

Incidence of lymphoid aggregates and associated factors in a large gastric biopsy series

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ABSTRACT

Introduction: Lymphoid aggregates (LA) in gastric biopsies have traditionally been linked to *Helicobacter pylori* (HP) gastritis and other inflammatory and neoplastic conditions. In the literature review on this subject, it is seen that the studies are limited and the number of patients in the studies is low. The aim of this study was to evaluate the relationship between the incidence of LA and patient's age, gender, HP, and other gastric mucosal pathologies in pathological examinations of gastric mucosal biopsies in a large series.

Materials and Methods: Endoscopic gastric mucosal biopsies taken from 1427 adult patients due to dyspeptic complaints were evaluated in terms of the relationship of LA with age, gender, HP, inflammation, gastric activity, and intestinal metaplasia (IM).

Results: LA was associated with HP positivity, age, inflammation, activity, and IM. No relationship was found with gender.

Conclusion: In our study, relatively young age, HP, and presence of inflammation were independent risk factors for lymphoid aggregates.

Keywords: Gastroscopy, Helikobakter Pylori, Intestinal metaplasia, Lymphoid Aggregat

Introduction

The term lymphoid aggregate (LA) is often encountered in biopsies performed in the upper and lower gastrointestinal systems; however, its importance cannot be fully comprehended by clinicians. Lymphoid tissue is normally concentrated in areas of our body that have a mucosal surface.^[1] The LA is cluster-like, composed of B cells, T cells, and supporting cells. LAs found in the gastric mucosal biopsy are associated with lymphoma and other mucosal pathologies. LAs are considered mucosa associated lymphoid tissue (MALT) precursors. For gastric MALT lymphomas to occur, MALT must be formed in the stomach. Healthy people do not have MALT in the stomach.

Although this relationship between MALT and LA has been shown in many studies, the importance of LA in the gastric mucosa is still controversial.

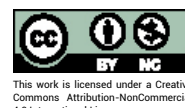
Studies on its relationship with LA and other mucosal pathological lesions in the gastric mucosa are insufficient. The existing studies^[2] have recommended screening for this association in large series. Some authors^[3] consider LA to be a normal finding in the antral region. Other studies^[4-7] suggest that it may be an immune response against *Helicobacter pylori* (HP) infection. Carpentieri et al.^[8] reported that HP infection was not associated with LA. As a result of these opposing arguments, there is no clear consensus on the relationship between



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an HP and an LA. This study aimed to identify risk factors for LA.

Materials and Methods

Ethical approval (Approval number: 2022/6/580) was provided by the Institutional Research and Ethics Committee of the university of health sciences kosuyolu higher specialty training and research hospital. Written informed consent for data assessment was obtained from all patients.

In this study, the pathology reports of 1427 patients who underwent gastroscopy and antral biopsy due to dyspeptic complaints between June 2017 and June 2021 in the Pendik state hospital endoscopy unit were retrospectively analyzed. Patient's age and gender information were recorded. Biopsy material taken from gastric antrum was fixed using 10% formaldehyde. Sections of 4–6 µm were made from paraffin blocks. Sections were painted with hematoxylin and eosin. The presence of HP was checked with Giemsa dye. At the end of the histopathological examination, HP, LA, intestinal metaplasia (IM), activity, and inflammation data were recorded.

All patients with cancer results and insufficient histological findings were excluded from the study.

Statistical Analysis

The software IBM® Statistical Package for the Social Sciences® version 22 (IBM Corp. Armonk, NY, USA) was used for statistical analysis. Qualitative data were presented as frequency and percentage. All numeric parameters showed non-normal distribution according to the Kolmogorov–Smirnov test and were given as median (interquartile range). The association of LA with categorical variables was analyzed using the Chi-square test. The Mann–Whitney U test was used to determine the relationship between LA and age. In determining the risk factors for LA, the significant parameters in the Chi-square test and the Mann–Whitney U test were subjected to multivariate logistic regression analysis. Significant parameters were subjected to multivariate analysis. $P \leq 0.05$ was considered significant.

Results

Demographic and histopathological characteristics of the patients according to LA are presented in Table 1.

Table 1. Patients' demographic and histopathologic characteristics according to lymphoid aggregate

Variables	Lymphoid aggregate				p
	Absence		Present		
	n=1068	74.8%	n=359	25.2%	
Age, years, median (IQR)	50 (38-61)		42 (34-54)		<0.001 ^a
Gender					
Female	640	75.7%	206	24.3%	0.396 ^b
Male	428	73.7%	153	26.3%	
Activity					
Absence	266	81.8%	59	18.2%	0.001 ^b
Present	802	72.8%	300	27.2%	
Inflammation					
Absence	52	92.9%	4	7.1%	0.002 ^b
Present	1016	74.1%	355	25.9%	
H. Pylori					
Absence	561	81.4%	128	18.6%	<0.001 ^b
Present	507	68.7%	231	31.3%	
Metaplasia					
Absence	948	74.4%	326	25.6%	0.279 ^b
Present	120	78.4%	33	21.6%	

^aMann-Whitney U test; ^bChi-Square tests. IQR: Interquartile Range.

While the median age of those with LA was 42, the age of those who did not was 50, which was higher, and this difference was statistically significant ($p < 0.001$). The presence of LA was detected in 27.2% of the patients with positive gastric activity ($p = 0.001$). In those with inflammation, the LA rate was 25.9% ($p = 0.002$). This rate was 31.3% in HP-positive patients, and a significant correlation was observed with LA ($p < 0.001$). No effect of gender and IM on LA was observed ($p > 0.05$).

Table 2 shows the identification of risk factors for LA by multivariate analysis.

It was seen that an increase in age by one unit significantly reduced the risk of LA by 1.02 times (OR: 0.978, 95% CI: 0.970–0.986, $p < 0.001$). The presence of inflammation was approximately 3.5 times the risk of LA (OR: 3.493, 95% CI: 1.229–9.930, $p = 0.019$), while HP positivity increased 1.8-fold (OR: 1.805, 95% CI: 1.372–2.374, $p < 0.001$).

Discussion

In the study of Fakhro et al.,^[9] the incidence of LA is reported as 24.5%. In our study, we found this rate to be 25.2%, which is consistent with the literature. Although the evidence is associated with HP and LA,^[4,5] some studies^[10] state that LA formed in the stomach cannot be attributed to the presence of HP alone. According to the literature review, the presence of LA did not discriminate by gender, similar to our study. In addition, LA is more common in the elderly than in the young.^[11,12] However, a significant result of our study was that the median age of those with LA was younger than the other group (42 vs. 50, respectively). Similar results were shown by Jaśkiewicz and Kobierska.^[13]

Many studies have reported that LA is directly proportional to gastric activity and the presence of HP.^[14,15] This information was supported in our results.

Table 2. Identification of risk factors for lymphoid aggregate by multivariate analysis

Variables	Odds ratio	95% CI	p
Age, years	0.978	0.970-0.986	<0.001
Activity, present	1.113	0.784-1.579	0.550
Inflammation, present	3.493	1.229-9.930	0.019
H.Pylori, present	1.805	1.372-2.374	<0.001

CI: Confidence Interval.

In a study involving 214 patients, the LA was significantly higher in the HP-positive group than the HP-negative group.^[16] In another study, it was reported that a significant increase in LA was detected in the HP-positive group.^[17] The LA rate of those with HP in our study was 31.3%.

Mete et al. report HP positivity as 90% in patients with LA.^[18] In our study, we found this rate to be 64.3%.

Furthermore, the coexistence of mucosal inflammation and LA was found to be significant. HP may have caused lymphoid aggregation and inflammation with the proliferation of B cells with the release of cytokines by stimulating T cells. This correlation may also have existed when there was inflammation due to any cause other than HP.

In our study, no relation with retrospective MALT was examined. However, it is a study conducted with a very large patient population, that is, 1427 patients. It is one of the limited numbers of studies showing the independent risk factors of LA.

Conclusion

In our study, relatively young age, HP, and presence of inflammation were independent risk factors for LA. Although the association of LA and HP is advocated in a small number of studies, since the cause of LA is not fully understood, it may be considered to reveal this relationship with its molecular etiology.

Disclosures

Ethics Committee Approval: Ethical approval (Approval number: 2022/6/580) was provided by the Institutional Research and Ethics Committee of the university of health sciences kosuyolu higher specialty training and research hospital.

Peer-review: Externally peer-reviewed.

Conflict of Interest: None declared.

Authorship Contributions: Concept – M.R.S.; Design – S.G.; Supervision – S.G.; Materials – M.R.S.; Data collection and/or processing – M.R.S.; Analysis and/or interpretation – M.R.S.; Literature search – M.R.S.; Writing – M.R.S.; Critical review – S.G.

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