Gastroenterology and Hepatology From Bed to Bench.

ORIGINAL ARTICLE

Association of *Helicobacter pylori* with central serous chorioretinopathy in Iranian patients

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ABSTRACT

Aim: This study was conducted to investigate a possible association between *H. pylori* infection and CSR.

Background: *Helicobacter pylori* infection is one of the most common infections worldwide. Central Serous Chorioretinopathy (CSR) is a serious macular detachment that usually affects young people. The etiopathogenesis of the disease is still not completely understood.

Patients and methods: A prospective study was performed and we evaluated a total of 35 CSR patients and control group of138 patients who referred to gastroenterology research center of Taleghani Hospital, Shahid Beheshti University of Medical Sciences, Tehran, Iran. Central serous chorioretinopathy was diagnosed on the basis of findings in ophthalmic examinations and confirmed by fluoresce in angiogram. All patients underwent a 13C-urea breath test (UBT) to detect *H. pylori* infection. Patients were defined as *H. pylori* infected, if breath test was positive.

Results: The mean duration of symptoms before diagnosis was8.3± 2.5 days. Overall, no statistically significant difference was found between left and right eyes, bilateral CSR was observed in 5 patients (14.2%).The incidence of *H. pylori* infection was 85.7% in CSR patients and 55.1% in control subjects (p=0.001). Odd's ratio was 4.895.

Conclusion: These results indicate that the prevalence of *H. pylori* infection is significantly higher in patients with CSR than in controls. No effect of age or sex was seen on H.pylori test results. Further multiple centers, randomized, case control trials are necessary to confirm the potential contributory role of the H. pylori infection in the pathogenesis of CSR as a possible association between infectious agents and endothelial dysfunction.

Keywords: Central cerouschorioretinopathy, *Helicobacter Pylori*, Macula, Retina.

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Introduction

There is increasing evidence that *Helicobacter pylori* is an important pathogen in human infections. It is confined to the stomach, and induces a strong systemic immune host response (1). It is, therefore, plausible that untoward effects of these responses may contribute to the development of disease in areas other than the gastrointestinal tract (2). 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 multi factorial and *H. pylori* can be, one of the causative factors. *H. pylori* has been implicated in focal occlusive arterial diseases in young people (3). CSR defined as suspected

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vascular occlusive disease of choriocapillaris, but precise pathophysiology of CSR is still poorly understood. CSR is a disease that is 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 (4-6). Patients have usually visual loss and one eye is predominantly affected and recurrences have been documented in 50% or more of cases (6).Additional retinal findings ilude Retinal Pigment Epithelium (RPE) detachment, RPE atrophic tracks, capillary teleangiectasis, retinal or choroidalneovascularisatious and intraretinal or subretinal depositions (3,5-7). Most cases (80-90%) of CSR spontaneously resolve with recovery of visual function within one to six months of the onset of symptoms (4-6), but in some cases a chronic or progressive disease with widespread decomposition of the RPE and severe vision loss may develop (5). The precise pathophysiology of CSR is still poorly understood (4). A possible correlation between CSR and the *H. pylori* infection has recently been hypothesized (8, 9). The purpose of this study is the evaluation of association of Helicobacter pylori with central serous chorioretinopathy in Iranian patients.

Patients and Methods

Study Population

From 2009 to 2011, during a two-year period, we set up a clinical program to evaluate total of 35 CSR patients (32males and three females, mean age 34.14± 5.73years) who were consecutively selected and after being matched with case group, they were followed in our center. All patients underwent a complete ophthalmic examination and fluoresce in angiography to confirm the diagnosis of acute CSR. Classic CSR was defined as alocalized neurosensory retinal detachment associated with a focal leak or leaks at the level of the RPE by fluoresce in angiography in the absence of associated uveitis, opticdisc edema, choroidalin filtrates. 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 amicroperimetric examination (5). Demographic data, medical history, pasthistory of previous peptic ulcer were recorded.

H. pylori infection was confirmed by 13C-urea breath test (C13 UBT Test, Kibion Uppsala, Sweden). Patients were defined as *H. pylori* infected, if UBT was positive. A control group of 138 patients without CSR (10 female, 128 male; mean age34.01±10.98 years) who came to the gastroenterology outpatient clinic with different complaints, 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 Gastroenterology and Liver Disease Research Center, Shahid Beheshti University of Medical Sciences Ethics Review Committee approved the study protocol, and consent for an interview was taken from each participant.

Statistical analysis

Results were expressed as the mean ± standard deviation (SD) for quantitative variables and percentages for categorical variables. Continuous variables were compared by independent samples t test for variables with normal distributions and Mann-Whitney test for variables with non-normal distributions. P values of 0.05 or less were considered statistically significant. All the statistical analyses were performed using SPSS version 16.0.

Results

During the study period, 35 patients with CSR were enrolled to this study. Thirty two patients (91.4%) of them were males and others were females. Their mean age was 34.14± 5.73years. Clinical characteristics of the study and control groups are summarized in table 1.

Table 1. Demographic characteristic of the case study and control groups

sex	Male (N/%)	Female (N/%)	Total (N/%)
case	32(91, 4%)	3(8.6%)	35(100%)
control	128(92.8%)	10(7.2%)	138(100%)

The mean duration of symptoms before diagnosis was 8.3±2.5 days. Overall, no statistically significant difference was found between left and rights eyes, bilateral CSR was observed in 5 patients (14.2%). 24.1% of patients had experienced recurrence. Initial visual acuity was 20/60-20/40 in 28 patients (80.0%) and ≥20/40 in7 patients (20.0%). The incidence of *H. pylori* infection was 85.7% in CSR patients and55.1% in control subjects (p=0.001) (table 2).

Table 2. *H.pylori* test results in case and control groups

H.pylori	Case (N/%)	Control (N/%)	Total (N/%)
Positive	30(85.7)	76(55.1)	106(100)
Negative	5(14.3)	62(44.9)	67(100)

Discussion

A correlation between CSR and the *H. pylori* infection has recently been hypothesized (2, 10).Visual acuity improvement was correlated significantly with successful eradication of the bacterium utilizing the standard antimicrobial therapy (7).

In study of affected either by active long-lasting CSR, or by diffuses retinal epithelopatly, the prevalence of *H. pylori* infection was found to be significantly higher in subjects with CSR. 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 (3).

In our study, the prevalence of *H.pylori* was significantly higher in case group. Their mean age was 34.14± 5.73 years. Considering the previous studies and current related texts, male preponderance and mean age of our patients - case group- were compatible with them.

CSR occurs primarily in healthy men between 25 and 55 years of age. This association is still unclear. However, a possible explanation might indirectly arise from other correlations already found, e.g. between the *H. pylori* infection and the development of atherosclerosis (11).

It has been documented that *H. pylori* cytotoxin associated *cag A* positive strains may contribute to and significantly increase the risk of atherosclerosis development (11). It has been suggested that anti-*cagA* antibodies may cross-react with vascular wall antigens, triggering an immunological cascade that causes arterial cell wall damage and leads to the development of atherosclerosis (11, 12). 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 (13). Although infection interactions and autoimmune mechanisms may not solely explain the pathology of microangiopathies such as CSR, which are more likely to represent organ response to multi factorial insults, a contributory mechanism for H. pylori could be hypothesized in this condition (7). Focal occlusion of the choroidal microcirculation may also promote choroidal neovascularisation and the associated serosanguineous complications observed in CSR (5). 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).

Although the precise pathophysiologic event leading to macular detachment in CSR in not known (1, 4), 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 fluoresce in leak (1, 4). These sequences of events are believed to produce detachment of the neourosensory retina and a myriad of secondary RPE and choroidal manifestations (4).

One study reports recurrences of the disease were always associated with HP-positivity, whereas improvements of both retinal findings and visual acuity were significantly correlated with a successful eradication of the bacterium (9).

A possible explanation might indirectly arise from the published hypothesis of a pathogenetic link between HP infection and atherosclerosis (11).In the study by Misiuk-Hojlo, et al, *H.pylori* infection was statistically significant among the patients with CSR diagnosis than in healthy population (14).

Much speculation surrounds the role potentially played by HP in determining CSR. In particular, CSR seems not to be more a merely retinal pigment epithelium (RPE) disease, but the final result of a general involvement of the choroidal microcirculation.

A HP-dependent immune mechanism, based on a “molecular mimicry” between pathogenic antigens expressed on the bacterium and homologous host proteins (e.g., those of the endothelial vascular wall), might also be involved in the pathophysiology of CSR. Although further multicenter, randomized, case-control trials are necessary to confirm the role potentially played by the HP infection in the pathogenesis of CSR, if this hypothesis is confirmed in the near future, a novel medical, antimicrobial approach to the disease management might be possible waiting for a successful vaccine therapy that will surely stimulate the scientific interest of many authors.

The results of this study show that the prevalence of *H. pylori* infection seems to be significantly higher in patients with CSR than in the controls. In conclusion, this study supports an association between H. pylori infection and CSR. Further multiple centers, randomized, case control trials are necessary to confirm the potential contributory role of the *H. pylori* infection in the pathogenesis of CSR as a possible association between infections agents and endothelial dysfunction.

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