Gastrointestinal lesions and Helicobacter pylori in patients with myeloproliferative disorders

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ABSTRACT

Objective: The aim of this study is to investigate the endoscopic lesions, and *Helicobacter pylori* (*H. pylori*) positivity in patients with myeloproliferative disorders (MPD).

Methods: Thirty patients with MPD and 93 controls with functional dyspepsia were enrolled in this study after informed consent obtained between March 2000 and July 2003. The study was held at the Departments of Hematology and Gastroenterology, Adnan Menderes University Faculty of Medicine, Adnan, Turkey. Physical examination, hemogram, peripheral blood examination, upper endoscopic examinations were performed in all patients. *Helicobacter pylori* positivity was evaluated by rapid urease test, and by histopathological examination of the biopsies obtained from antrum and corpus.

Results: The *H. pylori* positivity was 46.7% in MPD and 19.4% in control group ($p<0.05$). The prevalence of gastritis was much higher in MPD patients than control group ($p<0.05$). There was no gastrointestinal bleeding in control group but 8 patients in MPD group (26.7%; $p<0.05$).

Conclusion: The higher susceptibility of *H. pylori* infection and high frequency of gastric lesions in patients with MPD suggests a surveillance of these patients. The eradication of *H. pylori* to avoid probable gastrointestinal problems is advised in MPD patients

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Peptic ulcer (PU), esophageal varices resulting from portal hypertension, and platelet function disorders may cause gastrointestinal bleeding in patients with myeloproliferative disorders (MPD). Moreover, anti-aggregan drugs used in treatment of MPD can cause gastrointestinal bleeding.[1-5] It is well known that PU disease in patients with Polycythemia Vera (PV) is 4 times more frequent than in normal population. Its incidence is 8-23% in patients with PV.[1,2,6-8] There are few case reports on PU in patients with chronic myelogenous leukemia (CML), and essential thrombocytosis (ET).[1,5,9-11] Peptic ulcer of the esophagus and duodenum may be found in patients with agnogenic myeloid metaplasia (AMM) as a result of extramedullary hematopoiesis.[12,13] Increased histamine secretion of the basophils, gastric acid hypersecretion (hyperchlorhydria), hyperviscosity, and ischemia due to thrombosis of local mucosal vasculature are the reasons of increased prevalence of PU in MPD.[1,2,9,14-16] But the clinical impact of *Helicobacter pylori* (*H. pylori)* positivity in patients with MPD is controversy.

In this study, upper gastrointestinal endoscopic lesions, and *H. pylori* positivity were investigated in patients with MPD.

Methods. Thirty patients with MPD (19 females, 11 males) were enrolled to the study after

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informed consent obtained between March 2000 and July 2003. The study was held at the Departments of Hematology and Gastroenterology, Adnan Menderes University Faculty of Medicine, Adnan, Turkey. Mean age of patients was 57 ± 16 years. Ninety-three patients diagnosed as functional dyspepsia by history, physical examination, and upper endoscopic examinations were included to the study as a control group (59 females and 34 males, mean age was 44 ± 13 years). Distribution of the MPD patients was as follows: 14 with ET, 7 with CML, 5 with PV, and 4 with AMM. Myeloproliferative disorders' diagnosis was constituted according to appropriate and last criteria.[17-20] Physical examination, hemogram, peripheral blood examination, bone marrow aspiration and biopsy, chromosomal analysis for Philadelphia chromosome, erythrocyte mass measurement by Cr51 in PV suspicion and abdominal ultrasonography were carried out in all patients. Upper gastrointestinal system endoscopic examinations performed by experienced endoscopist using Pentax EG-2940 video endoscope device. *Helicobacter pylori* positivity was evaluated by rapid urease test, and by histopathologic examination of the biopsies obtained from antrum and corpus. Patients with any previous gastric operation, malign disease; patients who had taken proton pump inhibitors, antibiotics, histamin-2 receptor antagonists, or bismuth within 4 weeks prior to participation to the study were excluded.

All statistical analyses were performed using Statistical Package for Social Sciences software for Windows (release 10.0, SPSS Inc. Chicago, IL). Results were given as mean±SD. One-way analysis of variance, Mann-Whitney U tests were used for numerical variables in comparison of groups, and Continuity correction (Yates). Chi-square test was used for nominal variables. Yates Chi-Square test was performed to evaluate the relationship between the endoscopic findings and drugs used, and *H. pylori*-positivity. The multivariate test was used to evaluate the significance of parameters affecting gastrointestinal bleeding. Results were considered statistically significant at level $p<0.05$.

Results. Demographic features were given in **Table 1**. Agnogenic myeloid metaplasia was more frequent in males, and splenomegaly was more frequent in patients with ET and with CML. But, there was no significant difference in terms of

Table 1 - Demographic features of patients with myeloproliferative disorders.

Demographic features	Essential thrombocytosis (n=14)	Chronic myelogenous leukemia (n=7)	Polycythemia Vera (n=5)	Agnogenic myeloid metaplasia (n=4)	Myeloproliferative disorder (N=30)
Mean age	56 ± 13	52 ± 15	67.6 ± 22.7	55.8 ± 15.9	57 ± 16
Gender					
Males	3	3	2	3	11
Females	11	4	3	1	19
Disease duration	36 ± 31.8	29 ± 25	47.4 ± 45.4	24.8 ± 11.6	35 ± 33
Hemoglobin (g/dl)	12 ± 2.3	10.8 ± 2.6	15.3 ± 1.8	8.6 ± 2.7	11.8 ± 3
White blood cells (x10^3/mm^3)	12.1 ± 6.1	61.6 ± 60.7	18.2 ± 7.1	9.1 ± 4.6	24.3 ± 35.1
Platelet count (x10^3/mm^3)	1003.9 ± 468	555.8 ± 315.6	801 ± 280.8	184.5 ± 138.5	727.7 ± 474.5
Thrombocytosis (>400000/mm^3)	11	4	4	-	19
Chromosomal abnormality	-	5	-	-	5
Philadelphia chromosome positivity	-	5	-	-	5
Ultrasonographic findings					
Normal	7	-	1	-	8
Splenomegaly	7	7	2	4	20
Hepatomegaly	3	4	2	4	13
Cholelithiasis	-	-	1	1	2
Bile sludge	1	-	-	-	1
Portal vein thrombosis	-	-	1	-	1
Liver hemangiomatosis	1	-	-	-	1
Renal parenchymal disease	-	1	-	-	1
Gastrointestinal bleeding	2	1	3	2	8
Treatment					
Anagrelide	10	-	2	-	12
Interferon-alfa	11	4	2	-	10
Hydroxyurea	13	6	5	-	24
Splenectomy	-	-	-	2	2
Steroid	-	-	-	2	2
cytosine arabinoside	-	1	-	-	1
Acetyl salicylic acid	13	2	4	2	21
Exitus	2	1	1	-	4
Cerebrovascular accident	2	-	1	-	3
Chronic renal failure	-	1	-	-	1

gender, age, disease age, hypertension, gastrointestinal bleeding, organomegaly, survival and death rates between the groups (p>0.05).

Endoscopic findings of the study groups were given in **Table 2** The prevalence of gastritis was much higher in MPD patients than control group (p<0.05). Antral gastritis was 26.7% in MPD and 12.9% in control patients. There was no significant difference in terms of atrophic gastritis between MPD and control group patients (p>0.05). There was one patient with a duodenal ulcer in PV patients (3.3%) in MPD group, whereas there were 3 patients with a duodenal ulcer, and one with gastric ulcer (4.3%) in control group, but the difference was not significant (p>0.05). There was no significant difference in terms of erosive lesions between MPD and control group (10% and 7.5%; p>0.05).

The *H. pylori* prevalence was 46.7% in MPD and 19.4% in control group (p<0.05). These differences in terms of *H. pylori* positivity, and endoscopic lesions were not significant between MPD subgroups (p>0.05).

There was no relationship between endoscopic lesions and administration of drugs such as anagrelide, hydroxyurea, acetyl salicylic acid, or cytosine arabinoside. There was a relationship between steroid administration and having atrophic gastritis. Two of 5 patients with atrophic gastritis were on steroid treatment (p<0.05).

There was no gastrointestinal bleeding in control group but 8 patients in MPD group (26.7%; p<0.05). There was no relationship between drug administration, *H. pylori* positivity, age, gender, and hypertension with gastrointestinal bleeding according to Multivariate test results (p>0.05).

Discussion. The prevalence of PU has been reported between 3-10% in different populations.[21,22] This prevalence ranges between 2.6-10.9% in Turkey.[23,24] Clinical studies showed that PU prevalence in PV and CML patients is higher than normal population.[1,2,6,8] We did not find any difference between the 2 study groups in terms of the prevalence of PU. There are few case reports on co-existence of PU in ET and AMM patients.[1,5,9-11] Torgano et al[2] reported that PU prevalence was higher in patients with PV than normal population (29% and 7%). In this study, an increased rate of PU is more probably resulting from *H. pylori* positivity instead of increased histamine levels, and mucosal ischemia. Chronic *H. pylori* infection is known as a cause of PU, chronic antral gastritis, gastric adenocarcinoma, mucosa associated lypmpoid tissue and supposed to play a role in pathogenesis of coronary heart diseases.[25] Our results reveal that *H. pylori* positivity is significantly higher in MPD group (83%) than the control group (57%) (p<0.05). Besides,

Table 2 - Endoscopic findings in patients with myeloproliferative disorders and control group.

Endocopic findings	Essential thrombocytosis (n=14)	Chronic myelogenous leukemia (n=7)	Polycythemia Vera (n=5)	Agnogenic myeloid metaplasia (n=4)	Myeloproliferative disorder (N=30)	Control (n=93)	*p* value
Helicobacter pylori	6	3	3	2	14	18	0.006*
Normal endoscopy	1	-	-	-	1	60	0.000*
Gastritis	12	5	4	5	26	23	0.000*
Atrophic gastritis	1	1	1	2	5	4	NS
Antral gastritis	3	3	1	1	8	12	NS
Pangastritis	3	1	1	-	5	6	NS
Alkaline reflux gastritis	5	1	-	1	7	1	0.000*
Superficial gastritis	-	-	-	1	1	-	NS
Erosive lesions	1	-	2	-	3	7	NS
Erosive gastritis	-	-	1	-	1	4	
Erosive bulbitis	1	-	-	-	1	2	
Erosion in cardia	-	-	1	-	1	1	
Ulcer	-	-	1	-	1	4	NS
Duodenal ulcer	-	-	-	-	1	3	
Gastric ulcer	-	-	-	-	-	1	
Other lesions							NS
Bulbitis	1	-	-	-	1	2	
Esophagitis	-	-	-	-	-	1	
Enterogastric reflux	-	2	-	-	2	-	
Esophageal varices	-	-	1	-	1	-	
Intestinal metaplasia	-	-	-	-	-	1	

*between myeloproliferative disorders and control groups, NS - non-significant (p>0.05)

gastrointestinal bleeding rate is higher in patients with MPD than the control group ($p<0.05$). Gastritis was significantly more common in MPD patients than controls. The solely relationship of *H. pylori* positivity was only between pangastritis.

In conclusion, the prevalence of gastritis and *H. pylori* positivity was higher in patients with MPD. The higher susceptibility of *H. pylori* infection and high frequency of gastric lesions in patients with MPD suggests a surveillance of these patients. The eradication of *H. pylori* to avoid probable gastrointestinal problems is advised in MPD patients even without gastrointestinal complaints.

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