HELICOBACTER PYLORI INFECTION AND THE DEVELOPMENT OF GASTRIC CANCER

Alina Preda¹, F. Burada², Cristina Soare², Amelia Birca², E. Moraru², M. Cruce²

1. NATIONAL INSTITUTE OF LEGAL MEDICINE “MINA MINOVICI”
BUCHAREST  2. DEPARTMENT OF CELLULAR AND MOLECULAR BIOLOGY, FACULTY OF MEDICINE, UMPH CRAIOVA
predaalina2006@yahoo.com

Summary

*Helicobacter pylori*, a Gram negative bacteria, is capable of modifying cell turnover in the interior of gastric glands, by influencing cell proliferation and apoptosis ratio. Gastric carcinogenesis is a complex, multifactorial process in which *Helicobacter pylori* persistence plays an important role. Initially *Helicobacter pylori* determines a superficial gastritis which can lead to glandular loss and multifocal atrophic gastritis; this is followed by intestinal metaplasia which can develop later in some patients in gastric displasia and cancer. This carcinogenic model is currently accepted for distal gastric cancer; cardial cancer is correlated with *Helicobacter pylori* infection. Usually intestinal pathologic type is associated with gastric atrophy and diffuse type is associated with non-atrophic chronic gastritis. *Helicobacter pylori* seems to be involved in both pathological forms of gastric cancer; epidemiological studies couldn’t find significant differences between those types regarding infection prevalence. Regarding the high prevalence of *Helicobacter pylori* infection in general population must be explained firstly why just some individuals develop gastric cancer and secondly why others develop peptic ulcer.

**Keywords**: *Helicobacter pylori*, gastric mucosa, gastric cancer

Introduction

*Helicobacter pylori* is the etiologic agent of chronic active gastritis, gastric and duodenal ulcers, also being involved in the development of gastric cancer and MALT lymphomas (Blaser and Berg, 2001). It was recently included by OMS as a first degree carcinogen, because its involvement in atrophic gastritis with intestinal metaplasia (considered premalignant lesions) development (Graham, 2000]. Atrophic chronic gastritis is associated with an increased risk of developing intestinal type gastric cancer; the most frequently met is multifocal atrophic gastritis, usually determined by *Helicobacter pylori* infection and which is associated with intestinal metaplasia. The highest risk of gastric cancer development is associated with incomplete type intestinal metaplasia (type III) (Uemura *et al.*, 2001). This paper tries to review some of pathological particularities induced by *Helicobacter pylori* infection to gastric mucosa up until definite neoplastic changes.

Material and method

Gastric biopsies were taken from patients with gastric symptoms (abdominal pain or discomfort); about 70% of patients with early gastric cancer are presenting dyspeptic syndrome, 30% are asymptomatic, the clinical diagnosis not being sensitive enough to differentiate organic from functional diseases; for this reason all patients with high risk of developing gastric carcinoma must be evaluated throughout endoscopy (Robbins and Cotran, 2005), the upper gastro duodenal endoscopies are establishing lesion site, macroscopic type and allowing to take biopsies which can differentiate between different types of gastric cancer and their grading (Peek and Blaser, 2005).
For a correct histopathological result one must take at least eight biopsies from the lesion centre and margins; always from these biopsies tests for *Helicobacter pylori* identification must be done. The tissue fragments were immersed in 10% neutral formalin (buffered with cu potassium carbonate 10%) for 12-48h (depending from the piece size) and embedded in paraffin; 4-5 micrometers tissue sections were obtained and stained with haematoxylin eosin and examined microscopically for the overall study of gastric mucosa or gastric wall, gastritis grading (Sydney System), inflammation grading; *Helicobacter pylori* was found in the mucosal layer, even if its count was low, as right or slightly curved, comma-like pink bacilli (Figure 1).

**Results and discussions**

*Helicobacter pylori* colonizes human gastric mucosa, establishes a chronic infection of the gastric mucosa, gastritis and is associated with the development of peptic ulcer disease, atrophic gastritis and gastric cancer. The patients are aged between 60-70 years (males and females); after upper gastro duodenal endoscopies, the biopsy were analyzed by histopathology alone (using haematoxylin eosin staining) to reveal gastric diseases but also to determine the presence of *Helicobacter pylori* (Figure 2). Diseases for which endoscopic diagnosis was used were: duodenal ulcer, gastric ulcer, gastritis, including non-ulcer dyspeptic (seeming normal mucosa); *Helicobacter pylori* was positive in all patients, there is a significant association between *Helicobacter pylori* and gastric diseases (gastritis, gastro duodenal ulcer); the most frequent *Helicobacter pylori* colonization site is the antrum; gastric cancer diagnosis is more frequent in persons with a positive history of *Helicobacter pylori* positive active gastritis. There are more possible mechanisms of *Helicobacter pylori* induced gastric carcinogenesis; a major mechanism is represented by the production of chronic inflammation secondary to *Helicobacter pylori* infection (Figure 3), inflammation (Figure 4) will determine an increased in oxidative stress with free radicals formation and subsequent DNA lesions, increased cytokines production, increased cell turnover and diminished DNA repairs. The association between *Helicobacter pylori* infection and the inflammatory response determined by it leads to an increased proliferation rate and apoptosis in epithelial gastric cells in vivo (Blaser and Atherton J, 1999).

The mechanism by which *Helicobacter pylori* chronic infection favors gastric cancer includes an atrophic gastritis stage (Figure 5); initially *Helicobacter pylori* infection determines a superficial which can progress to gastric atrophy. Gastric atrophy is following by intestinal metaplasia (Figure 6), which can progress to gastric dysplasia and cancer. ( Figure 7) (Misra et al, 2000).

CagA positive strains (s1a-vacA:iceA1) are more pathogenic than CagA negative ones (s2-vacA:iceA1); first ones are colonizing the proximal mucosal layer associating intense inflammation, the second ones are colonizing the proximal mucosal layer associating diminished inflammation; this is the reason why some patients are developing gastric cancer while others are developing peptic or duodenal ulcer.

**Conclusions**

Gastric cancer can develop both in infected with *Helicobacter pylori* and non infected persons. Those with histological findings of severe gastric atrophy, predominantly in gastric corpus or intestinal metaplasia are at increased risk. Persons with *Helicobacter pylori* infection, nonulcer dyspepsia, gastric ulcers have an increased risk of developing gastric cancer compared to those with duodenal ulcers.

**References**


Figure 1. Superficial and antral active chronic gastritis with moderate activity, positive for \textit{Helicobacter pylori} ++

Figure 2. \textit{Helicobacter pylori} ++

Figure 3. Superficial and antral chronic gastritis with moderate activity

Figure 4. \textit{Helicobacter pylori} ++

Figure 5. \textit{Helicobacter pylori} + focal

Figure 6. Chronic gastritis with moderate activity and atrophy, associated with incomplete intestinal metaplasia.

Figure 7. Adenocarcinoma of the stomach, tubular type, well differentiated, with displasic lesions