

Histopathologic Feature of Breast Cancer Patients in Young Women

M. S. Sitorus¹, L. I. Laksmi²

¹Department of Anatomy, Universitas Sumatera Utara

²Department Of Pathology Anatomy, Universitas Sumatera Utara

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Abstract : Breast malignancy is still the most common cancer in the worldwide that attacks women. Causing a high mortality rate that is about 15% of all deaths in women. The incidence of breast cancer cases in young age under the 40 years of age is low but they have particular attention because of its unique behavior. Breast cancer biology in young women is more aggressive than women of premenopausal age. This is related to many factors associated with poor prognosis, including high proliferation index, grade three and four disease and negative Estrogen Receptor expression. This study aims to explore further histopathologic feature, immunohistochemical expression, and subtype of breast cancer biology, in women under 40 years of age. It was found that the most common type, of breast cancer histopathology was invasive breast cancer (88%). The most histopathologic grading was grade I which is 74%. Based on the ER immunohistochemical staining found that 60% gives a negative expression, only 40% gives positive. A total of 68% gave a positive PR expression, 68% Her-2 positive one, 30% Her-2 positive three. As many as 56% positive Ki-67. All cases are Her-2 positive and have a moderate to poor prognosis.

1 INTRODUCTION

Breast cancer is the most common malignancy in women. Each year affects 1.5 million women, with a high number of deaths. By 2015, 570,000 women die caused by breast cancer - about 15% of all deaths in women (WHO, 2018). The incidence of breast cancer is more frequent in developing countries while the death is higher in less developed countries (Ghoncheh, 2016). In Indonesia, this cancer is also the most cancer with a number of cases 48,998 in 2014, with a mortality rate of 21.4% (WHO, 2014).

Now, it is so rapidly progressing concerning therapeutic and screening of breast cancer to reduce mortality at all ages. However, breast cancer in young age although rarely encountered has its uniqueness compared with old age sufferers. However breast cancer in young age woman has an aggressive behaviour (Lee HB, 2014). Around 7% of breast cancers are found in young women under 40 years old. The survival rate is worse than that of older people (Anders CK, 2009). This paper aims to obtain a histopathologic feature, immunohistochemical expression, and subtype of breast cancer biology, in young women under 40 years old.

2 METHODOLOGY

The sample of the study was female breast cancer patients aged under 40. Patient has performed surgery and histopathology examination of the network in Installation of Pathology Anatomy of Adam Malik Hospital Medan. Anatomy Pathology examination results indicate the presence of breast cancer. The number of samples is 50 people with a distribution showed in table 1.

Table 1 : Distribution of breast cancer patients by age.

Age (years)	Number(person)	Percentage (%)
35-40	45	90
30-34	3	6
25-30	2	4
<24	-	-
	50	100

Some breast cancer patients aged 35-40 people were found as much as 90%. Only two persons (4%) aged 25-30 years, which are one person age 29 years and one person aged 26 years. There were no breast cancer patients under 24 years of age.

3 RESULTS

3.1 Histopathology Feature

A tumor had removed and sent to Installation of Pathology Anatomy. The tissue is processed in the Installation of Pathology Anatomy RS Adam-Malik Medan to become a slide. Then stained with Hematoxylin-Eosin to be observed with a light microscope. The type and grading histopathologic breast cancer are established. The most frequently type of histopathologic breast malignancy is invasive breast cancer with no specific type (44 cases) (88%), five patients are invasive lobular cancer and one clear cell carcinoma patient as shown in table 2.

Table 2: Breast malignancy types.

Breast cancer malignancy types	Number	Percentage (%)
Invasive breast carcinoma	44	88
Invasive lobular carcinoma	5	10
Clear cell carcinoma	1	2
	50	100

The Bloom & Richardson classification determines histopathologic grading. Classification is determined by tubular formation, cell atypia, and mitosis. The histopathologic Grading was found in Table 3.

Table 3: Grading breast cancer.

Grading breast cancer	Number	Percentage (%)
<i>Grade I</i>	12	24
<i>Grade II</i>	37	74
<i>Grade III</i>	1	2
	50	100

The most histopathologic grading was grade I of 74%, at least grade III of 2%.

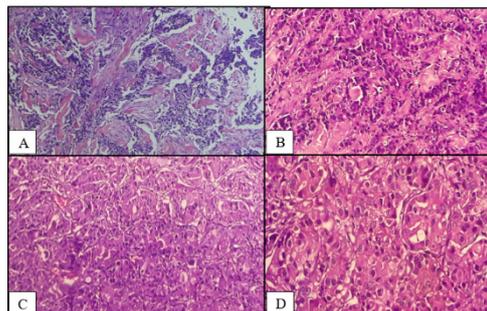


Figure 1: Microscopic view of invasive ductal carcinoma of breast. A. Grade III (HE, 50x), B. Grade III infiltratif pattern (HE,50x), C.Solid pattern (HE,50x), D(HE,100x).

3.2 Immunohistochemical (ihc) Expression

Then all histopathologic tissue blocks were immunohistochemically stained (ihk) with Estrogen Receptor (ER), Progesterone Receptor (PR), Her-2, and Ki-67 antibodies. The immunohistochemical examination is assessed on a scoring system. Immunohistochemical examination are shown in Table 4.

Table 4: Immunohistochemical expression of breast cancer.

Ihc expres sion	ER(%)	PR(%)	Her-2(%)	Ki-67(%)
Negati ve	30(60)	34(68)	1(2)	22(44)
+	20(40)	16(32)	34(68)	28(56)
++	0	0	0	0
+++	0	0	15(30)	0
	50(100)	50(100)	50(100)	50(100)

Based on the ER ihc expression found that 60% gives a negative expression, only 40% gives a positive. A total of 68% gave a positive PR expression, 68% Her-2 positive one, 30% Her-2 positive three. As many as 56% positive Ki-67.

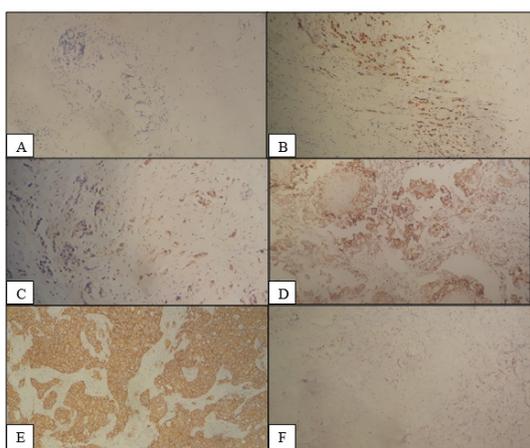


Figure 2: ER expression negative (A), PR +(B), Her-2 +1(C), Her-2 2+(D), Her-2 3+(E), Ki6 +(F).

3.3 Histopathology Subtypes

Through ihc examination, a subtype of breast cancer can be grouped based on a classification of St. Gallen. There were five intrinsic subtypes of breast cancer, Luminal-A, Luminal-B, Her-2 overexpression, Basal-like and Normal-like as in table 5.

Table 5: Classification of molecular subtypes of breast cancer (Dai X, 2015).

Intrinsic Subtype	Ihc
Luminal A	[ER+ PR+] HER2-KI67-
Luminal B	[ER+ PR+] HER2-KI67+ [ER+ PR+] HER2+KI67+
HER2 Overexpression	[ER-PR-] HER2+
Basal (Triple neg)	[ER-PR-] HER2-, basal marker+
Normal-like	[ER+ PR+] HER2-KI67-

In this study, it was found that all cases were Her-2 positive, and had a moderate to poor prognosis (table 6). No Luminal-A subtype was found.

Table 6. Molecular subtypes of breast cancer.

Intrinsic Subtype	Number	Percentage (%)
Luminal A	0	0
Luminal B	21	52
HER2 Overexpression	28	56
Basal (Triple neg)	0	0
Normal-like	1	2
Jumlah	50	100

4 DISCUSSION

The risk of breast cancer will increase with age. Also, will decrease in young age. So the amount of breast cancer patients in young age women is lower. In United States, an estimated 11,000 women diagnosed with invasive breast cancer are under 40 years old. That is 4.7% -4.9% of all breast cancer patients (Lee HB, 2014). The less number of breast cancer in young age is associated with pathogenesis and breast cancer risk factors. There are two risk factors: internal and external factors. The internal factors are age, hormonal status (age of menarche, menopause, breastfeeding) and genetics. External factors are the form of low-fiber diet, carcinogenic food, radiation exposure, smoking, hormonal therapy also play an important role in the pathogenesis of breast malignancy (Cable AM , 2015).

In this study, the most common type of breast cancer was invasive breast cancer in 44 cases (88%). While invasive lobular carcinoma were 5 cases (10%). When viewed from the literature, this type of cancer is indeed the most cases of 60-75% (Eliyatkin N, 2015, Malhotra GK, 2010).

Breast malignancy at a young age, although slightly but has unique biological characteristics. This makes the researchers interested in exploring more about this. Breast cancer biology in young age women is more aggressive than women of premenopausal age. This is related to many factors associated with poor prognosis, including high proliferation index, grade three and four disease and negative ER (Lee HB, 2014).

In this study, no luminal-A subtype had a good prognosis. In fact, 98% of cases show positive Her-2 and 56% of cancer with Her-2 overexpression. The presence of Her-2 overexpression has been stated to be an adverse prognostic factor of breast cancer. This situation is found in 20-25% of cases that can be detected with ihc. Her-2 is a member of the epidermal growth factor receptor functioning in the stimulation of cell growth, survival and differentiation (Punglisi F, 2015).

The existence of these different subtypes of breast cancer biology, as well as the basis for determining prognosis, may also determine appropriate treatment measures. In breast cancer that expressed positive ER will be treated with antihormonal, Her-2 positive will be treated with anti-HER-2. Targeting therapy can increase the life expectancy rate and the death rate decreases.

Another worse prognostic factor is triple negative breast cancer (ER-/PR-/Her-2-). In some papers, it is said that this subtype more often found at a young

age. This will make two bad things together. The risk of death would be 2.7-fold if a triple negative was encountered at a young age. There was no triple negative subtype in this study (Bano R et., 2015).

World Health Organization – Cancer country profile, 2014. Indonesia. Available at www.who.int/country-profiles/idn_en.

5 CONCLUSION

Breast cancer at a young age woman is a rare case. However, cancer cases in young age will show a worse prognosis. The grading, ihc appearance and subtype biology of breast cancer are worse compared with cancer found in older age.

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