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Evaluation of Histopathological Correspondence of Atrophic Gastritis Observed in Endoscopy: Systematic Review

Endoskopik Atrofik Gastrit Görünümünün Histopatolojik Karşılığının Değerlendirilmesi: Sistematik İnceleme

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ABSTRACT Objective: Atrophic gastritis (AG), which is defined as the loss of gastric glands, can be precancerous. The objective of this study is examination of histopathological correlation of our patients with AG, considered according to endoscopic findings and determination of the other concomitant pathological findings. **Material and Methods:** Biopsy was performed in the atrophic areas and/or different areas on a total of 201 patients during gastroscopic evaluation due to the pre-diagnosis of AG between 2013 and 2014 in our clinic. Their pathological evaluation was performed and the cases of these patients were examined retrospectively. Endoscopic diagnosis of AG was made based on observation of the gastric mucosa as pale compared to the normal gastric mucosa and the separation of this area from the normal gastric mucosa, which can be defined as an endoscopic atrophic border with the prominence of submucosal thin vascular structures. Diagnosis of AG was pathologically defined as loss of glands. **Results:** The average age of the total 201 patients, who were 133 (67%) women and 68 (33%) men, was 69 years. Endoscopic and histological AG correlation in the whole group was 63 (31%). Considering the gastric localisation of the cases with confirmed diagnosis of AG in histopathological examination; it was determined that 89% affect the proximal, 9% the distal and 2% the distal and proximal together. Intestinal metaplasia (IM) was accompanied in 68% of cases with chronic active gastritis (21%) and neuroendocrine cell hyperplasia (NEHD) (14%). Chronic active gastritis was detected in 32% and IM 17% in cases without histopathological AG. While *Helicobacter pylori* positivity was 6% in those with histopathologically AG, it was 24% in those without AG (p=0.003). When evaluated in terms of accompanying pathological findings, NEHD, IM and lymphoid follicle hyperplasia were found with a higher rate in patients with histopathologically AG, and found statistically significant. **Conclusion:** Pathological examination must be performed if AG is suspected in endoscopy. While IM and NECH were more commonly concomitantly observed in patients with AG in pathological examination, the rate of H. pylori was lower compared to the patients who did not have AG.

Keywords: Atrophic gastritis; intestinal metaplasia; neuroendocrine cell hyperplasia

ÖZET Amaç: Mide bezlerinin kaybı olarak tanımlanan atrofik gastrit (AG), prekanseröz olabilir. Bu çalışmanın amacı; endoskopik bulgular ile öngörülen AG'li vakalarımızın, histopatolojik korelasyonunun incelenmesi ve eşlik eden diğer patolojik bulguların saptanmasıdır. **Gereç ve Yöntemler:** 2013-2014 yılları arasında kliniğimizde gastroskopik değerlendirmesi yapılmış olan toplam 201 hastada saptanan atrofik alanlardan ve/veya farklı alanlardan biyopsi yapıldı. Patolojik değerlendirmeleri yapıldı ve bu hastalar retrospektif olarak değerlendirildi. AG tanısı endoskopik olarak; midede mukozanın normal mide mukozasına göre soluk olarak izlenmesi ve bu alanın endoskopik atrofik sınır şeklinde tanımlanabilecek şekilde normal mide mukozasından ayrışması, submukozal ince vasküler yapıların belirgin hâle gelmesi olarak tanımlandı. AG tanısı patolojik olarak gland kaybı olarak tanımlanmıştır. **Bulgular:** Yüz otuz üçü (%67) kadın, 68'i (%33) erkek olan toplam 201 hastanın ortalama yaşı 69 yıldır. Tüm grupta endoskopik ve histolojik AG korelasyonu 63'tür (%31). Histopatolojik incelemede, AG tanısı kesinleşen vakaların mide lokalizasyonuna bakıldığında; %89'unun proksimali, %9'unun distali, %2'sinin distali ve proksimali birlikte etkilediği tespit edilmiştir. Histopatolojik olarak AG saptanan vakaların %68'inde intestinal metaplazi (İM), %21'inde lenfoid hiperplazi, %21'inde kronik aktif gastrit ve %14'ünde nöroendokrin hücre hiperplazisi (NEHH) eşlik etmektedir. Histopatolojik olarak AG saptanmayan olgularda ise kronik aktif gastrit %32, İM %17 oranında saptanmıştır. Histopatolojik olarak AG saptananlarda *Helicobacter pylori* pozitifliği %6 iken saptanmayanlarda %24'tür (p=0,003). Eşlik eden patolojik bulgular açısından değerlendirildiğinde NEHH, İM ve lenfoid folikül hiperplazisi, histopatolojik olarak AG saptanan hastalarda daha yüksek oranda mevcut olup, istatiksel olarak da anlamlı bulunmuştur. **Sonuç:** Endoskopik AG şüphesinde, patolojik inceleme mutlaka yapılmalıdır. Patolojik incelemede, AG vakalarına İM ve NEHH daha sık eşlik ederken, H. pilori sıklığı AG saptanmayan vakalara göre daha düşüktür.

Anahtar Kelimeler: Atrofik gastrit; intestinal metaplazi; nöroendokrin hücre hiperplazisi

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The gastrointestinal system has a mucosa that has a fast turnover characteristic. Stem cells differentiate in stomach mucosa and they replace the cells that get damaged or spilt to lumen. This process determines the structure of glands in antral and oxyntic mucosae and mucosal thickness.[1] As chronic inflammation continues in the stomach, it might not be possible to repair all of the damaged cells with new cells, and in this case, the mucosa gets thinner. With the chronic inflammation of this thinned mucosa, atrophic gastritis (AG), which is defined as the loss of gastric glands and can be precancerous, occurs. AG is identified with pale mucosa, glossy surface, pale pili and significant submucosal veins in the gastroscopic examination.[1,2] Various classifications have been presented to define AG in terms of endoscopy but it was observed in some studies that sensitivity and specificity of identification of AG based on only endoscopic findings was low.[3] The objective of this study is the examination of histopathological correlation of our patients with AG considered according to endoscopic findings and evaluation of the other concomitant pathological findings.

MATERIAL AND METHODS

Endoscopic and histopathological findings of a total of 201 patients, who were diagnosed with AG during gastroscopic evaluation in our clinic in the last one year and who had a biopsy performed in the atrophic area and/or different areas and a histopathological evaluation, were examined retrospectively. Endoscopic assessments were performed with Fujinon EG-450 WR5 flexible fibre optic endoscopes with white light. Endoscopic diagnosis of AG was made as pale observation of the gastric mucosa compared to the normal gastric mucosa and the separation of this area from the normal gastric mucosa, which can be defined as an endoscopic atrophic border, with the prominence of submucosal thin vascular structures.[4] For pathological assessment, biopsy specimens collected from the atrophic area and/or different areas through endoscopy were sent to the pathology department in 10% neutral buffered formalin packs. In the histopathological examination, diagnosis of AG was established pathologically based on the loss of mucous glands. The existence of *Helicobacter pylori* was evaluated with Giemsa staining in all patients. SPSS version 16.0 was used in the statistical assessment of our study. A Chi-square test of independence was used in the comparison of independent variables. The study was carried out in accordance with the Helsinki Declaration principles.

RESULTS

In our study, the endoscopic findings of a total of 201 patients, who were diagnosed with AG after endoscopy, were examined. Of these patients, 133 (67%) were female and 68 (33%) were male. As the age distribution of the patients was evaluated, it was observed that the average age was 69 and there was a total of 83 (42%) patients aged above 65 years. Endoscopic and histologic AG correlation was provided in 63 (31%) patients in the entire group. Thirty eight of the patients who were diagnosed with AG after histopathology, were aged below 65 and 25 of them were aged above 65. While pathological and endoscopic AG correlation was 30% in patients aged above 65, the said rate is 32% in the patients aged below 65. As the patients were evaluated in terms of gender, 39 of the patients who were pathologically diagnosed with AG were female and 24 of them were male. Stomach localisation of the patients who were diagnosed with AG in the histopathological examination was examined. With proximal section defined as fundus and corpus and distal section defined as antrum, it was observed that the proximal section was affected in 89% of them, the distal section was affected in 9% of them and distal and proximal sections were affected in 2% of the patients.

As the histopathological findings of all patients were evaluated, it was observed that the most commonly observed pathological finding was intestinal metaplasia (IM) with a rate of 32% followed by active chronic gastritis with a rate of 28.4%. The distribution of the most commonly observed histopathological findings other than AG in the entire group of patients is summarised in Table 1.

IM was concomitantly observed in 68% of the patients who were diagnosed with AG after histopathology, lymphoid hyperplasia was concomitantly observed in 21% of them, chronic active gas-

TABLE 1: The most commonly observed histopathological findings other than atrophic gastritis in the entire group of patients.

		Frequency	Percentage
Pathological findings	Intestinal metaplasia	66	32.8%
	Active chronic gastritis	57	28.4%
	Inactive chronic gastritis	31	15.4%
	Reactive gastropathy	25	12.4%
	Foveolar hyperplasia	20	10.0%
	Lymphoid hyperplasia	20	10.0%
	Erosive gastritis	19	9.5%
	Oedema	17	8.5%
	Normal histological findings	16	8.0%
	Vascular congestion	11	5.5%
	Neuroendocrine cell hyperplasia	10	5.0%
	Pyloric metaplasia	7	3.5%
	Dysplasia	3	1.5%

tritis was concomitantly observed in 21% of them and neuroendocrine cell hyperplasia (NECH) was concomitantly observed in 14% of them. The distribution of the most commonly observed pathological findings in patients with endoscopic and histopathological AG correlation is summarised in Table 2.

The most commonly observed concomitant pathological finding was IM in patients who were diagnosed with AG after histopathology. This was followed by lymphoid hyperplasia, active chronic gastritis and neuro endocrine cell hyperplasia, respectively, and the rates of occurrence of all these findings in AG were statistically significantly high. In Table 3, the statistical evaluation of the most commonly observed concomitant pathological findings according to the existence of AG is summarised.

It was observed that the rate of occurrence of *H. pylori* was higher in the group of patients who did not have AG based on histopathological examination; according to this, while the rate of positivity of *H. pylori* was 23.9% in the group of patients who were not diagnosed with atrophy based on histopathological examination, the rate of positivity of *H. pylori* was 6.3% in the patients who were diagnosed with AG based on histopathological examination. The rate of positivity of *H. pylori* regarding IM, which is the

TABLE 2: The most commonly observed pathological findings in patients with endoscopic and histopathological atrophic gastritis correlation.

		Frequency	Percentage
Pathological findings	Intestinal metaplasia	43	68.3%
	Lymphoid hyperplasia	13	20.6%
	Active chronic gastritis	13	20.6%
	Neuroendocrine cell hyperplasia	9	14.3%
	Inactive chronic gastritis	7	11.1%
	Foveolar hyperplasia	5	7.9%
	Pyloric metaplasia	5	7.9%
	Reactive gastropathy	3	4.8%
	Inactive chronic gastritis	3	4.8%
	Dysplasia	2	3.2%
	Erosive gastritis	2	3.2%

TABLE 3: Distribution of the most commonly observed concomitant pathological findings in patients diagnosed with atrophic gastritis after histopathology.

			Atrophic gastritis			
			No	Yes	Total	Sig.
Intestinal metaplasia	No	Number of patients	115	20	135	0.000
	Yes	Number of patients	23	43	66	
		Total	138	63	201	
			Atrophic gastritis			
			No	Yes	Total	Sig.
Neuroendocrine cell hyperplasia	No	Number of patients	137	54	191	0.000
	Yes	Number of patients	1	9	10	
		Total	138	63	201	
			Atrophic Gastritis			
			No	Yes	Total	Sig.
Lymphoid hyperplasia	No	Number of patients	131	50	181	0.001
	Yes	Number of patients	7	13	20	
		Total	138	63	201	

most commonly observed concomitant pathological condition in patients diagnosed with AG based on histopathological examination, was 4.7%.

DISCUSSION

Flexible gastroscopes have been used since 1932 and since then, a long distance has been covered in gastroscopic diagnosis and treatment.[5] Identification of precancerous lesions in the oesophagus and stomach with the conventional white-light gastroscopes, which we frequently use in our daily practice, is important in terms of measures that can be taken and prolonging the survival period.

In this study, in which we evaluated correlation of the endoscopic picture of AG, which is a precancerous lesion, with histopathology, we observed that only 1/3 of the lesions, which we identified as AG with endoscopy, had a histopathological correspondence. Although there are scarce studies that evaluate the histopathological correlation of AG observed in endoscopy, Radeen et al. conducted a study that evaluated the relationship between *H. pylori* infection and endoscopic attributes in gastritis and histopathological findings in the general population. It was stated that sensitivity of the histopathological correlation with the definition of AG that was provided from mild to severe according to the existence of veins observed in antrum was 14% and its specificity was 91%.[6] In the study conducted by Poudel et al. to examine the endoscopic and histopathological correlation of the gastric lesions, histopathological correlation was observed only in 1 of 5 patients who were diagnosed with AG in endoscopy.[7] In the study conducted by Ramin et al. in the rural population of İran to evaluate the relationship between gastric endoscopic findings and histological premalignant lesions, gastric endoscopic findings were grouped into three: normal, existence of ulcerated lesion regardless of concomitant abnormal findings and existence of non-ulcerated abnormal findings (AG was also included in this group as a sub-group). In the existence of non-ulcerated abnormal findings that constituted one of the three groups of gastric endoscopic findings, the rate of observing histological premalignant lesions was significantly higher compared to the group with normal endoscopic findings.[8] In the study conducted by Lee et al., endoscopic, histologic and serologic correlations were evaluated in AG and sensitivity was 65.9% and specificity was 58% in the endoscopic and histologic correlation of antral AG.[9] Despite the fact that there are few studies evaluating the histopathological correlation of endoscopic AG at the present time, on the one hand, correlation was weak in some studies and on the other hand, it was demonstrated that there was a strong relationship in others. The factors taken into consideration in diagnosis of endoscopic AG such as mucosal changes, ex-

perience of the endoscopist and stomach area in which a biopsy was performed are the factors that are effective in correlation with histology. Histopathological correlation of AG, which is a premalignant lesion, should be evaluated with endoscopic imaging with more extensive studies in which all of these factors are taken into consideration.

Endoscopy techniques such as chromoendoscopy, high resolution magnifying endoscopy and narrow band imaging (NBI) are helpful in identifying the premalignant gastric lesions.[10] In a study conducted by Lisette et al., the efficacy of conventional white-light endoscopy (WLE) and NBI in identifying the gastric premalignant lesions was compared and it was observed that NBI increased the efficacy of diagnosis in identifying the advanced premalignant gastric lesions compared to WLE.[11] In our study, IM was diagnosed in 32% of patients. In a study conducted by Cossio et al. on 338 patients, they found the prevalence of IM to be 23%, and this rate was similar to our study group.[12] In a study conducted by Güner et al. with 150 people, they evaluated patients with *H. pylori* positive and negative duodenal ulcers together with the control group. In this study, the association of AG and IM was found to be 15-18%. This rate was found to be well below that in our study. The reason for this was thought to be that the group included in our study included patients who were endoscopically defined as AG, that is, with abnormal endoscopic findings.[13]

The rate of positivity of *H. pylori* was 30.2% in the entire study group in our study. This rate was 6.3% in patients diagnosed with AG based on histopathological examination and 23.9% in patients who did not have AG. As atrophy was associated with the proximal section of the stomach in 89% of the patients with the final diagnosis of AG in our study, the low rate of positivity of *H. pylori* in the group of patients diagnosed with AG necessitates considering the contribution of autoimmune processes rather than *H. pylori* in the etiopathogenesis of atrophy.

Since the study is not a randomised controlled study, it naturally brings some limitations in terms of study design. First of all, because the procedures were evaluated by different endoscopists and pathologists, intra-observer differences could not be stated in the study. Another limitation of the study is that the biopsies taken from the stomach (in terms of number-localisation) are not standardised.

The lesions observed during occurrence of stomach cancer are chronic gastritis, AG, IM, dysplasia and adenocarcinoma, respectively. IM, which is a precancerous lesion, constitutes one of the intermediate steps in the occurrence of stomach cancer.[14] In our study, it was observed that IM was the most commonly observed concomitant pathology in the group of patients diagnosed with AG based on histopathological examination, with a rate of 68%.

CONCLUSION

Correlation was provided with pathology only in 1/3 of the patients considered to have AG in endoscopic examination. IM was the most commonly observed concomitant pathology in AG in patients who had correlation with pathology. Pathologic examination must be performed if AG is suspected in endoscopy.

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Conflict of Interest

No conflicts of interest between the authors and / or family members of the scientific and medical committee members or members of the potential conflicts of interest, counseling, expertise, working conditions, share holding and similar situations in any firm.

Authorship Contributions

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