



Unique Breast Cancer Features Within the Vietnamese Population

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Unique Breast Cancer Features Within the Vietnamese Population

Abstract

BACKGROUND: Breast cancer is known to be a heterogeneous disease across women, and even within individual tumors. However, relatively little is known about heterogeneity across cultures. There has been some evidence to suggest that Asian women are more likely to have HER2+ breast cancer than their Caucasian counterparts.

PURPOSE: The aim of this study was to further investigate the unique pattern of breast cancer incidence and subtype in the Vietnamese population.

METHODS: We retrospectively collected data on all Vietnamese women diagnosed with invasive breast cancer at the Lester & Sue Smith Breast Center in Houston, Texas over a four year period. We recorded the subtype of breast cancer, tumor grade, age at diagnosis, and menopausal status for each woman. We then compared these characteristics between our population of Vietnamese breast cancer patients, and an ethnically diverse group of American women from the 2010 SEER registry.

RESULTS: We discovered that 15 of 33 Vietnamese patients diagnosed in our breast center had HER2 over-expressing breast cancer, resulting in a 45% rate of HER2 positivity. Compared with the 2010 Surveillance, Epidemiology, and End Results (SEER) registry data that encompasses 28% of all US breast cancer patients diagnosed that year, regardless of race, the Smith Clinic Vietnamese cohort had a statistically significant higher rate of HER2+ breast cancer, with an odds ratio of 4.7 (45% vs. 15%, p

CONCLUSIONS: Vietnamese breast cancer patients, especially those older than 50 years old, tend to have higher rates of HER2+ breast cancer than the general population. This unique pattern of breast cancer merits further study, as it may reflect a genetic mutation or environmental exposure which is more common among Vietnamese women.

Keywords

HER2+ breast cancer; Vietnamese; epidemiology; genetics



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ABSTRACT

Background: Breast cancer is known to be a heterogeneous disease across women, and even within individual tumors. However, relatively little is known about heterogeneity across cultures. There has been some evidence to suggest that Asian women are more likely to have HER2+ breast cancer than their Caucasian counterparts.

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Conclusion: HER2-overexpressing breast cancer is over-represented in our small sample of Vietnamese patients, especially in those older than 50 years old. This corroborates some other study findings which suggest the same phenomenon in this population. This unique pattern of breast cancer merits further study, as it may reflect a genetic mutation or environmental exposure which is more common among Vietnamese women.

Keywords: Breast Cancer, Vietnamese, HER2, epidemiology

INTRODUCTION

Breast cancer is the most commonly diagnosed cancer and the leading cause of cancer death in women worldwide (Matsudea & Saika, 2012). However, the incidence of breast cancer varies significantly across the globe. For example, age-adjusted incidence is 124.5 per 100,000 females in the US (Anderson, et. al. 2005), but only 17.5 per 100,000 in Vietnam (Thang, et al. 2011). This well-known discrepancy is likely due to known and unknown genetic, lifestyle, and environmental factors. However, a less commonly described phenomenon is the differing biology seen in Asian women as compared to Caucasian women.

For example, there has been some evidence that Vietnamese and Vietnamese-American women with breast cancer have up to a 40% rate of HER2 overexpression (Thang, et al. 2011 and Telli, et al. 2011), compared to 15-23% in the general American population (Owens, et al. 2004 and Howlader, et al 2014). In Hanoi, a retrospective study of 242 breast cancer patients discovered that 41% of patients had HER2+ disease, with post-menopausal women having a higher rate of HER2 positivity. Furthermore, a strong age association was observed in this study, with 55% of post-menopausal women having HER2-amplified tumors, compared to only 36% of pre-menopausal women (Thang et al. 2011). This differs from several other studies of diverse races within the general population which have not shown a higher proclivity for post-menopausal women to have HER2+ breast cancer (Beeghly-Fadiel et al, 2008 and Wang, et al 2009 and Borreson, et al. 1990).

In fact, this phenomenon of an increased proportion of HER2+ breast cancer may not be unique to only Vietnamese women. One study has also looked at Asian women living in California via the California Cancer Registry, and they found that Vietnamese women were 1.3 times more likely to have HER2+ breast cancer than non-Hispanic white women. Similarly, Korean and Filipino women had higher incidence of HER2+ breast cancer, up to 36% and 31%, respectively (Telli, et al. 2011 and Chuang, et al. 2012). Other Californian studies have also found that Asians/Pacific Islanders, as a group, are 1.3 to 2 times as likely to have HER2+ breast cancer as compared to Caucasian women (Parise, et al. 2009 and Kwan, et al. 2009). A study of 1170 Chinese breast cancer patients revealed that up to 65% were HER2 positive by FISH analysis (Zeng, et al. 2008). Though it has only been sporadically and rather superficially studied up until this point, some Asian women may have differing breast cancer biology compared to women of other ethnicities. It is not clear at this point as to what may be driving this disparate biology. However, this is clearly a very fertile area for further research.

METHODS

In our breast oncology clinic, the Lester and Sue Smith Breast Center (LSSBC) in Houston, Texas, we conducted a database search within our breast oncology clinic to look for all Vietnamese women diagnosed with invasive breast cancer between September 2010 and September 2014. Through the electronic medical record, we individually examined each woman's chart and recorded data on the patient's age, menopausal status, stage of breast cancer, tumor grade, Estrogen Receptor (ER), Progesterone Receptor (PR), and HER2 status. Unfortunately, due to the nature of our database, we were not able to collect comparable data from the general population at the clinic during the same time period because we do not have complete racial and ethnic data on the majority of our patients. Due to previous grant funding, however, the Vietnamese patients have been accurately identified. HER2 status at our institution is determined according to ASCO/CAP guidelines (Wolff, et al. 2013). Immunohistochemistry (IHC) testing for HER2 was first conducted on each breast biopsy sample. Those samples which

had IHC staining of 0 or 1+ were deemed to be HER2 negative. Samples with IHC staining of 3+ were deemed to be HER2 positive. For those samples which exhibited intermediate IHC staining of 2+, they were automatically reflexed to Fluorescent In-Situ Hybridization (FISH) testing. A ratio of HER2:CEP17 greater than or equal to 2, or an average number of HER2 signals/nucleus greater than or equal to 6, were called HER2 positive. Estrogen receptor (ER) and progesterone receptor (PR) status were also determined through ASCO/CAP guideline recommendations for immunohistochemical testing of ER and PR (Hammond, et al. 2010).

In order to have a comparator population, we utilized publicly available SEER database information. Corresponding summary counts from SEER were taken from the published report (Howlander, et. al. 2014). Fisher's exact test was used to compare HER2 positive rates between our small Vietnamese cohort and counts of cases reported by SEER, overall and within subsets such as high grade or ER positive. P-values were adjusted for multiplicity using the Holm method. Odds ratios (maximum likelihood estimate) and associated 95% confidence intervals were used to summarize the association between HER2 status and population source. Cases with unknown HER2 status were excluded. Analyses were performed using R version 3.2.2 (R Core Team (2015). R: A language and environment for statistical computing. R Foundation for Statistical Computing, Vienna, Austria. URL <https://www.R-project.org/>).

RESULTS

A thorough search of our database records from September 2010 through September 2014 revealed a total of 44 Vietnamese patients seen at the Breast Center during this time period. Six of these women had DCIS. Two women had invasive cancer with unknown biomarkers because they were diagnosed and treated elsewhere. Three women were seen for risk assessment only with no personal history of breast cancer. This left 33 Vietnamese women diagnosed with invasive breast cancer during the time period in question (Table 1). Out of these 33 Vietnamese patients, 15 (45%) of had HER2+ breast cancer. Among the patients who were greater than 50 years old, 52% were HER2 positive. Nearly half of the HER2 group had grade 3 tumors. These data are similar to other studies that have looked at the Vietnamese breast cancer population.

Table 1: Characteristics of Vietnamese Breast Cancer Patients at LSSBC and Cases reported by SEER

	LSSBC		SEER [6]		Odds Ratio (95% CI)	Holm Adjusted P-value
	HER2 Positive n= 15 (%)	HER2 Negative n=18(%)	HER2 Positive n= 7568 (%)	HER2 Negative n=43,003 (%)		
Total HER2+ cancer	15 (45%)		7568 (15%)		4.7 (2.22-9.95)	<.001
Age at dx						
≤50	4 (27%)	8 (44%)	2,127 (28%)	8,518 (20%)	2.0 (0.44-7.48)	0.55
>50	11 (73%)	10 (56%)	5,441 (72%)	34,485 (80%)	7.0(2.69-18.3)	<.001
Menopausal status						
Pre	5 (33%)	8 (44%)	NR	NR	--	
Post	9 (60%)	10 (56%)	NR	NR	--	
Peri	1 (7%)	0	NR	NR		
Tumor grade						

3	7 (47%)	3 (17%)	3320 (44%)	9679 (23%)	6.8 (1.55-40.8)	0.016
1-2	3 (20%)	15 (83%)	3026 (40%)	27883 (65%)	1.8 (0.34-6.5)	0.55
unknown	5 (33%)	0	1222 (16%)	5441 (13%)	Inf (4.073-Inf)	0.001
ER/PR						
Positive	7 (47%)	16 (89%)	5240 (69%)	36810 (86%)	3.1 (1.07-7.9)	0.056
Negative	8 (53%)	2 (11%)	2328 (31%)	6193 (14%)	10.6 (2.12-102.9)	0.004

We then compared our data to data from the SEER database that were used to examine population-based information on molecular subtypes in breast cancer (Howlander, et al. 2014); these data were compiled from 17 population-based cancer registries that participate in the SEER program and included 50,571 women diagnosed in 2010 with known breast cancer biomarkers and represented approximately 28% of US breast cancer patients diagnosed in 2010. These women comprised various races, including 70.9% White, 10.5% Black, 7.6% Asian, and 9.9% Hispanic women. Only 15% of these women had HER2+ breast cancer, and within this group, 31% of cancers were hormone receptor negative (Howlander, et al. 2014). In contrast, our subset of Vietnamese patients, as well as the larger group from Hanoi (Thang, et al. 2011), exhibited a 50% rate of hormone negativity in the HER2+ group. Also similar to the Hanoi analysis, we found that 50% of our post-menopausal patients had HER2+ breast cancer, as compared to only 36% of pre-menopausal patients. This is contrary to other population studies which have shown a lower rate of HER2+ breast cancer associated with older age and post-menopausal status (Dickens, et al. 2014 and de Kruijf, et al. 2014).

When we compared the 2010 SEER data and the Smith Clinic Vietnamese cohort, we found that the Smith Clinic group had a statistically significant higher rate of HER2+ breast cancer, with an odds ratio of 4.7 (45% vs. 15%, $p < 0.001$). Among the women greater than 50 years old in both groups, the Vietnamese women had a higher rate of HER2+ breast cancer than the same age group in the SEER data group (odds ratio 7.0, $p < 0.001$).

DISCUSSION

In this report, we examined the rate of HER2+ breast cancer in Vietnamese-American women and compared this to the national average in the United States. We found that HER2+ breast cancer is over-represented in Vietnamese women, as compared to the general American population, especially in older post-menopausal Vietnamese women. This group has not been extensively studied, and the distribution of breast cancer sub-types in this population is poorly understood. Most studies that have been done in the US included relatively small numbers of Vietnamese women. The study conducted in Vietnam has the largest sample size, but it is the only study done in Vietnam which examines this question. In some Asian countries, including Vietnam, many centers do not perform HER2 testing as a standard for all breast cancer specimens. Some of the centers who do test for HER2 may perform IHC staining for HER2, but they do not use in-situ hybridization for the HER2 equivocal cases which have 2+ IHC staining (Bilous, 2013).

It is important to note that there are clear limitations to our current report. First and foremost, our clinical sample size is very small, being composed of only 33 Vietnamese breast cancer patients. We have undertaken a collaborative project with several clinical practices in California that see larger numbers of Vietnamese women. With this collaboration, we will significantly increase our sample size and, thus, our power to detect statistically significant

different patterns of breast cancer within this population. In the meantime, it is reassuring that our data mirror many larger Vietnamese groups represented in the literature.

Additionally, aside from simply comparing the proportion of HER2+ breast cancer cases between populations, we would like to understand more about the epidemiology of breast cancer in the Vietnamese population, as this may provide clues as to why we see a disparate biology in this group. For example, we would like to learn more about the women's gravity and parity data, age at first childbirth, breastfeeding history, menarche, menopausal status, family history, environmental exposures, where they grew up, and genetic information. This data was not available within our database. It is interesting that all the women except for one were born in Vietnam and came to the United States as adults. A clearer understanding of the aforementioned factors would help us to better understand what may be driving the preponderance of HER2+ breast cancer among Vietnamese women.

CONCLUSION

We have preliminary confirmation that HER2-positive breast cancer is over-represented in the Vietnamese population, particularly among those women who are greater than 50 years old. This suggests a profound racial difference in the biology of Vietnam women's breast cancer which could be rooted in genetic or environmental differences. This may have important implications for genetic testing within Asian populations, or it may suggest certain environmental exposures which pre-dispose to a higher risk of HER2-positive breast cancer. Additionally, the increased rate of HER2 positive breast cancer in the Vietnamese population has several implications in terms of diagnosis, prognosis, and treatment. For all patients, but especially for those Vietnamese patients who live in their native country, it is very important to have standardized, high quality testing for HER2. Within the financial and practical constraints of the Vietnamese system, the guidelines for HER2 testing and diagnosis should align as closely as possible with the published ASCO/CAP guidelines for HER2 testing in breast cancer (Wolff, et al. 2013) so that we can correctly identify all the women who have HER2-overexpressing breast cancer. For those women who are found to be HER2 positive, it is imperative that they have anti-HER2 agents available to them as part of their treatment course. Breast cancer which is HER2-amplified carries a much worse prognosis if not treated with anti-HER2 agents. The addition of trastuzumab to standard chemotherapy for HER2+ breast cancer decreases the breast cancer death rate by at least one third (Romond, et al. 2005). If the phenomenon of increased HER2 positivity in the Vietnamese population is better understood and disseminated, policy changes can feasibly be made in Vietnam to allow for high quality testing and availability of necessary anti-HER2 medications.

As we begin to understand more about the heterogeneity of breast cancer, study of under-represented groups are likely to reveal more information about unique subtypes of breast cancer within these groups. This could lead to valuable insights regarding the prevention, diagnosis, and treatment of breast cancer within certain populations, based on a clear understanding of the biology of their disease.

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