Original Research Article

Correlation of tumor size and immunohistochemistry status with lung metastasis in carcinoma breast

S. P. Gayathre, S. Maniselvi*

Department of General surgery, Stanley Medical College and Hospital, Chennai, Tamil Nadu, India

*Correspondence:
Dr. S. Maniselvi,
E-mail: arvindr84@gmail.com

ABSTRACT

Background: Breast cancer is common cancer among females in rural India and is rapidly catching up to cervical cancer in rural India. Metastasis can occur after the initiation of treatment or at the time of diagnosis. The stage at initial presentation and underlying biology of the tumor has an impact on prognosis and metastasis of the tumor. The objective of the study was to study the correlation between tumor size and lung metastasis and to find the correlation between ER, PR status, and lung metastasis.

Methods: This study was conducted in 82 patients with breast carcinoma coming to the department of the general surgery and oncology at Government Stanley Medical College and Hospital. Details of cases and full history obtained. Routine blood investigations were done. Tumor size is evaluated by clinical examination and imaging. For all patients, core needle biopsy is done to confirm the diagnosis and receptor status. IHC status of the tumor is obtained from the pathologist. Presence of lung metastasis documented by CECT chest.

Results: In this study, the prevalence rate of lung metastasis in carcinoma breast patients is 9.75% Total number of Carcinoma Breast are 82, in which lung metastasis is seen in 8 cases and CECT chest is normal in 74 patients. The prevalence rate of lung metastasis in ER-positive patients is 9.90%. The prevalence rate of lung metastasis in ER-negative patients is 10.81%. The prevalence rate of metastasis in PR positive patients is 9.52%. The prevalence rate of metastasis in PR negative patients is 10%. Of 34 cases with HER-2 positive status 3 patients presented with lung metastasis with a prevalence rate of 8.82%. Of 48 cases with HER-2 negative status 5 cases presented with lung metastasis with a prevalence rate of 10.42%.

Conclusions: In this study prevalence of lung metastasis in carcinoma breast is 9.75%. There seems to be no correlation between ER, PR and HER-2 neu status and lung metastasis. There is also no correlation between clinically T2 and T3 tumors and lung metastasis. Whereas clinically T4 tumors seem to have a higher incidence of lung metastasis.

Keywords: Breast carcinoma, Lung metastasis, Estrogen receptor, Progesterone receptor

INTRODUCTION

Breast cancer is common cancer among females in rural India and is rapidly catching up to cervical cancer in rural India. An estimated about 1 Million cases of breast carcinoma been diagnosed annually worldwide.[1] Of these, most common site of distant metastasis is bone followed by the lung. Metastasis can occur after the initiation of treatment or at the time of diagnosis.[2] The stage at initial presentation and underlying biology of the tumor have an impact on prognosis and metastasis the of the tumor. The Tumor size, grade, nodal involvement, lymphovascular invasion, estrogen, and progesterone receptor (ER, PR) and human epidermal growth factor receptor 2

(HER2) statuses are all independent risk factors for metastasis and relapse. However, we need to have a comprehensive understanding of the pattern of spread and specific sites of recurrence.[3] Models of metastatic spread describe a complex interaction of factors involving tumor intravasation, circulation, extravasation, proliferation, and angiogenesis and the microenvironment of the tissue. Characteristics of the metastatic tumor usually follow the primary tumor.[4] Among patients with breast cancer, some associations with metastatic disease have been identified. Lung and bone metastasis gene signatures have been reported and HER2 and ER expression status have been associated with increased risk of spread to specific sites.[5] A better understanding of patterns of metastatic spread will influence adjuvant therapy and surveillance decisions and determine the investigations and therapies are appropriate once distant metastasis has been diagnosed.[6] Currently, treatment options for bone metastasis include alleviation of pain, reducing pathological fractures, prevention cord compression in spinal metastasis. It is achieved by radiotherapy and chemotherapy. Treatment options for lung metastasis are limited to chemotherapy.[7]

METHODS

This study was conducted in 82 patients with breast carcinoma coming to the department of the general surgery and oncology at Government Stanley Medical College and Hospital. The period of study was around 10 months between November 2016 to August 2017. Details of cases and full history obtained. Routine blood investigations were done. Tumor size is evaluated by clinical examination and imaging. For all patients, core needle biopsy is done to confirm the diagnosis and receptor status. IHC status of the tumor is obtained from the pathologist. Presence of lung metastasis documented by CECT chest. Core Needle Biopsy was done under aseptic conditions, parts prepare and draped. Trucut biopsy needle is inserted into suspected mass and chunk of tissue is removed. The procedure is repeated 5 to 8 times till obtaining sufficient sample. The site is chosen such that scar will be included in the surgical incision. Prevalence rate of lung metastasis in carcinoma breast patient. Age wise distribution of carcinoma breast patient with and without mets. Correlation between clinical T staging and Lung metastasis. Correlation between tumor size greater than 6 cms with lung metastasis. Correlation between ER status and lung metastasis. Correlation between PR status and lung metastasis. Correlation between HER-2 neu status and lung metastasis.

RESULTS

In this study, the prevalence rate of lung metastasis in carcinoma breast patients is 9.75% Total number of Carcinoma Breast are 82, in which lung metastasis is seen in 8 cases and CECT chest is normal in 74 patients.
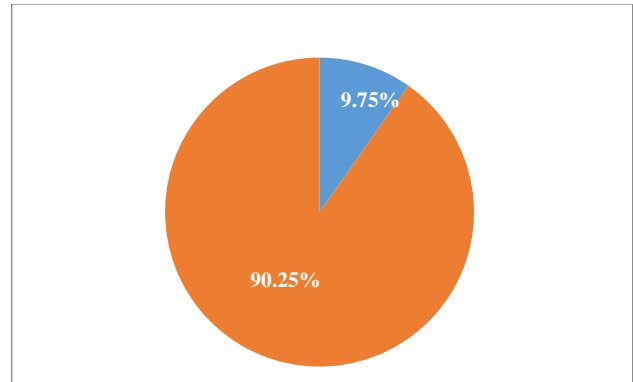

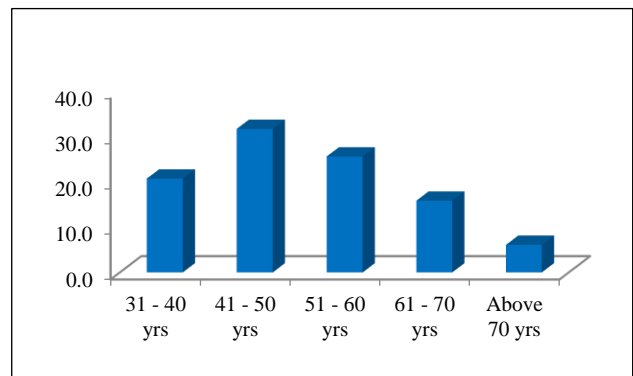**Figure 1: The prevalence of lung metastasis among breast carcinoma patients.**

Figure 2: The prevalence age distribution among breast carcinoma patient.

In this study patients are classified into three groups as less than or equal to 40 years of age, in the age group 41-60 and age above 60 years to find any correlation between age group and lung metastasis.
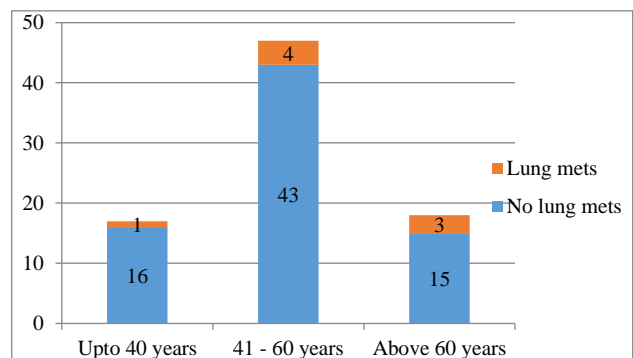

Figure 3: The prevalence age and prevalence of metastasis among breast carcinoma patient.

In our study prevalence of carcinoma, breast is 20.73% (17 cases) in the age group below 40 years, 57.31% (47 cases) in the age group 21.95% (18 cases) in the age group above 60 years. Of the 17 cases under the age group, 40 prevalence of lung metastasis is 6.25% (1 case). Of the 47 cases in the age group 41-60 years 4

cases are diagnosed with lung metastasis. Hence the prevalence of lung metastasis in the age group 41-60 years is 8.51%. Of the 18 cases above age group, 60 prevalence of lung metastasis is 16.67% (3 cases).
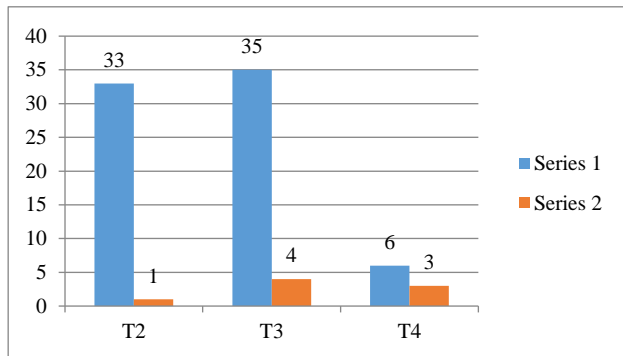

Figure 4: The prevalence t- clinical staging among breast carcinoma patient.

In this study of 82 cases, 34 cases are categorized under clinical tumor staging of T2 with a prevalence rate of 41.46%. 39 cases are categorized under clinical tumor staging of T3 with a prevalence rate of 47.56%. Nine cases are categorized under clinical tumor staging T4 with a prevalence rate of 10.97%.
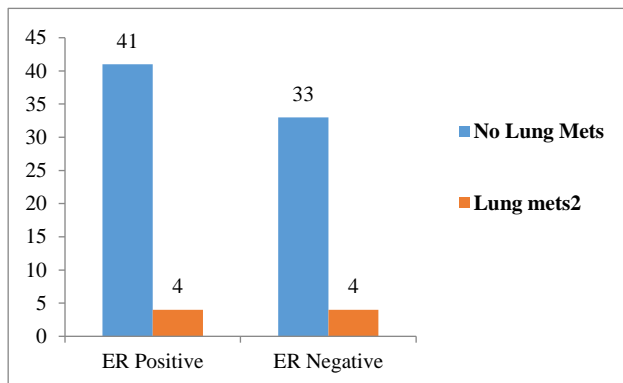

Figure 5: The prevalence ER status among breast carcinoma metastasis patients.

In this study, of 82 cases 45 cases are found to be ER positive with a prevalence rate of 54.9%. The prevalence rate of lung metastasis in ER-positive patients is 9.90%. The prevalence rate of lung metastasis in ER-negative patients is 10.81%.

In this study of 82 patients, 42 patients are found to be PR positive with a prevalence rate of 51.2%. The prevalence rate of metastasis in PR positive patients is 9.52%. The prevalence rate of metastasis in PR negative patients is 10%.

In this study, of 82 cases 34 cases are HER-2 neu receptor positive with a prevalence rate of 41.46%. Of 34 cases with HER-2 positive status 3 patients presented with lung metastasis with a prevalence rate of 8.82%. Of

48 cases with HER-2 negative status 5 cases presented with lung metastasis with a prevalence rate of 10.42%.
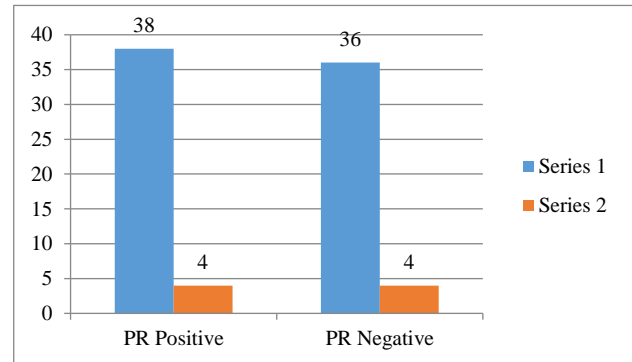

Figure 6: The prevalence PR status among breast carcinoma metastasis patients.
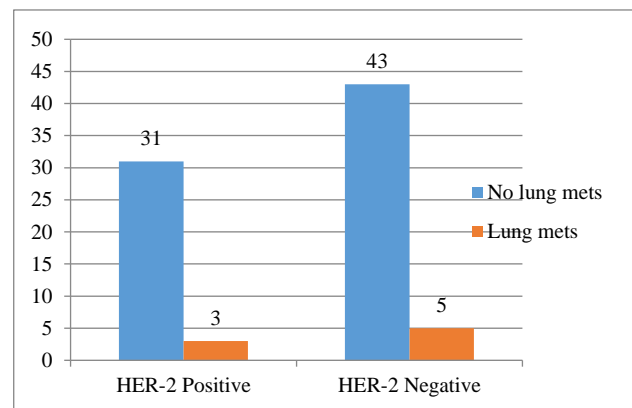

Figure 7: The relation to HER-2 neu status among breast carcinoma metastasis patients.

DISCUSSION

Carcinoma breast is one of the most common cancer in incidence and one of the most common causes of cancer-related mortality. The lifetime risk of developing cancer breast is approximately 1 in 8% to 1 in 12% and the risk of death from the disease in a person lifetime is approximately 2.4%.[8] Complete maturation of breast occurs only after pregnancy. Hence age at first childbirth is an important risk factor for carcinoma breast as the disease is linked with the action of estrogen on the immature breast. Age at first childbirth is directly proportional to the risk of malignancy.[9] Distant metastasis in the body usually spreads via the bloodstream. Cancerous cells have decreased cell adhesion hence tumor cells are seeded into blood vessels supplying cancerous mass and carried via the bloodstream.[10] Spinal metastasis occurs via venous drainage of breast i.e. Batson plexus. BRCA1 located in Chromosome 17 (17q21) long arm with autosomal dominant trait with high penetrance, 90% chance for of breast cancer, 40% for ovarian cancer, using high-grade tumor, with negative receptor status, affecting younger

age group, a higher prevalence of bilateral breast cancer. BRCA2 located on chromosome 13q, autosomal dominant trait and has a high penetrance, Carrier 100-fold risk in the male population, IDC type, with receptor status positive.[11] Accounts for 5 to 7% of breast cancer, Poor differentiation nuclei, a syncytial growth pattern, circumscribed border, lymphocyte and plasma cell intense infiltration, and little or no DCIS are the characteristic histological features of this type of a tumor.[12] Prognosis is favorable; however, they have a prognosis similar to that of invasive ductal carcinoma in case of mixed variants. Approximately more than one million women are diagnosed with breast cancer each year and approximately 700.000 of these have positive (+) hormone receptors (HR) The hormone receptors are expressed proteins both in the epithelium and in breast stroma which bind to circulating hormones, mediating their cellular effects.[13] The HR best studied in breast cancer is estrogen receptor (ER) and progesterone receptors (PR). Breast cancers classified by positive immunohistochemistry (IHC) expression of ER and PR have different clinical, pathological, and molecular characteristics. It is postulated that risk factors are closely associated with breast tumors ER+ and PR+ and may involve mechanisms related to exposure to estrogen and progesterone, while etiology of breast cancer ER− and PR− should be independent of hormone exposure.[14] The ER and PR are highly associated with patient age at diagnosis, rising continuously with age. Correlation between tumor size and lung metastasis is calculated by comparing clinical T staging and prevalence of lung metastasis using Chi-square test. The null hypothesis is assumed. The chi-square statistic is 3.0639. The p value is 080048. The result is not significant at $p<0.005$. Hence no correlation is found between clinically T2 stage tumor and lung metastasis. In this study patients are classified into two groups one with tumor size less than or equal to 6 cms and other with tumor size more than 6cm. The correlation between tumor size and lung metastasis is evaluated. Of 82 cases 14 cases presented with tumor size less than or equal to 6cm with the prevalence of 17.07%.[15]

CONCLUSION

In this study prevalence of lung metastasis in carcinoma, breast is 9.75%. There seems to be no correlation between ER, PR and HER-2 neu status and lung metastasis. There is also no correlation between clinically T2 and T3 tumors and lung metastasis. Whereas clinically T4 tumors seem to have a higher incidence of lung metastasis. In accordance with tumor size patients having tumor more than 6cm have a higher incidence of lung metastasis. Still a larger study with larger sample size is needed to get a reliable outcome of the study. Chemotherapy remains the backbone of systemic treatment in TNBC. Since the disease has become incurable, treatment goals have become prolongation of survival and palliation of symptoms.

REFERENCES

1. Yang XR, Chang-Claude J, Goode EL, Couch FJ, Nevanlinna H, Milne RL, et al. Associations of breast cancer risk factors with tumor subtypes: a pooled analysis from the Breast Cancer Association Consortium studies. J Natl Cancer Inst. 2011;103(3):250-63.
2. Ghosn M, Hajj C, Kattan J, Farhat F, El Karak F, Nasr N, et al. Triple-negative breast cancer in Lebanon: a case series. Oncologist. 2011;16(11):1552-6.
3. Bauer KR, Brown M, Cress RD, Parise CA, Caggiano V. Descriptive analysis of estrogen receptor (ER)-negative, progesterone receptor (PR)-negative, and HER2-negative invasive breast cancer, the so-called triple-negative phenotype: a population-based study from the California Cancer Registry. Cancer. 2007;109:1721-8.
4. Park YH, Lee SJ, Cho EY. Clinical relevance of TN staging system according to breast cancer subtypes. Ann Oncol. 2011;22(7):1554-60.
5. Nelson HD, Tyne K, Naik A, Bougatsos C, Chan BK, Humphrey L, et al. Screening for breast cancer: An update for the U.S. Preventive Services Task Force. Ann Intern Med. 2009;151:727-37.
6. Berg WA, Blume JD, Cormack JB, Mendelson EB, Lehrer D, Böhm-Vélez M, et al. Combined screening with ultrasound and mammography vs mammography alone in women at elevated risk of breast cancer. JAMA. 2008;299:2151-63.
7. Turnbull L, Brown S, Harvey I, Olivier C, Drew P, Napp V, et al. Comparative effectiveness of MRI in breast cancer (COMICE) trial: A randomised controlled trial. Lancet. 2010;375:563-71.
8. Murphy JO, Moo TA, King TA, et al: Radioactive seed localization compared to wire localization in breast-conserving surgery: Initial 6-month experience. Ann Surg Oncol. 2013;20:4121-7.
9. Rosen PR. Rosen's breast pathology, ed 2, Philadelphia, 2001, Lippincott Williams & Wilkins.
10. Fisher B, Costantino JP, Wickerham DL. Tamoxifen for prevention of breast cancer: Report of the National Surgical Adjuvant Breast and Bowel Project P-1 Study. J Natl Cancer Inst. 1998;90:1371-8.
11. Hartmann LC, Sellers TA, Frost MH. Benign breast disease and the risk of breast cancer. N Engl J Med. 2005;353:229-37.
12. Stefanick ML, Anderson GL, Margolis KL, Hendrix SL, Rodabough RJ, Paskett ED, et al. Effects of conjugated equine estrogens on breast cancer and mammography screening in postmenopausal women with hysterectomy. JAMA. 2006;295:1647-57.

13. Vogel VG, Costantino JP, Wickerham DL, Cronin WM, Cecchini RS, Atkins JN, et al. Effects of tamoxifen vs raloxifene on the risk of developing invasive breast cancer and other disease outcomes: The NSABP Study of Tamoxifen and Raloxifene (STAR) P-2 trial. JAMA. 2006;295:2727-41.

14. Cuzick J, Powles T, Veronesi U, Forbes J, Edwards R, Ashley S, et al. Overview of the main outcomes in breast-cancer prevention trials. Lancet. 2003;361:296-300.

15. Perou CM, Sorlie T, Eisen MB, van de Rijn M, Jeffrey SS, Rees CA, et al. Molecular portraits of human breast tumors. Nature. 2000;406:747-52.