

Brief Report

Breast fibroadenomas are less frequent in women with uterine fibroids

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Abstract.

BACKGROUND: The etiology and incidence of Fibroadenoma (FA) as the most frequent benign breast mass and uterine fibroma (UF) as the most benign gynecological disorders are unknown.

OBJECTIVE: Considering the dependency of FA and UF to sex hormones, our objective was to investigate the association of these two neoplasms.

METHODS: Among women attending the hospital Gynecology Clinic, those with typical uterine fibroids in their pelvic ultrasound constituted cases and those with no pathology the controls. All participants underwent breast ultrasound for FA. Criteria for diagnosis of FA were a typical image for lumps <2 cm in women aged <40 and <1 cm in ages ≥ 40, and a histologic diagnosis for all other participants or larger lumps.

RESULTS: The mean age of cases and controls was 42.4 and 41.7 years, respectively. FA were detected in 140 (23%) of all participants; 19.7% of the cases, and 26.2% of the controls ($p = 0.07$). FA and UF had a borderline reverse association (OR = 0.69, 95% CI = 0.46–1.02, $p = 0.07$).

CONCLUSION: The incidence of FA is lower in patients with UF. Further studies are needed to find the selective effects of estrogen and progesterone on hormonal receptors of these two tumors.

Keywords: Breast, case-control study, fibroadenoma, sex hormones, uterine fibroma

1. Introduction

Fibroadenoma (FA) is the most frequent benign breast mass and uterine fibroma (UF) is the most benign gynecological disorders [1]. The actual incidence and etiology of both disorders are unknown. As members of a team whose main concern is women's health, and practicing in women's hospital, we had noticed that many women harbored both UF and breast FA. We wondered whether this was a true association, or a coincidence related to the high frequency of both disorders. The sex hormone dependency of FA and UF made the association more probable. The incidence of

FA is higher in women whose inherent and reproductive characteristics are in favor of a higher endogenous steroid hormone milieu [2]. Also, UF are associated with sex hormones, although the exact relationship still needs to be investigated [3]. Few studies had previously approached the subject, including Spinos et al. [1] who found a direct association and Kénéme et al. who found a common mutation between these two lesions [4].

The detection of such a link could help in clarification of the pathophysiology of both diseases, and be a basis for the relation of other uterine and breast disorders, including malignancies. Also, if a strong association existed between FA and UF, it could propose a guideline toward screening women who were affected by one of these tumors for the other disorder. Therefore, we carried out the present study to find out if FA was more common in women with UF.

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2. Materials and methods

Among women who attended the Gynecology Clinic of Arash Women's Hospital for routine gynecology checkup and who underwent pelvic ultrasound exam, we selected those whose imaging had revealed one or more uterine fibroids and no other internal genital pathology as the case group. The control group was also chosen out of the same population, among those with no pathology in the pelvic exam and ultrasound. All participants filled out forms about demographic and reproductive data, and underwent breast ultrasound and breast exam for detection of FAs. Criteria for diagnosis of FA consisted of lumps with a typical picture and the largest diameter under 2 cm in women less than 40 years or under 1 cm for those above 40, or a histologic diagnosis of FA. All breast examinations were performed by an Oncologic Breast Surgeon, and ultrasounds were performed by radiologists dedicated to imaging of women.

SPSS software (version 20, SPSS, Inc, IL, USA) was used for all statistical analyses. Results were presented as mean \pm standard deviation (SD) for continuous variables and frequency for categorical variables. Logistic analysis was performed by considering fibroadenoma as dependent variable, and age and age of menarche, parity, menopausal status, and uterine fibroma as covariates in the model. Variables were entered to the model on the basis of evidence of an association from the literature.

3. Results

Each group consisted of 305 participants. Characteristics of the case and control groups are demonstrated in Table 1. The mean age of participant was 42.06 \pm 8.25 (range: 18–73 year). The two groups were not significantly different regarding age, age at menarche, parity and OCP use. However, the number of postmenopausal women was significantly higher among the controls. Fibroadenomas were detected in 140 (23%) of all participants; 19.7% of the cases, and 26.2% of the controls ($p = 0.07$). There were no significant differences in the history of infertility and use of assisted reproductive technology (ART), abortion, and hormone replacement therapy (HRT) between the two groups (data not shown in table). Considering menopausal status, in menopause women 19.2% and 21.4% ($p = 0.82$) FA and in premenopausal women 19.7% and 27.5% ($p = 0.04$) FA were detected in the case and control groups, respectively.

Logistic regression analysis showed that age (OR = 0.97, 95% CI = 0.94–0.99, $p = 0.008$) and fibroma (OR = 0.69, 95% CI = 0.46–1.02, $p = 0.07$) had a reverse association with FA; although the association between FA and UF was on borderline statistical significance.

4. Discussion

In the present study, we found a reverse association with borderline statistical significance (p -value = 0.07) between FA and UF in our population. Based on our knowledge, only one other epidemiologic study has evaluated the incidence of FA in women with and without UF up to the present time. In contrast to our study, they reported a higher frequency of FA (65%) in the patients with UF compared with the control group (35%) [1]. Contrarily in our study, when we considered menopausal status as an effective factor, the difference between the two groups was statistically significant in premenopausal women, and the frequency of FA was higher in the control group. This result may suggest a possible pathway other than hormonal factors, or may be in favor of a reverse effect of different hormones on FA and UF. To draw a best conclusion, hormonal levels measurement is helpful as well as considering other related factors that increase the risk of FA.

FA, as the most frequent benign breast mass, occurs in 25% of women [5]; this is consistent with the present study results, which showed a 23% incidence for FA in all participants; but the true incidence is not known because many FAs are small, non-palpable and asymptomatic. When palpable, it has a characteristic presentation consisting of a round or oval mass that is extremely mobile [6]. The ultrasound image also is typical, and is seen as a horizontal-lying, hypoechoic regular mass with circumscribed borders [7]. The etiology of FA has not been ascertained, but a role for sex steroids is highly probable because of the effects of these hormones on the size and appearance of FA [2,6,8]. The diagnosis of FA is based on histologic results of needle biopsy or excision, but small lumps with a typical presentation can be diagnosed as FA with a high accuracy in young women based on exam, and especially on ultrasound [7,9]. Actually and in clinical practice many breast lumps that have a typical picture of FA are diagnosed as such without biopsy.

The actual incidence of UF is unknown. It is around 4% in women in their third decade of life, and 33% between the ages of 40 to 60; based on the population under study and the diagnostic modality, figures up to 77% have been reported for it [10]. Although the

Table 1
Characteristics of participants in the two groups

Variable	Case group (n = 305)	Control group (n = 305)	P-value
Age	42.42 ± 7.35	41.70 ± 9.05	0.28
Age of menarche	13.12 ± 1.56	13.30 ± 1.53	0.19
Parity	1.46 ± 1.33	1.44 ± 1.23	0.83
Menopause	26 (8.5%)	56 (18.5%)	<0.001
OCP use	149 (49%)	144 (47.4%)	0.69
Fibroadenoma	60 (19.7%)	80 (26.2%)	0.07

Table 2
Results of some studies about the relation of female sex hormones and their receptors with fibroadenoma

First author	Publication year	Relevant results
Rao [10]	1981	Expression of PR in FA, but not ER
Kuttann [11]	1981	Expression of both ER and PR in FA
Balakrishnan [12]	1987	High affinity for estrogen binding in FA
Pasqualini [13]	1997	Estradiol, estrone, and their sulfates levels much higher in FA than normal breast
Cericatto [14]	2005	Higher expression of ER- α in FA than normal breast
Estevao [15]	2007	Decreased FA size with progestin-OCP, but inhibited by added estriol
Branchini [3]	2009	Higher levels of PR-A and PR-B in FA, but ER similar in FA and normal breast
Bidgoli [7]	2011	Increased incidence of FA with increased environmental estrogen exposure
Khanna [16]	2012	Higher serum estradiol and ER expression in FA than normal breast
Grouthier [17]	2020	Exogenous progestins decrease dimensions of FA

ER = estrogen receptor, FA = fibroadenoma, PR = progesterone receptors.

etiology is not clear, the growth of UF is increased by estrogen, and inhibited by progesterone. Interestingly, the risk of having a UF increases after the age of 40, but decreases with menopause [10].

The mutual dependency of FA and UF to sex hormones carries the notion of a common etiologic basis, and the consequent expectation of a higher frequency of FA in women with UF. However, results were just the opposite in our study. This might be due to diverse effects of estrogen and progesterone on these tumors due to different expressions of various hormone receptors. This subject has not been widely studied, but some relevant researches [5,8,11–18] are demonstrated in Table 2. Although our study participants were around age 40 and this entity share some similar characteristics, however, fibroadenoma and uterine fibroma are multifactorial diseases susceptible to many external and internal stimuli. In the present study, we didn't consider all the possibly effective factors such as caffeine consumption, cigarette smoking, race, breastfeeding, and body mass index (BMI).

Well-matched case-control studies should investigate the association between fibroadenoma and uterine

fibroma, and evaluation of the selective effects of estrogen and progesterone on hormonal receptors of these two common female tumors is required.

Considering the known relation of UF and estrogen and the reverse association with progesterone, our study suggests a different hormonal background for FA, which warrants further study.

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Conflict of interest

None.

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