

TOXICOSIS IN HELICOBACTER PYLORI INFECTION - A HYPOTHESIS

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Abstract

Background and aim. We present a new clinical entity in relation to the *Helicobacter pylori* infection characterized by complex and varied clinical extra-digestive manifestations.

Clinical findings such as asthenia, adynamia, sleep disorders, hair and nails modifications, digestive symptoms and heart rhythm disorders describe the clinical aspect of toxicosis associated with Helicobacter pylori infection.

Methods. The clinical presentation and therapy of patients with *Helicobacter pylori* infection were analyzed.

Results. Combined drug therapy: antibiotics + proton pump inhibitors + colloidal bismuth compound determinate remission of the symptoms in the first 3 to 5 days.

The characteristic of the relation between Helicobacter pylori and the mucus-epithelial cell complex, the properties of the bacterial cell components, and the inflammatory and immunological response targeting other organs describe the immuno-pathological outbreak of Helicobacter pylori.

Conclusion. We support the term of toxicosis associated with *Helicobacter pylori* infection in selected cases.

Keywords: *Helicobacter pylori*, mucus-epithelial cell complex, drug combination, immuno-pathological outbreak, toxicosis.

Introduction

The clinical symptoms associated with the *Helicobacter pylori* (*H. pylori*) infection are various digestive and extra-digestive manifestations. In practice, the clinical symptomatology is dominated by dyspeptic syndromes consisting of epigastric pain, gastric burns and nausea. Other clinical symptoms may also occur. These symptoms are often polymorphic manifestations generally dominating the first clinical symptoms: profound asthenia, extreme adynamia, extreme and continuous fatigue, malaise, sleep disorders, lack of creative activity, lack of initiative, loss of appetite, nausea, frequent and loose stools, itching, tachycardia. The objective examination evidences pale and peeling skin, wrinkles, depressed physical appearance, brittle hair and nails, hypotension.

Observation. Patients with positive test for *H. pylori* can associate clinical states similar to toxicosis under certain circumstances.

Therapeutic test. The administration of specific medication for the treatment of *H. pylori* infection can rapidly determine the remission of the symptoms in the first 3 to 5 days. A complex drug combination consisting of: Proton pump inhibitors (PPI) + Colloidal bismuth subcitrate + Antibiotics (Amoxicillin and Clarithromycin) must be used.

Material and Methods

I evaluated 89 patients presenting for clinical symptoms associated to *H. pylori* infection, 62.9% were females and 87.6% had a positive diagnosis of *H. pylori* infection [1,2,3,4,5].

During the first 7 days I used the following medication : Omeprazole or Esomeprazole 20 mg twice daily + Colloidal bismuth subcitrate 120 mg four times/day + Amoxicillin 1000 mg twice daily and Clarithromycin 250 mg four times/day. Between days 8 and 28, I used Omeprazole or Esomeprazole 20 mg/ day + Colloidal bismuth subcitrate 120 mg twice daily.

The treatment for *H. pylori* infection was conducted according to the guidelines of Romanian National Congress,

Sinaia, 1996 [6], European Consensus Maastricht, 1997 (Gut, 1997) [7] and Consensus Maastricht II 2000 [8] using first line therapy: PPI 20 mg twice daily + Clarithromycin 500 mg twice daily + Amoxicillin 1000 mg twice daily or Metronidazole for at least 7 days. In case of failure, second line therapy can be used: PPI 20 mg twice daily + Colloidal bismuth subcitrate 120 mg four times/day + Metronidazole 500 mg four times/day + Tetracycline 500 mg twice daily for at least 7 days.

Taking into consideration the beneficial effects of the Colloidal bismuth compound in gastric and duodenal ulcers during pain periods, the clinical experience of Doctor Bulbuc Traian from County Hospital Bistrita between 1968-1997 and also the use of Colloidal bismuth compound in University Hospitals from Cluj-Napoca [9] and other clinical research trials, I decided to use Colloidal bismuth subcitrate [10,11,12].

Considering the particularities of *H. pylori* infection in the gastric mucosa, the tendency of the bacteria to penetrate into the gastric mucus and to attach to the epithelial cells and avoid the immune system, to persistently multiply and infect areas difficult for the antibiotics to penetrate, I decided to extend the use of PPI and Colloidal bismuth subcitrate.

I communicated my personal experience with this treatment combination during the Maastricht Consensus III in 2005.

Results

Case no.1

Male, 48 years old, computer engineer working in a multinational company, active 8-10 hours daily. In 2001 he presented with malaise, asthenia, adynamia, sleep disorder, reduced mental and physical activity. Clinical diagnosis was Toxicosis with *H. pylori* and chronic duodenal ulcer.

Para-clinical examinations performed were superior endoscopy which showed antral chronic gastritis with high grade activity, positive *H. pylori*, exulcerations and immune-reactive lymphoid aggregates in the deep chorion; urea test was positive for *H. pylori*. Treatment combination used was Omeprazole + Colloidal bismuth subcitrate + Amoxicillin + Clarithromycin. The clinical evolution of the patient was very good.

In October 2003 *H. pylori* was detected positive and the patient didn't follow any medication.

In April 2004 the patient described epigastric pain accompanied by gastric burn after eating food at normal room temperature and having a "cold" sensation. He couldn't eat cold food, he had to heat water and food. The clinical diagnosis were allergy to cold or *H. pylori* infection. The serological test for *H. pylori* was positive. The clinical diagnosis was Toxicosis with *H. pylori*. Treatment combination used was Omeprazole + Colloidal bismuth subcitrate + Amoxicillin + Clarithromycin. The clinical evolution of the patient was very good.

In November 2004, the patient complained of painful dyspeptic syndrome located in the epigastric region, sleep disorder, lack of concentration, daily tiredness and depressive mood. The serological test for *H. pylori* was positive. Treatment combination used was Omeprazole + Colloidal bismuth subcitrate + Amoxicillin + Clarithromycin. The clinical evolution of the patient was very good.

In December 2004 a superior endoscopy was performed and the result was: gastric mucosa with discreet erythema. The urea test for detecting *H. pylori* was negative.

Case no.2

Male, 57 years old, professor at the University, came to the medical practice unit on the 20th of October 2002 complaining of asthenic syndrome during spring and summer seasons, headaches, tiredness, couldn't get up in the morning to go to the work. Blood pressure was 110/70 mmHg.

Superior endoscopy was performed and the result showed antral gastritis with positive *H. pylori* infection. Treatment combination used was Omeprazole + Colloidal bismuth subcitrate + Amoxicillin + Clarithromycin. The clinical evolution of the patient was excellent, the patient describing himself as being tireless and having very good appetite.

On the 8th of January year 2003 the patient was in very good health.

On the 6th of February the patient performed both serological and respiratory tests and they were both negative.

Case no.3

Male, 65 years old, retired colonel, came to the medical practice unit complaining for asthenia, extreme adynamia, very pale skin, sleep disorder, loss of appetite, nausea and weight loss.

Superior endoscopy was performed and the result showed antral gastritis with positive *H. pylori* infection. The urea test was positive. Treatment combination used was Omeprazole + Colloidal bismuth subcitrate + Amoxicillin + Clarithromycin. The clinical evolution of the patient was very good.

Case no.4

Male, 48 years old, priest, referred to the medical unit for nausea, epigastric pain, asthenia, profound adynamia, difficulty in conducting work activities. Superior endoscopy was performed and the result showed antral gastritis with positive *H. pylori* infection. The urea test was positive.

Treatment combination used was Omeprazole + Colloidal bismuth subcitrate + Amoxicillin + Clarithromycin. The clinical evolution of the patient was excellent in the first 5-7 days.

Case no.5

Female, 26 years old, school teacher, addressed to the medical unit for nausea, loss of appetite, asthenia, adynamia, agitated sleep, tiredness. Superior endoscopy

was performed and the result showed antral gastritis with positive *H. Pylori* infection. The urea test was positive.

Treatment combination used was Omeprazole + Colloidal bismuth subcitrate + Amoxicillin + Clarithromycin. The clinical evolution of the patient was very good.

One year later, the patient came to the medical practice for asthenia, adynamia, pale and peeling skin, depressed physical appearance, brittle hair and nails. The serological test for *H. pylori* was positive. I decided to perform a serological test to the family members living in the same apartment: the mother and the husband. Both relatives had positive tests and they were asymptomatic. I recommended treatment for the *H. pylori* infection to all family members with Omeprazole + Colloidal bismuth subcitrate + Amoxicillin + Clarithromycin.

The clinical evolution was very good; the patient regained the lust for life, shiny hair and smooth skin. Before coming to the medical practice the patient had been admitted to the psychiatry hospital for psychiatric disorders.

Discussions

The clinical observation of the patients infected with *H. Pylori* bacteria drew our attention to certain clinical manifestations, especially extra-digestive, that are not listed as symptoms for gastric disease described in *H. pylori* [13].

Clinical manifestations are very varied and they are compound by asthenia and depressive symptoms: asthenia, adynamia, lack of strength; sleep disorders: insomnia, nightmares, headaches, dizziness; trophic disorders: brittle hair, dry, pale, itchy and peeling skin; tachycardia, hypotension; extra-digestive manifestations: loss of appetite, weight loss, frequent and loose stools followed by constipation.

We analyzed the manifestations and decided to name them TOXICOSIS TO *H. PYLORI* INFECTION similar to other clinical states such as giardiasis, uremia [14], duodenal intoxication [15].

The treatment I used was antibiotics combinations with PPI and Colloidal bismuth subcitrate. All clinical symptoms disappeared after following the treatment.

H. pylori has increased bacterial virulence due to bacterial lipoproteins which determine the persistence of the infection by destroying the gastric mucosa integrity and the quality of gastric mucus, as well as the inflammatory process through the neutrophils activating protein [23,24].

The persistency of *H. pylori* is caused by the structural similarity between polysaccharide A and Lewis blood group antigens present on gastric epithelial cell creating a "camouflage" of the bacteria in the gastric ecological niche favoring the infection [24].

The presence of *H. pylori* strains with phenotype I VacA + CagA, increases gastric acidity [24] and induces a more intense gastric inflammatory response, but the position of *H. Pylori* in the mucus-epithelial cell complex

determines a specific inflammatory and immunologic response by releasing immuno-genetic factors, pro-inflammatory and immuno-modulatory cytokines: interleukin 8 (IL-8), necrosis tumoral factor (TNF-alpha) and interleukins 1 (IL-1) and interleukins 6 (IL-6) [23,24].

In this complex pro-inflammatory process, gamma-interferon is produced from IL-12 and activates NK (Natural Killer) cells and T helper cells (Th1 subset), which release IL-2 and interferon with pro-inflammatory response and dominates chronic infection with *H. pylori*. T helper cells (Th2 subset) activate the immune response through IgG and IgA [23,24].

These characteristics of *H. pylori* can determinate particular clinical manifestations on systems such as the nervous system, digestive system, cardiac system, skin.

Efficient therapeutic measures similar to tonsillectomy can stop these clinical manifestations. The effect of antibacterial medications, antibiotics, combined with the local immunosuppressive and immunomodulator [25] effects of Colloidal bismuth compound and PPI targeting *H. pylori* multiplication can determine rapid recovery.

Further studies are needed to verify the findings described.

Conclusions

Our treatment methodology, similar to other medical practitioners, was administrated also based on personal beliefs. The recommendation is to use Clarithromycin for *H. pylori* infection treatment and prophylaxis of gastric cancer [25,26,27,28].

We propose a new clinical term called *Toxicosis in H. pylori infection* for describing a multiform clinical symptomatology associated with the *H. pylori* infection. We performed an interpretation for the pathogenesis of inflammatory and immunological mechanisms implicated in the immuno-pathological outbreak determined by *H. pylori*.

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