Case Report
Middle East Journal of Cancer; April 2023; 14(2): 332-337

Clinicopathological Characteristics of Patients with *BRCA* Mutation Breast Cancer in North Sumatera: Case Report

Dedy Hermansyah♦, MD, Gracia Pricilia, MD, Yolanda Simamora, MD, Denny Rifsal Siregar, MD

Department of Surgery, Faculty of Medicine, Universitas Sumatera Utara, Medan, Indonesia

Please cite this article as: Hermansyah D, Pricilia G, Simamora Y, Siregar DF. Clinicopathological characteristics of patients with *BRCA* mutation breast cancer in north sumatera: case report. Middle East J Cancer. 2023;14(2):332-7. doi: 10.30476/mejc.2022.92503.1659.

Abstract

The most common cancer in women is breast cancer (BC) with an incidence of 24.2%. BC in younger patients will in general be more forceful, prompting more awful results and a requirement for more forceful treatment which may bring about a higher probability of long-haul treatment-related harmfulness and novel psychosocial issues. Furthermore, family inclination to BC as BRCA1 and BRCA2 mutations is more prevalent in this age group. There were a total of five ladies who had tumor pathology testing with negative results. All intrusive BC examples were regularly assessed for estrogen receptor, progesterone receptor, and human epidermal growth factor receptor-2 (HER2)/neu status utilizing immunohistochemistry. Cases with HER2/neu staining of 1+, 2+ or 3+ on immunohistochemistry examination were additionally assessed by fluorescent in situ hybridization for the enhancement of the HER2/neu quality. In this examination, we distinguished clinicopathological attributes of patients with BC. We partitioned into two gatherings, *BRCA* positive change and *BRCA* negative transformation. Roughly 5%-10% instances of BC have a positive family ancestry and about 20%-40% BC development were in acquired variations. Our study revealed that 20% of cases included individuals who had a family history of BRCA mutation. Male relatives with BC, earlier age at onset, a greater prevalence of reciprocal breast disease, and a connection to various malignancies in the ovary, colon, prostate, pancreas, and endometrial are only a few of the clear clinical characteristics of BRCA1/2-related BC.

Keywords: Breast neoplasms, Genes, *BRCA1*, *BRCA2*, Immunohistochemistry

♦Corresponding Author:
Dedy Hermansyah, MD
Department of Surgery, Faculty of Medicine, Universitas Sumatera Utara, Medan, Indonesia
Tel: +6281396743472
Email: escape744@gmail.com

Introduction

The most common cancer in women is breast cancer or carcinoma (BC) with an incidence of 24.2%. This type of cancer is the second-highest prevalence of incidence in the world with an incidence rate of 11.6%. Approximately 2,089 million new cases of BC were found in 2018. On the Asian continent, for example,

Received: August 25, 2021; Accepted: July 12, 2022

BC is the main malignancy of women, which occurs in around 22.4% of the population with 911,014 new cases and 137,514 cases of which come from Southeast Asia.[1] As the phenomena of this case is discovered at an advanced stage, the prevalence of new BC cases is rising quickly in emerging nations. The most recent phenomenon is examined by data from GLOBOCAN 2020, which reveals that BC is the most prevalent cancer in women with an estimated 58,256 new cases or 30.9%, and that this disease will be the leading cause of death for women in Indonesia in 2020 with an incidence rate of 22,692 cases or 12.56%.[2]

BC in younger age populations is generally described as "more-severe", as a requirement of longer yet aggressive approach will be applied which may bring about a higher probability of long treatment-related harmfulness and novel psychosocial issues. Furthermore, familial inclination to BC, as *BRCA1* and *BRCA2* transformations, is more normal in this age. Regarding high penetrance rates among such transformation carriers, it is critical to distinguish patients who may require extra danger decrease intercessions like two-sided mastectomies and oophorectomies. BC were divided into those with high articulation of the estrogen receptor (ER) quality (luminal A and luminal B subtypes) and those that do not express ER in light of the sub-atomic profiling of malignancies. Inside the ER-negative gathering, tumors that overexpress the human epidermal growth factor receptor-2 (HER2)/neuoncogene are named the HER2/neu-positive subtype.[3-5] ER negative tumors that express qualities found in basal epithelial cells and can be stained with antibodies to keratin 5/6 were distinguished as basal-like tumors. A larger part of these basal-like tumors is accepted to comprise of BC subtype in which does not express ER, progesterone receptor (PR), or HER2/neu (i.e., triple-negative breast cancer or TNBC). A few examinations have exhibited that *BRCA1*-change carriers are bound to be determined to have TNBC than non-carriers.[6]

Moreover, carriers of *BRCA2* changes appear to have comparable pathologic attributes with non-carriers. Furthermore, previous analyses have often ignored critical clinical parameters that could influence the total tumor improvement. Hence, as the consequence, this study aims to overview the clinicopathological characteristics of patients with *BRCA*-positive and *BRCA*-negative BC in North Sumatera region in Indonesia.

Case Presentation

Five women in total were included from the Division of Oncology in Department of Surgery of Universitas Sumatera Utara General Hospital with confirmed TNBC by immunohistopathological evaluations in the surgical pathology in our center. The ethical consideration of this study was approved by the ethical committee of the same institutions with the registered ethics code of 130/UN5.2.1.1.1.19/PPM/2022. The collected data include family history of cancer, cancer history, age, BC grade and stage, immunohistochemistry (IHC) testing, nodal metastasis, and sites of metastasis including lung, liver, brain, and bone.

Tumor pathology for the examples with BC was looked into by the pathologists. Data with respect to the histologic sort of BC; tumor grade utilizing the adjusted Black's atomic reviewing framework; and ER, PR, and HER2/neu status of BC tests were acquired from the patients' institutional pathology reports. All intrusive BC examples were regularly assessed for ER, PR, and HER2/neu status utilizing IHC. Cases with HER2/neu staining of 1+, 2+ or 3+ on IHC examination were additionally assessed by fluorescent in situ hybridization for the enhancement of the HER2/neu quality. The clinicopathological attributes of patients with *BRCA*-positive and *BRCA*-negative BC appeared on the table 1.

Discussion

Similar to our own Indonesia, BC in developing countries is associated with unusual highlights that are often under-represented in Western-culture of attention. In the first place, middle age at determination is at any rate 10 years younger than that of the West, a reality that should be

contemplated when planning early-location programs and furthermore managing psychosocial outcomes and long treatment confusions in a younger age. Second, a huge level of patients presents with privately progressed or metastatic infection, even among the most youthful.[7]

We distinguished clinicopathological attributes of patients with BC. We divided into two groups: BRCA negative transformation and BRCA positive change. As we presumably all know, this illness has a strong genetic component but may also develop in an atypical way. BRCA was a significant characteristic that signified as a propensity or risk factor in this circumstance. Roughly 5%-10% instances of BC have a positive family history and about 20%-40% BC development was in acquired variations. Our examination shows that one case (20%) was in the patients that has family ancestry in *BRCA* transformation. This outcome is in accordance with an investigation of 207 families that foreseeing changes in the *BRCA* qualities utilizing family ancestry data and was expanded by including the ER and PR receptor status and pathologic evaluation of the tumor. Extrapathologic factors that may anticipate *BRCA1* change status incorporate Ki67 and epidermal development factor receptor. In young (age less than 54 years) ladies with BC development, significant degrees of Ki67 articulation anticipated an opportunity of having a *BRCA1* change as high as 75%. In light of these studies and mounting evidence that suggests *BRCA1* tumors exhibit unusual pathologic characteristics, doctors may want to consider combining pathology findings with family ancestry information, when determining if a patient is at increased risk for genetic BC. This might be especially valuable when family ancestry data brings about a moderate worry for innate malignancy. Notwithstanding, on the grounds that apparently *BRCA2*-related malignancies have pathology like that of non-*BRCA* carriers, it is right now indistinct whether pathologic outcomes might be utilized in foreseeing *BRCA2* change status. Extra examination ought to be led to decide how much accentuation ought to be set on tumor pathology and how this data can be remembered for effectively settled models.[8,9]

Table 1. Sample characteristics

Characteristics	*BRCA* + (%)	- (%)
Family history	1	4
History of cancer	-	5
Age		
<30	-	-
30-40	1 (20)	3 (60)
41-50	-	1 (20)
>50	-	-
Grade		
1	-	-
2	-	2 (40)
3	1	2 (40)
Stadium		
1	-	-
2	1 (20)	-
3	-	1 (20)
4	-	3 (100)
IHC		
ER		
Positive	-	2
Negative	1	2
PR		
Positive	-	1
Negative	1	3
HER2		
Positive	-	1
Negative	1	3
Nodal metastasis		
Positive	-	3
Negative	1	1
Site of metastasis		
Lung	-	2
Brain	-	1
Liver	-	-
Bone	-	1

BRCA: Breast cancer gene; ER: Estrogen receptor; HER2: Human epidermal growth factor receptor-2; IHC: Immunohistochemistry; PR: Progesterone receptor

In 2009, Kwong et al. announced the clinicopathological qualities of Chinese patients with *BRCA*-related BC development. Among 226 high-hazard Hong Kong Chinese ladies, 28 (12.4%) conveyed *BRCA* transformations (*BRCA1* change, 11 patients; *BRCA2* changes, 17 patients), and 55.6% of these carriers were determined to have BC before age 40 contrasted and 36.0% of non-carriers ($P = 0.05$). A family history of breast and ovarian cancer, high-grade tumors, and TNBCs is a given for BRCA change carriers. TNBC was essentially more prevalent in *BRCA1* carriers (67.7%) than in *BRCA2* carriers (35.3%) and non-carriers (25.6%). Negative cancer found in the

emergency department was mostly linked to *BRCA1* mutations, especially in individuals under the age of 40.[10]

Period of beginning had significant role as one of clinical qualities in innate tumors particularly patients in youthful beginning. In innate BC development, the patients endure this carcinoma in the youthful beginning. As in our reports, the patient determined to have BC development with *BRCA* transformation and positive family ancestry were in younger age. This outcome is in accordance with meta-examinations indicate that *BRCA1* and *BRCA2* carriers have a 57%-65% and 45%-49% likelihood of creating BC over lifetime, individually. Patients with a familial history of breast or ovarian cancer, a personal history of BC at a younger age, or triple-negative aggregate have *BRCA1/2* germline alterations that are more common (for *BRCA1* as it were). As of late, Lang et al. revealed the pervasiveness of *BRCA* transformation and highlights of *BRCA*-related BC in Chinese patients using cutting edge sequencing on 2,991 BC patients and 1,043 solid people as controls. *BRCA* transformations were available in 9.1% (232/2,560) of patients with in any event one danger factor for genetic BC development contrasted with 3.5% (15/431) in irregular patients and 0.38% (4/1,043) in sound controls. Family background of breast/ovarian malignant growth, younger age, negative HER2, high Ki-67 list, and high tumor grade were related with *BRCA* transformations. Though *BRCA2*-changed BCs were guaranteed to be ER- or PR-positive, *BRCA1* carriers were guaranteed to be ER- or PR-negative compared to *BRCA1* non-carriers. Patients with *BRCA1* mutations also presented a higher stage at the hour of conclusion, while *BRCA2* mutation carriers had more precise lymph nodes. There were no distinctions in infection free endurance among *BRCA1* carriers, *BRCA2* carriers, and non-carriers. In any case, among non-TNBC patients, *BRCA2* transformation carriers showed diminished disease-free survival contrasted with *BRCA2* change non-carriers (risk proportion, 1.892; 95% certainty stretch, 1.132 to 3.161; $P = 0.013$).[11,12]

As in the site of metastasis, it was appeared in *BRCA*-negative patients that there are two cases with lung metastasis, and every last one of the cerebrum and bone metastasis. These results were also consistent with a study that was shown on television, which found that 63 (15.1%) individuals had metastatic disease, with 13 (20.6%) having bone-only metastasis and 50 (79.4%) having instinctive metastases to the liver, lung, or brain. A significant number of the 354 patients with non-metastatic sickness had poor clinical and neurotic highlights, including 237 (66.9%) with positive axillary lymph hubs, 182 (51.4%) with grade III, 100 (28.2%) with T3 or T4 infection, and 172 (48.6%) with positive lymphovascular attack. Both ERs and PRs were positive in 284 (68.1%) patients, while 52 (12.5%) others had ER-or PR-positive sickness and 80 (19.2%) had chemical receptor-negative infection. Not all patients were tried for HER2; notwithstanding, 122 (31.5%) of the 387 those tried patients were HER2-positive on immunohistochemical staining or fluorescence in situ hybridization.[13,14]

The clinical stages of BC were logically shown in *BRCA*-with three cases in the IV stage, yet one case in III stage. On the other hand, one patient with II stage had *BRCA*+ alongside them. In 2014, Yu et al. examined the characteristics of BC from 55,387 irregular breast tumors from the Korean BC Registry and 181 *BRCA1/2* transformation carriers' cases (80 patients with *BRCA1* alteration and 101 patients with *BRCA2* transformation). In this report, middle patient age was fundamentally lower in the *BRCA1* and *BRCA2* change groups than in the registry group (37 and 41 years versus 48 years; $P < 0.001$ for both). Tumor size was not diverse between *BRCA1* and *BRCA2* gatherings and the registry group. The extent of patients with axillary hub metastasis was not essentially unique between *BRCA1* and library gatherings; nonetheless, axillary nodal association was available more regularly in the *BRCA2* group than in the registry group (45.5% versus 33.5%, $P = 0.002$).[12]

The *BRCA1* and *BRCA2* populations showed no significant relationships between tumor size and axillary nodal association. When compared

to the library group's tumors, *BRCA1* tumors performed better (64.3% versus 27.5%, $P < 0.001$) In comparison with the registry group, the *BRCA1* group had a larger percentage of chemical receptor-negative tumors and a lower percentage of HER2-overexpressing tumors. TNBCs were more pervasive in the *BRCA1* group than in the registry group (61.3% versus 12.4%, $P < 0.001$). Moreover, chemical receptor articulation was not altogether unique between the *BRCA2* group and registry group. The recurrence of ductal carcinoma in situ was lower in the *BRCA1* (3.7%) and *BRCA2* (5%) groups than in the registry group (10.3%).[15]

Conclusion

In this case report, we found one patient who had a *BRCA 1/2* mutation with a triple negative type of BC grade 3 and had a family history of BC. According to the existing theory, BC related to *BRCA 1/2* has aggressive characteristics, high grade, and is often found in the triple negative type.

Informed Consent

Before beginning any medical or legal processes, we got the participants' informed consents; in other words, patients have given their consent to participate in formal scientific research ever since they registered at our facility. The verbal agreement from all patients regarding the data documentation, discussion, and possible publication of the cases had been obtained since we explained the main objective of this report is solely on scientific purpose.

Conflict of Interest

None declared.

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