



Immunohistochemical Characteristics of Nodular Mastopathy

¹ Khalikova Firuza Sharofovna

² Bukhara State Medical Institute, Uzbekistan

Annotation: The physiology and pathology of the mammary glands has always been one of the most difficult areas of medical science and practice. This is a complex problem, the scientific, therapeutic, diagnostic, methodological and organizational aspects of which have a pronounced interdisciplinary character. The system of medical care for the female population that has developed in our country determines the important role of the obstetric and gynecological service in the prevention, diagnosis and treatment of most inflammatory and benign diseases of the mammary glands.

Keywords: mastopathy, nodular, morphofunctional, fibrocystic.

It is well known that the main phases of morpho-functional formation of the organ proceed postnatally and are clearly synchronized with the periods of ovulatory and hormonal functions of the ovaries and the realization of the reproductive function of the woman. The most pronounced growth spurt of the mammary glands occurs during puberty, during pregnancy and lactation, and involutive tissue transformations occur on average after the age of 40 and occur most intensively in postmenopause. The development of glands from the period of establishment of the ovarian cycle is carried out cyclically, with activation in the second phase of the menstrual cycle. Recent years have been characterized by a sharp increase in the frequency of hyperplastic processes and breast cancer. This is probably due to the progressive growth of civilization diseases associated with metabolic disorders (obesity, hypertension, hyperlipidemia, hyperinsulinemia, and diabetes mellitus), environmental problems, peculiarities of the reproductive function, psychogenic loads. The greatest proportion among the benign pathology of the mammary glands is mastopathy or fibrocystic disease. The evolution of the concept of mastopathy for more than two centuries took place in a wide range: from the recognition of this pathology as a mandatory stage of neoplastic transformation to the denial of the definition as a "disease". For a long time mastopathy was considered as a precancerous condition, which determined the implementation of a medical examination program in the Soviet Union in the second half of the last century, within the framework of which work was carried out to identify, treat and monitor patients with this pathology

The histological verification used the recommendations of the histological classification of breast tumors (WHO, 2003). The following forms of fibrocystic disease were distinguished:

1. non-proliferative;
2. proliferative (without cell atypia) with a moderate and pronounced degree of proliferation of the milky epithelium;
3. Proliferative form with cell atypia.

The non - proliferative form was characterized by the following main features:

1. the lobules are not altered or atrophic;
2. ducts are not changed or expanded;
3. the epithelium lining the intra-lobular and inter-lobular ducts is not changed, is represented by 1-2 layers or is atrophic;
4. cell nuclei are normochromic;
5. there are no pathological mitoses;
6. Changes in the interlobular and intralobular stroma (increased development and/or hyalinosis). Depending on the prevailing morphological changes among the proliferative forms of fibrocystic breast changes, the following variants were distinguished: lobular; ductal; mixed.

In the lobular type, epithelial proliferation took place mainly in the intra—lobular ducts; in the ductal type, in the extra-lobular ducts; in the mixed type, a combined pattern was observed. The histological description of the structure of the mammary gland in the non-proliferative and proliferative form of fibrocystic changes took into account the presence of: cysts; lymphocytic infiltration; myoepithelial hyperplasia; cribriform structures in the ducts; fibrosis of the false (intra-lobular) stroma; solid proliferates in the lobules and ducts; false and true papillae; fibroadenoma and its histologists-ical type (intracanalicular, pericanalicular, mixed). The proliferative activity and apoptosis were evaluated using the immunohistochemical method of investigation. Proliferative activity was performed based on the analysis of the content of endogenous markers of proliferation - nuclear antigen Ki-67. To identify the factors involved in the regulatory mechanisms of apoptosis, immunohistochemical determination of the Vcl-2 protein was carried out. Markers were examined on paraffin sections (thickness 5 microns) by the avidinbiotin immunoperoxidase method. Previously, breast tissue was fixed in neutral formalin (pH-7.2). Before the reaction with antibodies to the intracellular markers Ki-67 and Vcl-2, high-temperature unmasking of the antigen was performed in a citrate buffer (pH 7.6).

Immunohistochemical study was performed using monoclonal mouse antibodies Ki-67, Clone MIB1 Ki-67 (1:100, Dako); Vcl-2 clone 124 (1:75, Dako). A universal kit containing biotinylated anti-mouse and anti-rabbit immunoglobulins was used as the second antibodies. A complex of DAB chromogen and DAB substrate was used to visualize the reaction.

The degree of expression of the stained cells was assessed as weak, moderate and high. If less than 10% of the stained cells were found in the sections in one field of view, the expression was assessed as weak. If there were from 10 to 90% of the stained cells, then the expression was considered moderate. In the presence of more than 90% of stained cells - high expression. The study used a light microscope MBI 1120, a digital camera DCM 130, a personal computer based on Intel Pentium 4.

Biopsies of nodular breast formation of 28 patients were subjected to morphological and immunohistochemical studies. The control group included biopsy materials taken from corpses in the same age range who died from other causes, in which no pathology of the mammary glands was verified.

Histological examination of breast biopsies is dominated by its non—proliferative forms - in 20 (71.4%) patients. Proliferative forms of nodular mastopathy without atypia were histologically verified in 8 (28.6%) patients, of which 4 had a pronounced degree of epithelial proliferation. At the same time, depending on the prevailing morphological changes, lobular, ductal and mixed types of epithelial proliferation are distinguished.

Intracanalicular or mixed fibroadenomas were microscopically determined, often with cystic-dilated ducts, in the lumen of which polypoid connective tissue outgrowths covered with one or more rows of cubic epithelium protrude. The stroma of the neoplasm is multicellular with areas of myxomatosis, hyalinosis, cartilage and bone tissue. Stroma cells are predominantly spindle-shaped with elongated nuclei, folded into bundles intertwined with each other. There are also areas with proliferation of smooth muscle fibers. The neoplasm resembles the so-called mixed, or mesodermal tumors, which are occasionally found in the mammary gland. In places, there were areas in the tumor

containing ugly polymorphic cells, mitoses, foci of hemorrhages and necrosis, despite the fact that this tumor remains benign. Microscopically, proliferation of both glandular and epithelial cells took place.

It is important to note that sometimes the acinuses of glandular lobules proliferate evenly and retain all morphological features of the structure of physiological adenosis - a uniform order of cell enlargement. At the same time, the excretory ducts of the tubules and the alveoli of the gland are covered with a saturated cytoplasmic cubic epithelium, in the second myoepithelial layer there is an epithelium with hyperchromic nuclei and vacuolinized cytoplasm.

When studying the biopsy material, it was also revealed that if the glandular alveoli proliferate and pass into adenosis, then the glandular lobules have a solid and cribric structure. At the same time, the excretory ducts and alveoli of glandular lobules proliferate evenly and are covered with monomorphic small epithelial cells

Uniform proliferation is observed in the initial stages of the disease, and over time polymorphic proliferative changes of glandular tissue are already determined. Polymorphic proliferation of glandular acinuses and ducts. Hemotoxylin-eosin staining. Magnification is 10x40.

At the same time, there is a cystic expansion of the excretory ducts of the gland, the appearance of papillomatous growths in the glandular lobules, lymphocytic infiltration, false and true papillae, cribric proliferates, as well as solid proliferates in the ducts and lobules.

Normally, breast tissue consists of lobules, each lobule, in turn, is divided by loose connective tissue into small lobules, which end in small lobules with alveoli and ducts (Fig.3).

Collagen fibers are found little in the interlobular fibrous tissue. It is rich in cellular elements, fibroblasts, macrophages, mast cells, eosinophils and lymphocytes are found between collagen fibers. The growth of the alveoli is subject to the menstrual cycle.

The ducts of the mammary gland in diameter are covered with a single-layer cubic epithelium or cylindrical. Closer to the nipples, they turn into a two-layer epithelium. In the nipples, the epithelium is layered.

As is known, the rate of tumor growth is the most important integral indicator of the features of its clinical course. To determine the proliferative activity of the breast node, we used antibodies to Ki-67. Mono-clonal antibodies to Vcl-2 were used to study the blocking of the apoptotic mechanism. Out of 28 breast biopsies, a positive immunohistochemical result was verified in every 7th on Ki-67, in every 3rd on Bcl-2. Microscopically revealed changes in the excretory ducts. The epithelium lining the gland cavity is formed during metaplasia the usual epithelium of the alveoli and ducts. At the same time, the appearance of various papillary growths of different types and sizes due to cell proliferation is visible. In such an epithelium, the nuclei turn brown, which indicates the presence of the Ki-67 gene in the tissue and the progression of tumor growth

In proliferative areas with the transition to papillae, an increase in the expression of Ki-67 and vacuolated epithelium was found. And also, an increase in myoepithelium in proliferative foci with apocrine metaplasia.

In the stroma of the gland, connective tissue of various types has been verified, sometimes sclerosed and fibrotic, in places with areas of hyalinosis, as well as with swelling and myxomatosis. However, in the stroma of the glands, the cell nucleus is colored in the usual purple color, which indicates that proliferative activity is insignificant in stromal cells.

One of the main apoptosis inhibitor proteins is Vcl-2. It is located on the outer membrane of mitochondria and is found in many types of normal cells.

With nodular mastopathy, papillary growths inside the expanded ducts are covered with a single-row or multi-row cubic epithelium. In some places, the epithelium is apocrinized and passes into the lumen of the duct. At the same time, foci of expression of the Vcl-2 gene with brown coloration were found in the glandular tissue (Fig.5).

Cancer markers Ki-67 and Vcl-2 cells differed in three degrees of expression: weak, moderate and high (Table 11).

When less than 10% of the stained cells were detected in the field of vision, it was assessed as weak expression. The presence of 10 to 90% of stained cells was regarded as moderate expression. The presence of more than 90% of colored cells in the field of vision was considered a high degree of expression.

tumors. None of our observations revealed a high expression of the studied markers.

At the same time, a combination of moderate expression of Vcl-2 and Ki-67 was observed in sections of 2 patients, a combination of moderate expression of Vcl-2 and weak expression of Ki-67 was verified in 2 more patients. The remaining 4 patients with proliferative mastopathy were diagnosed with weak expression of Hcl-2. The proliferative form of mastopathy was histologically noted in all 8 patients. Of these, half – 4 patients had a histologically marked degree of epithelial proliferation; these patients were diagnosed with a combination of moderate expression of Vcl-2 and Ki-67. Conclusions. Thus, histological and immunohistochemical studies of the epithelial component of nodular mastopathy revealed two forms of mastopathy - proliferative and non-proliferative with the development of different types of proliferative changes. Thus, foci of intracanalicular proliferation appear in the glandular epithelium, and the single-row epithelium turns into a multi-row one with the appearance of various solid and cribric structures. At the same time, epithelial proliferation increases with the simultaneous absence of apoptosis. Subsequently, polymorphism and cell growth appear in the foci of intracanalicular proliferation, and the normal ratio to the basement membrane is disrupted. The presence of Hcl-2 with a moderate degree of expression in combination with Ki-67 in patients with nodular mastopathy should be considered as a marker of the progression of the proliferative process and the need for long-term monitoring of these patients by a mammologist.

References:

1. Aslonov S. G. et al. Modern Approaches to Oropharyngeal Cancer Therapy //International Journal of Discoveries and Innovations in Applied Sciences. – 2021. – T. 1. – №. 3. – C. 38-39.
2. Aziza Zokovna Olimova, Sanoev Bakhtiyor Abdurasulovich. OVARIAN diseases IN women OF reproductive age: dermoid cyst. // Volume: 01 Issue: 06/2021. 154-161 p
3. Aziza Zokovna Olimova. The frequency of occurrence of my uterus In women of reproductive age. // JOURNAL OF ADVANCED RESEARCH AND STABILITY (JARS). Volume: 01 Issue: 06/2021. 551-556 p.
4. B.A. Sanoev, G.S. Niezova, N.I. Hikmatova MACRO- AND MICROSCOPIC MANIFESTATIONS OF UTERINE LEIOMYOMAS // New day in medicine. Number 2. 2020. pp. 526-528
5. Hikmatova N.I. Improving the effectiveness of infertility prediction in women with inflammatory diseases of the pelvic organs // FIGO 23 World Congress of Gynecology and Obstetrics. - Australia. Sydney, 2021. - p.10.
6. Hikmatova N.I., Pakhomova Zh.E. Association with the antigen HLA-variant of the DRB1 gene, genotype DQA1 and DQB1 with infertility of reproductive disorders in the Bukhara region of Uzbekistan // News of dermatovenerology and reproductive health. Tashkent. 2022.-pp.28-31.
7. Hikmatova N.I., Pakhomova Zh.E. Clinical indicators of individualized approaches to the treatment of infertility of inflammatory genesis // News of dermatovenerology and reproductive health. – Tashkent, 2021. - p.19-22.
8. Ilkhomovna K. D. MANIFESTATIONS OF POST-MASTECTOMY SYNDROME, PATHOLOGY OF THE BRACHIAL NEUROVASCULAR BUNDLE IN CLINICAL MANIFESTATIONS //Innovative Society: Problems, Analysis and Development Prospects. – 2022. – C. 225-229.

9. Ilkhomovna K. D. Modern Look of Facial Skin Cancer //BARQARORLIK VA YETAKCHI TADQIQOTLAR ONLAYN ILMIY JURNALI. – 2021. – T. 1. – №. 1. – C. 85-89.
10. Ilkhomovna K. D. Modern Look of Facial Skin Cancer //BARQARORLIK VA YETAKCHI TADQIQOTLAR ONLAYN ILMIY JURNALI. – 2021. – T. 1. – №. 1. – C. 85-89.
11. Ilkhomovna K. D. Morphological Features of Tumor in Different Treatment Options for Patients with Locally Advanced Breast Cancer //International Journal of Innovative Analyses and Emerging Technology. – 2021. – T. 1. – №. 2. – C. 4-5.
12. Khodjaeva D. I. Magnetic-resonance imaging in the diagnosis of breast cancer and its metastasis to the spinal column //Scientific progress. – 2021. – T. 2. – №. 6. – C. 540-547.
13. Khodjayeva D. I. MORPHOLOGY OF IDIOPATHIC SCOLIOSIS BASED ON SEGMENT BY SEGMENT ASSESSMENT OF SPINAL COLUMN DEFORMITY //Scientific progress. – 2022. – T. 3. – №. 1. – C. 208-215.
14. Khodjayeva D. I. MORPHOLOGY OF IDIOPATHIC SCOLIOSIS BASED ON SEGMENT BY SEGMENT ASSESSMENT OF SPINAL COLUMN DEFORMITY //Scientific progress. – 2022. – T. 3. – №. 1. – C. 208-215.
15. Khodzhaeva D. I. Changes in the Vertebral Column and Thoracic Spinecells after Postponement of Mastoectomy //International Journal of Innovative Analyses and Emerging Technology. – 2021. – T. 1. – №. 4. – C. 109-113.
16. Khodzhaeva D. I. Modern Possibilities of Ultrasounddiagnostics of Skin Cancer //IJTIMOIY FANLARDA INNOVASIYA ONLAYN ILMIY JURNALI. – 2021. – T. 1. – №. 1. – C. 101-104.
17. R. I. Israilov, B. A. Sanoev, A. Z. Olimova Pathologically undifferentiated morphology of the placenta in primary placental insufficiency // American Journal of Medicine and Medical Sciences. Volume: 10 Issue: 09/2020. 660-663 p.
18. Sanoev Bakhtiyor Abdurasulovich MORPHOLOGICAL AND MORPHOMETRIC CHARACTERISTICS OF THE PLACENTA IN NORMAL PREGNANCY.// DEVELOPMENT OF THE MODERN EDUCATION SYSTEM AND CREATIVE IDEAS FOR IT, REPUBLICAN SCIENTIFIC AND PRACTICAL ONLINE CONFERENCE "PROPOSALS AND SOLUTIONS" Issue: 06/2020. 94-96 p.
19. Sanoev Bakhtiyor Abdurasulovich, Olimova Aziza Zokovna. Pathology of precancerous ovarian conditions in women of reproductive age. // Volume: 01 Issue: 06/2021.
20. Ходжаева Д. И. Современные возможности ультразвуковой диагностики рака кожи лица //Вопросы науки и образования. – 2021. – №. 25 (150). – С. 21-24.