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ORIGINAL RESEARCH

Vimentin expression in Invasive Ductal carcinoma- A tertiary care hospital study

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Abstract

Introduction: Breast cancer is the most common malignant tumor and leading cause in carcinoma deaths in women, with more than 2 lakh cases occurring worldwide annually. Vimentin is a 57 kDa intermediate filament protein, which forms a part of cytoskeleton. Vimentin is expressed in mesenchymal origin of cells and also expressed in epithelial cells undergoing EMT under both pathological and physiological situations.Aim of this study is to determine the expression of vimentin in breast carcinomaand correlate with patient age, histologic grade and type and lymphnode status.

Material and method: This was a cross sectional, retrospective study done in National Institute of Medical sciences and Research, Jaipur from March 2020 to November 2021. We included 70 cases of mastectomy specimen of Invasive duct carcinoma of breast received in Department of Pathology. Immunohistochemical analysis of vimentin expression was done with clincopathological correlation.

Result: Majority of the cases were in age grow was of 35-44 years. Youngest patient in this study was 26 years old and oldest was 85 years.

The result of Mann whitney U test and chi square test shows no correlation between age and vimentin expression.

Conclusion: Vimentin expression is strongly associated with poor prognostic factors of invasive ductal carcinoma. Hence we concluded that expression of vimentin is a potent indicator of biologically aggressive tumors. Discovery of drug, WFA (Withaferin A) that binds and inhibits vimentin can play a major role in preventing cancer cell growth.

Keywords: Invasive ductal carcinoma, Vimentin, Lymphnode, histological grade.

Introduction

Breast cancer is the most common malignant tumor and leading cause in carcinoma deaths in women, with more than 2 lakh cases occurring worldwide annually.[1] There is evidence that breast cancer is associated with exposure to hormones, late menopause, early menarche and hormone replacement therapy.[2] Immunohistochemistry assessment based on hormone receptor expression and Her2neu oncoprotein expression is now being widely used to delineate surrogate luminal, her-2 and basal like immunophenotypes.[3]

Epithelial to mesenchymal transition (EMT) is a key point in the progression of cancer metastasis. EMT is a critical process in which epithelial cells lose their apical basal polarity, cell-cell contacts and transdifferntiate into fibroblastic migratory cells with mesenchymal characteristics. Vimentin is a 57 kDa intermediate filament protein, which forms a part of

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cytoskeleton. Vimentin is expressed in mesenchymal origin of cells and also expressed in epithelial cells undergoing EMT under both pathological and physiological situations.[4]
Upragulation of vimentin, slug, snail, twist, H-ras is responsible for EMT.[5] Vimentin is one of the important marker of EMT and a requisite regulator of mesenchymal cell migration.[6] In breast carcinoma, it is known to be expressed significantly in high grade infiltrating ductal carcinoma, medullary carcinoma but not in lobular carcinoma in breast.[7]it is associated with low ER, low PR, increase basement membrane invasiveness and drug resistance.[8,9,10]
Its expression is identified as a marker of basal like breast cancer cells that may represent the clinical triple negative tumor associated with a poor prognosis.[11]the mechanism underlying the functional contribution of vimentin to epithelial cell migration remains unclear. However, it is not known whether it functionally contributes to the gene expression pattern responsible for EMT phenotype or whether its expression is merely a result of EMT.[12]
Aim of this study is to determine the expression of vimentin in breast carcinomaand correlate with patient age, histologic grade and type and lymphnode status.

Methods and materials
This was a cross sectional , retrospective study done in National Institute of Medical sciences and Research, Jaipur from March 2020 to November 2021. We included 70 cases of mastectomy specimen of Invasive duct carcinoma of breast received in Department of Pathology. Immunohistochemical analysis of vimentin expression was done with clincopathological correlation.

Inclusion criteria
1. All mastectomy cases diagnosed as invasive duct carcinoma of breast during study period

Exclusion criteria
1. Inadequate sample
2. Male breast
3. Paget's disease
4. Mesenchymal tumor
5. Patients not giving their consent

In this study, we received properly labeled mastectomy specimen that were preserved in 10% formalin, sent with patient's history and proper clinical details on requisition form.
Following adequate fixation for about 12-24 hours, the representative tissue sections were submitted for routine processing, following which the paraffin embedded serial sections of 3-4 microns thickness were obtained. These were stained with hematoxylin and eosin stain and immunohistochemistry of vimentin was applied thereafter. Vimentin is expressed as distinct granular positivity. Five hundred cells were counted in an area of maximum vimentin positivity and score of >10% was considered as significant. Less than <10% staining was taken as negative. Stromal cells expressing vimentin served as internal control.
The collected data were transferred into variable, coded and entered in Microsoft excel. Data was analysed and statistically evaluated using SPSS-PC-17 version.

Result
Table 1: distribution of cases according to age of patients (number=70)

Age	Frequency	Percentage
25-34 years	7	10
35-44 years	20	28.5
45-54 years	16	23.3
55-65 years	15	21.7

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65 years and above	12	16.7
Total	70	100

Majority of the cases were in age grow was of 35-44 years. Youngest patient in this study was 26 years old and oldest was 85 years.

Table 2: distribution of cases according to histological grade (n=70)

Histological grdae	Frequency	Percentage
Grade 1	14	20
Grade 2	26	36.7
Grade 3	30	43.3
Total	70	100

Table 3: distribution of cases according to lymphovascular status (n=70)

Lymphovascular invasion	Frequency	Percentage
Absent	48	68.3
Present	22	31.7
Total	70	100

Table 4: distribution of cases according to Vimentin expression (n=70)

Vimentin	Frequency	Percentage
Negative	39	55
Positive	31	45
Total	70	100

Total 5: Relationship between vimentin expression and age

vimentin expression	Positive (31)	Negative (39)	Test statistic	P-value
Age (Mean±SD)	52.38±11.91	53.28±14.32	528	0.906

The result of Mann whitney U test and chi square test shows no correlation between age and vimentin expression.

Table 6: relationship between vimentin expression and histological grade (n=70)

Histological grade	Vimentin positive		Total	Fisher's exact statistics	p-value
	Negative	Positive			
1	13 (91.7%)	1 (8.3%)	14(100%)	32.11	0.001
2	21 (81.8%)	5 (18.2%)	26 (100%)		
3	5 (15.4%)	25(84.6%)	30 (100%)		
Total	39	31	70		

The result of Fisher's exact test shows positive correlation between histological grade and vimentin expression.

Table 7: relationship between vimentin expression and lymphovascular invasion (n=70)

Lymphovascular invasion	Vimentin positive		Total	Chi-square statistic	P-value
	Negative	Positive		10.23	0.005
Absent	33 (68.3%)	15 (31/7%)	48(100%)		
Present	6 (26.3%)	16 (73.7%)	22(100%)		
Total	39	31	70		

The result of Chi-square test shows positive correlation between lymphovascular invasion and vimentin expression.

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Discussion

This study was conducted in National Institute of Medical sciences from march 2020 to November 2021. 70 modified radical mastectomy specimens reported as Invasive ductal carcinoma were taken.

In our study 45% of cases showed vimentin positivity. This is consistent with findings of other previous studied in which the range of vimentin expression varies from 45% to 57%.[13,14,15,16] Majority of studied considered vimentin expression in at least 10% of tumor cells to be significant. Some studies like Khillare et al[17] and Elzamly et al[18] demonstrated higher percentage of vimentin positivity as they considered tumors to be vimentin positive irrespective of the percentage of cells, i.e. even <10%. They showed 75.7% and 91.3% positivity respectively.

No significant correlation was found between vimentin expression and the patient's age at presentation in our study (p value- 0.806). It is accordance with the studied done by Hemalatha et al[19](p value- 0.52) and Vora et al[14](p value- 0.67)which showed no association between the two. Similar results were seen in other studied done by Niveditah et al[8] (p value- >0.05) and Khillare et al[17]. (p value- 0.08) . Contrary to this Kusinka et al[20] found a significant correlation between age of the patient and vimentin expression(p value- 0.024). Another study done by Yamashita et al[21] also showed correlation between these two (p value- 0.016).

In our study, significant correlation was found between positive vimentin expression and histological grade of tumor (p value-0.001). Our findings are accordance with Kusinka et al[20], Raymond et al[15], Hemalatha et al[19], Domogala et al[22], Sheshadri et al[23] and Korsching et al[24]. But Khillare et al[17] could not derive a significant correlation in between these two variables and showed that increase expression of vimentin is associated with increase histological grade.

In the present study, significant correlation was found between vimentin expression and the presence of lymphovascular invasion (p value- 0.005). these findings are accordance with study done by Khillare et al[17] (p value- 0.04). however studied done by Wang et al[25] (p value- 0.09) and Lakhtakia et al[26] (p value- 0.066) showed no correlation between the two. A significant positive correlation of vimentin expression with lymphovascular invasion reflects the fact that vimentin is expressed when there is epithelial to Mesenchymal transition. Its increase expression denotes more chances of lymphovascular invasion thus leading to widespread and aggressive disease.

Conclusion

Vimentin expression is strongly associated with poor prognostic factors of invasive ductal carcinoma. Hence we concluded that expression of vimentin is a potent indicator of biologically aggressive tumors. Discovery of drug, WFA (Withaferin A) that binds and inhibits vimentin can play a major role in preventing cancer cell growth.

Conflict of interest

None

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None

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