BRITISH MEDICAL JOURNAL

British Medical Journal

Volume 3, No.1, January 2023

Internet address: http://ejournals.id/index.php/bmj
E-mail: info@ejournals.id
Published by British Medical Journal
Issued Bimonthly
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THE STUDY OF THE EXPRESSION OF THE PROLIFERATION MARKER KI -67 IN FIBROUS MASTOPATHY NODULAR FORM.

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Abstract. The study of proliferative conditions of the mammary glands is an important diagnostic and prognostic problem, the solution of this problem to the fullest extent will reliably indicate the possibility of developing breast cancer (BC), and therefore reduce the development of the tumor process in it.

In recent years, much attention has been paid to the study of tumor receptor status in breast cancer (estrogen receptors, progesterone receptors, HER-2/ neu status, Ki-67 proliferative activity). At the same time, there are no sufficiently convincing data on the role of cell division proteins , i.e. proliferative activity of cells in benign mammary dysplasia.

The aim of the study was to study and comparative analysis of morphological data and immunohistochemical parameters of the expression of the proliferation marker Ki-67 in the nodular form of fibrocystic disease and in C - r in situ .

The obtained materials can be used in the development of a diagnostic algorithm aimed at detecting precancerous transformation of the gland tissue into a malignant tumor, which will provide more information about the pathogenesis of the malignant process, and can also be taken into account when developing practical recommendations for the management of patients with benign breast dysplasia.

Keywords: fibrocystic mastopathy, nodular form, proliferative conditions of the mammary gland, immunohistochemical analysis (IHC analysis)

Introduction. Among the proliferative conditions of the mammary glands, I single out t fibrocystic disease (FCD), fibroadenomas of various structures, cysts, intraductal papillomas. FCD is the most common pathological process in the mammary gland. Determining the probability of malignancy in these pathological processes is difficult, and sometimes impossible, without performing a trephine biopsy of the breast tissue [1-4]. In recent years, much attention in the domestic and foreign press has been paid to the developed morphoimmunohistochemical , molecular genetic characteristics in breast cancer (BC), with particular importance given to such factors as the determination of estrogen receptors, progesterone, HER-2 / neu -status, proliferative tumor cell activity. The identification of these biological markers of breast cancer makes it possible to identify the molecular genetic subtypes of breast cancer, and therefore to assess the prospects and tactics of chemotherapy treatment [5-10]. However, in some cases, when performing ultrasound diagnostics and mammographic examination of the breast, there are problems associated with a full and competent intravital diagnosis of precancerous and tumor processes in it. Morphological examination of the surgical material does not always give a complete judgment about the presence or absence of malignancy of the pathological process, including proliferative processes of the ductal epithelium. The solution of these issues is extremely important in the conditions of early diagnosis of breast cancer, which can significantly reduce the risk of recurrence and metastasis. A few works devoted to the role of precancerous conditions in the genesis of breast cancer are

based on experimental material. Thus, in some publications there are indications of the role of myoepithelial cells of the ducts of the mammary gland in the development of an oncosuppressive effect on the appearance of neoplastic cells in the glands [2]. Some authors discuss the likelihood of developing a staged occurrence of breast cancer through transformation from the normal glandular epithelium of the ducts [3, 9]. There is a histogenetic model of the occurrence of cancer, according to which its appearance is preceded by proliferative-hyperplastic and atrophic-dystrophic changes in the epithelium, accompanied by a gradual morphological transformation of cells, which is most pronounced in precancerous processes, regarded as severe dysplasia. Further growth of dysplastic changes can lead to a qualitatively new stage - malignant transformation of cells [2, 3, 9]. These studies do not provide information on the role of cell division proteins (Ki-67) and apoptosis (TP53) in areas of neoplastic cell transformation. Undoubtedly, the solution of these issues will make it possible to develop a unified diagnostic algorithm aimed at identifying early pre-tumor and tumor fields in the mammary gland.

In this regard, the purpose of our study was to study and comparative analysis of morphological data and immunohistochemical parameters of the expression of the proliferation marker Ki-67 in the nodular form of fibrocystic disease and in C - r in situ

Research materials. Breast tissue obtained by trepanobiopsy and sectoral resection from 100 women of reproductive age (mean age 45 years), of which patients with breast cancer - C - r in situ was 45 people, with benign dysplasia - 55. The morphological study was carried out according to the traditional method using hematoxylin-eosin staining. The IHC stage of the study was carried out on a Bench Mark Ultra apparatus using ready-made sets of antibodies.

Research results. FCD was characterized by the formation of cystic dilatations of individual groups of ducts with areas of uneven proliferation of their epithelium. Cystic structures expressed the Ki-67 protein mainly in the basal regions. Mutant p53 protein was not detected in ductal structures. The level of proliferation of the Ki-67 protein did not exceed 10-15% of nuclei with moderate expression. It is important to note that individual ductal structures were filled with glandular epithelium with pronounced proliferation, filling with clusters of cells of the lumen of the glands, while the basement membrane of the ducts was intact. This created a false impression of the presence of malignant growth in the glandular structures (Fig. 1).

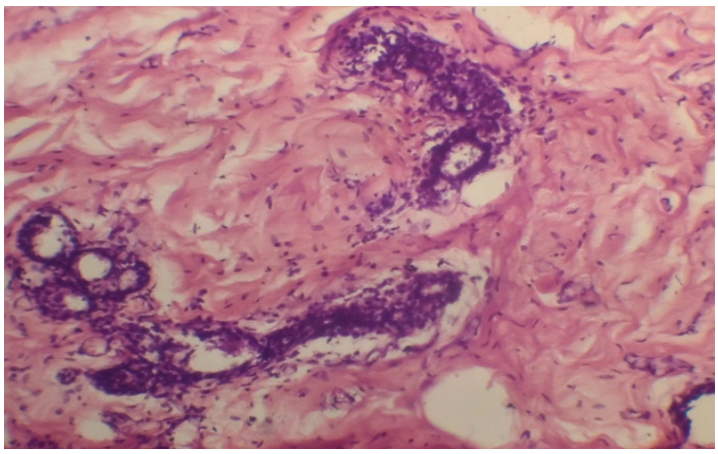

Fig. 1

Patient A.A., born in 1982 Fibrocystic mastopathy, nodular form (Staining with hematoxylin and eosin, x 200). In the micropreparation among the fibrous tissue, there are ducts of the mammary glands, with hyperplasia, separate areas with dystrophic changes, in some loci there are tumoral vessels

In this regard, for the differential diagnosis of precancerous conditions, an IHC study was performed. In some observations, we encountered ductal structures containing papillary formations consisting of hyperchromic cells, while the basement membrane was preserved. These morphological features indicated the presence of an intraductal papilloma with marked proliferation of glandular epithelial cells . However, it is difficult to judge the probable potential for malignant growth of this category of tumor based on morphological examination alone. At high magnification, the structure of papillary formations was represented by two types of cells - secretory and basal, separated from each other by thin fibrovascular layers of connective tissue. Around the areas of pronounced proliferation of duct cells and lobules, a picture of invasive lobular carcinoma was observed in 35% of cases. However, such diagnosis was not always easy, which is associated with the location of solid areas along with pronounced proliferation of ducts and lobules. One of the criteria for the presence of invasive carcinoma was the location of cell clusters that build solid areas in the hyalinized stroma around small thin-walled vessels (Fig. 2).

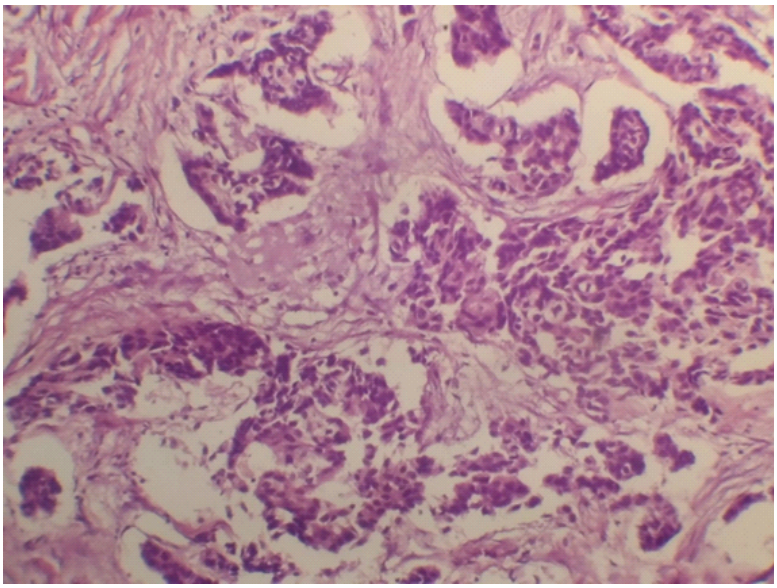

Fig. 2.
Patient T.Z. born 1971 Encapsulated ductal carcinoma in situ breast papillary structure (Staining hematoxylin and eosin, x 200) Loose fibrous connective tissue is determined in the micropreparation. In separate foci, dilated ducts, in the ducts the epithelium is hyperplastic and fills the entire duct, the nuclei are hyperchromic , single pathological mitoses.

To assess the prognostic value of some IHC markers, a comparative study of proliferative conditions and neoplastic formations in the mammary gland was carried out. The level of proliferative activity of Ki-67 in ductal papillomas was low, not exceeding 10-15% of cell nuclei with the expression of the nuclear protein Ki-67 in the basal sections of the gland ducts (Fig. 3).

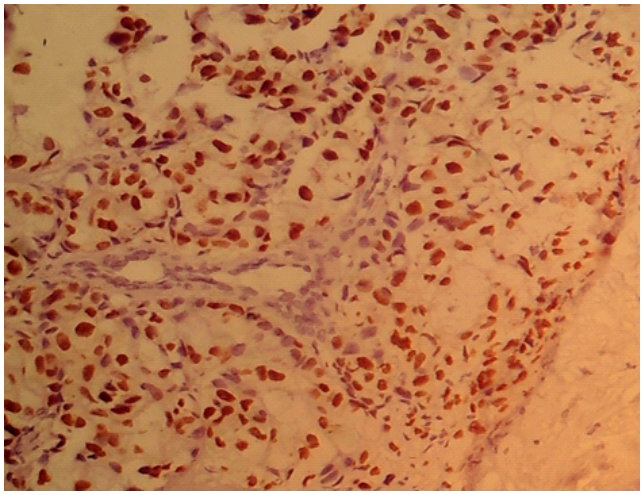

Fig. 3.
Patient B. Positive reaction, high expression of proliferative activity protein Ki - 67 in breast cells. ok. 10 x , ob.40 x

In places of pronounced proliferation of the glandular epithelium, only single cells expressed the Ki-67 protein. This, in our opinion, indicated the predominance of secretory changes in the cells of the ductal epithelium in comparison with its proliferation.

Thus, the study showed the presence of foci of increased cell proliferation in FCD with an unstable growth potential, preservation of estrogen and progesterone receptors. We believe that the role of proteins with proliferative activity is important for the onset of tumor transformation of ductal and lobular structures of FCD, intraductal papillomas in breast cancer. Undoubtedly, the detection of Ki - 67 expression in the areas of proliferation of the ductal and lobular epithelium of the mammary gland on the material of trephine biopsies will significantly facilitate the differential diagnosis of FCD and breast cancer, and therefore determine further treatment tactics.

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