Familial breast cancer in Hong Kong Chinese

W Yeo, WH Kwan, WY Lee, TWT Leung, PML Teo, W King, PJ Johnson

Breast cancer is known to be associated with familial aggregation in the West. However, similar data has not been collected in a Chinese population. In a survey of 820 newly-diagnosed breast cancer patients treated in our centre from January 1989 through December 1994, 6.6% had a family history of breast cancer. This group presented at an earlier age and had a significantly higher proportion with the histological subtype of mucinous carcinoma. Although 31.5% of patients with a family history presented with early breast cancer, only 12.7% of those without familial breast cancer presented with early disease—perhaps reflecting a delay in consultation in women who are less aware of the disease. Our results suggest that the incidence of familial breast cancer in Chinese is much lower than it is in the West, and may partially explain the lower incidence of breast cancer found in our population compared with the West.

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Introduction

The epidemiology of breast cancer has shown a familial aggregation in patients with the disease. In the West, family relatives of a woman with breast cancer have a two- to three-fold increased risk of developing breast cancer.[1,2] It has also been reported that 10% to 30% of breast cancer patients have at least one female relative who has had breast cancer.[3-5] Familial breast cancer has also been associated with specific histological features.[3,6-9]

Although it is known that the incidence of breast cancer in Chinese living in the East is much lower than it is in the West, there have been no family studies of this disease in a Chinese population. This study was undertaken to explore the incidence of familial breast cancer in a Chinese population and the association with specific histological subtypes and pathological staging of the disease.

Prince of Wales Hospital, Sir YK Pao Cancer Centre, Shatin, Hong Kong:
Department of Clinical Oncology
W Yeo, MB, BS, MRCP
WH Kwan, MB, BS, FRCR
WY Lee
TWT Leung, MB, BS, MD
PML Teo, MB, BS, FRCR
PJ Johnson, MD, FRCP
Department of Surgery
W King, FRCS (Edin), FRCR (C)
Correspondence to: Dr W Yeo

Material and methods

During the study period from January 1989 through December 1994, the records of all patients with primary breast cancer seen in the Prince of Wales Hospital were reviewed. The data extracted included any family history of breast cancer and other variables such as the age of the patient at the time of diagnosis of breast cancer, menopausal status and information regarding the tumour, including specific histological subtypes, size of the primary tumour, number of axillary lymph nodes involved, and the stage of the disease based on the American Joint Committee on Cancer (AJCC) criteria.[10] Because of incomplete data collection in earlier years, other associated factors such as previous benign breast disease, menstrual and obstetric history have not been assessed.

The family history of breast cancer was recorded as first-degree (mother, sisters, daughters) and as second-degree (aunts, grandmothers, cousins, etc.). Information regarding other non-breast malignancies in the family of patients was not recorded. Patients with a family history of breast cancer were considered as one group, and those with no known family history as another. The Chi-square (χ^2) test was used to compare the menopausal status, the stage of the disease and the histological subtypes found in the two groups of patients. Stratifications of AJCC staging were made in both groups as early disease (defined in this study as AJCC stages 0 and I) and more advanced disease

(AJCC stages II, III and IV). The student's *t*-test was used to compare the mean age at the time of diagnosis between the groups.

Results

From January 1989 through December 1994, 889 patients with newly-diagnosed primary breast cancer were seen at our centre. Of these, 820 patients had their family history recorded. Fifty-four patients (6.6%) reported one or more relatives with known breast cancer. Of these, thirty-nine (72.4%) had a known first-degree relative with carcinoma of the breast: 14 patients (26.0%) had mothers who had breast cancer; 16 patients (29.5%) had one sister with a known history of breast cancer; 3 patients (5.5%) had one daughter each with the disease; 1 patient (1.9%) had an affected mother, two affected sisters and one affected maternal aunt; 1 patient (1.9%) had two affected sisters; 1 patient (1.9%) had an affected mother and sister; 1 patient (1.9 %) had an affected mother and maternal aunt; 1 patient (1.9%) had an affected mother and maternal grandmother; and 1 patient (1.9%) had an affected daughter and half-sister.

Fifteen patients (27.6%) had affected second-degree relatives: 6 patients (11.0%) had an affected grandmother; 3 patients (5.5%) had an affected maternal

Table 1. Breast cancer patient characteristics

	Patients with a family history of breast cancer No. (%)	Patients without family history of breast cancer No. (%)	P value (χ^2)
No. of patients	54	766	
Menopausal status:			
premenopausal	38 (68.5)	436 (56.9)	0.05
postmenopausal	16 (31.5)	330 (43.1)	
Age:			
mean (y)	45.7	49.7	0.02
range (y)	30-77	24-91	(*t*-test)
Stage of breast cancer:*			
stage 0	1	9	<< 0.01
stage I	16	88	
stage II	26	479	
stage III	4	117	
stage IV	2	42	
not known	5	31	
Histological features:			
IDC	1 (1.8)	9 (1.2)	0.50
IFDC	45 (83.3)	682 (89.0)	0.20
IFLC	2 (3.7)	33 (4.3)	1.00
medullary	1 (1.9)	9 (1.2)	0.50
mucinous	5 (9.3)	16 (2.1)	0.01
others†	0	17 (2.2)	0.62

IDC = Intraductal carcinoma
IFDC = Infiltrating ductal carcinoma
IFLC = Infiltrating lobular carcinoma
*Stratified according to stage, i.e. stages (0+I) versus stages (II+III+IV)
†Others includes 3 sarcomas of the breast, 2 signet ring carcinomas, 2 cribriform carcinomas, 1 anaplastic carcinoma, 1 intralobular carcinoma, 1 carcinoid tumour, 1 tubular carcinoma, 1 colloid carcinoma, 1 mixed infiltrating ductal carcinoma and medullary carcinoma, 1 mixed infiltrating ductal and lobular carcinoma, 1 mixed mucinous and infiltrating ductal carcinoma, 1 mixed infiltrating lobular carcinoma and ductal carcinoma-in-situ, 1 mixed papilloma and ductal carcinoma-in-situ.

aunt; 1 patient (1.9%) had an affected paternal aunt; 2 patients (3.7%) had two affected maternal aunts; and 3 patients (5.5%) had an affected half-sister.

Due to the small number of patients with a family history of breast cancer in our series (6.6%), individual subgroup analysis of each type of family relationship was not conducted. Patients with a family history were considered as one group, and compared with those with no known family history (Table 1). At the time of diagnosis, patients with a family history had a significantly lower mean age (45.7 vs 49.7 y, P = 0.016, *t*-test) and a significantly higher proportion of early stage disease (stages 0, I) when compared with patients without such a family history (31.5% vs 12.7%, P = 0.003, χ^2 test). In addition, the proportion of patients found to have the histological subtype of mucinous carcinoma was significantly higher in patients with a family history (9.3% vs 2.1%, P = 0.012, χ^2 test). Although the proportion of pre-menopausal patients was higher in the group with a family history (68.5% vs 56.9%), the difference was not significant (P = 0.053, χ^2 test).

Discussion

Studies in Western populations have reported the incidence of a family history of breast cancer among patients with this disease to be in the range of 10% to 30%.[3-5] There is no agreement about the tumour histopathology encountered in familial breast cancer. The observations most often cited are of an increased frequency of lobular carcinoma,[3,4,6,7] especially in patients with a history of maternal cancer. Anderson reports an increased association of invasive carcinomas in maternal breast cancers,[8] and an increased association of intraductal carcinoma and medullary carcinoma in the sister's pedigrees. Other reported findings include an increased incidence of tubular carcinoma in familial cancers.[9] Our findings differed in that mucinous carcinoma was the histological subtype found more often in patients with familial breast cancer.

It is known that the risk of developing breast cancer for a woman who has a positive family history is highest in pre-menopausal women who have a first-degree relative diagnosed with breast cancer at a pre-menopausal age.[11] Our finding that women with a family history tend to be diagnosed at an earlier age agrees with this. However, we did not find a significantly higher proportion of pre-menopausal women in the same group. The fact that fewer patients presented with early stage disease in the group without a family history suggests that in Hong Kong, women ignore early signs or symptoms of breast cancer and present later with their disease.

Our data showed a lower incidence of familial breast cancer in the Chinese population in Hong Kong compared with the West.[3-5] The reason for the difference in the frequencies is probably multifactorial. There may be under-reporting of breast cancer in relatives in our patients. Until recently, the occurrence of cancer was often not discussed in Chinese families, particularly in the older generation, who may also know little of the medical history of previous generations. Also, in Hong Kong, many relatives have emigrated and the precise details of disease among those living abroad is often not available. Nonetheless, the fact that the incidence of breast cancer in Hong Kong (35 per 100 000 female population),[12] is lower than the incidence in the West and may be explained by a lower incidence of familial breast cancer in Hong Kong.

Several genetic alterations have been reported to be involved in breast tumour development including the p53 gene,[13] the ataxia telengiectasia gene,[14] and the estrogen receptor genes.[15] However, mutations in these genes can only account for a minority of breast cancer families.[16] Recently, germ-line mutations on chromosome 17q, located on the breast cancer gene-1 (BRCA1), have been reported to be responsible for many inherited breast and ovarian cancers.[17,18] In the United States, it is estimated that as many as 1 in 200 women carry BRCA1 genetic mutations, making it one of the most common gene markers for which genetic testing could be feasible.[19]

Another breast cancer gene, BRCA2, has been identified on chromosome 13q. Unlike BRCA1, it does not confer a substantial risk of ovarian cancer, but may increase the risk of breast cancer in male carriers.[16] These two genes are two of the most promising genetic markers to date. Identification of the frequencies of these gene mutations will provide more information as to the true incidence of familial breast cancer. However, before such genetic markers can be proven to be of practical value, high risk subjects—particularly those who have a strong family history of breast cancer—should participate in breast cancer screening programmes. Genetic counselling and ethical issues have to be carefully considered before genetic testing is introduced.

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