

Helicobacter pylori infection and primary open-angle glaucoma: is there a connection?

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Abstract: Glaucoma, the most common form of which is primary open-angle glaucoma (POAG), is a neurodegenerative disease which is the second most common cause of blindness worldwide. Among the factors that have been implicated in the pathophysiology of this disease is infection with *Helicobacter pylori*. This alleged association has caused a great deal of scientific discussion during the past decade, as the establishment of such a correlation might lead to therapeutic applications for all glaucoma patients. In this review, we assess all relevant major studies and trials in an effort to elucidate the issue.

Keywords: *Helicobacter pylori*, primary open-angle glaucoma, apoptosis

Introduction

Glaucoma is a neurodegenerative disease which is the second most common cause of blindness worldwide. It is estimated that 60 million people in the world are affected by the disease and 8.4 million are bilaterally blind.¹ Various factors, among them infection with *Helicobacter pylori* (HP), a Gram-negative bacterium associated with the occurrence of Alzheimer's disease, gastritis, gastric ulcers, and gastric carcinomas,²⁻⁴ have been implicated in the pathophysiology of the disease. Over the last decade, researchers around the world have focused on the issue; however, the controversial results of studies have left the subject open to further discussion. Another question that will require answers is whether an association between HP infection and glaucoma is proven, is whether these two entities are linked by a causal relationship or whether they share common predisposing or precipitating factors.

Studies

Kountouras et al⁵ were among the first to investigate the putative association between HP infection and glaucoma. In a prospective study (based on a sample of 32 patients with primary open-angle glaucoma (POAG), nine patients with pseudoexfoliation glaucoma (PEG) and a control group of 30 age-matched anemic patients), they concluded that HP infection is more frequently encountered among glaucoma patients than in the general population; this finding was based on both biopsy-based campylobacter-like organism tests as well as on serological examinations. Glaucoma patients also had, to a statistically significant extent, more frequent pathologies in the form of antral gastritis and peptic ulcers. In an extension of this study,⁶ the same authors proved that in the long term, glaucoma patients benefit in terms of regulation of intraocular pressure and visual field parameters in those cases where HP is successfully eradicated. It was again the

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same team⁷ who conducted a prospective study on 26 POAG patients and 27 PEG patients undergoing glaucoma surgery and 31 patients undergoing phacoemulsification cataract surgery and concluded there was an increased concentration of IgG HP antibodies in the aqueous humor of surgical eye specimens from glaucoma patients. These studies by Kountouras et al were used in correspondence⁸ addressed to Weinreb et al,⁹ in which Kountouras criticized the lack of mentioning of the role of HP in glaucoma by Weinreb.

Deshpande et al¹⁰ also performed a similar prospective, nonrandomized comparative study based on the serological and aqueous humor examination of 50 glaucoma patients and a control group of patients undergoing phacoemulsification cataract surgery. They found a statistically significant difference between POAG patients and PEG and control patients, as far as the concentration of serum HP IgG antibodies was concerned. However, they did not find any significant correlations between the patient groups in regard to HP IgG antibody concentration in the aqueous humor. Galloway et al¹¹ performed a prospective study based on a sample of 97 patients with POAG, PEG, and ocular hypertension and an analogous control group; they did not find statistically significant differences in the concentration of serum HP-IgG antibodies between groups, thus leaving an open field for further research and scientific discussion. Similarly, Kurtz and associates¹² investigated seropositivity to HP and to its cytotoxin-associated gene A (CagA) product in 51 patients with various types of glaucoma and compared the findings to those of a control group of 36 cataract patients. They found no significant association between HP infection and CagA seropositivity with glaucoma. Handa et al noted the connection of CagA to various pathological pathways, leading to irregular gastric cell activity, apoptosis, and carcinogenesis.¹³

There has also been much debate regarding the mechanisms that might be involved in the possible association of HP infection with glaucoma. Is there a causal relationship between them or do they share common predisposing or precipitating factors and pathophysiological backgrounds? Various authors^{14–19} believe that HP infection acts through the release of proinflammatory and vasoactive substances, through the release of endothelin-1, nitric oxide, and oxygen free radicals, and through the induction of oxidative stress, the destruction of mitochondrial DNA and the induction of apoptotic cell death, which may be the main reason for glaucomatous neuropathy. This apoptotic process may be linked with the FASL protein, a type-II transmembrane protein belonging to the tumor necrosis factor (TNF) family. The binding of this protein with

its receptors differentiates the response of the immune system, is believed to play a role in oncogenetic processes, and is also connected with apoptotic cell death.^{14,15,18}

Discussion

Over the last decade, various researchers have examined the existence of a possible link between HP infection and glaucoma. Some studies have supported such an association, with suggested underlying mechanisms including the induction of inflammatory responses as well as apoptotic processes that lead to glaucomatous neuropathy. Although some support for this seems to exist, contradictory results from other related studies leave room for further investigation. This controversy is best reflected in the scientific debate that took place between Weinreb et al⁹ and Kountouras et al,⁸ with Kountouras et al claiming there was a positive correlation between HP and glaucoma. The establishment of such a causal relationship will probably have important practical applications as the eradication of HP might lead to developments in the treatment of glaucoma.

Disclosure

The authors report no conflicts of interest in this work.

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