Patterns of E.cadherin and Estrogen receptor Expression in Histological Sections of Sudanese Patients with Breast Carcinoma

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Abstract

 Background: Breast cancer in Sudan reached 1.968 or 0.53% of total death, and the age adjusted death rate is 16.3 per 100.000 of population ranks Sudan # 96 in the world. E.cadherin is a calcium dependant epithelial cell adhesion molecule; it is associated with metastasis in breast cancer. The relationship between breast cancer and estrogen has been demonstrated by bilateral oophorectomy that resulted in remission of breast cancer in menopausal women. Our aim is to study the correlation between loss of E.cadherin and expression of estrogen receptor in breast cancer patients in Sudan.

Materials and methods: A total number of thirty seven (37) Formalin fixed-paraffin embedded sections were collected from Sudanese female patients with breast carcinoma; the median age was 54.4 years (range, 29-80 years) registered in Radiation and isotope centre of Khartoum [RICK]. H&E and immunohistochemistry for E.cadherin and estrogen receptor were done for all samples of patients with invasive breast cancer.

Results: Invasive carcinomas were classified as thirty one (31/37) were ductal Carcinomas, two (2/37) were lobular Carcinomas, two (2/37) were papillary, one metablastic, and one medullar carcinoma. of the positive E.cadherin expression, 50 %(15/30) had positive estrogen receptor expression, and 50 %(15/30) had negative estrogen receptor expression. And Of the negative E.cadherin expression 28.6 %(2/7) had positive estrogen expression and 71.4 %(5/7) of the negative E. cadherin expression had negative estrogen   receptor expression. Statistically P value was 0.416; which is considered insignificant.

Conclusions: according to these findings we conclude that there is no correlation between loss of E.cadherin and expression of estrogen receptor.

Key words: E.cadherin, Estrogen, Breast Cancer

Introduction

Breast cancer in Sudan reached 1.968 or 0.53% of total death, and the age adjusted death rate is 16.3 per 100.000 of population ranks Sudan # 96 in the world [1]

E. Cadherin is a transmembrane glycoprotein that mediates calcium-dependent intracellular adhesion and is specifically involved in epithelial cell-to-cell adhesion   [2].

Among the novel prognostic marker is E. Cadherin a calcium dependant epithelial cell adhesion molecule, it loss has been associated with metastases, Therapy providing evidence for role as invasion suppressor. The relationship between breast cancer and estrogen has been recognized for more than 100 years, since George Beetson demonstrated that bilateral oophorectomy resulted in the remission of breast cancer in premenopausal women [3]. The studies have different findings, one of them have been demonstrated aberrant expression of E. Cadherin is associated with high-grade, estrogen receptor (E.R.) negative and metastatic breast cancer, whereas others studies have failed to confirm this result. So this current study aimed to investigate the relationship between loss of E.cadherin and expression of estrogen receptor in breast cancer.

Materials and methods

The study comprised thirty seven cases (37) of Formalin fixed paraffin embedded breast cancer tissue of Sudanese female patients registered in the national institute of nuclear medicine centre during the period of October 2013 – July 2014 identified using computerized data bases. The median age of patients was 54.4 years (range, 29-80 years), The cases were selected according to availability of the paraffin blocks.

Representative sections from formalin fixed paraffin embedded tissues were taken from the 37 cases of Breast cancer and immunohistochemical stain of E.cadherin and estrogen were performed.

Histopathology was based on Haematoxylin and eosin (H & E) stained slides. The specimens were reviewed independently by two consultant Histopathologist to sub classify the tumors without knowledge of immunohistochemical results.

Immunohistochemical staining:

The procedure was done as follows: Two sections (3mm) from formalin fixed paraffin Embedded tissues were cut and mounted into salinized slides (fisher-brand) following deparaffinization in xylene, slides rehydrated through a graded series of alcohol and steamed for antigen retrieval for E. Cadherin and estrogen using pt link slide. slides placed in coplin jars containing sodium citrate buffer (PH 9.0), then boiled at high temp for 10 minutes, then cool at RT. Endogenous peroxidase activity blocked with 3% hydrogen peroxidase and methanol for 10 minutes for two slides, then slides incubated with 100-200 ml of primary antibodies for 10 minutes at room temperature for primary antibodies (E. Cadherin in one slide and for estrogen in second slides), and then rinsed in phosphate buffer saline for 3 minutes, binding of antibodies detected by incubating for 20 minutes with dextran labeled polymer (Dako-E.n vision TM Flex kit), finally two sections washed in three changes of PBS, followed by adding 3.3 diaminobenzidine tetra hydro chloride (DAB) (Dako) as chromogen to product the characteristic brown stain for the visualization of antibodies/ enzyme complex for up to 5 minutes), slides counterstained with Haematoxylin, for each run of staining, positive and negative control slides prepared "the positive control slides will contain the antigen under investigation and the negative of primary antibodies-each slide evaluated with investigator then results confirmed by two consultant Histopathologists.

Ethical clearance for this study is provided by ethical committee of Faculty of medical laboratory sciences –AL-Neelain University, Khartoum, Sudan.

Results

Immunohistochemical results

-Representative sections of tumors from 37 breast cancer patients were evaluated. Thirty one (31) cases were invasive ductal carcinomas; two cases lobular carcinomas, two cases papillary carcinomas, one case medullary carcinoma and one case metablastic carcinoma (figure1). Immunohistochemical resulted of the 37 cases showed positive E.cadherin staining in 81% (30/37) of invasive carcinomas, and negative E.cadhrerin staining in 19% (7/37) of

the cases. Immunohistochemical results of 37 cases showed positive estrogen receptor expression in 46 %(17/37) of invasive carcinomas, and negative estrogen receptor expression in 54 %(20/37) of invasive carcinomas. (Table1).

Of the positive E.cadherin staining 50% (15/30) had positive estrogen receptor expression, and 50% (15/30) had negative estrogen receptor expression. - Of the negative E.cadherin staining 28.6 %(2/7) had positive estrogen expression and 71.4 %(5/7) of the negative E.cadherin staining had negative estrogen receptor expression. (table2).
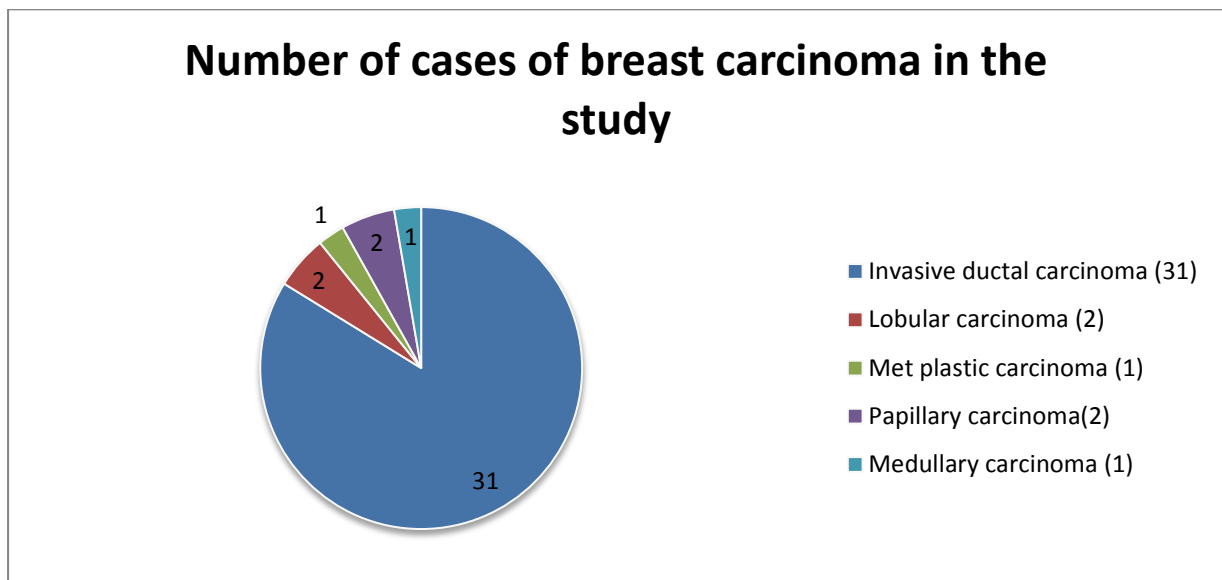

Figure (1) shows Number of cases of breast carcinomas included in the study.

Statistics analysis

Associations between E.cadherin and estrogen were assessed with the chi square tests .p value 0.416 was considered statistically insignificant, this data indicate that no correlation between loss of E.cadherin and expression of estrogen.

Table (1): Show the relation between Histological type, E.cadherin and estrogen expression status in a total number of 37 cases

Histological Type	No of cases	E.cadherin status		Estrogen receptor status	
		+ve	-ve	+ve	-ve
Invasive ductal carcinoma	31	26	5	15	17
Lobular carcinoma	2	0	2	0	2
Metaplastic carcinoma	1	1	0	0	1
Papillary carcinoma	2	2	0	2	0
Medullary carcinoma	1	1	0	0	1
Total	37	30	7	17	20

Table (2) show the relation between E.cadherin and estrogen receptor expression status

		E.cadherin status		Total
		Positive	negative	
Estrogen	positive	15	2	17
	Negative	15	5	20
Total		30	7	37

Discussion

Breast cancer comprises a heterogeneous group of diseases with regard to presentation, morphology, biological characteristics, clinical behavior, and response to therapy(11,12).The immunohistochemical staining of paraffin sections using antibody panels has been shown to

be a reliable surrogate for the molecular classification of invasive breast cancers through gene expression profiling studies, and the association between loss of E.cadherin and development of breast cancer has been extensively studied but the results had variable findings.

-In the current study Our data showed 81% of the invasive carcinoma had positive E.cadherin staining and this results are close to those of Howard et al[4] which their study demonstrated 84% of E.cadherin positively in invasive ductal carcinomas cases, but less than those of Molle et al which demonstrated 97% positivity[5].

-All of lobular carcinomas were negative for E.cadherin expression, which is consistent with most of the published data, Moll R,[5], Gamelloc[6].

-Other type of carcinomas (medullary carcinoma, papillary carcinomas, and metablastic carcinoma) had positive E.cadherin expression. In our study E.cadherin expressions not correlate with expression of estrogen receptor, and this is support those of ASC et al [7] and Lipponen et al [8]]; which they found no correlation between the loss of E.cadherin and other prognostic parameters as ER. But our against those of Siitonen SM,et al[9] and Oka H,et al[10]; which their results indicated loss of E.cadherin was associated significantly with ER status.

Conclusion

According to these findings we conclude that there is no correlation was found between loss of E.cadherin and expression of estrogen receptor.

Acknowledgments

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