CENTRAL SEROUS CHORIORETINOPATHY AS AN EXTRADIGESTIVE MANIFESTATION OF HELICOBACTER PYLORI GASTRIC INFECTION

CORIORRETINOPATÍA SEROSA CENTRAL COMO MANIFESTACIÓN EXTRADIGESTIVA DE INFECCIÓN GÁSTRICA POR HELICOBACTER PYLORI

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ABSTRACT

Objective: Helicobacter pylori (HP) gastric infection has been implicated as an important factor in occlusive arterial pathology. Nowadays, it is suspected that central serous chorioretinopathy (CSC) is due to a multifocal vascular occlusive disease of the choriocapillaris. The aim of this study was to determine the relation between gastric HP infection and CSC.

Materials and methods: We evaluated a group of 16 patients with CSC and 20 controls. HP infection was assessed by the 13C-urea breath test (UBT). Clinical CSC diagnosis was confirmed by fundus biomicroscopy and fluorescein angiography.

Results: Out of 16 patients with CSC, 11 (68.75%) were males and 5 (31.25%) females, with a mean age of 46.3 years. HP infection was positive in 11 patients (68.75%) and negative in 5 (31.25%). Men were HP-positive (HP+) in 72.7% of cases, compared to women who were HP+ in 60% of cases. The difference in prevalence of HP between the CSC-group (68.75%) and the control-group (30%) was found to be statistically significant ($p< 0.05$). HP+

RESUMEN

Objetivo: La infección gástrica por Helicobacter pylori (HP) es considerada como un factor de riesgo importante en la patología arterial oclusiva. Actualmente se piensa que la coriorretinopatía serosa central (CSC) es una enfermedad por oclusión multifocal en la coriocapilar. El objeto de este estudio es valorar una posible relación patogénica entre la infección gástrica por HP y la CSC.

Material y método: Se estudió un grupo de 16 pacientes con CSC y 20 controles. El estudio de la infección por HP se realizó con el test respiratorio de la urea-13C (TRU). El diagnóstico clínico de CSC se confirmó con biomicroscopía posterior y angiografía fluoresceínica.

Resultados: De los 16 pacientes CSC, 11 (68,75%) fueron varones y 5 (31,25%) mujeres con una edad media de 46,3 años. La infección por HP fue positiva en 11 pacientes (68,75%) y negativa en 5 (31,25%). Los hombres fueron HP positivo (HP+) en el 72,7% de los casos frente a las mujeres que fueron HP+ en el 60%. La diferencia en prevalencia de HP entre el grupo-CSC (68,75%) y el grupo-con-

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patients had more gastric pain than HP negative (HP-) patients (72.73% vs 20%).
Conclusions: These results indicate a possible statistical association between Helicobacter pylori gastric infection and CSC. HP should thus be considered a risk factor in CSC patients. *(Arch Soc Esp Oftalmol 2008; 83: 177-182).*

Key words: CSC, Helicobacter pylori, urea breath test, gastric infection, extradigestive manifestation, risk factor.

trol (30%) fue significativa (p< 0,05). Los pacientes HP+ tenían más dolores gástricos que los pacientes HP negativo (HP-) (72,73% vs 20%).
Conclusiones: Estos resultados indican una posible asociación estadística entre la infección gástrica por Helicobacter pylori y la coriorretinopatía serosa central, pudiendo considerar la infección por HP como un posible factor de riesgo en los pacientes CSC.

Palabras clave: CSC, Helicobacter pylori, test respiratorio de la urea, infección gástrica, manifestación extradigestiva, factor de riesgo.

INTRODUCTION

Typically, central serous chorioretinopathy (CSC) is defined as a neurosensory serous retina detachment of unknown origin which affects the macula generally during emotional stress periods, exhibiting a preference for young males in the 25-45 age bracket (1). The majority of cases have a spontaneous functional recovery but sometimes it can become chronic in older patients, with signs of decompensation of the retinal pigmentary epithelium (PE) and severe vision loss (1,2). The ethiopathogeny of CSC is unknown (1,2) although it has always been related to type A characters, anxious and stress-prone individuals, considering that in the acute phase there is a release of corticoids (cortisole) and adrenaline. The latter can cause damage to the choriocapillaris and increase its permeability. In turn, cortisole can enhance the constricting action of chatecolamines. The collagen-synthesis inhibiting action of cortisole can cause a thinning of the capillary wall, increasing its fragility and enhancing the permeability of the choriocapillary (1-3). Helicobacter pylori (HP) is a gram-negative bacteria of spiral appearance, associated to multiple digestive and extra-digestive pathologies (4-10). Only recently has HP attracted the interest of ophthalmologists (11-13). This paper aims at establishing a possible pathogenic relationship between gastric Helicobacter pylori infection and central serous chorioretinopathy.

SUBJECTS, MATERIAL AND METHODS

This study was approved by the Research and Teaching Committee of our hospital. Patients were recruited at the retina consulting room. A total of 36 individuals were studied (16 patients and 20 controls) between 2002 and 2006. Table I shows the demographic characteristics of both groups. The inclusion criteria for the CSC group patients were as follows:

To accept participation in the study, signing an informed consent.

Not having a previous diagnosis of infection by HP.

Not having been treated 3 months prior to the study with antibiotics, corticoids, sildenafil citrate of sympathetic-mimetic drugs. For women in fertile age, negative pregnancy test.

Eye fundus: retinal serous detachment associated or not to a serous detachment of the pigmentary epithelium.

Fluorescein angiography: one or more escape points at the level of the retinal pigmentary epithelium.

The inclusion criteria for the control group were:

— Accepting to participate in the study with signature of informed consent.

— Being the spouse or sibling of a patient of the CSC group.

— Not having CSC history, past or present.

— Not having a prior diagnostic of HP infection

— Not having been treated 3 months prior to the study with antibiotics, corticoids, sildenafil citrate

Table I. Demographic characteristics

	Control group	CSC Group
#	20	16
Sex	13 (65%) male	11 (68.75%) males
Age	50.2 SD 12.4	46.3 SD 13.2

CSC: Central Serous Chorioretinopathy; #: Number.

or sympathetic-mimetic drugs. For women in fertile age, negative pregnancy test.

The exclusion criteria were:

— Not accepting the conditions of the study.

— Inability to comply with follow-up.

— Pregnancy, breastfeeding and postpartum.

— Treatment with antibiotics, corticoids, sildenafil citrate, sympathetic-mimetic drugs or vitamins at the time or 3 months prior to the study.

— Collagen-related disorders or transplants.

The assessment of gastric pain was made with:

Simple descriptive or verbal evaluation scale (VRS): classified as no pain, mild, moderate, intense an unbearable

Andersen scale: measurement of pain from the dynamic viewpoint, quantified as spontaneously described, at rest, with slight movements or with cough.

A full ophthalmological exploration was made, including fluorescein angiography . The HP study was made with a non-invasive method, the urea respiratory test (URT): each patient was given a solution of 100 mg of urea C 13 associated to citric acid. When HP colonizes the gastric mucous, bacterial urease metabolizes urea into NH3 (ammonia) and in CO2 (carbon dioxide) which is eliminated with exhaling air. A mass spectrometer was used to measure C13. Our lab set the threshold value at 2.5 C 13 °/00 (HP + >2.5 C 13 °/00).

In order to compare the qualitative variables between patients and the control group, chi square and t of Student were utilized for the quantitative variables.

RESULTS

Table II shows a comparison between patients and the control group with respect to HP. Of the 16 patients with CSC, eleven (68.75%) were HP positive while 5 cases (31.25%) were negative. In the control group, six (30%) were positive for HP and 14 (70%) negative. Table 3 shows the percentage of HP per sex. In the CSC group, 72.73% of men were positive against 60% of women. In the control group, 30.77% of men were positive against 28.57% of women. A stratified analysis of the sample per gender shows that HP is associated to a younger age of CSC diagnostic in the group of men (HP+ = 32.l2 SD 4.1; HP- = 39.8 SD 5.7: $p<0.001$). A comparison of the proportion of HP positive cases in the control group (30%) and the CSC group (68.75%) was significant ($p < 0.05$).

Table II. Comparison of Helicobacter pylori

	Control group	CSC Group
HP +	6 (30%)	11 (68.75%)
HP -	14 (70%)	5 (31.25%)

HP: Helicobacter pylori, CSC: Central Serous Chorioretinopathy.

The HP- positive patients had more gastric pain (eight out of eleven, 72.73%) than HP-negative patients (one out of five, 20%).

DISCUSSION

Central Serous chorioretinopathy is a macular serous detachment which typically affects young men in the 25-45 age bracket and which usually resolves spontaneously with good visual prognosis (1). A small percentage of patients develop a chronic or progressive disease with EP decompensation and severe vision loss (1,2). At present the ethiopathogeny of CSC is not fully known and no effective treatment has been developed. CSC has been associated to toxic products such as tobacco, drugs such as corticoids, sympathetic-mimetic, antibiotic and, more recently, sildenafil citrate, pregnancy, several systemic processes such as high arterial pressure, collagen-related disorders, asthma and eye diseases such as pigmentary retinopathy (14-16).

There has been widespread speculation about the psychosomatic origin of CSC due to it being associated to type A personalities (3,14). In CSC patients, Iijima H et al (17) described an increase of inhibitor 1 of the plasminogen tissue activator. At the level of the choriocapillary, occlusion areas would occur with ischemia in the pigmentary epithelium and this would mean the CSC is a microvascular process generally affecting the PE. This matches the clinical findings.

Table III. Comparison of Helicobacter pylori

	Control group	CSC Group
HP +	M= 4 (30.77%)	M= 8 (72.73%)
	F= 2 (28.57%)	F= 3 (60%)
HP -	M= 9 (69.23%)	M= 3 (27.27%)
	F= 5 (71.43%)	F= 2 (40%)

HP: Helicobacter pylori; CSC: Central Serous Chorioretinopathy; M: Males; F: Females.

It has recently been documented that CSC could be an extra-digestive expression of HP (18-21). HP is a spiral-shaped gram negative microaerophile bacteria which colonizes the stomach of 50% of all humans. Its presence is associated to the inflammation of gastric mucous due to the infiltration of inflammatory cells. Before the discovery of HP in 1984, it was believed that stress and lifestyle-related factors accounted for peptic ulcers (22). However, we know now that the bacteria is responsible for at least 905 of duodenum ulcers and 80% of gastric ulcers. This paper studies the relationship between HP and CSC in a group of patients vis-à-vis a control group. As the control group is comprised mainly of spouses of CSC patients, the environmental and socioeconomic variables which may influence the colonization of HP are minimized (22). The URT test is the main non-invasive method for detecting active infection by HP with a sensitivity of 90%. The limits of this test lie in its cost and the need of a high level of equipment (23). The series presented herein shows that CSC affects more men (68.75%) than women (23.1%), with a mean age of 46.3 years. HP infection was positive in 11 patients (68.75%) and negative in 5 (31.25%). Men were HP positive in 72.73% of cases against women, who were HP positive in 60%. These results match those of other studies which also showed a greater prevalence of HP infection in males in general, independently of the ocular involvement (24).

The different prevalence of HP between the CSC group (68.75%) and the control group (30%) was significant ($p< 0.05$). It is important to emphasize that HP+ patients had more gastric pain than HP- patients (72.73% vs. 20%). In clinical practice, this difference has typically been associated to anxiety and stress levels of patients (3). The verbal assessment tool (VRS), introduced by Keele in 1948 was used to measure pain because it is the most basic approach for measuring pain and is useful for the researcher due to ease of application. The patient does not find it difficult to utilize this scale to indicate his/her pain level. Anderson's scale measures pain from the dynamic point of view. The good correlation observed between the latter and other scales is enhanced by its interest in acute pain, associated to the reduction of physical activity. We have no explanation about the association found between HP and an earlier expression of CSC in males, although the hormone and gastrine levels (which control the secretion of parietal cells) surely play a role (11,22). In a prospective study with 16 CSC patients in the South of France, Mauget-Faysse M et al (18) detected HP infection in 56.3% of patients. This percentage is much higher than the 27.5% of the control group. In turn, in a study with 78 patients, Ahnoux-Zabsonre et al (19) established an association between HP infection and CSC (39.7% vs. 25.4% of the control group). Cotticelli L et al (25) proved that the prevalence of HP is significantly higher in patients with CSC than in the control group (78.2% vs. 43.5%).

From the above studies, it can be considered that HP could be a risk factor in patients with CSC, which could be involved with their physiopathology the same way it affects vascular, cerebral and dermatological pathologies: bacterial antigens would be equivalent to proteins expressed by the human body, for example vascular endothelium, producing an attack by the immune system against structures such as the choriocapillary, with blood flow reduction and damages to the EP (11,20).

Why is it that HP does not produce CSC in every case? Perhaps because of the different HP strains, each having a different genetic imprint and therefore different biochemical and pathogenic characteristics. To this we must add cytokines, prostaglandins and leucotriens (12,22,26), which increase their concentration in blood in varying quantities as a result of the infection and appear to be active in choroidal vessels. Another important limiting factor for the development of CSC is the genetically determined susceptibility of individuals (22,26). The patients diagnosed with chronic CSC and treated with photodynamic therapy may reduce their clinical expressions such as choroidal permeability. However, visual acuity improvement can be variable (27). Anti-angiogenics could be a therapeutic option for chronic CSC. However, more studies are needed before their use can be generalized (28). The limitations of this paper are due to the number of cases studied and the lack of genetic-bacterial research. If these findings were confirmed with randomized, multi-centre studies with control cases, the treatment of CSC would be mainly anti-microbial as an extra-gastric expression of Helicobacter pylori.

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