BENIGN BREAST DISEASE AND THE RISK OF BREAST CANCER IN THE NEXT 15 YEARS

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BENIGN BREAST DISEASE AND THE RISK OF BREAST CANCER IN THE NEXT 15 YEARS (Abstract): Aim: Fibrocystic mastosis (FCM) is defined by the totality of dystrophic changes of the mammary tissue, the grouping in the form of fibrosis of epithelial, cystic, metaplastic and hyperplastic alterations. A very good estimation of the cancer risk is related specifically to the microscopic aspect. Other factors, the family history as well as the presence of an inherited gene determining the increase in the risk of breast cancer are also considered. But, if a woman known with fibrocystic mastosis has not undergone any biopsy, then it is impossible to calculate the specific individual risk of developing cancer. Material and methods: The data collected as a study material and considered refer to: the total number of cases investigated and diagnosed with fibrocystic mastosis, the annual distribution of this disease cases, the distribution of the cases according to age groups, admission reasons, clinical examination, personal pathologic history clinically significant for the basic disease (the main diagnosis), the family medical history significant for the basic disease, the anatomo-pathological diagnosis. Results: Between 2004 and 2006, at “Cuza Vodă” Obstetrics and Gynecology Hospital of Iași, a maximum number of cases is noticed in 2006, when there were 147 cases, and the lowest number of cases was in 2005. There was high frequency of the anatomo-pathological examinations that highlighted the presence of fibrocystic lesions (both proliferative and non-proliferative), and the second most often diagnosis is fibroadenoma. Though fibrocystic mastosis is not clearly defined, it is still admitted that in order to support this diagnosis it is first compulsory to exclude malignant tumours. Conclusions: Only in 5% of the women with fibrocystic mastosis cellular changes can be revealed in the form of atypical hyperplasia, which are a risk factor for cancer. The lesion that delimits cancer from non-cancer is ductal carcinoma in situ. An incidence of over 20% is present in the countries that use mammographic screening programmes, mammographic surveillance programmes and programmes for the guided localization of nonpalpable lesions of the mammary gland. Keywords: FIBROCYSTIC MASTOSIS, BREAST CANCER, BREAST SCREENING, ATYPICAL HYPERPLASIA.

From the histopathological point of view, fibrocystic mastosis (FCM) is defined by the totality of the dystrophic changes of the mammary tissue, the grouping in the form of fibrosis of epithelial, cystic, metaplastic and hyperplastic alterations. The elementary lesions in fibrocystic mastosis are varied as regards both quality
and quantity, forming a characteristic polymorphism.

The classification of the disease is different, the French authors classifying it as mammary dystrophy: fibrocystic mastosis (FCM), and American authors classifying it as benign breast disease. Currently there is no consensus on the content of this notion. Welling and Alpers asserted that the fibrocystic disease of the breast can be like a dominant morbid process, in most histopathological images. Fibrocystic mastosis (FCM) is the most frequent benign mammary lesion according to Nielsen’s study, with over 61% incidence.

Both in the surgical specimens of breast biopsy, sectoring, partial or full mastectomies and in the necropsy specimens, FCM is most often accompanied by other benign mammary lesions, some of them with malignifying risk.

The causes of FCM are not fully known, but it is believed that they are associated to ovarian hormones, because the condition is reduced at menopause. It is clinically found that the maximum frequency of FCM is at puberty and in perimenopause, which correspond to the periods of progesterone insufficiency, and after menopause, FCM regresses, and the progesterone insufficiency causes relative endogenous hyperestrogenism (therefore the disorder of the normal estrogens/progesterone ratio). The histologic elements of the terminal ducto lobular unit in the FCM suffer from changes that create varied histopathologic pictures, each of them representing a different risk for breast cancer for the following 15 years.

Taking into account this essential criterion, Dupont and Page proposed a classification of different histopathological pictures, which was accepted and agreed by the College of American Pathologists, therefore benign lesions were classified into: non-proliferative lesions, proliferative lesions without atypias, atypical hyperplasia.

A very good estimation of the risk of cancer is related specifically to the microscopic aspect. Other factors, the family history and the presence of an inherited gene determining the increase in the breast cancer risk are also considered. But, if a woman known with fibrocystic mastosis has not undergone any biopsy, then it is impossible to calculate her specific individual risk of developing cancer. The patients with FCM – either operated on or not – must be monitored rhythmically and on a long term, especially if atypical hyperplasia was found. Even if FCM lesions regress with age, we must not forget that the breast cancer risk increases with age. Both the diagnosis and the actual treatment of benign breast diseases remain a challenge, and the indication for surgery is not clearly defined.

The anatomopathological examination is useful for the precise determination of the benign character of a lesion and for the exclusion of the cancer diagnosis. Lefranc mentions that a diagnosis of high accuracy – of up to 99% - is based on the tripod: clinical diagnosis – imaging diagnosis (mammography and ultrasonography) – morphologic examination (cytological or anatomopathologic). Using only one of the diagnosis means reduces the probability of its accuracy: clinical examination – 62%, mammography – 83%; and the association of the clinical examination and the mammography is 79% accurate, and the association of the clinical and cytological examinations is 87% accurate.

From the point of view of the risk of breast cancer for the following 15 years any of the 3 categories of histopathological
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lesions runs a different risk as regards the possibility of developing breast cancer for the following 15 years, therefore non-proliferative lesions do not increase the risk of breast cancer, even if there is family history of breast cancer, proliferative lesions without epithelial atypia run a risk of around 2 for breast cancer, taking into account the associated epidemiologic factors. Starting from the initial evaluations of Page and Dupont and continuing with elements supplied by subsequent studies and the protocol recommended by the College of American Pathologists, 5 risk categories of invasive cancer were emphasized based on the examined lesions (tab. I).

### TABLE I
**Categories of invasive cancer**

<table>
<thead>
<tr>
<th>RISK CATEGORY</th>
<th>LESION TYPES</th>
</tr>
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<tbody>
<tr>
<td>Absence of risk</td>
<td>• sclerosing adenosis</td>
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<tr>
<td></td>
<td>• apocrine metaplasia</td>
</tr>
<tr>
<td></td>
<td>• micro- and macro-cysts</td>
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<tr>
<td></td>
<td>• ductal actasia</td>
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<tr>
<td></td>
<td>• fibroadenoma</td>
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<tr>
<td></td>
<td>• mastitis</td>
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<tr>
<td></td>
<td>• mild hyperplasia</td>
</tr>
<tr>
<td>1.5-2 times risk</td>
<td>• moderate hyperplasia</td>
</tr>
<tr>
<td></td>
<td>• intraductal papilloma</td>
</tr>
<tr>
<td>5 times risk</td>
<td>• atypical ductal hyperplasia</td>
</tr>
<tr>
<td></td>
<td>• atypical lobular hyperplasia</td>
</tr>
<tr>
<td>8-10 times risk</td>
<td>• ductal carcinoma in situ</td>
</tr>
<tr>
<td></td>
<td>• lobular carcinoma in situ</td>
</tr>
<tr>
<td>Insufficient data or different opinions</td>
<td>• single papilloma of the lactiferous sinus</td>
</tr>
<tr>
<td></td>
<td>• radial scar</td>
</tr>
</tbody>
</table>

### MATERIAL AND METHOD

The collection, processing and interpretation of the information necessary for the clinical-statistical study led to knowledge on the particularities of the cases of fibrocystic mastosis admitted in the 2nd Obstetrics – Gynecology Clinic of “Cuza-Vodă” Hospital of Iași between 2004 and 2006; we used the data recorded in the observation charts and in the computerized system.

The retrospective study on three years (2004 – 2006) included female patients diagnosed with fibrocystic mastosis in the above mentioned clinic. Between 2004 and 2006, 359 cases of fibrocystic mastosis were diagnosed and investigated, based on clinical examination and specialized complementary explorations.

The clinical observation charts was used as a source of information.

The data collected as a study material and taken into consideration refer to: the total number of cases investigated and diagnosed with fibrocystic mastosis, the annual distribution of the disease cases, the distribution of the cases according to age groups, the reasons for admission, clinical examination, personal pathologic history clinically significant for the basic disease (the main diagnosis), family pathologic history significant for the basis disease, anatomopathological diagnosis.

Based on the processing and evaluation of the 359 cases of fibrocystic mastosis
recorded in the 2\textsuperscript{nd} Obstetrics and Gynecology Clinic of “Cuza-Vodă” Obstetrics and Gynecology Hospital of Iaşi between 2004 and 2006, from the point of view of the temporal variable, a maximum number of cases is noticed in 2006, when 147 cases (40.9\% of the total) were recorded, and the lowest number of cases were in 2005 (fig. 1).

Results

Most of the patients that came to our unit were from the urban environment (66.9\%), and the patients from the rural environment represented only 1/3 of the recorded cases (33.1\%). In socio-economically developed countries, both from Europe and the U.S.A. they represent 15-20\% of the cases of death because of cancer in women. The most admissions were of persons over 45 – 50 years of age, which was associated with the “enrichment” of the morbid status with age. In our study, we divided the patients into 12 five-year groups of age. The data processing revealed a maximum value of the frequency in the group of 45 – 49 years (17\% of the total number 359 studied cases). Relatively equal shares (over 14\%) are noticed for the age groups of 35-39 and 40-44 years. Minimum values are recorded in patients over 70 years old.

More than half of the studied cases (226 cases, namely 62.95\%) had as a main reason of the check-up the presence of a tumour in one of the breasts. Only in approximately 1/3 of the cases the main admission reason was mastodynia (112 cases, namely 31.19\%). 80 of these cases were represented by unilateral mastodynia (19.93\%), and only one case of bilateral mastodynia (0.57\%). Mastodynia was accompanied by other symptomatology in few cases, namely: association with the presence of a tumour in one of the breasts in 28 cases (7.8\%), association with galactorrhea in 3 cases (0.84\%).

From the point of view of the distribution of the studies cases according to the clinical diagnosis, as regards our study, the most frequent clinical diagnosis was breast nodule (203 cases, namely 56.54\%), followed by fibrocystic mastosis (75 cases, namely 20.89\%), and depending on the distribution of the studied cases depending on the significant personal pathologic hist-
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tory, 239 of the total number of patients did not state the existence of this history (namely 66.6%), and the remaining 120 mentioned different conditions of the breast or of the genital system. In our study, breast cancer is reported only in one case, which means 0.28%.

The most “quotes” as regards family pathological history refer to the maternal line (15 cases, namely 4.17% of the total). Among the 35 patients who could mention family pathological history, the family history reveals the existence of cancer to a relevantly important extent (26 cases, namely 76.47%). If we refer to the total number of patients, the values are obviously lower (7.24%). In conclusion, most cases are on maternal line (10, namely 2.79% of the total). The family pathological history on paternal line is one unit away (9 cases, namely 2.51% of the total).

The processing and analysis of the data obtained in the study done on the 359 cases recorded between 2004 and 2006 revealed a higher frequency of the anatomopathological examinations that showed fibrocystic lesions (both proliferative and non-proliferative) – 190 cases, namely 52.92% of the total number of cases, and the second most often diagnosis is fibroadenoma – 56 cases (15.60%). Though FCM is not clearly defined, in order to assert this diagnosis, malignant tumours must be excluded first. We must not omit that the fibro (sclero) cystic change is also present in the normal tissue, especially in perimenopausal women.

Haagensen (7) did a study on over 2,000 women and published results specifying the fact that the localization in the left breast was revealed in 36.7% of the cases, the one in the right breast in 27.9%, and the remaining 35.4% were localized bilaterally.

Niţescu (11) also mentions that lesions emerge more often in the left breast, but bilateral location is noticed in half of the cases. The results of our research reveals nevertheless a more frequent localization of lesions or symptoms in the right breast – 185 cases, namely 51.53%; localization in the left breast are found in 137 cases (37.16%), and bilateral in 36 patients (namely 10.03%), and there was an additional case of right axillary lipoma (0.28%). In our

DISCUSSION

Based on a study on 333 patients, McFarlane (9) shows that most benign lesions were given by fibrocystic diseases (41%) and fibroadenomas (33%). The conclusion of the study reveals the fact that benign breast diseases develop, in the studied population, especially in young women, under 30. Of the total biopsies performed in women with a suggestive clinical picture, 80% reveal benign lesions. Anlauf (1) investigated the association between biopsies that revealed benign lesions in the breast and the subsequent development of cancerous lesions, and the study results highlighted a rate of the risk of developing breast cancer in 480 women of the 14,602 participants in the study.

In our study the high frequency of the anatomopathologic examinations that revealed the presence of fibrocystic lesions (both proliferative and non-proliferative) – 190 cases, namely 52.92% of the total cases, the second diagnosis is fibroadenoma – 56 cases (15.60%). Though FCM is not clearly defined, in order to assert this diagnosis, malignant tumours must be excluded first. We have to mention that the fibro (sclera) cystic change is also present in the normal tissue, especially in perimenopausal women.

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study, breast cancer is reported only in one case, namely 0.28%.

Breast cancer is the most frequent malignant localization in women worldwide. In socio-economically developed countries, both in Europe and the U.S.A., it is 15-20% of the cases of death by cancer in women. In fact, the high standard of life characteristic to the socio-economically developed countries is a risk factor for this disease. In 1993, the incidence of breast cancer was 33.4 cases out of 100,000 women and increased to 40.94 cases out of 100,000 in 1995. Currently, its incidence is estimated to 85 new cases in 100,000 women a year, but the frequency is growing. It emerges before the age of 30 (unlike fibrocystic mastosis, which is quoted as an exception before this age) and predominates between 30 and 50 years of age (4, 5, 7).

CONCLUSIONS

In our study we established that the individual risk for each woman of developing a neoplasia in the breast is higher if a patient has a family history and inherited gene specific for this disease. These cases with high risk of breast cancer need increased clinical and mammographic surveillance. A higher frequency of breast cancer was determined in patients with atypical hyperplasia.

REFERENCES