

QUALITY OF LIFE IN BREAST CANCER PATIENTS HISTOLOGICAL TYPES, RARE FORMS

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Abstract

Purpose: The present work proposes an approach to breast cancer in the light of the complexity of malignant histological forms, but also of high-risk lesions with potential malignancy.

Keywords: breast cancer, hyperplasia, carcinoma in situ, invasiveness, multidisciplinary, quality of life.

Material and method of work:

Typical and atypical hyperplasia, increased risk injuries, clinical follow-up, imaging and histology are essential in hyperplasia to ensure therapeutic interventions at an optimal time of disease evolution. In situ carcinoma, ductal and lobular, invasive carcinoma with specific forms as well as rare forms of breast cancer, benefit from specific treatment, analyzed in the multidisciplinary team surgeon, oncologist, radiotherapist, psychotherapist.

Conclusions: histological forms are varied, follow-up and therapeutic approach takes into account these aspects, the multidisciplinary approach allows for the optimal performance of therapeutic interventions, adaptation to the particularities of the case, allowing Increasing survival and improving the quality of life.

1. High risk injuries:

Hyperplasia is an increase in the number of ductal or lobular epithelial cells, cells that may or may not have atypia and the overall loss of apicobasal orientation. The most frequent is ductal hyperplasia without atypia, if the process is marked, it is called florid hyperplasia or papillomatosis.

Atypical ductal hyperplasia (HAD) must be differentiated from carcinoma in situ. Median hyperplasia is characterized by the presence of 3 or more cell layers near the basement membrane in a lobular or ductal unit. Such lesions are an "inflammatory" form of hyperplasia, with a clear separation between epithelial and inflammatory cells and are found in over 20% of biopsies. Their clinical significance is that they involve an increased risk of 1.5 to 2 times the occurrence of invasive carcinoma¹.

All proliferative changes of breast tissue signify an increased risk for the further development of breast cancer, but this risk is significantly different depending on the type of proliferation; Although most carcinomas after a benign biopsy with proliferative changes occur in those with typical hyperplasia, a relatively higher risk is associated with atypical hyperplasia².

The multidisciplinary approach, the clinical follow-up, the imaging and the histology is essential in the hyperplasia, in order to ensure the therapeutic interventions in an optimal moment of the evolution of the disease, which will allow the preservation of the quality of life of the patients and the cure³.

2. Ductal/lobular carcinoma in situ (CDIS/CLIS)

In situ carcinoma is characterized by the fact that tumor cells remain strictly localized in ducts or lobules, without evidence of invasion of the surrounding stroma by ordinary microscopy; theoretically, such lesions could not occur regionally or remotely, but in practice there are cases of carcinomas in situ documented histologically as such but with the involvement of regional nodules. A notion that complements from this point of view that of in situ carcinoma is that of microinvasive carcinoma, a less well defined entity that cannot be circumvented in practice and which would refer to a lesion with an existing stromal invasion but both so small that the risk of metastasis, although theoretically existing, is negligible in practice.

In situ carcinomas are of two categories: ductal in situ carcinomas and lobular in situ carcinomas; it should be mentioned that the distinction is made on the basis of growth pattern and cytological characteristics, rather than on the basis of anatomical localization.

Ductal and lobular carcinomas in situ differ as clinical presentation, morphology, biological behavior and, therefore, as prognosis.

In situ ductal carcinomas comprise a heterogeneous group of lesions with difficult to predict biological and clinical evolution, so that none of the

¹ Angelescu N., treatment of Surgical Pathology, vol. 1, Medical Publishing House, Bucharest, 2003

² Simion S., Surgical Pathology, vol.1, Carol Davila University Publishing House 2002

³ Wild L., Makopoulos C., Leidenius M., Senkus-Konefka E., Breast Cancer Management for Surgeons, A European Multidisciplinary Textbook, Springer International Publishing AG, 2018

classifications that have been made are fully relevant in terms of their management and prognosis. A simple classification that best correlates with the potential for recurrence after limited excision divides the ductal carcinomas in situ into high-grade (intermediate), intermediate-grade and low-grade (low-grade) carcinomas in the Lagio classification, respectively weakly differentiated, intermediary differentiated and well differentiated, the European classification⁴:

- I. high-grade in situ carcinomas exhibit aneuploidy, hyperexpression of the oncogene c-erbB-2, mutations of the p53 gene, high proliferation rate, lack of estrogen and progesterone receptors, angiogenesis in the surrounding stroma;
- II. low-grade in situ carcinomas have a low proliferation rate, very rarely show alterations of biological markers, are positive for estrogen and progesterone receptors;
- III. the intermediate carcinomas are between these two models both in terms of morphology and frequency of alterations of biological markers.

In situ lobular carcinomas, in contrast to the ductal ones, have a very homogeneous appearance and a less aggressive biological behavior (less aggressive than the low-grade ductal ones); they are never clinically presented as a palpable mass and do not have special mammographic features, so they represent an accidental microscopic finding; these reasons make lately in situ lobular carcinoma less regarded as neoplasia per se and more as a marker of the developed risk of invasive carcinoma (the risk of invasive carcinoma occurring in patients with in situ lobular carcinoma is 1% per year throughout life, but the invasive neoplasms that appear have no topographic connection or histological resemblance to the in situ carcinoma found)⁵. The mammary puncture is the one that establishes the diagnosis of certainty. Correlation of imaging examinations with histopathological outcome, clinical examination, multidisciplinary approach taking into account the particularities of the case allow, the establishment of therapeutic conduct.

3. Infiltrative carcinomas:

- a. ductal or common infiltrative, most commonly, 70-80%; it can be well differentiated, intermediate or poorly differentiated; In varying proportions, in situ ductal carcinoma is associated, which is an

⁴ N. Jitea, I. Bălanescu, Al. Blidaru, Fl. Isac, Ileana Boianu – Surgical Pathology of the breast. In the "Treatise of Surgical Pathology" under the editorial of N. Angelescu, Medical Publishing House, Bucharest, 2001.

⁵ Dickson R.B. Lippman M.E. - Advances in Cellular and Molecular Biology of Breast Cancer, Boston, 1996.

- important prognostic factor in patients treated with conservative surgery on the breast;
- b. lobular invasive, 2nd in frequency, 5-10%, classically with better prognosis than the first; lobular carcinoma is often associated in situ, frequently bilateral and multicentric;
 - c. - tubular, can represent up to 10% of breast carcinomas and has a much better prognosis than invasive ductal carcinoma, although in 75% of cases it is associated with low grade in situ ductal carcinoma;
 - d. mucinous (colloid), 1-2%, occurs more frequently in elderly patients and has a favorable prognosis;
 - e. marrow, 5-10%; spinal cancer and colloid cancer have the characteristics of benign tumors, which can lead to diagnostic errors.
 - f. papillary, metaplastic, adenoid cyst, etc., 1-2%.

A surprising type of cancer is triple negative breast cancer (HER2-, ER-, PR-) which has a high mortality rate and whose cells resemble the basal cells of the skin and sweat glands. These mammary cells create a support structure for the mammary ducts. It was observed that it was different from any other type of breast cancer, more closely resembling to ovarian and lung cancer.

Two other types of breast cancer appear from the luminal cells lining the breast ducts. These types of cancers have on their surface proteins that attract estrogen, thus ensuring their growth. Almost all patients suffering from estrogen cancer receive the same treatment. In some cases it results, in others it does not. Genetic analysis has divided these cancers into two distinct types. Patients suffering from luminal cancer A have made progress, while in patients suffering from luminal cancer B no improvement has been observed. This suggests that patients with the first type of cancer could recover only with hormone therapy, which prevents estrogen from feeding the tumor, while people with the second type of cancer are more likely to be subjected to chemotherapy⁶. In some cases, genetic abnormalities were so strongly associated with one type of luminal cancer that they seemed to have been the basis of the respective tumor formation. Another type of cancer is called enriched Her2 researchers, some types of breast cancer often have additional copies of a Her2 gene that causes them to grow.

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4. Rare types

Inflammatory cancer - carcinomatous mastitis (tumor invasion in dermal lymphatics) may be primary (rare) or secondary (inflammatory relapse); It is an aggressive form of carcinoma, intensely angiogenic and angioinvasive; at presentation, almost all patients have lymph node involvement and more than one third have systemic metastases; breast skin biopsy reveals tumor emboli in superficial lymphatics; the vital prognosis is poor. This type of disease, framed between locally advanced breast cancer forms, is not a special histological type, in most cases the tumor being ductal, but the very high capacity of angiogenesis seems to be an intrinsic feature of the tumor. From the point of view of cell kinetics, the growth rate is very high; from the point of view of molecular genetics, there are common alterations with other carcinomas (c-erbB-2 hyperexpression, p53 mutation) and inflammatory carcinoma-specific alterations (RhoC-GTP-axis hyperexpression and LIBC loss, an insulin-like growth factor)⁷.

Paget's disease of the nipple (carcinoma in situ with galactophore channels starting point). It is a rare form of breast cancer, about 2-3% of the total mammary carcinomas. It occurs more frequently in women over 40 and the evolution is slow. It is characterized by itching, erythema and then nipple ulceration. Periodically the ulceration is covered with scales, which gives the false impression of healing. It originates in the epithelial cells of the large caliber galactophore channels and is characterized by the presence of Paget cells that are voluminous with pale cytoplasm and chromatin arranged in thick grunts. The histogenesis of this type of cancer has provoked controversy by setting out two hypotheses. The first hypothesis claims that the disease would be epidermal in nature and that Paget cells would appear as the result of a degenerative process leading to the

⁷ Simion S., Surgical Pathology, vol. 1, University publishing house "Carol Davila" 2002

installation of an epidermal neoplasm, at present this hypothesis is abandoned in favor of a theory that tumorigenesis is located in galactophore channels, the disease spreading -is by invasion in tegument. The arguments are immunohistochemical. It can take 3 clinical forms:

- I. lesion limited to the nipple and areola without tumor in the breast;
- II. breast tumor without nipple injury;
- III. areola and nipple lesion associated with breast tumor.³

When the lesion is limited only to the nipple the disease is classified in the Tis stage (carcinoma in situ), when the breast tumor is also present then the classification takes into account the characteristics of the tumor. Sometimes a bloody nipple leak may occur. Axillary lymph node invasion is relatively common.

The breast schstring occurs more frequently in older age. It is characterized by a slow progressive evolution and determines the retraction of the perileional teguments, reaching the global retraction of the breast.

Breast cancer associated with pregnancy is a very rare form of cancer. Statistics show the existence of this cancer in very young women 23-25 years. Diagnosis is generally easy to make, 10-year survival is only 33%, and relapses and bilateralization are more common.

Bilateral breast cancer accounts for 7% of all breast cancers. It may be concomitant when bilaterality is found less than 1 year after the diagnosis of the first or successive cancer. If both cancers are in stage I, the prognosis of the disease does not worsen due to bilaterality. If one of the cancers is more advanced than stage I, the prognosis is worse than in unilateral cancer with the same stage.

5. Other rare primary cancers of the breast are:
 - a) phyllodes maligna tumor,
 - b) lymphomas,
 - c) sarcomas.

Malignant lymphomas of the breast may be Hodgkin's, non-Hodgkin's, and a particular form Burkitt's lymphoma, which occurs more frequently in pregnant or lactating women. It is usually bilateral and has a very rapid evolution. In contrast, primitive hodgkinian and non-hodgkin's lymphomas are one-sided and affect older age groups. The evolution is determined in relation to the known prognostic factors for lymphomas.

Phyllodes cystosarcoma is the sarcomatization of a Phyllodes tumor due to delayed treatment, when it was benign, or because of relapses that result from incomplete surgical treatment. Benefits from modified radical mastectomy, and axillary dissection must be performed because axillary

metastases are an important prognostic factor⁸. This form of sarcoma can cause axillary lymph node invasion.

The malignant melanoma can be located either at the level of the breast skin or at the level of the areolomamellar complex. Surgery for diagnostic and therapeutic purposes should be tailored to the size and depth of the melanoma, excision including the tegument, subcutaneous tissue, gland, including the pectoral fascia. Axillary lymphadenectomy is performed according to Clark's⁹ level of invasion. The role of chemotherapy, radiotherapy and biological therapy is the same as for other skin locations of melanoma.

The treatment of breast neoplasm is a complex process that is performed following the decision of the oncology committee, depending on the histological type, with the patient's involvement, a customized therapeutic plan is developed, conservative surgery / radical surgery with or without breast reconstruction, neoadjuvant or adjuvant chemotherapy, hormone therapy, molecular therapy, depending on the histological form and the patient's history. The psychological impact is high at each stage from diagnosis to healing or the death of the patient, which requires the creation of a support team for the patient.

Conclusions

A diagnosis like breast cancer is like a harsh sentence for the person receiving it. The decision-making process for a woman opting for a radical procedure is complex and includes both the physical and the psychoemotional and cognitive components.

The histological forms are varied, the follow-up and the therapeutic approach takes into account these aspects, the multidisciplinary approach allows the optimal time to perform the therapeutic interventions, the adaptation to the particularities of the case, which will allow to increase the survival and improve the quality of life.

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⁹ Wild L. ,Makopoulos C. ,Leidenius M., Senkus-Konefka E., Breast Cancer Management for Surgeons, A European Multidisciplinary Textbook, Springer International Publishing AG, 2018

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