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GASTROESOPHAGEAL REFLUX DISEASE AND AUTOIMMUNE THYROIDITIS: FEATURES OF PATHOMORPHOLOGICAL MANIFESTATION IN YOUNG PEOPLE

T. Pasiyeshvili, T. Bocharova, N. Zhelezniakova, L. Pasiyeshvili

The aim of the work. To study the effect of concomitant autoimmune thyroiditis (AIT) on the pathomorphological features of lesions of the esophageal mucosa in young patients with gastroesophageal reflux disease (GERD).

Material and research methods. The study included 165 individuals. The contingent of the surveyed was students of Kharkov higher educational institutions. The main group consisted of 120 patients with a combined course of GERD and AIT, the comparison group included 65 individuals with an isolated GERD. The morphological form of the GERD was revealed during esophagogastroduodenoscopy ("Fuginon" system). A histomorphological study of the obtained biopsy material from the mucous membrane of the esophagus was carried out. Samples were studied on an Olympus BX-41 microscope. Morphometric study of the esophageal mucosa was performed using the Olympus DP-Soft.

Research results. Histological examination of biopsy specimens revealed that the main pathomorphological signs of GERD in both groups were hyperplasia of the basal zone, lengthening of epithelial papillae, leukocyte infiltration, intercellular edema, expansion of the intercellular space, dystrophic changes, submucous fibrosis, the presence of severe inflammatory infiltration in the submucosal layer. Presence of concomitant AIT was associated with a statistically higher frequency of occurrence of certain signs: hyperplasia of the basal layer of the epithelium, elongation of the papillae, epithelial edema, expansion of the intercellular space, dystrophic changes in the epithelium ($p < 0.05$).

Conclusions. The presence of concomitant AIT in young patients with GERD does not affect the incidence of erosive GERD, but is associated with a significant increase in the severity of erosive esophagitis. The comorbid course of GERD and AIT in the student population is accompanied by a significant increase in the incidence and statistically significant intensification of the severity of hyperplasia of the basal layer of the epithelium, elongation of connective tissue papillae and leukocyte infiltration compared with isolated GERD

Keywords: gastroesophageal reflux disease, autoimmune thyroiditis, students, pathomorphological features

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1. Introduction

Gastroesophageal reflux disease (GERD) takes one of the first places among internal diseases which determines not only the medical problem, but also significant socio-economic implications [1, 2]. A systematic review demonstrated that the prevalence of GERD ranged from 10 to 30 % in adult population [3–5]. Ye B.X. et al. (2017) in their study showed the increasing of erosive forms of GERD from 3.1 % to 16.0 % [6]. It was previously believed that the incidence of GERD increases with age. But epidemiological studies in recent years noted the tendency of rising GERD rate in young population [7, 8]. Among young people, students should be singled out as a separate group. The young age of this contingent, high hormonal levels, the lack of an orderly way of life in eating habits, the quality and quantity of food intake, as well as lack of sleep amid stressful situations, the prevalence of viral infections in large groups contribute to the chronicity of diseases. Balmus I. M. et al. (2019) in their work showed that more than 40 % of students had changes in gastrointestinal manifestations during stressful periods (tests, exams) [9]. Martinucci I. et al. (2018) in their study demonstrated that 26.2

% students had typical GERD symptoms occurring at least once a week; 47 % had episodes of heartburn, regurgitation was registered in 53 % of respondents. Many comorbidities affect the features of the clinical picture and the severity of GERD [10]. One of the diseases that often accompanies GERD is autoimmune thyroiditis. Like GERD, autoimmune thyroiditis (AIT) belongs to the group of psychosomatic diseases in the pathogenesis of which psychoemotional disorders play an important role. The prevalence of AIT in the world among the adult population is 5–10 % [11, 12].

The aim of the work. To study the effect of concomitant AIT on the pathomorphological features of lesions of the esophageal mucosa in young patients with GERD.

2. Material and research methods

Study was conducted in 2017–2019 years on the basis of the Municipal Non-profit Enterprise of Kharkiv Town Council "City Student Hospital" (Kharkiv). The study included 165 individuals. The contingent of the surveyed was students of Kharkov higher educational institutions. The main group consisted of 120 patients with a combined

course of GERD and AIT, the comparison group included 65 individuals with an isolated GERD. The mean age in the groups was 21.9 ± 2.7 and 21.2 ± 2.4 years, respectively. The anamnesis of diseases did not exceed three years. The control group consisted of 20 practically healthy people matched with age and sex of examined patients.

Verification of the GERD diagnosis was performed according to the protocol for the management of patients with GERD and recommendation of the Montreal Consensus (2006). The morphological form of the disease was revealed during esophagogastroduodenoscopy ("Fuginon" system). Endoscopic severity of esophagitis was assessed according to the recommendations of the Los Angeles classification. A histomorphological study of the obtained biopsy material from the mucous membrane of the esophagus was carried out. Samples were studied on an Olympus BX-41 microscope. Morphometric study of the esophageal mucosa was performed using the Olympus DP-Soft. The severity of basal layer hyperplasia, leukocyte infiltration and Elongation of the connective tissue papillae were assessed on a 3-point scale: 0 – no sign, 1 – mild, 2 – moderate, 3 – severe degree [13].

Protocol for the management of patients with AIT was used. The functional activity of the thyroid gland was assessed using enzyme immunoassay of the level of thyroid hormones (thyroid-stimulating hormone (TSH), free thyroxine (fT4) and free triiodothyronine (fT3)) and the presence of antibodies to thyroid peroxidase and thyroglobulin. There were no changes in hormone levels. An ultrasound examination of the thyroid gland was performed.

The study adhered to diagnostic and treatment standards and requirements in relation to the ethical component of clinical trials (GCP, 1997). Consent to participate in the study in accordance with the recommendations of the ethical committees for biomedical research in the legislation of Ukraine, the Declaration of Helsinki 2000 and the directives of the European Society 86/609 on the

participation of people in biomedical research was signed by every examined patient. Study was approved by ethics committee of Kharkiv National Medical University (protocol No. 11 of 05.12.2018).

The obtained results were processed using the licensed program Statistica Basic Academic 13 for Windows local. Methods of non-parametric statistics were used: Kraskel-Wallis test, median test, Mann-Whitney test. The results were processed by the method of variation statistics and considered reliable at $p < 0.05$.

3. Research results

Comparative analysis of the results of endoscopic examination found no significant differences in the incidence of erosive and non-erosive forms of GERD in the examined groups of patients: erosive lesions of the esophagus were observed in 28.3 % (34 patients) of cases in the main group and 24.4 % (11 people) of patients in the comparison group; non-erosive forms was registered in 71.7 % (86 patients) and 75.6 % (34 patients), respectively ($df=1$, $\chi^2=0.025$, $p=0.617$).

Analysis of the incidence of erosive esophagitis various degrees according to the Los Angeles classification in patients with comorbid pathology revealed grade A – 6 (17.7 %), grade B – 18 (52.9 %), grade C – 8 (23.5 %), grade D – 2 (5.9 %) patients; in the comparison group, these indicators were 7 (63.6 %), 3 (27.3 %), 1 (9.1 %) and 0 (0 %), respectively. Statistical processing of the results according to the severity of esophagitis has established a predominance of grade A esophagitis ($df=1$, $\chi^2=8.557$, $p=0.003$) in patients with isolated GERD. At the same time, an integral analysis of the frequency of occurrence of GERD various degrees by groups showed statistically significant reallocation towards strengthening esophagitis in patients with comorbid disorders ($df=3$, $\chi^2=8.772$, $p=0.033$) (Fig. 1).

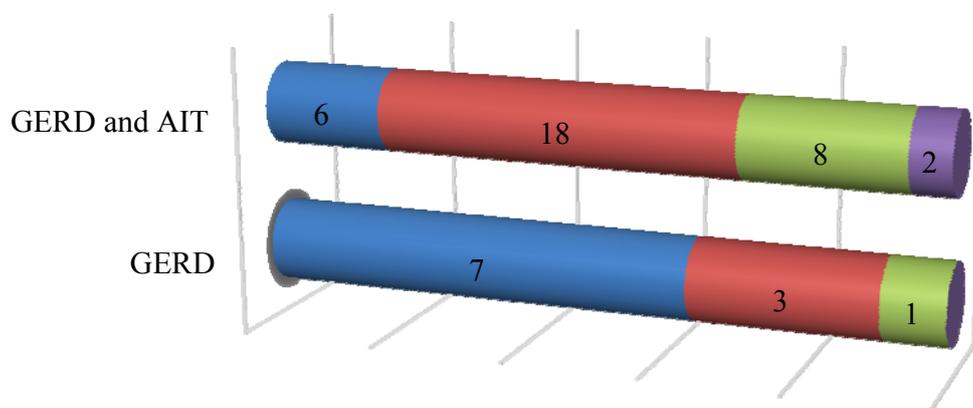


Fig. 1. The structure of the incidence of various degrees of esophagitis according to the Los Angeles classification in the examined patients

A small number of cases of erosive lesions of the esophagus among the examined patients, who, moreover, had different degrees of esophagitis, made further statistical analysis impossible for morphological study, samples of patients with a non-erosive form of the disease were taken: 50 biopsies of the main group and 35 – of the comparison group.

Histological examination of biopsy specimens revealed that the main pathomorphological signs of GERD in both groups were hyperplasia of the basal zone, lengthening of epithelial papillae, leukocyte infiltration, intercellular edema, expansion of the intercellular space, dystrophic changes, submucous fibrosis, the presence of severe inflammatory rice infiltration in the submucosa (Fig. 2, 3).

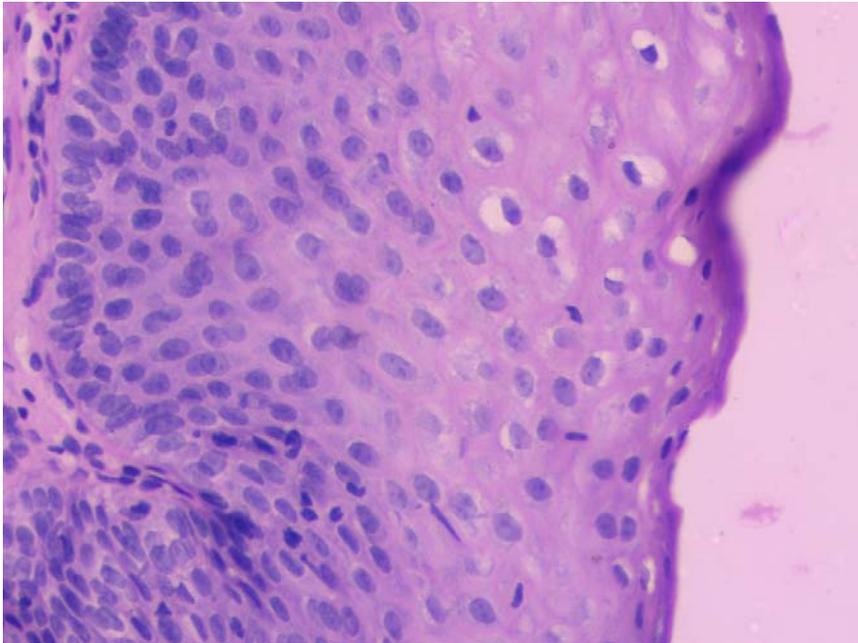


Fig. 2. Thickening of the epithelium of the esophagus and hyperplasia of the basal layer in a patient with comorbid pathology (staining with hematoxylin and eosin, magnification $\times 400$)

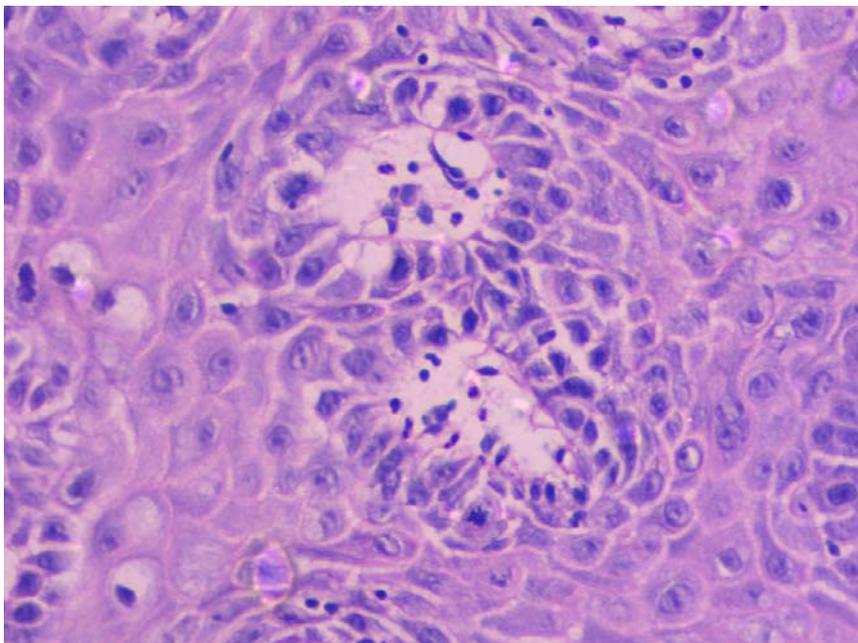


Fig. 3. Inflammatory leukocyte infiltration of the esophageal mucosa in a patient with comorbid pathology (staining with hematoxylin and eosin, magnification $\times 400$)

However, it should be noted that the presence of concomitant AIT was associated with a statistically higher frequency of occurrence of certain signs. Thus, hyperplasia of the basal layer of the epithelium was observed in 22 patients of the comparison group and 44 patients of the main group (df=1, $\chi^2=7.499$, p=0.006), elongation of the papillae – 20 and 41 (df=1, $\chi^2=5.049$, p=0.025), epithelial edema – 21 and 41 (df=1, $\chi^2=5.049$, p=0.025), expansion

of the intercellular space 19 and 39 (df=1, $\chi^2=5.342$, p=0.021), dystrophic changes in the epithelium – 23 and 45, respectively (df=1, $\chi^2=7.589$, p=0.006).

To assess the intensity of inflammatory changes in the mucous membrane of the esophagus, a more detailed analysis of the leading pathomorphological markers was conducted, taking into account their degree of severity (Table 1).

Table 1

The structure of the severity degrees of individual morphometric indicators of the esophageal mucosa in the examined patients

Sign		GERD (n=35)		GERD and AIT (n=50)		Significance of differences (χ^2) ¹
		Abs.	%	Abs.	%	
Hyperplasia of the basal layer of the epithelium	In general, by group	22	62.9	44	88.0	df=1 $\chi^2=7.499$ p=0.006
	I degree	14	63.6	7	15.9	df=2 $\chi^2=15.625$ p<0.001
	II degree	7	31.8	29	65.9	
	III degree	1	4.6	8	18.2	
Elongation of the connective tissue papillae	In general, by group	20	57.1	41	82.0	df=1 $\chi^2=6.278$ p=0.012
	I degree	13	65.0	14	34.1	df=2 $\chi^2=7.424$ p=0.024
	II degree	5	25.0	22	53.7	
	III degree	2	10.0	5	12.2	
Leukocyte infiltration	In general, by group	22	62.9	39	78.0	df=1 $\chi^2=2.33$ p=0.127
	I degree	12	54.5	7	17.9	df=2 $\chi^2=10.218$ p=0.006
	II degree	8	36.4	18	46.2	
	III degree	2	9.1	14	35.9	

Note: ¹ p<0.05 – the difference is statistically significant between groups

At the same time, it was found that even in cases where the frequency of occurrence of the sign in the groups had no statistical differences – leukocyte infiltration – the presence of concomitant AIT led to a significant increase in the severity of the indicators.

4. Discussion of research results

The last decades have been marked by significant advances in the study of the main pathogenetic mechanisms of the initiation and progression of GERD. Therefore, at the present stage of medical science, significant attention of researchers is attracted by ways of implementing reflux esophagitis in conditions of comorbid pathology. One of the most unfavourable companions of any disease is autoimmune pathology, since it is characterized by the development of systemic inflammatory reactions and, as a consequence, unpredictability of manifestation, rapid progression and early formation of complications. In this aspect, the AIT can be considered as a disease that is often formed at a young age, but usually remains undiagnosed for a long time. Data on the features of the pathomorphological realization of GERD in patients with AIT are practically absent in the modern literature. Reva T.V. et al. observed the predominance of hyperregenerative changes on inflammatory in patients with GERD and reduced thy-

roid function, according to the authors, may be due to prolonged contact of the epithelium with the contents of the stomach and has a compensatory character [14]. Most researchers consider the expansion of the intercellular space, hyperplasia of the basal layer, lengthening of the connective tissue papillae and leukocyte infiltration as the classic histological characteristics of GERD [13, 15].

The presented study revealed a significant aggravation of these deviations in patients with AIT, which may have been a consequence of the involvement of an additional autoimmune inflammatory component in the pathological process. At the same time, in a study by van Malenstein et al. it was shown that the expansion of the intercellular space in the esophageal epithelium may be a consequence of psychological stress, which may act as an additional initiating mechanism for the implementation of GERD in the studied student population [16].

Study limitations. The study was not conducted in case of identified concomitant pathology of other organs and regarding the patients refuse to participate in the study.

Prospects for further research. In the future it is planned to study common pathogenetic mechanisms and develop ways of its correction.

5. Conclusions

The presence of concomitant AIT in young patients with GERD does not affect the incidence of erosive GERD, but is associated with a significant increase in the severity of erosive esophagitis.

The comorbid course of GERD and AIT in the student population is accompanied by a significant increase in the incidence and statistically significant intensification of the severity of hyperplasia of the basal layer of the epitheli-

um, elongation of connective tissue papillae and leukocyte infiltration compared with isolated GERD.

The obtained data allow us to consider concomitant AIT as a prognostically unfavourable factor in the progression of GERD in the student population.

Conflict of interest

The authors declare that they have no conflicts of interest.

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