Recovery of Thrombocytopenia after Eradication of *H. pylori* Infection in Chronic Idiopathic Thrombocytopenic Purpura

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Abstract

Introduction: Recent studies have shown a relationship between *H. pylori* and chronic idiopathic thrombocytopenic purpura (CITP).

Objective: The present study was performed to evaluate this relationship in Iranian patients.

Methods: The antibody (IgG) against *H. pylori* was studied in sixty-two patients with CITP, comprising 25 males and 37 females (mean age: 30.38±12.23 yrs) The patients positive for *H. pylori* were given quadruple therapy including omeprazol, metronidazol, amoxicillin, bismuth subcitrate for two weeks and antibody assay was repeated after six months to determine the rate of *H. pylori* eradication. Platelet counts at onset of the study were less than 100×10⁹/L. After eradication therapy, increases in platelet counts above 150×10⁹/L and those above 30×10⁹/L of the basal values were considered as complete and partial responses (CR and PR) respectively. The *H pylori*-negative patients served as control group.

Results: The study included 28 patients with *H. pylori* infection, including 11 males and 17 females and aged from 16-63 yrs (29.7±11.58 yrs). *H. pylori* infections were eradicated in 25 patients (89%) comprising 16 women and 9 men. Platelet response was achieved in 11 cases (44%) including 3CR and 8PR with mean age of 26.86±7.84 yrs. Control group did not show any significant alteration of the platelet count during the follow-up period.

Conclusion: The eradication of *H. pylori* infection led to a good platelet response in CITP patients. It is therefore suggested to search for *H. pylori* infection in these patients.

Keywords • *H. pylori* • eradication therapy • idiopathic thrombocytopenic purpura

Introduction

Helicobacter Pylori is an important cause of gastritis and peptic ulcer disease. It has also been implicated in the pathogenesis of gastric adenocarcinoma and lymphoma. In recent yrs several studies have investigated the role of *H. pylori* in some autoimmune disorders such as autoimmune thyroid disease, rheumatoid arthritis, Sjogren's...
syndrome and idiopathic thrombocytopenic purpura (ITP). In 1998, Gasbarrini and colleagues reported a good platelet response to *H. pylori* eradication in most cases of CITP. Similar investigations from Japan and Italy showed 50-100% response in H. pylori eradication. Although another study reported a very low response of CITP to *H. pylori* treatment. Regarding *H. pylori* epidemiology in developing countries including Iran with 50-70% rate of *H. pylori* infection, this prospective study was designed to determine the frequency of *H. pylori* infection in CITP and evaluate the platelet response to *H. pylori* eradication therapy.

### Patients and Methods

The present study comprised adult patients having normal bone marrow with CITP of more than six months duration and excluded secondary causes such as drugs, viral infections and collagen vascular diseases. In spite of problems with their measurement and interpretation, auto-antibodies certainly appear to be involved in the pathogenesis of ITP. However, laboratory assays for anti-platelet antibodies in ITP remain investigational; they have not yet been demonstrated to be important for either diagnosis or management. So anti-platelet antibody assay was not performed. Patients with thrombocytopenia of more than 100×10^9/L and those with active bleeding were ruled out from this study. Thus, 62 patients with CITP, 25 males and 37 females, were studied in two University hospitals in Tehran and Bandar-Abbas from 1999 to 2002. The anti-*H. pylori* antibody (IgG) assayed by Elisa was used for the detection of *H. pylori* infection in each patient. Gastroscopy was performed on 6 patients and the presence of *H. pylori* was confirmed by histologic examination of the gastric mucosal biopsy. Thirty patients (48%) tested positive for *H. pylori* of which two cases were omitted because of their non-compliance at follow-ups. Thus, 28 patients (17 females and 11 males) were eligible for present investigation. Patients undergoing immunosuppressive therapy entered the study 3 months after discontinuation of this treatment. The patients who tested negative for *H. pylori* were taken as control group. Having explained the aim of the study, informed consent was obtained from *H. pylori*-positive patients and the quadruple therapy of omeprazol 20mg bid, amoxicillin 1000mg bid, bismuth subcitrate two tablets bid, metronidazol 500mg bid, was administered for 2 weeks. Six months after such treatment, repeat antibody assay for *H. pylori* was made and considered as eradicated, if reduced to that below normal level.

Rise of platelets above 150×10^9/L was considered as a complete CR and a rise of 30×10^9/L above previous count was considered as PR. Platelet count was made every two months and the assessment of patient's response was made after six months and all responders were observed for another six months following eradication of *H. pylori*.

### Statistics

Data are presented as Mean±SEM. Unpaired Student t-test and Chi-square test were used when appropriate.

### Results

The study comprised 62 patients (37 females and 25 males) with CITP and aged from 16-73 yrs (30.38±12.2). Thirty patients (11M, 19F) had IgG antibody against *H. pylori* ranging from 64 to 136U/ml (89±26) with disease duration between 6 to 36 months (13.6±5.4). Twenty patients were treated with prednisolone for CITP and 4 cases underwent splenectomy. Two patients were excluded from the study because of their non-compliance regarding observance of medication. The remaining 28 patients, 11 males and 17 females, aged from 16-63 yrs (29.7±11.58) were given the quadruple therapy. *H. pylori* was eradicated in 25 (89%) patients (16 females and 9 males) after six months. The mean age in the control group including 34 patients was younger than the *H. pylori* positive patients (25.35±10.66 vs. 29.1±11.43 yrs). The mean platelet counts in all *H. pylori*-positive patients before and after eradication therapy were (52.40±20.69 and 85.00±45.42)×10^9/L respectively (p<0.0005). The mean platelet number before and after therapy in 3 patients (12%) with CR were (26.66±4.71 and 188.00±31.53)×10^9/L respectively (p<0.0005). The respective number of platelet counts in 8 patients (32%) with PR were (51.87±28.61 and 91.125±21.50)×10^9/L (p<0.005). In all, CR and PR rate was 44% with corresponding mean platelet counts of (39.26±28.99 and 139±22.22)×10^9/L before and after treatment (p<0.005). The responsive patients consisted of 4 (36% of males) and 7 (41% of females) with the mean age of 26.86±7.84 yrs. Regarding the response to treatment, no obvious difference was found between the male and female patients. In the control group, no significant change was observed in the platelet count during the follow-up.
Discussion

The direct and indirect evidences show that the infectious agents may play a role in the development and course of some autoimmune diseases.16,17 Regarding the H. pylori, it is shown that it does result in immunological response with the production of pro-inflammatory substances causing mucosal injury by the process of autoimmunity.20,21 On the other hand the role of some bacteria and viruses in the development of CITP is well known.17-19 The role of H. pylori in the development of CITP is probably through the production of antibody against platelets or due to antigenic similarity and cross-mimicry between the H. pylori and platelet.22 Our findings are consistent with those of similar studies which showed a relationship between the H. pylori infection and chronic CITP. Although a cross-reactivity between H. pylori and platelets’ antigen does not exist, a relationship between the HLA class-II, H. pylori and CITP has been reported.22 Our study showed a rate of 48% of H. pylori infection as compared with 43% to 61% from Italy,6,11 62.5% from Japan,12 71% from Spain13 and 29% from France.23 In a similar study from Tehran and performed on the elderly, the rate of H. pylori infection was reported to be about 55%.16 The reason for the lower infection rate in our study is probably due to the younger age of the patients studied as the rate of H. pylori infection increases with age.14,15

In this study a platelet response of 44% (CR and PR) was noted after the eradication of H. pylori infection, whereas the corresponding rate was reported to be 50% by Emilia,14 63.2% by Kohda,12 5% by Jarque,16 and 100% by Gasbarrini,8 as well as 2 case reports with complete response.9,10 Perhaps such discrepancies in the treatment response is due to the presence of different strains of H. pylori in various societies with different immunological response.

The reason for 100% response rate8 was probably because of short duration of 4 months follow-up, which missed out the relapsed cases. Although Jarque does not consider the search for H. pylori as a part of initial workup in CITP patients,13 the unclear pathogenicity of H. pylori induced thrombocytopenia warrants a search for the presence of H. pylori at the time of CITP diagnosis in adults and to eradicate it, if positive. This kind of approach may be effective in reducing the rate of immunosuppressive therapy in some patients. It is also necessary to conduct wider studies with larger number of patients to determine the prevalence rate of H. pylori infection with longer follow-up, to confirm the lasting response to the eradication of H. pylori in patients with chronic CITP.

References

13 Jarque I, Andrew R, Llopis I, et al. Absence of platelet response after eradication of Helicobacter pylori infection in pa-
H. pylori infection in CITP