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Analysis of Endoscopic Primary Bile Reflux Gastritis Diagnosis and Histopathological Findings: A Retrospective Study on 73 Patients

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Abstract: Bile reflux gastritis (BRG) is a clinical diagnosis based on presence of bile and gastritis on endoscopy. We aimed to analyze relationship of pathological results, Helicobacter Pylori (HP), intestinal metaplasia (IM) between each other and with primary BRG diagnosed on endoscopy. Seventy-three patients with diagnosis of primary BRG on endoscopy was retrospectively analyzed. Age, gender, endoscopic gastric biopsy results were recorded. Type of gastritis, Helicobacter pylori (HP) and intestinal metaplasia were recorded on pathological analysis. The interrelation between pathological findings of primary BRG,HP and IM were analyzed. Seventy-three patients with a mean age of 51.01±16.4 years were included. Female/male ratio was 1.70. Twenty-eight (38.4%) of the patients were HP positive and 61.6% were HP negative. 16.4% of the patients were IM positive and 83.6% were IM negative. There was atrophy in 5.4%. Female dominance was contrary to male dominance of the literature. The incidence of HP positivity was lower than its negativity in BRG patients. There was not an increase in IM rate, contrary to the literature. Chronic inactive gastritis and chronic active superficial gastritis were significantly high. It was observed not to cause an increase neither in IM nor gastric mucosal atrophy.
Keywords: Primary biliary reflux, gastritis, helicobacter pylori, intestinal metaplasia.

INTRODUCTION

Bile reflux is caused by sphincter insufficiency, loss of bile storage after cholecystectomy, presence of surgical stoma or abnormal duodenal motility, where bile gets reflux retrogradely into the stomach [1].

Bile reflux gastritis (BRG) is a clinical diagnosis based on presence of bile and gastritis on endoscopy. Three criteria were proposed to diagnose biliary reflux gastritis on endoscopy: presence of biliary reflux, erythema of gastric mucosa and history of gastric or biliary surgery [2]. Most of the patients have epigastric pain unresponsive to proton pump inhibitors and antacids, pyrosis and bilious vomiting. There are not so many studies on primary biliary reflux in literature and most of studies are on secondary BRG following gastric or biliary surgery. The pylorus prevents bile reflux into stomach in normal circumstances. Thus, when pylorus has an injury or dysfunction, bile reflux might occur. It was reported that 10% of the patients who had endoscopic examination was found to have bile reflux into the stomach [3]. Bile and pancreatic fluid are alkaline and irritant for stomach mucosa and results in gastritis which was reported to occur following gastric resections, pyloroplasty, cholecystectomy or sphinchteroplasty procedures [3]. Its treatment is difficult and there is a wide spectrum of treatments varying from medication to surgery if the symptoms are intractable, especially for the BRG occurring after gastric surgery [4, 5].

We aimed to analyze relationship of pathological results, Helicobacter Pylori (HP), intestinal metaplasia (IM) between each other and with primary BRG which was not was not secondary to gastric or biliary surgery and diagnosed on endoscopy by direct visualization.

MATERIALS AND METHODS

The study was approved by hospital local ethical committee (12.02.2018 HNEAH-KAEK2018/KK/08) and conducted in accordance to the Declaration of Helsinki. Data of seventy-three patients who were diagnosed to have primary BRG macroscopically on upper gastrointestinal endoscopy between January2013 and December 2017 were analyzed.

The patients taking prokinetic drugs, proton pump inhibitors and H_2 receptor blockers for gastric symptoms; having gastric or biliary surgery history, having taken HP eradication treatment; who were

pregnant or younger than 18 years old were excluded. Every patient had 8 hours of fasting before upper GI endoscopy to obtain optimal results. Age, gender, endoscopic gastric biopsy results were recorded. All endoscopic interventions were performed by experienced endoscopists and the captured photos on endoscopy were analyzed and the diagnosis was verified by two endoscopists later. The visualization of presence of profuse bile along with hyperemic mucosa and edema on endoscopy was accepted as BRG. At least 4 consecutive mucosa biopsies were taken in every patient and fixed immediately in 10% formaldehyde solution. All specimens were analyzed by experienced pathologists. Type of gastritis, Helicobacter pylori (HP) and intestinal metaplasia were searched on pathological analysis. HP was researched on tissue by using Giemsa staining. The interrelation between pathological findings of primary BRG,HP and IM were analyzed.

Statistical analysis was made by MedCalc Statistical Software version 12.7.7 (Med Calc Software bvba, Ostend, Belgium; http://www.medcalc.org; 2013). Descriptive statistics (frequency N, percent%, mean, standard deviation, median, minimum and maximum) were used for categorical variables. Chi-Square (or Fischer Exact Tests where applicable) were used to analyze the relation between categorical variables. $p<0.05$ was significant.

RESULTS

Data of 73 patients with the macroscopic diagnosis of primary BRG on upper gastrointestinal endoscopy was retrospectively analyzed. The mean age was 51.01±16.4 (21-86) years (median =50). Female/male ratio was 1.70 (27 F [37%]) and 46 M [63%])) and significant (p=0.003). The mean time period between the initiation of complaints and endoscopic procedure was 28 ± 6 days. Twenty-eight (38.4%) of the patients with BRG were also HP positive and 45 (61.6%) were HP negative. Twelve (16.4%) out of the patients were IM positive and 61 (83.6%) were IM negative. There was atrophy in only 4 (5.4%) patients. The patient demographics, clinical and histopathological properties of the patients were given in table 1.

HP-IM relationship in BRG patients was given in table 2. BRG-related gastritis types of gastritis and comparison of them between each other were given in table 3. Pathology revealed normal gastric mucosa in 3 patients only. Atrophy rates and comparison between each other in HP positive and negative patients were given in table 4.

Table-1: Demographics, clinical and histopathological properties of biliary reflux gastritis patients

Variable		p value
No.patients	73	
Age, years (mean ± SD)	51.01 ± 16.4	
Sex		
Male	27 (37.0%)	0.003
Female	46 (63.0%)	
H.pylori infection		
Negative	45 (61.6%)	0.008
Positive	28 (38.4%)	
Intestinal metaplasia (IM)		
Negative	61 (83.6%)	<0.001
Positive	12 (16.4%)	
Atrophy		
Negative	69 (94.6%)	<0.001
Positive	4 (5.4%)	

SD; Standard deviation, $p<0.05$ was significant.

Table-2: The comparison of HP and IM relationship in BRG patientsTable 3. The comparison of gastritis types observed in BRG patients

Variable	n (%)	p value
HP+IM+	6 (8.2%)	0.763
HP-IM+	6 (8.2%)	
HP+IM+	6 (8.2%)	0.002
HP+IM-	22 (30.1%)	
HP+IM+	6 (8.2%)	<0.001
HP-IM-	38 (52.1%)	
HP-IM+	6 (8.2%)	0.002
HP+IM-	22 (30.1%)	
HP-IM+	6 (8.2%)	<0.001

HP-IM-	38 (52.1%)	
HP+IM-	22 (30.1%)	0.011
HP-IM-	38 (52.1%)	

HP; Helicobacter pylori, IM; intestinal metaplasia, +; positive, -; negative, p<0.05 was significant.

Table-3: The comparison of gastritis types observed in BRG patients

Variable	n (%)	p value
CIAG	45 (%61.6)	0.001[1]
CASG	23 (%31.5)	<0.001[2]
CAG	2 (%2.7)	<0.001[3]

CIAG; Chronic inactive gastritis, CASG; Chronic active superficial gastritis, CAG; Chronic active gastritis, CIAG vs. CASG[1], CIAG vs. CAG[2], CASGG vs. CAG[3], p<0.05 was significant.

Table-4: HP and atrophy relationship

Variable	None	Mild	Moderate	Severe	Total	p value
	n %	n %	n %	n %	n %	
HP+	27	0	1	0	1	0.660
	(36.9%)		(1.3%)		(1.3%)	
HP-	42	0	2	1	3	
	(57.5%)		(2.6%)	(1.3%)	(3.9%)	

HP; Helicobacter pylori, +; positive, -; negative, p<0.05 was significant.

DISCUSSION

Bile reflux is an irritant chemical for stomach and might cause histopathological changes in gastric mucosa. The mucosal injury that bile reflux causes was shown by in vitro and in vivo animal studies [6,7,8]. BRG is characterized by foveolar hyperplasia, edema in lamina propria, vasodilatation, and scarcity of acute and chronic inflammatory cells [9]. Cai *et al*. reported that histopathological changes in BRG were more severe in antrum and decreased in severity as getting closer to the cardia [10].

The most common risk factor in biliary reflux was reported to be gastric and biliary surgery in literature (ie resections and anastomoses) [2].

Our study was an analysis of interrelationship between biliary reflux, IM, HP and gastric atrophy in the patients with abdominal complaints or who underwent upper GIS endoscopy for screening.

Our female dominance was also contrary to male dominance in literature [2]. The mean age of our patients was correlated with the literature which reported that BRG was seen in older ages [2]. This was explained with increased numbers of gastric surgical procedures by age especially in male [11].

Today, close relationship between HP infection and atrophic gastritis is known well. However, there are few studies analyzing the relationship between biliary reflux and atrophy development in the patients who have HP infection or not. Association of BRG and HP makes mucosal injury more severe. Lots of studies reported that BRG following cholecystectomy initiated gastric mucosal injury and decreased HP colonization [12-15]. In correlation with the literature, lower incidence of HP positivity compared to HP negativity in BRG patients made us think that alkaline pH due to bile reflux might cause an inappropriate environment for HP colonization.

High pH and gastric total biliary acid concentration was found to be in close relationship with IM [14, 16, 17]. In spite of having been known that biliary reflux is a chemical irritant to stomach, we found there was not an increase in IM rate in our cases, contrary to the literature. Although underlying HP colonization and BRG was reported to increase mucosal injury synergistically, we found that their coexistence was significantly low. We think that mechanisms other than HP positivity might play role in IM development in BRG patients.

We found that BRG-related chronic inactive gastritis and chronic active superficial gastritis were significantly high in our study. Only in three patients, normal gastric mucosa was found.

The limitations in our study were as follows; first, we was not able to determine the time period between development of the present lesions and initiation of the biliary reflux as gastric mucosal injury progress step by step in a long period of time. Second, in situations where decreased acid production occurs, HP colonizes in gastric mucosa and increases the severity of proximally located atrophic gastritis [18]. In our study, only the antrum was biopsied. Third, the biopsy allowed diagnosis at only one point; all surface of the stomach was not biopsied.

CONCLUSION

As a result, in spite of being known that bile is a chemical irritant to gastric mucosa, it was seen not to cause an increase neither in IM nor gastric mucosal atrophy.

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