Past obstetric history and risk of malignant breast neoplasms

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Summary

Many studies indicate hormonal disorders as a crucial reason for breast pathology. They are also probably responsible for the development of benign neoplasms and play a role in the origin and development of breast carcinoma. Although the mammary gland is under the influence of many steroid and peptide hormones such as thyroid hormones, prolactin, growth hormone, glucocorticosteroids, it is estrogen that plays an important role in the development of breast cancer. The purpose of the study was to analyze the obstetrical past of patients and the potential influence on the risk of developing malignant breast neoplasms. The participants in the study were healthy women with no changes in mammary glands (control group) and women with diagnosed malignant or benign breast neoplasms (study group). The total number of participants was 555 females aged 35-70 years. The study was carried out in the Greater Poland and Lubuskie province between 2005 and 2006. Hormonal disorders in childhood and puberty symptoms of early menarche play a crucial role in increasing the risk of malignant breast neoplasms. In women who experienced one or more miscarriages the risk of malignant breast neoplasms is significantly increased. On the basis of our study we calculated the odds ratio (OR) of malignant breast neoplasms among women who during lactation experienced problems needing medical intervention (OR = 2.25; 95% CI, 1.20-4.19) in comparison to women who experienced no problems).

Key words: Breast cancer; Risk factors.

Introduction

Malignant breast neoplasms are the most common neoplasms in women in the majority of developed countries [1, 2].

There is much evidence showing that breast cancer has been concomitant with humans for a long time. It was first mentioned in Egyptian papyrus 5000 years ago [3].

Many studies indicate hormonal disorders as a crucial reason for breast pathology. They are also probably responsible for the development of benign neoplasms and play a role in the origin and development of breast carcinoma [4-7].

Although the mammary gland is under the influence of many steroid and peptide hormones such as thyroid hormones, prolactin, growth hormone, glucocorticosteroids, it is estrogen that plays an important role in the development of breast cancer [6, 7].

The influence of ovarian hormonal effects on the origin of breast cancer is proven by the fact that it occurs 100 times more often in women than in men and also that it appears after adolescence [7].

The purpose of this study was to analyze the obstetrical past of patients and the potential influence on the risk of developing malignant breast tumor.

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Material and Methods

The participants of the study were healthy women with no changes in mammary glands and women with diagnosed malignant or benign breast neoplasms. The total number of participants was 555 females aged 35-70 years. The study was carried out in the Greater Poland and Lubuskie province between 2005 and 2006.

The inclusion criteria for the first group (control) (n = 292) was an examination performed by a specialist that revealed no pathological changes, and correct mammography and/or ultrasound examination.

The second and third groups consisted of patients divided according to pathological examination of material gained by breast biopsy or operation: benign changes (n = 184) and malignant lesions (n = 79), respectively.

Every patient voluntarily filled out an anonymous questionnaire consisting of questions about menstrual and obstetric history, breastfeeding, and puerperium.

In the analyzed groups parameters like age, age of menarche, and age at first pregnancy were characterized by arithmetic means, standard deviation (SD) and minimal and maximal values. Agreement with the normal distribution was checked by the Shapiro-Wilk test.

Parameters presented in a nominal scale (miscarriages, medical treatments in puerperium) were described by numbers and percentage. To check relations between those parameters and inclusion in a group, the chi-square test, Fisher's exact test or the Fisher-Freeman-Halton test were used.

For the chosen parameters we calculated odds ratio (OR) of malignant breast neoplasms, with 95% confidence interval (CI):

$$OR = \frac{a^* d}{c^* b}$$

Statistical analyses were verified on the significance level of $p \leq 0.05$.

Statistical analysis was performed using StatSoft, Inc. (2005), STATISTICA (data analysis software system), version 7.1 and Cytel Studio version 7.0.0 (2005).

Permission for the study was obtained from the Bioethical Commission of K. Marcinkowski University in Poznan.

Results

Patient ages in the studied groups are shown in Table 1. Mean age differed only between patients suffering from malignant neoplasms (group CA: 53.4 years) and benign breast tumors (group BZ: 52.4 years) compared with group D (control), where it was the lowest – 47.5 years. Other differences were not statistically significant.

Earliest menarche occurred in the group of women with malignant breast neoplasms; the mean age of menarche was 13.1 years. The latest menarche occurred in group D consisting of women with no changes in breasts (control) – mean age 13.5 years. Statistically significant differences were noted only between groups CA and BZ, p = 0.02 (Table 2).

Patients experiencing menarche after 14 years of age had an OR = 0.12; 95% CI, 0.02-0.49 in relation to women whose menarche occurred before 11 years of age.

Other analyzed parameters included number of pregnancies and deliveries and the age at first conception. In the CA group the mean number of pregnancies was 2.3, mean number of deliveries 2.0 and age at the first conception 24 years. In the BZ group those numbers were 1.9, 1.8 and 23 years, respectively. Results in group D were different: the mean number of pregnancies was lower compared to the previous groups – 1.7 and the mean number of deliveries was 1.6; mean age at conception was the same as in the BZ group (Tables 3, 4, 5).

Table 1. — *Mean age of women in the studied groups*.

Mean age in a group (years)	Mean ± SD	Range (min-max)	ANOVA p < 0.05
CA - group with malignant neoplasms	53.4 ± 9.0	32-73	CA vs BZ
D - group with benign neoplasms	52.4 ± 8.06	5-73	D vs BZ
BZ - group with no changes	47.5 ± 7.96	35-71	

Table 2. — *Mean age of menarche in the groups*.

Mean age of menarche in groups (years)	Mean ± SD	Range (min-max)	ANOVA p < 0.05
CA - group with malignant neoplasms	13.1 ± 1.5	10-16	CA vs BZ
D - group with benign neoplasms	13.3 ± 1.4	9-18	
BZ - group with no changes	13.5 ± 1.2	10-18	

Table 3. — *Mean number of pregnancies in the groups*.

Mean age of pregnancies	Mean ± SD	Range (min-max)	ANOVA p < 0.05
CA - group with malignant neoplasms	2.3 ± 1.4	0-1	Not significant
D - group with benign neoplasms	1.7 ± 1.1	0-6	Not significant
BZ - group with no changes	1.9 ± 1.1	0-7	Not significant

Table 4. — *Mean number of deliveries in the groups*.

Mean number of deliveries	Mean ± SD	Range (min-max)	ANOVA p < 0.05
CA - group with malignant neoplasms	2.0 ± 1.2	0-6	
D - group with benign neoplasms	1.6 ± 0.9	0-4	D vs BZ
BZ - group with no changes	1.8 ± 1.1	0-7	

Differences between groups D and BZ are statistically significant (p = 0.01).

Table 5. — *Mean age of first contraception in the groups*.

Mean age of the first contraception (years)	Mean ± SD	Range (min-max)	ANOVA p < 0.05
CA - group with malignant neoplasms	24.1 ± 4	18-39	CA vs BZ
D - group with benign neoplasms	23.2 ± 3.8	18-38	
BZ - group with no changes	23 ± 3.5	17-38	

Only *differences* between groups CA and BZ are statistically significant, p = 0.02.

Women who delivered more than five children had an OR of 1.64; 95% CI, 0.61-4.41 for malignant breast neoplasms in relation to women who delivered one or two children.

Among women who had experienced pregnancy the number of miscarriages were analyzed. In the CA group miscarriages occurred in 21.52%, in group D 17.93% and in group BZ 10.9% (Figure 1). Statistically significant differences were observed between groups CA and BZ (p = 0.02) and between groups D and BZ (p = 0.04).

Patients who experienced at least one miscarriage had an OR of 2.22; 95% CI, 1.16-4.26 in comparison to women who had no history of miscarriages.

In women who delivered and breastfed the total duration of lactation was analyzed. Mean duration of breastfeeding in group CA was 8.3 months, group D 6.3 months and in group BZ 6.8 months. Differences among groups were not statistically significant.

Women who breastfeed more than six months had an OR of 1.65; 95% CI, 0.78-3.48 of malignant breast neoplasms in comparison to women who had not breastfeed.

Participants who breastfed were also asked about problems with their breasts during puerperium. In the CA group 24.32% of women needed medical treatment; in the D and BZ groups – 9.24% and 12.33%, respectively. Differences between the CA and BZ groups were statistically significant (p = 0.03).

If breastfeeding mothers experienced breast problems needing medical intervention in puerperium the OR was 2.25; 95% CI, 1.20-4.19 for malignant breast neoplasms in comparison to women who did not have any problems during breastfeeding.

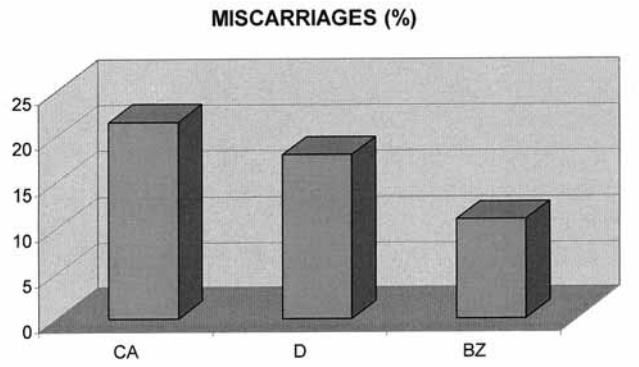

Figure 1. — Miscarriages in each group.

Discussion

Time of breast exposure to ovarian hormones is regarded as one of the most important and perhaps the most crucial among all known risk factors of breast neoplasms. Prolonged time of breast exposure to estrogens can be natural and results from early menarche and late menopause or can be caused by using contraceptive drugs or hormonal replacement therapy in the postmenopausal period.

The risk is twice as high in women whose hormonal activity lasted more than 40 years in comparison to women whose time of menstruation was shorter than 30 years. In women whose menarche occurred at the age of about 12 and cycles became ovulative within a year the risk of carcinoma is 3.7 times higher than in those who experienced menarche after 13 years of age and menstrual cycles were irregular in the next five years. The risk of breast cancer increases together with increasing number of ovulatory cycles in a lifetime, which is connected with the amount of estrogens which induce high mitotic activity in breast cells [6].

According to a 12-year study conducted in Holland the risk of breast cancer in women with long irregular menstrual cycles was significantly lower. Each year of delayed menopause resulted in an increased risk of breast cancer of 3% [8].

Our study shows that OR of breast neoplasms significantly decreases for patients who had menarche after 14 years of age (OR = 0.12; 95% CI, 0.02-0.49) in comparison to women who had menarche at the age of 11.

According to Budner and Przybylski [9] relative risk for the age of menarche is RR = 1.2-1.5 for women experiencing menarche before age 12 in comparison to women who experienced it after the 12th year of age. The period between menarche and first delivery also plays a crucial role. The shorter this time is, the more the risk of breast neoplasms decreases. It is connected with the number of menstrual cycles within that period and shorter or longer exposition to carcinogens [10-12].

Among our patients we observed the highest mean age of menarche in group BZ (13.5 years), and also women in this group delivered at the earliest age compared to the other groups (mean age 23 years) and differed statistically if compared to women in the group with malignant breast neoplasms. The risk is two times higher in comparison to women who delivered before 20 years of age [7, 9, 13-17]. The youngest women who delivered in group BZ was 17 years old. Budner and Przybylski [9] consider that the risk for women delivering after they are 30 years old is 1.3-2.2 in relation to those delivering before they are 20.

Some authors are of the opinion that apart from the age at delivery it is also the number of deliveries that matters [2, 3, 7, 10, 12, 18, 19]. The risk for multiparous females and women who delivered after 35 years of age is at the same level as for nulliparous females [3, 7, 19]. According to the study, OR for women who delivered five or more children was increased (OR = 1.64) in comparison to those who delivered only once or twice. However in a study conducted by Ostrowska *et al*. [20] the number of deliveries was not statistically significant.

According to Godlewski [11], Becher *et al*. [21], Tavani *et al*. [12] the first delivery at an early age and higher number of deliveries are protective factors against breast neoplasms. They also consider long breastfeeding to be protective.

Kamarudin *et al*. [22] revealed that the risk of morbidity was decreased by 61% for women who breastfed at least 13 months in comparison to those who did not experience breastfeeding, OR = 0.39; 95% CI, 0.17-0.87. They also observed that the OR of breastfeeding women who did not use oral contraceptives was decreased by 56% (OR = 0.44; 95% CI, 0.44-0.87) in comparison to breastfeeding women using oral contraception.

On the other hand according to Lee *et al*. [23], who studied a group of Korean women, the decreased risk occurs in non breastfeeding women (OR = 0.7; 95% CI, 0.5-1.1) in comparison to women who breastfed 14-24 months. What they also observed was that the risk was decreased (OR = 0.6; 95% CI, 0.3-1.0) for women who breastfed more than 24 months in comparison to those who breastfed for a shorter period.

Tessaro *et al*. [24] did not observe any protective effect for breastfeeding women (OR = 0.9; 95% CI, 0.8-1.2) in comparison to non breastfeeding women.

In our study we did not observe any protective influence of the length of lactation on the risk of morbidity. The mean length of breastfeeding in the CA group was the longest and lasted 8.3 months and in the D and BZ groups – 6.3 and 6.8, respectively. The OR was significantly increased for women who breastfed longer then six months in relation to non breastfeeding women (OR = 1.65; 95% CI, 0.78-3.48).

Jernstromi *et al*. [25] revealed that the length of breastfeeding was connected with risk reduction and that for each month OR was 0.98; 95% CI, 0.97-0.99. They also found that breastfeeding is protective and decreases risk among patients – carriers of mutated gene BRCA1.

On the basis of our study we calculated the odds ratio of malignant breast neoplasms among women who during lactation experienced problems needing medical intervention (OR = 2.25; 95% CI, 1.20-4.19) in comparison to women who had no problems).

Conclusions

1. Hormonal disorders in childhood and puberty with early menarche play a crucial role in increasing the risk of malignant breast neplasms.

2. In women who experienced one or more miscarriages the risk of malignant breast neoplasms is significantly increased.

3. In multiparous females who delivered more than five children and additionally experienced problems with breastfeeding the risk of malignant breast neoplasms is increased.

4. Factors like number of miscarriages and deliveries, length of breastfeeding and medical interventions in puerperium should be taken into account when qualifying women to a group of increased risk of malignant breast neoplasms.

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