

Helicobacter pylori infection and thrombocytopenia: A single-institution experience in Mexico

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ABSTRACT

The association between gastrointestinal *H. pylori* infection and thrombocytopenia was studied in a single institution in Mexico, over a 5-year period. In 99 individuals with *H. pylori* infection, the prevalence of thrombocytopenia was 14%, whereas in 23 consecutive patients with chronic refractory thrombocytopenic purpura, the prevalence of *H. pylori* infection was 60%, this figure being similar to that informed in the general population of Mexico (66%); the association between thrombocytopenia and *H. pylori* infection was not significant. In 14 patients who were found to have both thrombocytopenia and *H. pylori* infection, eradication treatment was given and the platelet count recovered in three. It is not still clear if detection of *H. pylori* infection should be routinely included in the initial workup of chronic thrombocytopenia.

Key words. *H. pylori*. Thrombocytopenia. Purpura. Mexico.

INTRODUCTION

Helicobacter pylori (*H. pylori*) is a gram-positive, spiral-shaped bacterium which resides in the stomach mucosa. Since its discovery by Marshall and Warren,¹ *H. pylori* has been considered as the etiologic agent of gastritis and peptic ulcer, and has been found to be associated with gastric cancer, mucosa-associated lymphoid tissue lymphoma,²⁻⁴ etc. More recently, *H. pylori* has been found to be associated with ischemic heart disease⁵ and a number of autoimmune disorders, such as rheumatoid arthritis,⁶ autoimmune thyroiditis,⁷ Sjögren's syndrome,⁸

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RESUMEN

Se investigó la asociación entre infección del tubo digestivo por *H. pylori* y trombocitopenia en una sola institución en México, en un periodo de cinco años. En 99 individuos infectados por *H. pylori*, la prevalencia de trombocitopenia fue de 14%; por otro lado, en 23 pacientes consecutivos con púrpura trombocitopénica crónica refractaria, la prevalencia de infección por *H. pylori* fue de 60%, cifra similar a la descrita para la población general de nuestro país, de alrededor de 66%; en consecuencia, la asociación entre trombocitopenia e infección por *H. pylori* no fue significativa. En 14 pacientes en quienes coexistieron púrpura trombocitopénica e infección por *H. pylori*, se administró tratamiento de erradicación de la bacteria y la cuenta de plaquetas se normalizó en tres. Los datos apoyan otras publicaciones que muestran falta de asociación entre estas variables y son insuficientes para recomendar si es prudente o no investigar la infección por *H. pylori* en el estudio inicial de todos los pacientes con púrpura trombocitopénica.

Palabras clave. *H. pylori*. Trombocitopenia. Púrpura. México.

Henoch-Schönlein purpura,⁹ autoimmune thrombocytopenic purpura (AITP)^{10,11} and others.

AITP is an acquired bleeding disorder in which autoantibodies bind to the platelet surface, leading to platelet destruction.^{12,13} The triggering mechanisms of the production of platelet autoantibodies are still poorly understood.¹⁴ There is information suggesting that the immune process leading into the platelet destruction may be associated with *H. pylori* infection¹⁰⁻¹¹ and that eradication of the bacteria may resolve the thrombocytopenia.¹⁵ We analyze herein data concerning the association between *H. pylori* infection and thrombocytopenia, in a single institution in Mexico.

MATERIAL AND METHODS

Laboratorios Clínicos de Puebla (LCP) and Centro de Hematología y Medicina Interna de Puebla (CHMI) are parts of the Clínica Ruiz de Puebla, located in Puebla, México. All patients referred to LCP between July 2002 and June 2006 to investigate the presence of *H. pylori* in stools were included in this study; a subset of these individuals in whom the platelet count was also assessed was analyzed separately. On the other hand all patients studied prospectively in the CHMI after July 2002 to define the etiology of chronic (more than 6 months) thrombocytopenia (less than $100 \times 10^9/L$ platelets), who had failed to respond to at least a single course of corticosteroids were also prospectively included in the study; the investigation of *H. pylori* was done in all of them as part of the initial laboratory work-up. Patients with overt autoimmune disease, malignancy or liver disease were excluded. The platelet counts were assessed by means of flow cytometry (*Beckman Coulter HmX*, Miami, FL), whereas *H. pylori* infection was assessed by means of an enzyme immunoassay for the detection of *H. pylori* antigens in stool (*Premiere Platinum HpSA® Plus*, *Meridian Bioscience*, Cincinnati, OH). No other methods were used to define the presence of *H. pylori*. The association of *H. pylori* infection and thrombocytopenia was analyzed in two ways:

1. In patients with chronic thrombocytopenia, the prevalence of *H. pylori* infection was studied.
2. In patients with *H. pylori* infection, the prevalence of thrombocytopenia was assessed.

RESULTS

742 individuals in a 5-year period were referred to *Laboratorios Clínicos de Puebla* to assess the digestive tract infection by *H. pylori*; in a subset of 237 of these patients the platelet count was also measured. In this group of 237 patients, *H. pylori* infection was identified in 99 patients (42%); the prevalence of thrombocytopenia in these 99 patients was 14% (14/99). On the other hand, nine patients with a low platelet count were identified in the 138 individuals without *H. pylori* infection (6.5%). The association between thrombocytopenia and *H. pylori* infection was not significant using the *chi square* test, see table 1.

On the other hand, in 23 consecutive patients with chronic refractory thrombocytopenic purpura prospectively studied and treated at the CHMI *H. pylori* infection was done as part of the initial labo-

Table 1. Association between presence (+) or absence (-), of *Helicobacter pylori* infection and platelet count (low = less than $100 \times 10^9/L$ platelets).

<i>H. pylori</i>	Platelet count	
	Low	Normal
+	14	85
-	9	129

p value assessed by means of the *chi-square* method is > 0.05 .

Table 2. Salient features of the three patients who normalized their platelet counts after a two-week eradication treatment of *H. pylori*. Age is expressed in years.

n	Sex	Age	Pre	Post	Rx	Response	Other
1	F	11	6	194	PDN	60 d	Splenectomy
2	M	56	88	220	PDN	> 150 d	-
3	M	61	5	239	PDN	> 210 d	-

F: female. M: male. Pre: platelet count ($\times 10^9/L$) before the treatment. Post: platelet count ($\times 10^9/L$). Rx: previous treatment. PDN: Prednisone. Duration of the response is expressed in days (d). Other: additional treatment.

ratory workup; in all these individuals overt autoimmune diseases had been ruled out. In this group the prevalence of *H. pylori* infection was 60% (14/23); this figure being similar to that informed in the general population of Mexico, which is around 66%.¹⁶ In the 14 patients who were found to have both thrombocytopenia and *H. pylori* infection, quadruple-drug (amoxicillin, clarithromycin, bismuth subsalicylate and pantoprazole) treatment was given during a two-week period, the platelet count recovering in three of them; the table 2 shows some features of the three individuals who normalized their platelet counts; *H. pylori* was cleared in all the patients, Patients numbers 2 and 3 have had sustained responses for over 150 and 210 days respectively, whereas patient number 1 had a transient response for 60 days with a subsequent relapse of the thrombocytopenia which lead into splenectomy. In this group of patients, median age was 53 years (range 7 to 78), there were 8 males and 6 females, whereas the platelet count has a median of $74 \times 10^9/L$ (range 5 to 98).

DISCUSSION

Several lines of direct and indirect evidence suggest that infectious agents may influence the occurrence or the course of some autoimmune diseases.¹⁷ The involvement of *H. pylori* has been suggested in

various autoimmune diseases.⁶⁻⁹ The role of *H. pylori* infection in the pathogenesis of AITP has been suggested and significant increases in the platelet count have been reported after eradication of *H. pylori* infection;¹⁰⁻¹² however, its role in the pathogenesis of AITP is still controversial.

Emilia, *et al.*¹⁰ and Gasbarrini, *et al.*¹⁵ both in Italy, reported that 43% and 61% respectively of a total of 48 AITP cases were infected with *H. pylori*, whereas the prevalence of *H. pylori* infection in the general population in Italy is 45%.¹⁹ On the other hand Kohda, *et al.*,¹⁸ in Japan, found that *H. pylori* was present in 62.5% of 40 AITP patients, the prevalence of the infection in the general population in Japan being 25-45%.²⁰ In the study which we are informing, we found a prevalence of *H. pylori* infection of 60% in AITP, whereas that in the general population in Mexico is 66%.¹⁶ All these figures indicate that the prevalence of *H. pylori* infection in patients with AITP is not very different from that informed in the general population in several countries, this being one possible reason of the lack of association between these two variables.

On the other hand, eradication of *H. pylori* infection has been informed to result in resolution of the thrombocytopenia in some, but not all cases.^{15,21,22} We delivered quadruple treatment to all the 14 patients with chronic thrombocytopenia who were found to be infected by *H. pylori*, and in three cases (21%) an increase in the platelet count was observed; these data are comparable to those informed by Jarque, *et al.*, in Spain, who recorded platelet increases in 3 of 56 patients (5%) given eradication treatment.²²

In conclusion, this study conducted in a single institution in Mexico fails to show a significant association between *H. pylori* infection and thrombocytopenia, despite the low number on individuals studied. However, since some cases were observed to increase the platelet counts after eradication of the bacteria, it may be adequate to deliver this simple and harmless treatment to patients with chronic refractory thrombocytopenia, prior to engaging in more aggressive or complicated medical actions. It is not still clear if detection of *H. pylori* infection should be routinely included in the initial workup of AITP.

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