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Original Article

Evaluation of intestinal metaplasia associated with alkaline reflux gastritis and Helicobacter pylori in patients without gastric surgery

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Abstract

Aim: Alkaline reflux gastritis is a term used for gastric mucosa damage due to reflux of duodenal and pancreatic content into stomach. In addition to many histopathological changes caused by alkaline reflux gastritis, the relationship of alkaline reflux gastritis with intestinal metaplasia is also important. Gastric intestinal metaplasia is a precancerous lesion that requires a follow-up protocol.

Material and Methods: This study included 1005 patients who underwent esophagogastroduodenoscopy and were diagnosed with alkaline reflux gastritis at Endoscopy Unit of Gastroenterology Department of Karabük University, Medical School between January 2013 and January 2016.

Results: When the data of these patients were retrospectively reviewed, intestinal metaplasia was detected in 203 patients (20.2%), whereas Helicobacter pylori was detected in 466 patients (46.4%). There was pyloric dysfunction in 359 patients (35.7%) but 646 patients (64.3%) did not have pyloric dysfunction.

Conclusion: In our study, it was found that there was an increase in the frequency of intestinal metaplasia in patients with alkaline reflux gastritis who had increased with age, male gender and Helicobacter pylori. This was a retrospective study indicating the association of H. pylori with intestinal metaplasia in patients with alkaline reflux gastritis. We think that there is a need for further prospective studies to investigate the presence of intestinal metaplasia in patients with alkaline reflux gastritis

Keywords: Duodenogastric Reflux; Metaplasia; Helicobacter Pylori.

INTRODUCTION

Alkaline reflux gastritis (bile gastritis) is generally seen in patients who undergo gastric surgery, cholecystectomy, ampullary or sphincteroplasty, and it is rarely seen in surgery-naive patients. Epigastric pain, nausea, vomiting, a burning sensation and distention may occur due to alterations in gastric functions resulting from enterogastric reflux (1). The pathogenesis includes damage of the gastric mucosal barrier due to bile acids (2).

Prolonged exposure of the gastric mucosa to biliary and duodenal content can lead to ulcers, intestinal metaplasia, dysplasia and malignancies (3). It is known that gastric intestinal metaplasia is a precancerous gastric lesion triggered by H. pylori (4). Despite an increased risk for cancer development in intestinal metaplasia, there is no established follow-up protocol by endoscopic evaluation (5). In this study, we investigated the association of H. pylori with intestinal metaplasia by assessing the changes of the gastric mucosa in surgery-naive patients who were diagnosed with alkaline reflux gastritis via endoscopic evaluation.

MATERIAL and METHODS

This study evaluated 1448 out of 5969 patients who underwent esophagogastroduodenoscopy (EGD) and were diagnosed with alkaline reflux gastritis at the Endoscopy Unit of Gastroenterology Department of Karabük University, School of Medicine between January, 2013 and January, 2016. Of these evaluated patients, 443 patients were excluded due to previous surgery or lack of pathological results. The data of the remaining 1005 patients were retrospectively reviewed.

Age, gender, endoscopic diagnoses, and results of endoscopic biopsy and abdominal sonography were

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retrospectively recorded for all the patients. The EGD procedure was performed by 2 experienced endoscopists using a Pentax videoendoscope. Observation of bile in the gastric lumen by endoscopy was used as a diagnostic criterion for erythematous gastric mucosa regardless of erosion (6). The results of gastric canal or incisura angularis biopsies were recorded and assessed according to the Sydney classification. H. pylori was shown in mucosal samples. The patients with a history of previous gastric surgery were excluded. This study was a retrospective study. Informed consent form was obtained from all patients before endoscopy.

Statistical Analysis

Statistical analysis was performed using the SPSS 16.0 software (SPSS Inc.; Chicago, IL, USA). Student's t test was used to compare numeric variables, while Pearson's chi-square test was used to compare categorical variables. Logistic regression analysis with a backward stepwise method (likelihood ratio) was used to assess factors influencing intestinal metaplasia. A P value<0.05 was considered statistically significant.

RESULTS

Of 1005 patients who were diagnosed with alkaline reflux gastritis (Figure 1), 380 (37.8%) were men and 625 (62.2%) were women. The male: female ratio was calculated to be 0.60. The mean age of included patients was 49.08 ± 15.65 years (range: 18-80 years).

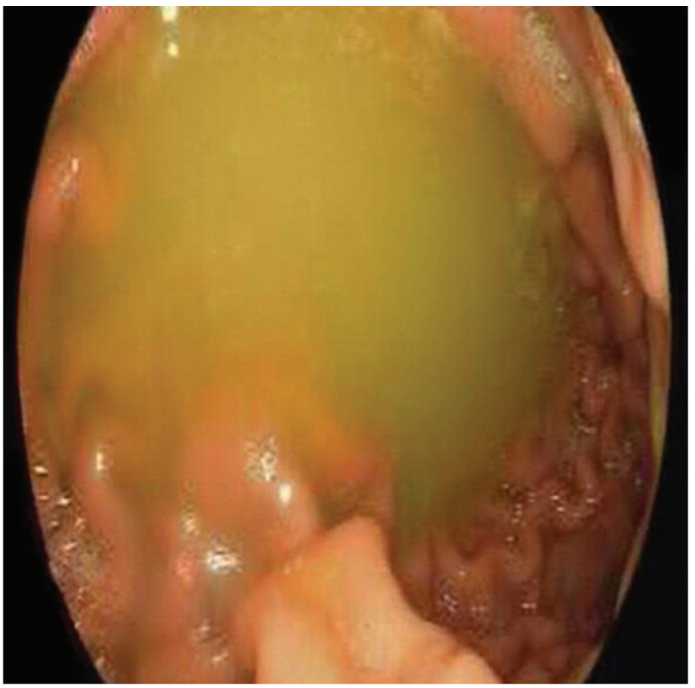

Figure 1. Endoscopic view of alkaline reflux gastritis

In the histopathological evaluation, tissue specimens obtained by endoscopic biopsy were stratified as chronic inflammation, acute inflammation, intestinal metaplasia, Helicobacter pylori, atrophy, lymphoid follicle, hyperplastic polyp, inflammatory polyp, adenomatous polyp and dysplasia (Table 1).

Intestinal metaplasia was observed in 203 cases (20.2%), whereas Hp was observed in 466 cases (46.4%) (Table 1).

Table 1. Histological changes in alkaline reflux gastritis

	Endoscopic pathology results			
	Positive	%	Nega-tive	%
Chronic inflammation	984	97.9	21	2.1
Acute inflammation	779	77.2	229	22.8
Intestinal metaplasia	203	20.2	802	79.8
Hp	466	46.4	539	53.6
Atrophy	397	39.5	608	60.5
Lymphoid follicle	43	4.3	962	95.7
Hyperplastic polyp	19	1.9	986	98.1
Inflammatory polyp	7	0.7	998	99.3
Adenomatous polyp	1	0.1	1004	99.9
Dysplasia	5	0.5	1000	99.5

The frequency of intestinal metaplasia was found to be significantly higher among women than in men, and it was observed that the occurrence of intestinal metaplasia increased with age (p<0.005; Table 2).

Intestinal metaplasia was found to be correlated to atrophy (p<0.05; Table 3).

Table 2. Distribution of alkaline reflux gastritis according to age and gender

		M(n)	%	F (n)	%	P	Age (mean)	P
Intestinal	Positive	113	11.2	90	9	0,001	56.35	0,001
	Negative	267	26.6	535	53.2		47.32	

Table 3. The relationship between intestinal metaplasia and atrophy in patients with alkaline reflux gastritis

	Intestinal metaplasia		
Atrophy	Positive (n)	Negative (n)	p
Positive	93	304	P<0.040
Negative	110	498	

In the backward stepwise regression analysis, significant correlations were found between intestinal metaplasia and age (p<0.05), gender (p<0.05), H. pylori (p<0.05) and atrophy (p<0.05).

Abdominal sonography was available for 550 patients. Based on sonography reports, the gallbladder and biliary tract was normal in 313 patients (56.9%). It was observed that 150 patients (27.3%) underwent cholecystectomy, while there was a gallstone in 73 patients (13.3%) and a gallbladder polyp in 14 patients (2.5%).

Of the patients with alkaline reflux gastritis, there was pyloric dysfunction in 359 patients (35.7%), whereas 646 patients (64.3%) did not have pyloric dysfunction.

DISCUSSION

Alkaline reflux gastritis is generally seen following peptic ulcer disease or tumor surgery. After cholecystectomy or biliary sphincterotomy, bile content increases in the duodenum and the stomach is exposed to bile for a prolonged period as a result of duodenogastric reflux. It is proposed that bile acids cause retrograde diffusion of hydrogen ions through damaged gastric mucosa, resulting from the facilitated contact of pepsin and acid to epithelial cells by changes in mucus layer of gastric mucosa. In endoscopy, observation of bile within the gastric lumen and presence of erythematous gastric mucosa regardless of erosion are the most important diagnostic criteria for alkaline reflux gastritis (6,7).

According to Vere et al. (1), histological changes include chronic inflammation, foveolar hyperplasia, intestinal metaplasia, acute inflammation, H. pylori infection, chronic gastritis, gastric polyp, dysplasia, benign ulceration, oedema and neoplasm. In our study, histological findings were classified as chronic and acute inflammation, intestinal metaplasia, H. pylori infection, atrophy, lymphoid follicle, dysplasia, and hyperplastic, inflammatory or adenomatous polyps.

Although alkaline reflux gastritis is classified within reactive gastropathies, the presence of H. pylori is controversial. It is proposed that H. pylori colonization would be decreased due to impairment of the gastric mucosal barrier by bile gastritis. In addition, it is shown via in vitro studies that the bile acids have a negative influence on Helicobacter viability and growth (8-10). In agreement with this finding, a decrease was observed in H. pylori colonization in individuals with bile reflux in some studies (10,11). Contrary to publications that indicate the absence of H. pylori as a diagnostic criterion of alkaline reflux gastritis (6), in our study and some other studies, it is shown that H. pylori could accompany bile gastritis. In the study by Vere et al.(1), H. pylori frequency was 16% in patients with alkaline reflux gastritis, while it was higher in our study population (46.4%). In our study, Hp was positive in 46.4% of patients with IM, while the Hp positivity rate was 73%, confirming that the presence of HP is an important factor for the development of IM (12). We believe that alkaline reflux gastritis contributed to the higher rate of intestinal metaplasia which was observed in our study.

Intestinal metaplasia develops as a result of bile reflux. Mucosal damage and erosions are important in intestinal metaplasia in the grounds of alkaline reflux gastritis. It is thought that the regeneration of cells induced by mucosal damage evolves to type II intestinal metaplasia and that the gastric mucosa returns to normal if this conversion results in regression, but type I or type III intestinal metaplasia develops in the case of further progression. The intestinal metaplasia is more persistent and generalized following repeated exposure to bile, if there is Helicobacter pylori related chronic gastritis in the background. This determines the evolution from intestinal metaplasia to cancer (3). In our study, intestinal metaplasia was found to be correlated with atrophy and chronic inflammation. We believe that a higher rate of H. pylori infection in the histopathological evaluation causes an increase in the rate of chronic inflammation and thus, an increase in the incidence of intestinal metaplasia. In support of this, there are many studies advocating that this process begins in the epithelium, which is repeatedly stimulated by Helicobacter pylori, as chronic active gastritis and progresses to chronic atrophic gastritis with intestinal metaplasia and eventually leads to dysplasia and gastric carcinoma (12). In the backward stepwise regression analysis, we found significant correlations between intestinal metaplasia and age, gender, H. pylori and atrophic gastritis.

All guidelines for reducing the risk of gastric cancer, recommend the eradication of H. pylori as a solution. In a recent meta-analysis including randomized-controlled studies, it was shown that gastric cancer incidence was decreased by 34% with H. pylori eradication. H. pylori gastritis evolved into chronic active gastritis in 10% of patients. As a result of its progression into chronic inflammation of the gastric mucosa, the incidence of intestinal metaplasia increased with age (4). In our study population, female gender was preponderant among patients with alkaline reflux gastritis; however, it was found that intestinal metaplasia incidence was significantly higher among men and it increased with age.

The worldwide prevalence of atrophic gastritis is 33.4%. The prevalence increases up to 42% in some countries in which the incidence of gastric cancer is high. The incidence of intestinal metaplasia is lower in Western countries than in Asian countries (13). In a meta-analysis including 16 studies, authors observed a significant resolution in atrophic gastritis at both the antrum and corpus following H. pylori treatment (14).

H. pylori is one of the most common causes of the evolution of pre-neoplastic gastric lesions into gastric cancer. H. pylori must be eradicated to prevent the progression of pre-neoplastic gastric lesions (4). In a study, the prevalence of intestinal metaplasia was higher in the presence of both bile gastritis and H. pylori compared to that in the presence of either entity alone. The incidence of intestinal metaplasia is increased when concentrations of bile acid in the gastric fluid are increased (3). In this regard, increased H. pylori incidence is important in patients with alkaline reflux gastritis.

CONCLUSION

In conclusion, our study included a large population of patients with alkaline reflux gastritis. In our study, intestinal metaplasia was increased in patients with alkaline reflux gastritis who had increased age, male gender and increased H. pylori incidence. There are some limitations of our study, which includes the missing data for some patients due to its' retrospective nature. In addition, we believe that the rate of intestinal metaplasia would be higher in prospective studies in which multiple

biopsies are obtained. Therefore, prospective studies are needed for this issue. We also believe that a follow-up protocol should be implemented and endoscopic monitoring should be performed in patients with alkaline reflux gastritis.

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REFERENCES

1. Vere CC, Cazacu S, Comănescu V, Mogoantă L, Rogoveanu I, Ciurea T. Endoscopical and histological features in bile reflux gastritis. Rom J Morphol Embryol 2005;46(4):269-74.
2. Chen SL(1), Mo JZ, Cao ZJ, Chen XY, Xiao SD. Effects of bile reflux on gastric mucosal lesions in patients with dyspepsia or chronic gastritis. World J Gastroenterol 2005;11:2834-7.
3. Sobala GM, O'Connor HJ, Dewar EP, King RF, Axon AT, Dixon MF. Bile reflux and intestinal metaplasia in gastricmucosa. J ClinPathol 1993;46(3):235-40.
4. Liu KS, Wong IO, Leung WK. Helicobacter pylori associated gastric intestinal metaplasia: Treatment and surveillance. World J Gastroenterol 2016;22:(3)1311-20.
5. Whiting JL, Sigurdsson A, Rowlands DC, Hallissey MT, Fielding JW. The long term results of endoscopic surveillance of premalignant gastric lesions. Gut 2002;50(3):378-81.
6. Feldman M, Friedman LS, Brandt LJ, editors. Sleisenger and Fordtran's Gastrointestinal and Liver Disease, 10th Edition, Elsevier, 1;881
7. Abdel-Wahab M, Abo-Elenein A, Fathy O, Gadel-Hak N, Elshal MF, Yaseen A, et al. Does cholecystectomy affect antral mucosa? Endoscopic, histopathologicand DNA flowcytometric study. Hepato-Gastroenterology 1999;47:621-5.
8. Marshall RE, Anggiansah A, Owen WA, Manifold DK, Owen WJ. The extent of duodeno gastric reflux in gastro-oesophageal reflux disease. Eur J Gastroenterol Hepatol 2001;13(1):5-10.
9. O'Connor HJ, Wyatt JI, Dixon MF, Axon AT. Campylobacter like organisms and reflux gastritis. J Clin Pathol 1986;39(5):531-4.
10. Fukuhara K, Osugi H, Takada N, Takemura M, Lee S, Taguchi S, et al. Duodenogastric reflux eradicates Helicobacter pylori after distal gastrectomy. Hepato-gastroenterology 2004;51(59):1548-50.
11. Scalon P, Di Mario F, Del Favero G, Meggiato T, Rugge M, Baffa R, et al. Biochemical and histopathological aspects in duodenogastric reflux gastritis patients with or without prior cholecystectomy. Acta Gastroenterol Belg 1993;56(2):215-8.
12. Craanen ME, Dekker W, Blok P, Ferwerda J, Tytgat GN. Intestinal metaplasia and Helicobacter pylori: an endoscopic bioptic study of the gastric antrum. Gut 1992;33(1):16-20.
13. de Vries AC, van Grieken NC, Looman CW, Casparie MK, de Vries E, Meijer GA, et al. Gastric cancer risk in patients with premalignant gastric lesions: a nationwide cohort study in the Netherlands. Gastroenterology 2008;134(4):945-52.
14. Kong YJ, Yi HG, Dai JC, Wei MX. Histological changes of gastric mucosa after H. pylori eradication: a systematic review and meta-analysis. World J Gastroenterol 2014;20(19):5903-11.