

Analysis of Clinicopathological and Immunohistochemical Profile in Invasive Ductal Breast Cancer Patients

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Abstract: Breast cancer is the most common malignant neoplasm among women worldwide. This cancer is the primary cause of mortality and morbidity in Indonesian women. The aimed of this study was to analyze the pattern of clinicopathological profile and immunohistochemical of ER, PR, and Her2 in invasive ductal breast cancer patients. This study was a retrospective design. A Histopathological diagnosis and immunohistochemical ER, PR, and Her2 from 105 patients with invasive ductal breast cancer were included during period January 2017 to June 2018. Information of clinical, pathologic and immunohistochemical examination was recorded and analyzed. Average of age patients is range from 25 to 80 years, 59% of cases are > 45 years. The majority of tumor size of patients is 2 – 5 cm, 57 patients (54,3 %). Majority of a tumor is grade 3. The Immunohistochemical overexpression of ER, PR, Her 2 and Triple negative was 59%, 59%, 46,7% and 10,5% respectively. Incidence of invasive breast cancer is highest in premenopause women. Analyze of tumor size, grade histopathology, lymph vessel invasion and immunohistochemical profile is important to therapeutic management in patients with invasive ductal cancer.

1 INTRODUCTION

Breast cancer is the most common malignant breast lesion in a woman with more than a million new cases per year in worldwide, representing 22% of all cancer diagnosed in women. It is the leading cause of death in the world with over 370.000 deaths per year, or 14% of cancer deaths in women (Isawi, 2016). From data and information center of Indonesian Health Ministry 2016, Incidence of breast cancer in Indonesia is 40/100.000 people and mortality rate is 16,6/100.000 people. Invasive Ductal Breast Cancer is the commonest type of epithelial breast cancer (Kementrian Kesehatan RI, 2016) (Komite Penanggulangan Kanker Nasional, 2016).

Treatment of breast cancer is multidisciplinary and depends on the age of patients, the tumor size, lymph node status and histological type, grade of the tumor, estrogen receptor (ER)/ Progesteron Receptor (PR) status and growth factor (Her-2). Prognosis and survival life years of breast cancer is worse with higher grade, subtype of tumor, lymph node metastase, negativity for ER, PR and positivity for

Her-2. Analysis clinicopathology characteristic and expression of Estrogen Receptor, Progesteron Receptor and Her-2 immunostaining are very useful tools to diagnose this cancer, important to management protocol therapy and prognosis of the patients (Kristina, 2010). The aimed of this study is to analyze the profile of clinicopathological parameters and immunohistochemical of ER, PR, and Her2, in invasive ductal breast cancer patients.

2 METHODS

The study was retrospective design and done as per standard ethics. The study was performed on medical record of eligible 100 patients with breast cancer who had undergone surgical treatment, pathological and immunohistochemical analysis at Murni Teguh Memorial Hospital in Medan Indonesia during period in January 2017 to June 2018. Medical record with missing data on clinicopathology and immunostaining ER, PR and Her2/ neu were

excluded. The data of age, tumor size (< 2cm, 2 – 5 cm, > 5cm), histopatological type is specified according to WHO classification of breast cancer, histopatological tumor grade was performed using the modified criteria of Bloom and Richardson as described by Elston and Ellis, lymphnode metastase, lymphvessel angioinvasion was collected as follows (1). The hormone receptor status (ER,PR) immunohistochemical stain was scored that positivity cells ≥ 10.0% is positive and < 10% is negative. Her2 according to immunohistochemical staining of cells can be divided into 0,1+. 2+ and 3+. Score 0 was negative (no reactivity), 1+ was negative, (faint, weak reactivity in > 10 % of tumor cells), but only a portion of the membrane is positive), 2+ was equivocal (circumferential) intense membran staining in < 30% of cells . Score 0 and 1 were considered negative, score 2 was considered weakly positive, and score 3 was considered strongly positive. Then only score 3 cases were considered as Her-2 overexpressing cases.(Almumen, 2015) (Zineb, 2012).

3 RESULT

In our study, 105 of histopathological of a tumor and immunohistochemical profile in patients with invasive ductal breast cancer were taken. Average of age patients was ranges from 25 – 80 years. The majority ages group was 45 – 54 (42,8%) patients. Majority of patients belonged to histologic grade III WHO (73,4%). Majority of tumor size is 2 – 5 cm (54,3%). Lymph vessel invasion was present in 54 patients (51,4%). Location of tumor commonly in right breast site. Over expression of Immunohistochemical profile ER, PR and Her2 was 62 (59%), 62 (59%) and 49 (46,7%) respectively. Immunoexpression Triple negative was found in 11 (10,5%) patients (Table 1).

Table 1. Clinicopathological and immunohistochemical profile

| Profile | | Number | Percentage |
|--------------------|---------|--------|------------|
| Age (years) | 25 – 34 | 6 | 5,7 |
| | 35 – 44 | 32 | 30,5 |
| | 45 - 54 | 45 | 42,8 |
| | 55 - 64 | 15 | 14,3 |
| | ≥ 65 | 7 | 6,7 |
| Tumor size (cm) | < 2 | 10 | 9,5 |
| | 2 - 5 | 57 | 54,3 |
| | > 5 | 38 | 36,2 |
| Histological Grade | I | 1 | 0,9 |
| | II | 27 | 25,7 |
| | III | 77 | 73,4 |

| | | | |
|---------------------------|-----------|----|------|
| Lymph-vessel invasion | Present | 54 | 51,4 |
| | Absent | 51 | 48,6 |
| Location | Right | 67 | 63,8 |
| | Left | 33 | 31,4 |
| | Bilateral | 5 | 4,8 |
| Estrogen Receptor (ER) | Positive | 62 | 59,0 |
| | Negative | 43 | 41,0 |
| Progesteron Receptor (PR) | Positive | 62 | 59,0 |
| | Negative | 43 | 41,0 |
| Her2/neu | Positive | 49 | 46,7 |
| | Negative | 56 | 53,3 |
| Triple Negative | | 11 | 10,5 |

Table 2. Comparison Clinic opathological profile and Immunohistochemicalexpression ER, PR, Her2 and Triple negative.

| Clinicopathological Profile | ER | | PR | | Her2 | | Triple Negative | |
|--------------------------------|----|------|----|------|------|------|-----------------|------|
| | N | % | N | % | N | % | N | % |
| Age (years) ≤ 45 | 25 | 40,3 | 24 | 38,7 | 27 | 55,1 | 7 | 63,7 |
| > 45 | 37 | 59,7 | 38 | 61,3 | 22 | 44,9 | 4 | 36,3 |
| < 2 | 6 | 9,7 | 3 | 4,8 | 3 | 6,1 | 1 | 9,1 |
| Tumor size 2 - 5 | 34 | 54,8 | 36 | 58,1 | 20 | 40,8 | 6 | 54,5 |
| (cm) > 5 | 22 | 35,5 | 23 | 37,1 | 26 | 53,1 | 4 | 36,4 |
| I | 1 | 1,6 | 1 | 1,6 | - | - | - | - |

| | | | | | | | | | |
|-------|-----|----|------|----|------|---|------|---|------|
| Grade | II | 15 | 24,2 | 15 | 24,2 | 3 | 22,4 | 3 | 27,3 |
| | III | 46 | 74,2 | 46 | 74,2 | 8 | 77,6 | 8 | 72,7 |

| | | | | | | | | | |
|-----------------------|--|----|------|----|------|----|------|---|------|
| Lymph vessel Invasion | | 35 | 56,5 | 30 | 48,4 | 30 | 61,2 | 5 | 45,5 |
| Present | | 27 | 43,5 | 32 | 51,6 | 19 | 38,7 | 6 | 54,5 |
| Negative | | | | | | | | | |

Comparison positivity immunohistochemical expression ER, PR and Her2 with age, tumor size, histopathological grade and lymph vessel invasion has been shown in table 2. Her2 positivity showed in age ≤ 45 (55,1%), tumor size > 5 cm (53,1%), histopathology tumor grade III (77,6%) and lymph vessel present (61,2%).

4 DISCUSSION

Our study comprised of 105 patients with invasive ductal breast cancer, Range of age of patients from 25 to 80 years old and majority patients are premenopausal women (45 – 54 years old. This is consistent with the study conducted by Sahu N and Almumen M, size of tumor, histopathologic grade and lymph vessel invasion are the traditional prognostic factor in invasive ductal breast cancer patients (Colditz, 2012). In our study, majority tumor size, the histological grade is 2 – 5 cm (54,3cm) and grade III (73,4%) respectively. The many studies have demonstrated a strongly association between grade of histological and survival of invasive ductal breast cancer patients (Heng, 2017) (Kouame, 2012). The grade is dominant prognostic factor and should be included as a component of the minimum dataset for histological reporting of breast cancer (Colditz, 2012). This was compatible to the result observed in Indian women, Mir MA et al showed that 72,3% patients were in histological grade III and tumor size range from 2 – 5 cm. E Gottfried studied showed 51,2% patients had been 2 – 5 cm size of a tumor. Five-years survival in breast cancer less than 1 cm is 93% while as it is

63% for more massive than 5 cm in size (Colditz, 2012) (Gottfried, 2004) (Schoppmann, 2010).

Lymph vessel present are found in 54 (51,4%) in patients with invasive ductal breast cancer. This is different result from studied of Schoppmann SF, where as lymph vessel invasion was present in 36,6% of case. Three molecular biomarker, Estrogen receptor (ER), Progesteron Receptor and Her2 are used in routine clinical management of patients with invasive ductal breast cancer. Our study shown ER, PR, Her2 positivity in 59%, 59% and 49 % respectively. Many studies have demonstrated that ER is strong predictive factor for response to hormonal therapies such as tamoxifen (Colditz, 2012) (Kristina, 2010). The over expression of the Her2 in a patients of breast cancer is a prognostic and predictive biomarker. Her2 expression is associated with diminished prognosis (higher risk of recurrence) (Heng, 2017).

Our study showed Triple negative positivity was found in 10,5% patients with invasive ductal breast cancer, and was seen in 63,7% women under 45 years old, 54,5% in 2 – 5 cm size of tumor and 72,7% in histopathological grade III tumor. Biswal P et al studied show that 35% cases are triple negative (Priyadharshini, 2015).

5 CONCLUSION

Analysis of clinicopathological and immunohistochemical profile is important in patients with invasive ductal breast cancer. They are provide valuable for prognostic, predictive and therapeutic management in patients. The accurate assessment of

the clinicopathological aspect and biomarker testing (ER,PR and HER2) is associated with a patient's overall clinical outcome.

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