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Research Article

Ultrastructure of Plasma Cells in Mucous Membrane of Digestion Organs in Pathology

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Abstract

By the JEM-100S electron microscope, reactive changes in the plasma cells of the mucous membranes digestive organs (antrum stomach, duodenum, colon and ampulla of the rectum) were studied 30 patients with various pathologies (gastro-duodenitis, irritable bowel syndrome, Crohn's disease). At the ultrastructural level, the number of plasma cells in the colon of 6 patients with irritable bowel syndrome was counted and in 3 patients without signs of pathology in all parts of the colon (control).

As a result of the study, the following are shown for the first time: ultrastructural changes in plasmacytes during their functional activity associated with the production of immunoglobulins (antibodies) in response to the effect of antigens; Two ways to separation immunoglobulin complexes from plasma cells; The structure of immunoglobulin complexes freely located in the loose connective tissue of the proper mucous plate. All the patients examined had an increase in the content of active plasmacytes. The reliable data on an increase in the amount of plasmacytes in the colon mucosa with irritable bowel syndrome have been obtained.

Keywords: *Plasma Cells; Gastroenterology; Ultrastructure*

Introduction

Interest in plasma cells increased after the establishment of their role in immunogenesis as a source of immunoglobulin (antibody) formation. The presence of lymphocytes and plasma cells in the lamina propria of the mucous membrane confirms the involvement of the immune system in the development of inflammatory reactions in it and according to a number of authors, serves as one of the indicators of an unfavorable course of the disease [1-3].

The digestive organs are directly exposed to various antigens (bacteria, viruses, food antigens, etc). For protection, the body has a general immune system (spleen, lymph nodes, tonsils, etc.) and local use in the form of immunocompetent cells, which include plasma cells [4,5]. They are formed from B-lymphocytes and are located in the organs of the immune system, and a significant part of them is distributed in the loose connective tissue of the mucous membranes of organs of various body systems [6,7].

The basis of humoral immunity is the differentiation of B-lymphocytes into plasma cells secreting antibodies. On this issue, recently (15 - 20 years), a large number of works have been published devoted to the determination of the role of plasma cells for the diagnosis of the disease and the severity of their course in the organs of the digestive system with various clinical manifestations [8,15]. In the digestive organs, three populations of plasma cells were identified in healthy and sick patients. Healthy - 72% plasmacytes produce only IgA, in 18% - double the content of IgA/IgG or IgG [9].

In clinical and experimentally induced pathological conditions in the digestive organs, an increase in the number of lymphocytes and especially plasmacytes in the mucous membrane, as well as an increase in the content of antibodies secreted by these cells, is noted [10-12]. Studies devoted to the study of the submicroscopic structure of plasmacytes during the period of their functional activity were reflected in a few studies carried out on experimental animals [10,11] and obtained during clinical examination of patients [1-3,7]. In them, in addition to an increase in the number of plasmacytes, an increase in the cytoplasm of the granular cytoplasmic reticulum, producing immunoglobulins, and disturbances characteristic of destructive and metabolic changes are described. The finding of plasmacytes in different functional states is mainly based on the identification of light and dark cells among them [7,13]. Changes in the submicroscopic structure of plasmacytes in the mucous membranes of the digestive organs during their transition from a state of rest to active production and excretion of immunoglobulins were not reflected in published studies.

Aim of the Study

The aim of the work is to study the submicroscopic structure of plasmacytes of the mucous membrane of the digestive organs in various types pathology.

Materials and Research Methods

The material for the study was biopsies obtained from various parts of the digestive organs (stomach, duodenum, colon and rectum) from patients (age from 25 to 62 years) with diagnoses: gastroduodenitis, irritable bowel syndrome (IBS), Crohn's disease. A total of 30 patients were examined. The clinical diagnosis was made on the basis of clinical and anamnestic data, as well as the results of laboratory and instrumental (fibrogastroscopy, colonoscopy) studies. The biopsy material was fixed in a 2.5% glutaraldehyde solution, followed by additional fixation in a 1% solution of osmium tetroxide and embedded in araldite M. in an electronic microscope JEM - 100S (Japan).

Determination of quantity

Plasma cells in the lamina propria of the colon mucosa were performed using an electron microscope in 6 biopsies obtained from patients with irritable bowel syndrome. Biopsies from the same section of the large intestine of 3 patients with an unconfirmed diagnosis of pathology in the colon during colonoscopy and ultrastructural examination of the mucous membrane served as control. Plasma cells were counted on a grid square, on which ultrathin sections (square area 0.27 μm^2, determined in a light microscope) were placed with a microscope magnification of 7000. Plasmacytes were counted in patients with IBS in 136 and in controls, in 74 fields of view microscope. Statistical processing of quantitative indicators was carried out taking into account the significance of differences according to the Student's criterion at $P \leq 0.05$.

Research Results

All examined patients have edema in the mucous membrane of the digestive organs, which occurs in the epithelium and the lamina propria. In the epithelium, in addition to edema expressed in varying degrees, dystrophic and destructive changes are observed, in its exocrine and endocrine cells. In some areas, swelling the epithelium is poorly expressed and is represented by small expansions of the in-

tercellular spaces in its basal part, in others it is more pronounced and the epithelial cells are separated from each other at a considerable distance from each other. The connection between them is maintained due to the contact of narrow outgrowths from the lateral surfaces of the cytoplasm epithelial cells.

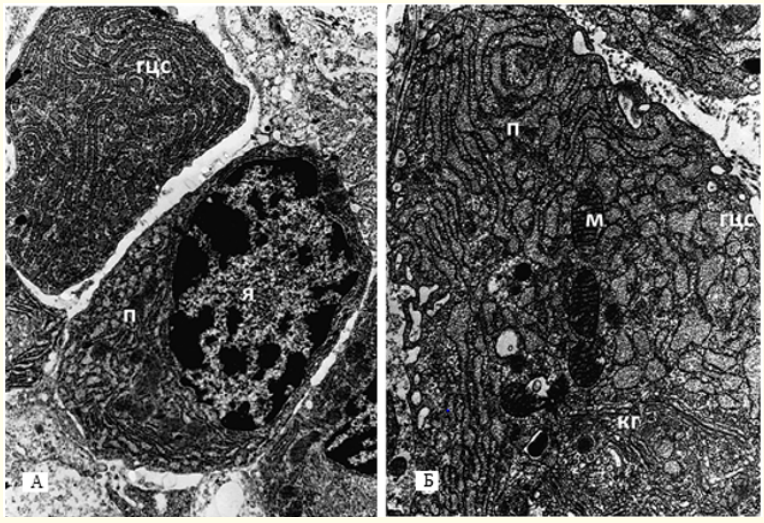

Figure 1: *Mucous membrane of the antral part of the stomach of patients with gastroduodenitis (a, b). P - plasmacyte, I: Nucleus; GCC: Granular Cytoplasmic Reticulum; M: Mitochondria; CG: Golgi Complex. Uv.: a - 14000, b - 20,000.*

Intercellular contacts (desmosomes and tight junctions) in the apical part of epithelial cells are in most cases without visible disturbances. In the lamina propria of the mucous membrane, edema of loose connective tissue is accompanied by an increase in the number of lymphocytes and especially plasma cells in it, as well as a change in the structure of the endothelium of blood capillaries. In most endotheliocytes, the cytoplasm contains numerous pinocytic vesicles, which indicates an increase in fluid transport through the endothelium.

Plasma cells are unevenly distributed in their own lamina, most often they are localized in groups of 3 - 7 cells in the field of view of an electron microscope and differ in structure. When counting the number of plasma cells in the mucous membrane of the colon in patients with IBS, there are 3.4 ± 1.3 plasmacytes per grid square, in the control - 0.3 ± 0.1. Plasmacytes in the lamina propria of the mucous membrane in all examined patients differ in structure. Among them, you can find cells that are at rest and at various stages of their functional activity. In plasmacytes in a state of rest (Figure 1a), most of the cytoplasm is occupied by a round-shaped nucleus with even or slightly wavy contours. Heterochromatin in the form of large clusters adjoins the inner nuclear membrane.

Cytoplasm contains numerous narrow tubules of the granular cytoplasmic reticulum filled with a fine-grained substance (immunoglobulin) of moderate electron density. The Golgi complex is poorly developed and occupies small areas of the cytoplasm near the nucleus. Oval mitochondria with parallel cristae are also located near the nucleus.

When plasmacytes enter the state of active functioning (initial stage), pronounced submicroscopic changes are observed in the cytoplasm (Figure 1b). The cells increase dramatically in size. On their surface, outgrowths and invaginations of the cytoplasm of various sizes appear. In the tubules of the granular cytoplasmic reticulum, vacuolar dilations appear, which are filled with immunoglobulin. The golgi complex occupies significant areas of the cytoplasm. No pronounced changes are observed in the structure of the nuclei.

In addition to the described plasmacytes, in all examined patients, most of them are elements that are in a state of active formation of immunoglobulin (antibodies) and its removal into the intercellular medium (Figure 2). On the sections, you can trace the various stages of the removal of immunoglobulin from plasma cells, which in vacuoles of the granular cytoplasmic reticulum it is located unevenly. Its granules can adhere tightly to each other, or they lie loosely, and clear areas are visible between them. Sections of the cytoplasm - immunoglobulin complexes - consisting of vacuoles of the granular cytoplasmic reticulum filled with immunoglobulin - are separated from the plasma cells and are freely located in the intercellular medium of loose connective tissue of various sizes. Some immunoglobulin complexes are surrounded by a narrow area of the cytoplasm and the plasma membrane, vacuoles of the granular cytoplasmic reticulum in them contain a large amount of immunoglobulin, and numerous ribosomes are associated with its membrane. In figure 2c and 2d you can see the separation of the immunoglobulin complex from the plasmoita.

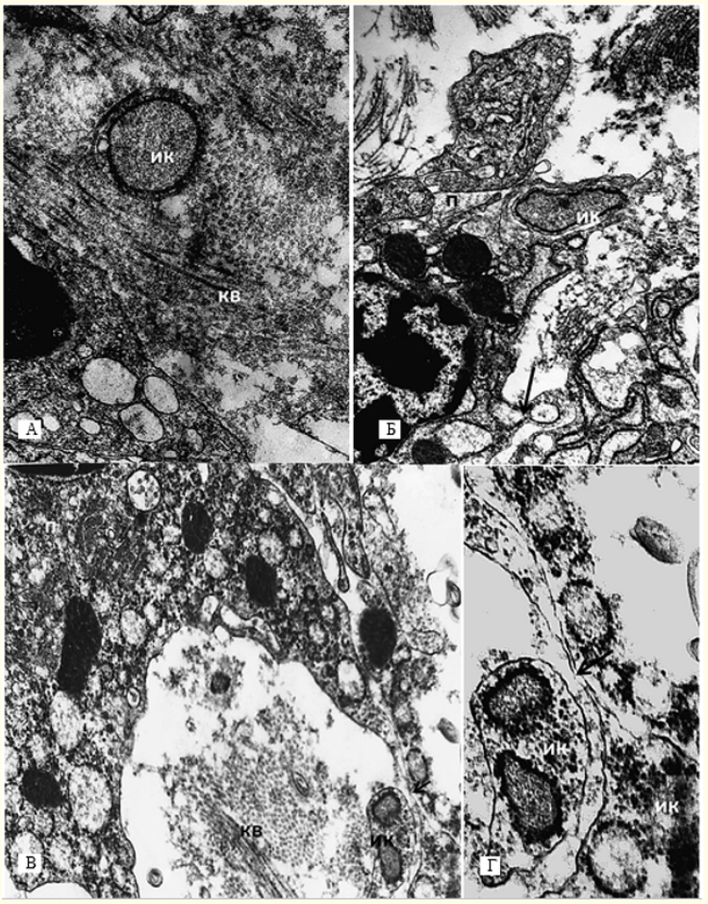

Figure 2: *The lamina propria of the gastric mucosa (a, c), duodenum (d) of patients with gastroduodenitis, and of the colon of patients with IBS (b) IR: Immunoglobulin complex, KB: Collagen fibers, arrow - junction of the immunoglobulin complex with a plasmacyte. The rest of the designations are the same as in figure 1. Uv.: a - 28000, b, c - 20,000, d - 40,000.*

It is also connected by a narrow isthmus with a plasma cell, which preserves the plasma membrane throughout its entire length. Other immunoglobulin complexes are separated from plasma cells without preserving the plasma membrane (Figure 3). They can be

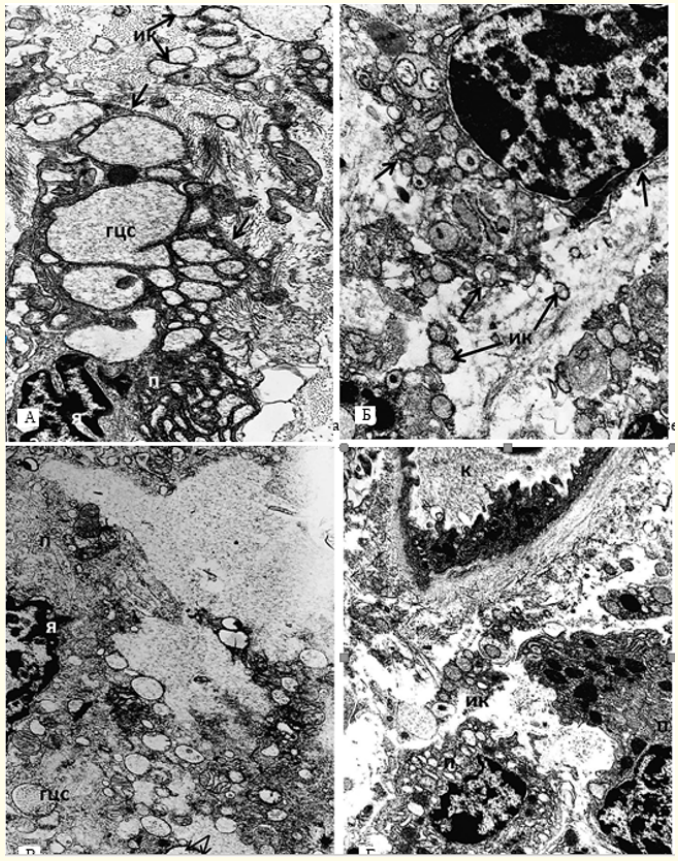

Figure 2: *Colonic lamina propria (a, b) in patients with IBS and rectum (c, d) in Crohn's disease. Arrow ka - areas of the cytoplasm devoid of a plasma membrane, double arrow - vacuole of the granular cytoplasmic reticulum with a destroyed membrane, the rest of the designations are the same as in figure 1, 2. Uv .: a - 20,000, b, c - 14,000, d - 11,000.*

represented in the intercellular medium of loose connective tissue by one vacuum of the granular cytoplasmic reticulum filled with immunoglobulin, with the membrane of which a reduced number of ribosomes is often associated, or by their whole group with scraps of cytoplasm. In this case, upon separation of the immunoglobulin complex, significant areas of the cytoplasm, devoid of the plasma membrane, remain on the surface of the plasmacytes (Figure 3a-3c). Mitochondria in separating areas of the cytoplasm are rare. In some cells, the nucleus, after the separation of a large number of immunoglobulin complexes, contacts with the surrounding intercellular medium only by the nuclear envelope (Figure 3b).

In the nuclei of plasmacytes in a state of increased functional activity, there is a slight swelling of the karyoplasm and deep invaginations of the nuclear envelope appear (Figure 3a), which indicates an increase in their surface and is also an indicator of the functional

activity of cells. Phagosomes are rarely found in actively functioning plasmacytes. Sometimes patients have plasma cells (Figure 3c), in the cytoplasm which show significant areas devoid of organelles and filled with finely granular substance, which is similar in size to granules and their electron density to those in the cavities of the granular cytoplasmic reticulum.

In the same the cell can see a vacuole, the membrane of which is partially destroyed and from it the immunoglobulin enters the cytoplasm. The separated immunoglobulin complexes are located throughout the lamina propria and near the capillaries (Figure 3d).

Discussion

The study showed that in all examined patients with various pathologies of the digestive organs, there is an increase in the lamina propria of the mucous membrane of plasma cells, most of which are in a state of active formation and excretion into the environment of immunoglobulins. Cells at rest are found in small numbers in all examined patients. As a result of the study, it was found that the removal of immunoglobulins (antibodies) from plasma cells is carried out as a result of separation from them of cytoplasmic sections - immunoglobulin complexes, which, without describing their structure and method of formation, are mentioned in two works [7,14]. In the first method of formation, immunoglobulin complexes, separating from the plasmacyte, retain on their surface the plasma membrane and the narrow rim of the cytoplasm, and have a structure characteristic of the vacuoles of the granular cytoplasmic reticulum at the initial stage of active synthesis of antibodies, and the plasma cells retain the integrity of the plasma. the cell membrane on the entire cell surface. The separated complexes of this structure, apparently, remain in the mucous membrane for a longer time. In the second method of their formation, vacuoles of the granular cytoplasmic reticulum contain a reduced amount of immunoglobulin, sometimes they look optically empty, and a reduced number of ribosomes is associated with their membranes. With this method, a large amount of immunoglobulin is separated from the plasmacytes.

Conclusion

Complexes without a plasma membrane or with its scraps, while the cytoplasm on a significant cell surface remains devoid of a plasma membrane. Both methods of excretion of immunoglobulin took place in all patients; it was not possible to determine the predominance of this or that method of separating the complexes, depending on the disease. Differences were only in the degree of development of these processes both in different pathological conditions and in the same diagnosis, which, apparently, is explained by the individual characteristics of the patients and the severity of the disease. Probably, the differences in the methods of formation of immunoglobulin complexes are determined by which plasmacytes are in a state of active synthesis and elimination of antibodies, since in the digestive organs among them 3 populations were identified according to the type of immunoglobulin produced [9] and according to life expectancy - living (memory cells) and short-living cells.

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