. This prevalence was also significantly higher when compared to that of an age matched control population in the same country as that of the participating subjects [1]. In the present study, we evaluated pylori infection in patients with CSCR and compared this with the control group (patients without CSCR). Our study showed that *H. pylori* infection was 68.5% in cases with CSCR and 65% of the control group (p=0.64).

These findings are not consistent with another study of the association between *H. pylori* and CSCR [9]. Although the precise pathophysiologic event leading to macular detachment in CSCR in not known [12-13]. Most ophthalmologists today believe that the pathology of case begins with a nonspecific disturbance of the choroidal circulation. Alteration in the exudative state of the choroids may lead to serous detachment of the RPE and a mechanical disruption of this tissue layer, possibly a small opening or a "blow out" of RPE, leading to the characteristic fluorescein leak [14]. These sequences of events are believed to produce detachment of the neourosensory retina and a myriad of secondary RPE and choroidal manifestations [15].

This association is still unclear. However, a possible explanation might indirectly arise from other correlation already found, e.g. between the *H. plyori* infection and the development of

atherosclerosis [10]. It has been documented that *H. pylori* cytotoxin associated gene A (cag A) positive strains may contribute to and significantly increase the risk of atherosclerosis development [16]. It has been suggested that anti-cage A antibodies may cross- react with vascular wall antigens, triggering an immunological cascade that causes arterial cell wall damage and leads to the development of atherosclorsis [10, 16].

In fact, the IgG antibody response to the infection by multiple and specific pathogens has been similarly considered to be a risk factor leading to the endothelial dysfunction. This fact may represent an additional mechanism by which pathogens such as *H. pylori* may contribute to atherogenesis [17]. Although infections interactions and autoimmune mechanisms may not solely explain the pathology of microangiopathies such as CSCR, which are more likely to represent organ response to multifactorial insults, a contributory mechanism for *H. pylori* could be hypothesized in condition [7]. Focal occlusion of the choroidal microcirculation may also promote choroidal neovascularisation and the associated serosanguineous complications observed in CSCR [18-21]. Interactions between *H. pylori* and vascular endothelial growth factor A might help to explain the choroidal ischemia and the secondary activation of host angiogenesis observed in some of these patients [7, 21].

In conclusion, even though this study does not support an association between *H. pylori* infection and CSCR, further multiple centers, randomized, case control trials are necessary to confirm the potential contributory role of the *H. pylori* infection in the pathogenesis of CSCR since diverging results regarding a possible association between infections agents and endothelial dysfunction.

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