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## MICROSCOPIC PECULIARITIES OF DIFFERENT FORM OF GASTROESOPHAGEAL REFLUX DISEASE

### Summary

The work devoted for investigation of the prevalence and significance of microscopic changes in the esophageal mucosa in gastroesophageal reflux disease (GERD) for the biopsy results. It was studied 223 patients with biopsy, which have been diagnosed with GERD. Material was divided after comparing endoscopic and histological data into three subgroups: non-erosive GERD was referred 104 cases or 46.64%; the picture of erosive ulcerous form corresponded in 77 patients, or 34.53%; Barrett's esophagus was detected in 42 patients (18.8%). The following histological features were evaluated: degree of hyperplasia of basal cells, epithelial papillae elongation, the level of infiltration with leukocyte lymphocytic elements, the presence of erosive or ulcerative changes, the presence of metaplasia and dysplasia. Study of esophageal biopsies indicates cases of metaplasia (Barrett's esophagus) and esophageal dysplasia in GERD. All patients with GERD, a comprehensive diagnostic approach that combines not only endoscopic examination, but histological analysis of biopsy samples. Diagnostically most significant are the basal layer hyperplasia, infiltration of inflammatory cells for all forms of metaplasia and dysplasia detection for Barrett's esophagus.

**Key words:** esophagus, reflux, histology, metaplasia.

There is no "gold standard" in the diagnosis of gastroesophageal reflux disease (GERD), but that is important due to a risk factor for esophageal adenocarcinoma development [1]. Such methods as esophagogastroduodenoscopy, daily intraesophageal pH monitoring are not 100% reliable [2, 3]. Histological analysis of the structure of the esophageal mucosa is a method that gives an objective diagnostic criteria and complements clinical GERD [4]. Biopsy investigation is not always used for the diagnosis of GERD.

Visual analysis and morphological data shows that reflux esophagitis diagnosed histologically 2.5-3 times more often than using only endoscopy. Study of esophageal biopsies with endoscopically negative GERD shows that a significant portion of these patients histologically revealed not only reflux esophagitis, but also its complications [5,6]. Application histological biopsy becomes the "gold standard" for the diagnosis of GERD, while histological criteria and their relative importance are still debated [7, 8].

**The aim** of our work was to identify the prevalence and significance of microscopic changes in the esophageal mucosa in GERD for the biopsy results.

### Material and methods

We studied 223 patients with biopsy, which have been diagnosed with GERD (72 women and 151 men, aged between 22 and 80). In accordance with the clinical and endoscopic classification adopted at the IX European Gastroenterology Week in Amsterdam, material was divided after comparing endoscopic and histological data into three subgroups: non-erosive GERD (NEGERD) was referred 104 cases or 46.64 %; the picture of erosive ulcerous form (EUGERD) corresponded in 77 patients, or 34.53 %; Barrett's esophagus (BE) was detected in 42 patients (18.8%).

The following histological features were evaluated: degree of hyperplasia of basal cells, epithelial papillae elongation, the level of infiltration with leukocyte lymphocytic elements, the presence of erosive or ulcerative changes, the presence of metaplasia and dysplasia. These signs were subjected to gradation. If there is no sign he was given a value of negative, if evaluated - ac-

ording to the recommendations of international experts - from 1 to 3 depending on the severity.

The slides were investigated under the microscope "Olympus BX -41" followed by the program "Olympus DP-software version 3.2", which was carried out using morphometric study.

**Results and discussion.** Among the studied traits of basal cell hyperplasia was observed in 92 patients with NEGERD (88.46 %), 77 patients EUGERD (93.51%), 41 patients with BE (97.62%). The I and II degree was observed in 91 (63 and 28) of a patient with NEGERD (98.91% overall). III degree basal hyperplasia was observed in only 1 patient with NEGERD. In patients with EUGERD first degree was observed in 30 patients, II degree was detected in 38 patients, III degree in 4 patients (1.39%, 78.95% and 5.56%, respectively). First degree BE hyperplasia was diagnosed in 24 patients (58.54%), level II in 17 patients (41.46 %).

Elongation of papillae was observed in 76 patients NEGERD (73.08 %). First degree was observed in 54 patients, II degree was observed in 19 patients, III degree in 3 patients (71.05 %, 25% and 3.95 %, respectively). Elongation of papillae was found in 72 patients with EUGERD (93.51 %). First degree was observed in 35 patients, II degree was detected in 32 patients, III degree in 5 patients (48.61 %, 44.44 % and 6.94 %, respectively). Patients with BE had elongation of papillae in 39 cases (98.86 %); of these 20, 17 and 2 cases, depending on the severity (51.28 %, 43.59 % and 5.13% respectively).

Infiltration of mononuclear elements was observed in all patients. First degree infiltration was observed in 49 patients (47.12 %), II degree was observed in 55 patients (52.88 %) in patients with NEGERD. III degree of infiltration was not detected in any patient in this group. First degree infiltration was observed in 5 patients (6.49 %), II degree was observed in 53 patients (68.83 %), III degree was found in 19 cases (24.68 %) in patients with EUGERD. That indicator was observed and in BE patients: I degree was observed in 17 patients (40.48 %), II degree in 23 patients (54.76 %), III degree in 2 cases (4.71 %).

Infiltration of polymorphonuclear cells was detected in 89 patients with NERD (85.58 %), all patients with EUGERD and 38 patients with BE (90.48 %). First degree observed in 67 patients (75.28 %) with NERD, II degree in 20 patients (22.47 %), III degree in 2 cases (2.25%). In patients with EUGERD first degree of infiltration was observed in only 4 patients (5.19 %), II degree was observed in 23 patients (29.87 %), III degree was found in 50 cases (64.94 %). Distribution of this indicator in BE patients was: I degree observed in 23 patients (60.53 %), II degree in 7 patients (18.42 %), III degree in 8 cases (21.05%).

The presence of erosive and ulcerative changes is a prerequisite for the verification of EUGERD (100%). I and II degree was met equally often - in 33 patients (42.86 % for each), III degree was found in 11 cases (14.26 %). Erosive and ulcerative lesions identified in 6 cases of BE (18.18%), while in all cases assessed as corresponding changes for the second degree.

Identification of esophageal metaplasia of the epithelium is crucial in the diagnosis of BE. Depending on the severity of the case BE 42 patients was as follows: first degree - 12 patients (28.57 %), II degree - 21 patients (50%), III degree - 9 cases (21.43 %).

Allocated signs of dysplastic changes were found in patients with first degree of NERD dysplasia was observed in 2 patients (1.9%), II degree was observed in 1 patient (1.1%), III degree was not detected. In patients with first degree EUGERD dysplasia was observed in 15 patients (52.9 %), II degree was observed in 2 patients (18.1%), III degree not found. When BE had been revealed we observed the following data: first degree was diagnosed in 9 patients (21.4%), II degree in 12 patients (28.6%), III degree was not found.

Morphological changes had been described in the mucosa of the esophagus and they should be considered in determining the diagnosis of GERD [8]. For the diagnosis of significant changes such biopsies: thinning of the epithelial layer; necrosis keratinocytes, preferably in the surface layers; basement membrane thickening and hardening; violation of layering epithelium; focal and diffuse lymphoplasmacytic inflammatory infiltrates; identification interepithelial lymphocytes and erythrocytes; swelling of muscle fibers [9,10].

One form of GERD should be considered as Barrett's esophagus, which is manifested by metaplasia of the epithelium in the esophagus by response to the chemical effects of gastric or duodenal reflux contents, with replacement of squamous epithelium by cylindrical gastric or intestinal epithelium [11, 12]. Metaplasia with prolonged presence is accompanied by dysplasia - a deviation from the normal structure of cells in the direction of non-ductile development, manifested cellular atypia and impaired epithelial differentiation with possible development of carcinoma [13]. Morphological features of dysplasia are: cellular atypia (nuclear polymorphism, hyperchromic nuclei, increased nuclear-cytoplasmic index, stratification of nuclei); violation of differentiation (decreased or disappearance of goblet cells and Paneth cells in the epithelium with metaplasia; reduction or cessation of mucus secretion of gastric epithelial cells); violation of the architectonics of the mucosa (proliferation and bundle glands with formation of the surface and inside the glandular papillary structures) [14, 15].

Statistical analysis showed that the epithelium metaplasia and dysplasia can be used as morphological diagnosis criteria complications of GERD.

Erosive and ulcerative changes are considered as one of the key markers of inflammation, allowing to assess disease activity. Our data indicate that in most cases, necrotic erosive GERD symptoms accompany complications, which are the rule.

Erosive GERD is characterized by histological features such as neutrophilic infiltration of the epithelium, erosive necrotic and metaplastic changes that combined with the data of other authors [6, 10]. Histological study provides important objective data on the form and severity of the disease. At the same time often marked discrepancy with endoscopy, which does not always reflect the true picture of the depth of change of the esophageal mucosa in GERD.

**Conclusions.** Study of esophageal biopsies indicates cases of metaplasia (Barrett's esophagus) and esophageal dysplasia in GERD. Metaplastic and dysplastic changes in the esophageal mucosa considered precancerous states, so these studies are relevant. All patients with GERD, a comprehensive diagnostic approach that combines not only endoscopic examination, but histological analysis of biopsy samples. Diagnostically most significant are the basal layer hyperplasia, infiltration of inflammatory cells for all forms of metaplasia and dysplasia detection for BE.

#### References:

1. Tutuian R. Update in the diagnosis of gastroesophageal reflux disease. // *J. Gastrointest Liver Dis.* – 2006. - Sep;15(3). P.243-247.
2. Champion G., Richter J.E., Vaezi M.F., Singh S., Alexander R. Duodenogastro-esophageal reflux: relationship to pH and importance in Barrett's esophagus. // *Gastroenterology.* – 1994. - 107(3). – P.747-754.
3. Thomas H., Wilhelm L., Petermann J., Rosenbaum K.D., Lorenz D. Simultaneous long-term measurement of duodenogastric reflux and gastroduodenal motility. // *Chirurg.* – 1997. - 68(6). – P.618-623.
4. Geboes K., Desmet V., Vantrappen G., Louvain A. Esophageal histology in the early stage of gastroesophageal reflux. // *Arch Pathol Lab Med.* – 1979. – 103. – P.205.
5. Papa A., Urgesi R., Danese S. et. al. Pathophysiology, diagnosis and treatment of non-erosive reflux disease (NERD) // *Minerva Gastroenterol. Dietol.* - 2004. - Vol.50. - P.215-226.
6. Weinstein W.M., Ippoliti A.F. The diagnosis of Barrett's esophagus: Goblets, goblets, goblets. // *Gastrointest Endosc.* – 1996. – 44. - P.91-94.
7. Egger K., Werner M., Meining A. et.al. Biopsy surveillance is still necessary in patients with Barrett's esophagus despite new endoscopic imaging techniques / *Gut.* – 2003. – 52. – P.18-23.
8. Vakil N., van Zanten S.V., Kahrilas P., Dent J., Jones R. The Montreal definition and classification of gastroesophageal reflux disease: a global evidence-based consensus. // *Am J Gastroenterol.* 2006. - 101(8) – P.1900-1920.
9. Oberg S., Wenner J., Johansson J., Walther B., Wilten R. Barrett esophagus: risk factors for progression to dysplasia and adenocarcinoma. // *Ann Surg.* – 2005. - 242(1). – P.49-54.
10. Mueller J., Werner M., Stolte M. Barrett's esophagus: histopathologic definitions and diagnostic criteria. // *World J Surg.* – 2004. - 28(2). – P.148-154.
11. Glickman J.N., Chen Y.Y., Wang H.H., Antonioli D.A., Odze R.D. Phenotypic characteristics of a distinctive

multilayered epithelium suggests that it is a precursor in the development of Barrett's esophagus. // Am J Surg Pathol. – 2001. - 25(5). - P.569-578.

12. Riddell R.H. The genesis of Barrett esophagus: has a histologic transition from gastroesophageal reflux disease-damaged epithelium to columnar metaplasia ever been seen in humans? // Arch Pathol Lab Med. – 2005. - 129(2). – P.164-169.

13. Lagergren J., Bergstrom R., Lindgren A., Nyren O. Symptomatic gastroesophageal reflux as a risk factor for

esophageal adenocarcinoma. // N Engl J. – 1999. – 18. - P.825–831.

14. Dent J. Microscopic esophageal mucosal injury in nonerosive reflux disease. // Clin Gastroenterol Hepatol. – 2007. - 5(1). P4-16.

15. Vieth M., Haringsma J., Delarive J., Wiesel P.H., Tam W., Dent J., et al. Red streaks in the oesophagus in patients with reflux disease: is there a histomorphological correlate? // Scand J Gastroenterol. – 2001. - 36(11). – P.1123-1127.

#### Резюме

### МИКРОСКОПИЧЕСКИЕ ОСОБЕННОСТИ РАЗЛИЧНЫХ ФОРМ ГАСТРОЭЗОФАГЕАЛЬНОЙ РЕФЛЮКСНОЙ БОЛЕЗНИ

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Работа посвящена исследованию распространенности и значимости микроскопических изменений в слизистой пищевода при гастроэзофагеальной рефлюксной болезни (ГЭРБ) по результатам биопсии. Было изучено 223 пациентов с биопсией пищевода, у которых была диагностирована ГЭРБ. Материал после сопоставления эндоскопических и гистологических данных был разделен на три подгруппы: неэрозивная ГЭРБ - 104 случая или 46,64%; эрозивно-язвенная форма - 77 пациентов, или 34,53%; пищевод Барретта - 42 больных (18,8%). Следующие гистологические изменения особенности были проанализированы: степень гиперплазии базальных клеток, удлинения сосочков эпителия, уровень инфильтрации лейкоцитарных и лимфоцитарных элементов, наличие эрозивных или язвенных изменений, наличие метаплазии и дисплазии. Исследование пищевода биопсии выявило случаи метаплазии (пищевод Барретта) и дисплазии при ГЭРБ. Все пациенты с ГЭРБ требуют комплексного диагностического подхода, который включает не только эндоскопическое исследование, но и гистологический анализ биопсии. Диагностически наиболее значимыми являются гиперплазия базального слоя, инфильтрация воспалительных клеток для всех форм, выявление метаплазии и дисплазии для пищевода Барретта.

**Ключевые слова:** пищевод, рефлюкс, гистология, метаплазия.

#### Тұжырым

### ГАСТРОЭЗОФАГЕАЛДЫ РЕФЛЮКСТІ АУРУДЫҢ ӨРТҮРЛІ ФОРМАЛАРЫНЫҢ МИКРОСКОПИЯЛЫҚ ЕРЕКШЕЛІКТЕРІ

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Биопсия нәтижелері бойынша гастроэзофагеалды рефлюксті аурулар (ГЭРА) кезіндегі өңеш шырышындағы микроскопиялық өзгерістердің таралуы мен маңыздылығын зерттеуге арналған жұмыс. Өңеш биопсиясымен 223 науқас зерделенді, оларда ГЭРА диагноздалды. Эндоскопиялық және гистологиялық мөлдіреттерді салыстырудан кейін материал үш кіші топтарға бөлінді: неэрозивті ГЭРА - 104 жағдай немесе 46,64%; эрозивті-ойық жара түрі - 77 науқаста, немесе 34,53%; Барретта өңеші - 42 науқаста (18,8%). Мынадай гистологиялық өзгерістер ерекшеліктер талданды: базалды ағзалар гиперплазиясы дәрежесі, эпителилер ұштарының ұзаруы, лейкоцитарлық және лимфоцитарлық элементтерді инфильтрация деңгейі, эрозиялық немес ойық жаралық өзгерістердің болуы, метаплазияның және дисплазияның болуы. Өңеш биопсиясын зерттеу метаплазия оқиғасын (Барретта өңеші) және ГЭРА кезіндегі дисплазияны анықтады. ГЭРА барлық науқастар кешенді диагностикалық әдісті талап етеді, ол эндоскопиялық қана емес сонымен қатар биопсияның гистологиялық талдауынан тұрады. барлық формалар үшін ісік жасушаларының инфильтрациясы, Барретта өңеші үшін метаплазияны және дисплазияны анықтау базалды қабаттың гиперплазиясы диагностикалық ең маңызды болып табылады.

**Негізгі сөздер:** өңеш, рефлюкс, гистология, метаплазия.