

PEPTIC DISEASE AND *Helicobacter pylori* ARE HIGHLY PREVALENT IN PATIENTS WITH THE INDETERMINATE FORM OF CHAGAS' DISEASE: REPORT OF 21 CASES

Luiz Carlos Marques de OLIVEIRA(1), Abadia Gilda BUSO(1), Luiz SIQUEIRA FILHO(1), Flávia MORAES(1), Humberto ALVES OLIVEIRA(1), Roseli Maria OLIVEIRA(1) & Eliana Chaves SALOMÃO(2)

SUMMARY

Given that chagasic patients in the indeterminate form of this disease, can have abnormal motility of the digestive tract and immunologic abnormalities, we decided to assess the frequency of peptic disease and *Helicobacter pylori* (Hp) infection in these individuals. Twenty-one individuals, 13 males and 8 females, mean age 37.6 ± 11.1 years, were examined. Biopsies of the duodenum, antrum, lesser and greater gastric curvature and esophagus were performed. The endoscopic findings were of chronic gastritis in 20 (95.2%) patients, duodenal ulcer in 3 (14.3%), gastric and duodenal ulcer in 3 (14.3%), gastric ulcer alone in 1 (4.8%), esophagitis in 5 (23.8%), and duodenitis in 5 (23.8%). The diagnosis of infection by the Hp was done by the urease test and histologic examination. Hp infection was found in 20 (95.2%) individuals: in 20 out of them in the antrum, in 17 in the lesser curvature, and in 17 in the greater curvature. Hp was not found in the esophagus and duodenum. The only individual with no evidence of infection by Hp was also the only one with normal endoscopic and histologic examinations. The histologic examinations confirmed the diagnoses of gastric ulcer as peptic, chronic gastritis in 20 patients, duodenitis in 14, and esophagitis in 9. In this series the patients had a high frequency of peptic disease, which was closely associated with Hp infection.

KEYWORDS: Chagas' disease; *Helicobacter pylori*; Chronic gastritis; Peptic ulcer.

INTRODUCTION

Chagas' disease, caused by *Trypanosoma cruzi*, occurs in about four million people in Brazil²². After the acute phase of the infection, the individual remains asymptomatic for a variable period of time, generally of years, during which are normal the conventional electrocardiogram, the cardiac size at radiological examination of the thorax, and the digestive tract assessed by a contrasted radiologic examination; this form is known as the indeterminate form of the disease⁸. These individuals may later develop the cardiac and/or the digestive form of the disease, the latter being a consequence of the neuronal destruction of the Auerbach's and Meissner's plexuses and consequent compromise of the motility, with formation of megaesophagus and/or megacolon^{6,11}.

Esophageal abnormalities at manometry¹⁹ and increased baseline pressure in the inferior sphincter¹⁸ have been described in individuals with the indeterminate form of Chagas' disease. Another study, also assessing the pressure of the esophageal

inferior sphincter in chagasic patients with radiologically normal esophagus, found it decreased⁷. These abnormalities could already be due to esophageal denervation.

Helicobacter pylori (Hp), curved or spiral, Gram negative and flagellated bacterium, is presently accepted as the main etiologic agent of chronic gastritis, of duodenal ulcers and of gastric ulcers^{14,15}. In patients with digestive form of Chagas' disease it was reported that the rate of antral infection by Hp is high, an evidence that this agent could have a role in the pathophysiology of chronic gastritis observed in these patients¹. This study aimed at assessing the frequency of peptic disease and Hp infection in patients with the indeterminate form of Chagas' disease.

PATIENTS AND METHODS

The study involved endoscopic examination of the upper gastrointestinal tract and biopsies of 21 individuals, 13 males and 8 females, mean age 37.6 ± 11.1 years (range 18 to 56

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(1) Serviço de Gastroenterologia and

(2) Serviço de Anatomia Patológica, Hospital das Clínicas. Universidade Federal de Uberlândia, Uberlândia, MG, Brazil.

Correspondence to: Luiz Carlos Marques de Oliveira. Rua Gonçalves Dias 455, Bairro Tabajaras, 38401-049 Uberlândia, MG, Brazil.

years). These patients were candidates to blood donation referred to the outpatient clinic from the blood bank for testing positive for Chagas' disease by immunofluorescence, hemagglutination and ELISA. These individuals, considered as being in the indeterminate form of the disease, were assessed consecutively. None had past history of alcoholism and denied the chronic use of non-steroidal anti-inflammatory drug.

After a 12-hour fast period the patients were submitted to endoscopic examination. Ten mg of a benzodiazepine and 30 drops of dimethicone were given one hour before the exam, performed under local anesthesia with lidocaine 10%, with the patient lying on his left side. A Pentax FG-28C or Olympus GIF type 3 endoscope was introduced in the oral cavity and, during the endoscopic examination biopsies of the duodenum, gastric antrum at about 5 cm from the pylorus, lesser and greater curvatures of the stomach, and esophagus, at least 2 cm above the gastro-esophageal junction, were obtained through a Fujinon K1816K2 forceps. The Sydney system¹⁷ was used to report the endoscopic diagnosis of the mucosal alterations observed in the stomach.

The urease test was performed separately for each biopsy site (*Hp uréia teste*, Laboratory of Research in Bacteriology of the Faculdade de Medicina da Universidade Federal de Minas Gerais – FUNDEP). The test was considered positive when the color changed from amber to pink in the first 24 hours, according to the manufacturer's instructions.

Histological examination of the fragments were processed after inclusion in paraffin, slicing in 4 to 6 micrometers, and staining with hematoxylin-eosin and carbolfuchsin; an optic microscopy with 10-, 20- and 40-fold magnification, was used for examination. Gastritis were classified according to the Sydney system¹⁷.

Informed consent was obtained from all patients before entry in the study protocol.

RESULTS

Out of the 21 patients submitted to endoscopic examination 20 (95.2%) had chronic gastritis, 3 (14.3%) had duodenal peptic ulcer, 3 (14.3%) had gastric and duodenal peptic ulcers, 1 (4.8%) had gastric peptic ulcer, 5 (23.8%) had esophagitis, and 5 (23.8%) had duodenitis; only 1 (4.8%) had a normal exam (Table 1).

The urease test was positive in 19/21 (90.5%) of the patients, being positive in the gastric antrum in 19, in the lesser curvature in 15, and in the greater curvature in 10. Hp was positive at histology in 20 (95.2%) subjects (20 in the gastric antrum, 17 in the greater curvature, and 17 in the lesser curvature). Only one patient showed a negative urease test and had a negative histology for Hp. Hp were not detected in the esophagus and duodenum of all patients.

TABLE 1

Endoscopic findings in the esophagus, stomach and duodenum of 21 individuals with the indeterminate form of Chagas' disease.

chronic gastritis	20 (95.2%)
duodenal peptic ulcer	3 (14.3%)
gastric and duodenal peptic ulcer	3 (14.3%)
gastric peptic ulcer	1 (4.8%)
esophagitis	5 (23.8%)
duodenitis	5 (23.8%)
normal	1 (4.8%)

The histologic examination showed active chronic gastritis in 20 patients, graded as mild in 11, moderate in 8 and severe in 1. Fourteen patients had duodenitis and 9 esophagitis. The only patient who had normal histologic examination had also normal endoscopic examination and negative tests for Hp. The gastric ulcers were histologically confirmed as peptic (Table 2).

TABLE 2

Histologic findings in biopsies of esophagus, stomach and duodenum of 21 individuals with the indeterminate form of Chagas' disease. All had *Helicobacter pylori* infection, except the patient with normal histology.

chronic gastritis	20 (95.2%)
gastric peptic ulcer	4 (19.0%)
esophagitis	9 (42.8%)
duodenitis	14 (66.7%)
normal	1 (4.8%)

Ten individuals had dyspeptic symptoms, and 11 were asymptomatic. Two patients with duodenal ulcer had symptoms, but one with duodenal ulcer, one with gastric ulcer, and all three with gastric and duodenal ulcers, were asymptomatic. Eight patients had non-ulcer dyspepsia. There was no relationship between age and Hp positive status.

DISCUSSION

The patients included in this study were recruited consecutively, non-selectively, as soon as the diagnosis of Chagas' disease in its indeterminate form was made. We found surprisingly high the number of patients with ulcers: 7 (33%) out of 21. Five of these 7 patients with ulcer had no dyspeptic symptom or pain. Four had gastric peptic ulcer, in three of them associated to a duodenal ulcer. It has been reported that in patients with chagasic megaesophagus, differently from the general population, the incidence of gastric and duodenal ulcers are similar²³. The frequency of infection by Hp in our patients was high, taking into consideration what has been described among the normal, nonchagasic population of a similar age group in our community⁹. This could explain the high prevalence of chronic gastritis^{3,24}, duodenal ulcer^{3,16,24} and gastric ulcer^{12,16} in these individuals.

It is unknown whether chagasic patients have a higher prevalence of Hp infection than individuals without Chagas'

disease. The fact that these patients, even in the indeterminate form of the disease, have impaired immunologic response² could lead us to hypothesize a higher susceptibility to Hp infection and/or difficulty to eliminate the bacterium. However, it has been described that even in immunologic normal individuals the immune system is usually unable to, by itself, eliminate the Hp, an infection that if not treated with antibiotics remains active for life^{10,15}. Moreover, the chronic gastritis observed in these patients may represent, in part, an immunologic response of the organism against the Hp^{10,16}.

In the chronic phase of Chagas' disease the stomach also presents, in a variable extent, destruction of intramural neurons⁵. This fact could lead to impaired gastric motility and therefore higher possibility of infection by the Hp. However it is unclear whether gastric hypomotility can facilitate the infection by the Hp. In individuals with nonulcerous dyspepsia the impaired gastric emptying was not shown to be a risk factor to infection by the Hp⁴.

Diabetic patients, either insulin-dependent or not, who may also be immunologically compromised and have impaired gastric emptying as a consequence of diabetic neuropathy, also have higher occurrence of Hp infection than nondiabetics^{20,21}.

Hp can cause duodenal-gastric reflux, what could be important in the pathophysiology of gastritis¹³. Biliary-duodenal-gastric reflux is a common finding in chagasic patients, at least in those with megaesophagus²³.

In our study the patients with the indeterminate form of Chagas' disease had a high prevalence of peptic disease, which was closely associated with Hp infection. The high frequency of peptic ulcer was a striking finding of this study. This finding need to be confirmed by further studies involving a higher number of subjects.

RESUMO

Doença péptica e *Helicobacter pylori* são freqüentes em pacientes com a forma indeterminada da doença de Chagas: relato sobre 21 pacientes

Uma vez que, pacientes chagásicos com a forma indeterminada da doença de Chagas podem apresentar dismotilidade do tubo digestivo e anormalidades imunológicas, decidimos verificar a freqüência de doença péptica e infecção por *Helicobacter pylori* (Hp) nestes indivíduos. Avaliamos 21 pacientes, sendo 13 do sexo masculino e 8 do sexo feminino, com idade média de 37,6 ± 11,1 anos. Realizamos biópsias no bulbo duodenal, antro, pequena e grande curvaturas gástrica, e esôfago. À endoscopia digestiva alta (EDA), 20 (95,2%) tinham gastrite crônica, 3 (14,3%) úlcera péptica duodenal, 3 (14,3%) úlcera gástrica e duodenal, 1 (4,8%) úlcera gástrica, 5 (23,8%) esofagite e 5 (23,8%) duodenite. Para o diagnóstico de infecção pelo Hp utilizamos o teste da urease e o exame histológico. Infecção pelo Hp estava presente em 20 indivíduos (95,2%): no antro gástrico em 20, e na pequena e grande curvaturas em 17. No esôfago e no

duodeno, a pesquisa para Hp, foi negativa em todos. O único indivíduo sem infecção pelo Hp também foi o único que teve EDA normal e exames histológicos sem alterações. A histologia confirmou as úlceras gástricas como pépticas, gastrite crônica em 20 pacientes, duodenite em 14 e esofagite em 9. Os pacientes deste estudo mostraram uma alta freqüência de doença péptica a qual estava intimamente relacionada à infecção por Hp.

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