

MEDICAL SCIENCES

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MODERN OPINION ON THE DEVELOPMENT OF EOSINOPHILIC GASTRITIS IN CHILDREN

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Abstract: The article reflects the peculiarities of morphological and immunohistochemical changes of stomach's mucosa in eosinophilic gastritis in children. Comparative analysis of morphologic investigation has demonstrated that eosinophilic gastritis is characterized by fibrosis and fibroblasts proliferation into basal and superficial parts of mucosa's lamina propria, multiple hemorrhages, thrombosis and erosions on the background of eosinophilic infiltration. Immunohistochemical indexes of cellular restoration in eosinophilic gastritis are characterized by increased proliferative activity and decreased indexes of proapoptotic and antiapoptotic activity. Eosinophilic gastritis course in children is characterized by remarkable inflammation, decreased regeneration of the mucosa, impairment of cellular restoration which is prognostic index of fibrous remodeling development.

Key words: eosinophilic infiltration, fibrosis, fibrous remodeling, cellular restoration, children

Introduction

Eosinophilic gastrointestinal disorders (EGIDs) represent a heterogeneous group of disorders that selectively affects the different segments of the

gastrointestinal tract and are characterized by eosinophilic inflammation in the absence of known causes for eosinophilia [1, p.107, 2, p. 20, 3, p.274]. EGIDs result from the interplay between genetic predisposition, intestinal dysbiosis and environmental triggers [4, p.96, 5, p.20]. Eosinophilic esophagitis (EoE) is the most common of these conditions [6, p.272]. Eosinophilic gastritis (EG), eosinophilic gastroenteritis, and eosinophilic colitis are thought to be less common than EoE, although the prevalence of these other EGIDs has not been well described [7, p. 1791, 8, p. 208]. Diagnostics the eosinophilic diseases of the gastro-intestinal tract (GIT) is quite problematic due to poorness of clinical symptoms and morphological investigation of the gut mucosa's bioplates is the own standard of eosinophilic diseases verification [9, p. 259, 10, p.989]. Modern notions about foundation and development of EG are based on generalizing conception of eosinophilic inflammation and have no strict morphological diagnostic criteria [11, p.1820]. Experts suggest that eosinophils can indirectly support a pro-inflammatory reaction in the mucous membrane of the GIT due to the release of cytokines, chemokines and lipid mediators [12, p.511].

Presented data are a serious argument in favor of necessity of study of morphofunctional and immunohistochemical regularities of stomach's mucosa eosinophilic inflammation development in EG.

The aim: to study peculiarities of morphological and immunohistochemical changes of stomach's mucosa in eosinophilic gastritis in children.

Materials and methods

Investigations have been carried out with a strict adherence to basic statements of the GCP Council of Europe Convention on Human right and biomedicine and basic statements of Ethical principles for medical research involving human subjects of World Medical Association Declaration of Helsinki.

We observed 65 children aged 8-16 years with verified chronic gastritis. Esophagogastroduodenoscopy (upper endoscopy, UE) with a target biopsy of stomach's mucosa has been performed in all children to verify the diagnosis with the help of morphological and immunohistochemical investigation. To assess histological

changes of stomach's mucosa a tissue fragments were stained with hematoxylin, eosin and picrofuchsin by van Gieson's. The results of study have been interpreted in accordance with Kyoto Consensus, 2015.

For immunohistochemical examination, sections 4-6 μm thick were applied to Super Frost Plus adhesive slides and an indirect streptavidin peroxidase staining method was used. Apoptosis was determined with murine monoclonal antibodies to antiapoptotic Bcl - 2 protein (Clone 124, DAKO, Denmark) and proapoptotic Bax protein (Clone 2D2, DAKO, Denmark). Proliferating cells nuclear antigen (Proliferating Cell Nuclear Antigen – PCNA) (Clone: PC10, DAKO, Denmark) was used to estimate proliferation.

Results

According to the results upper endoscopy, none of the children had destructive (erosion, ulcer) changes of the stomach's mucosa. Morphological assessment of stomach's mucosa biopates eosinophilic gastritis was detected in $64,1 \pm 6,0\%$ patients and lymphocytic gastritis – in $35,9 \pm 6,0\%$ ones.

Biopates of stomach's mucosa in lymphocytic gastritis were characterized by the violation of mucosa's relief in the form of shortening of holes and flattening of rollers and perivascular swelling signs. Superficial epithelium was found to be with areas of desquamation and flattened foci. Mucosa's lamina propria was infiltrated by lymphocytes up to 25 cells in the field of vision, single plasmocytes, eosinocytes and neutrophils which were basically localized in superficial parts of the mucosa and inside the rollers. Foci with atrophic mucosa with decreased quantity of glandules with impaired architectonics were detected as well (Fig.1).

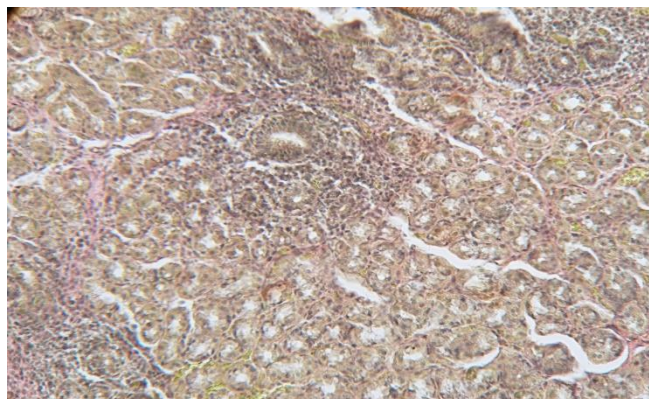
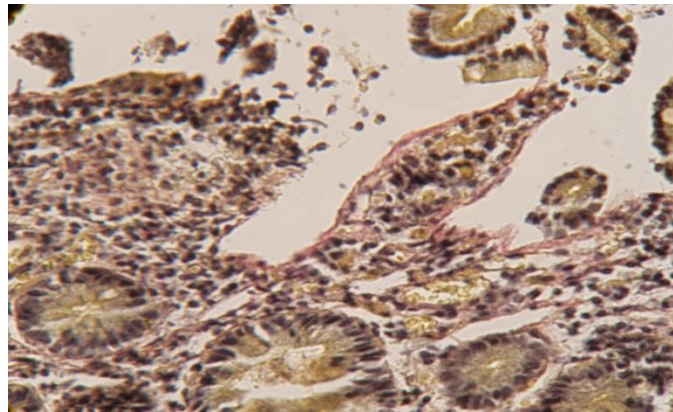


Fig. 1. Microphoto of stomach mucosa's biopate. Lymphocytic gastritis x 200.

Stomach's mucosa bioptate in eosinophilic gastritis was characterized by impaired mucosa's relief, shortened holes and flattened rollers in all samples. Superficial epithelium was marked with the fields of desquamation and foci of flattened areas. Lamina propria was infiltrated by lymphocytes to 7 cells in field of vision and eosinocytes to 25 – 30 cells in field of vision; areas of perivascular swelling, erosions, hemorrhages and microthrombosis were detected in all bioptates. Fibrotic foci sized from 50 – 70 μm to 100 – 150 μm , areas of proliferating fibroblasts and thin collagen fibers with unclear outlines in basal and superficial parts were detected in lamina propria. Glandules in lamina propria were located unevenly and contained centers of destruction (Fig. 2).



**Fig. 2. Microphoto of stomach mucosa's bioptate.
Eosinophilic gastritis x 200.**

Cellular restoration indexes assessment was performed by immunohistochemical examination. Immunohistochemical indexes of cellular homeostasis in eosinophilic gastritis were characterized by the increased proliferative activity due to increased expression of PCNA from 10.6% to 42.1% of positively colored glandular epithelium's nuclei and decreased proapoptotic activity – Bax expression from 10.3 to 29.1% of positively colored cells and Bcl-2 expression - less than 10% of positively colored cells (Fig.3).

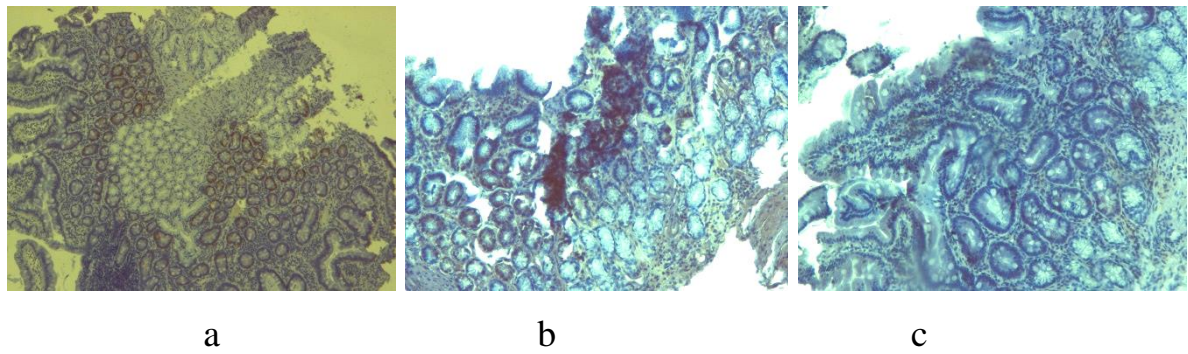


Fig. 3. Stomach mucosa's microphoto. Eosinophilic gastritis: a – immunohistochemical reaction with antibodies to PCNA x 200; b – immunohistochemical reaction with antibodies to Bax x 200; c - immunohistochemical reaction with antibodies to Bcl-2 x 200.

A tendency to Bax proapoptotic index increase from 82.4% to 96.1% of positively colored cells in low Bcl-2 expression (less than 10% of positively colored cells) and low PCNA expression from 0.9% to 2% of positively colored cells was detected during analyzing the levels of indexes of cellular restoration in patients with lymphocytic gastritis (Fig. 4).

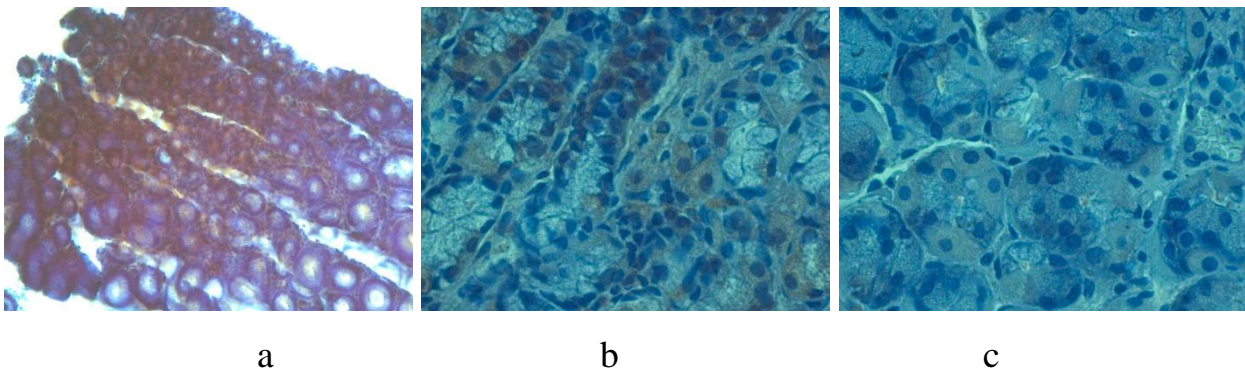


Fig.4. Stomach mucosa's biopate. Lymphocytic gastritis: a – immunohistochemical reaction with antibodies to PCNA x 100; b – immunohistochemical reaction with antibodies to Bax x 200; c – immunohistochemical reaction with antibodies to Bcl-2 x 200.

Discussion

On the basis of the results of the performed research stomach mucosa's morphological changes pathognomonic for eosinophilic gastritis were estimated; these changes were found to include eosinophilic infiltration, fibrosis of stroma of lamina propria, microcirculatory disorders with multiple hemorrhages, thrombosis and erosions. In our point of view microcirculatory disorders of stomach's mucosa

are caused by eosinophilic infiltration of lamina propria. As it is known eosinocytes contain high concentrations of peroxydase which increases vascular permeability and leads in vasculitis development.

Analysis of the results of immunohistochemical investigation demonstrated that structural peculiarities of dysregeneration characterized by dysbalance of cellular regeneration processes were detected in eosinophilic gastritis in children. Increasing of epitheliocytes proliferation index is associated with increasing of undifferentiated cells which are not able to fulfill their usual function leading in the development of stromal and epithelial rebuilding of the mucosa and its impaired regeneration.

Conclusions

Thereby comparative analysis of morphologic and immunohistochemical changes of stomach's mucosa demonstrated that eosinophilic gastritis is characterized by remarkable inflammatory changes and impaired regeneration of the mucosa with further development of fibrosis.

As conclusion we should note that the course of eosinophilic gastritis in children is characterized by dysbalanced processes of cellular restoration which leads in mucosa physiological regeneration violation and is prognostic index of fibrous remodeling.

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