Section: Miscellaneous

Original Research Article

A STUDY ON THE DIAGNOSTIC UTILITY OF TRPS1 EXPRESSION IN TRIPLE-NEGATIVE BREAST CANCERS

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ABSTRACT

Background: Trichorhinophalangeal syndrome type 1 (TRPS1) encodes a novel nuclear transcription factor, belonging to the GATA family. It is a recently identified IHC marker and is more sensitive and specific than the other breast-specific markers. The aim and objective is to understand the prevalence and potential role of TRPS1 protein expression in triple-negative breast tumors. To evaluate the diagnostic utility of TRPS1 in comparison with GATA3.To assess the impact of TRPS1 on histopathological parameters in triple-negative breast carcinomas. **Materials and Methods:** This was a study done in the pathology department in the last 3 years. A total of 15 triple-negative breast carcinoma cases were included in the study. All the relevant clinical and histopathological data were retrieved from the records. Immunohistochemical markers TRPS1 and GATA3 were used in all 15 cases. **Result:** In this study, 53% of cases were seen in age >50 years, and the left breast was involved in 60%. The typical histological type was Invasive ductal carcinoma (67%), grade 3 (60%), and lymphovascular invasion (LVI) was absent in 53% of cases. The ROC curve analyzed TRPS1 (p-value of < 0.05) as a highly sensitive and specific marker than GATA3 (p=0.7). TRPS1 correlated with the grade of the tumor with a significant p-value of 0.04. **Conclusion:** TRPS1 is a highly sensitive and specific marker to confirm breast origin and can be used as a diagnostic tool, especially for Triple Negative Breast Carcinomas.

INTRODUCTION

Triple-negative breast cancer (TNBC) can pose a diagnostic challenge because it may show both nonspecific morphological features and immunostain profiles.[1] Breast cancer is the most common cancer in females (38.8%) and is categorized into 4 types based on molecular classification.[1] Breast cancer is considered a heterogeneous group of diseases with highly variable clinical behavior.[1] Since TNBC is an aggressive tumor with a worse prognosis and a high tendency to relapse, accurate diagnosis is essential for optimal treatment.[2] Immunohistochemistry is used to identify primary breast in occult nodal metastases and to differentiate primary breast carcinomas against metastatic tumors to the breast.[3] Unlike ER, PR, and Her2neu positive breast cancer cases, where these IHCs may help to confirm breast primary, triple-negative breast cancers require other breast-specific markers like GATA3 (70-90%), mammaglobin (50-80%), and GCDFP15 (15-40%).[4] However, studies showed that these markers were not highly sensitive for use in TNBCs, hence, a search for a better IHC marker was initiated. Subsequently, trichorhinophalangeal syndrome type 1 (TRPS1), a novel nuclear transcription factor belonging to the GATA family, was identified and studied for its relevance in breast-specificity. It is expressed in normal mammary epithelial cells and also retained in cells that undergo malignant transformation.[5]

The study aims to understand the prevalence of TRPS1 protein expression in triple-negative breast tumors and elucidate the diagnostic utility of TRPS1 in comparison with GATA3. To assess the impact of TRPS1 on clinicopathological parameters in triple-negative breast carcinomas.

MATERIALS AND METHODS

This is a cross-sectional study done in the Pathology department for 2 years. A total of 15 Triple-negative breast Carcinoma cases diagnosed in mastectomy specimens were included in the study. All the relevant clinical and histopathological data were

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obtained. The IHC markers ER, PR, and Her2 neu negativity were checked. IHC markers TRPS1 and GATA3 were used in all 15 cases.

The Immunoreactivity scores of TRPS1 (ZR382/Rabbit/monoclonal from zeta corporation) were calculated by multiplying the score representing % of immunoreactive cells (0, <1%; 1, 1-10%; 2, 11-50%; 3, 51-100%) with the number representing staining intensity (0, negative; 1, weak; 2, moderate; 3, strong). The Immunoreactivity scores were considered negative (0-1), low positive (2), intermediate positive (3-4), and high positive (6-9).

The distribution of GATA3 (L50-823, Cell morque, Rockin, CA) was recorded as negative if < 5% of tumor cells showed nuclear staining and positive if >5% of tumor cells showed nuclear staining.

The data collected was expressed in percentage, and a comparison of TRPS1 and GATA3 was done using ROC curve analysis, the p-value was calculated, and <= 0.05 was considered significant.

Inclusion Criteria

All TNBC cases diagnosed on mastectomy specimens were included in the study

Exclusion Criteria

TNBC core needle biopsies/lumpectomy specimens and those with insufficient clinical/pathological data were excluded.

RESULTS

The clinicopathological characteristics have been tabulated in [Table 1].

Table 1: Clinicopathological characteristics of Triple negative breast carcinomas.

Parameter	Total number of cases (%)
Age(yrs)	
<50	7 (47%)
>50	8 (53%)
Multiplicity	
Multifocal	1 (7%)
unifocal	14 (93%)
Tumor size	
<2cm	2 (14%)
2-5cm	5 (33%)
>5cm	8 (53%)
Laterality	
Right	6 (40%)
left	9 (60%)
Histological grades	
Grade 1	1(7%)
Grade 2	5 (33%)
Grade 3	9 (60%)
Histological Types	
Invasive carcinoma (NST)	10 (67%)
Medullary carcinoma	2 (13%)
Invasive lobular carcinoma	2 (13%)
Metaplastic carcinoma	1 (7%)
Lymph nodal metastasis	
N0	8 (53%)
N1	2 (13%)
N2	2 (13%)
N3	3 (20%)

In this study, we investigated the immunohistochemical marker expression of TRPS1 and GATA3 in triple-negative breast carcinomas.

The diagnostic values of TRPS1 and GATA3 were evaluated for each case and tabulated in [Tables 2 and 3].

Table 2: Distribution of GATA3 and TRPS1 positive cases in the current study

IHC Marker	Number of cases	positive	Negative
GATA3	15	5 (33%)	10 (67%)
TRPS1	15	12 (80%)	3 (20%)

Table 3: Expression of TRPS1 and GATA3 in different histological types

Histological type	Number of cases	TRPS 1	GATA 3
Medullary carcinoma	2	+	+
Metaplastic carcinoma	1	+	-
Lobular carcinoma	1	+	+
	1	-	-
Invasive carcinoma of no special type	2	-	-
	2	+	+
	6	+	-

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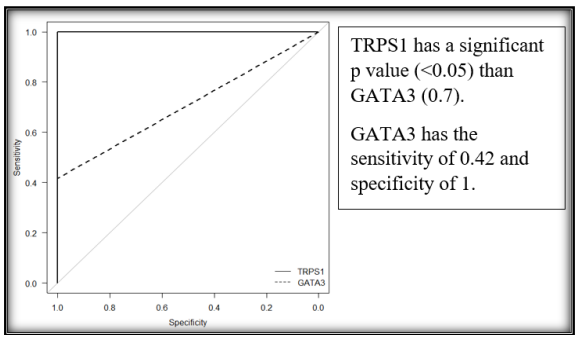

Figure 1: The comparative area under curve for TRPS1 and GATA3

To compare the sensitivity of TRPS1 with GATA3 Area under the curve was calculated which showed a significant p-value of <0.05 thus concluding that TRPS1 is a more sensitive marker than GATA3.
In this study, we compared the expression of TRPS1 with pathological parameters of breast carcinoma. There was a significant p-value with histological grade (0.04), and it is insignificant with tumor size, lymphovascular invasion, and pT stage, as shown in [Table 4].

Table 4: Fisher Exact Test Results

Parameter	TRPS1 positive	TRPS1 negative	P Value
Size			
<2 cms	2	0	0.98
2-5 cms	5	1	
>5 cms	5	2	
Histological Grade			
1	0	1	0.044
2	3	2	
3	9	0	
LVI			
Present	5	2	0.076
Absent	7	1	
pT stage			
T1	2	0	1.00
T2	4	1	
T3	5	2	
T4	1	0	

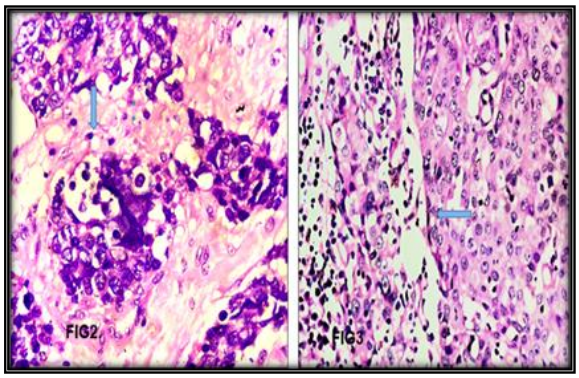

Figure 2: shows ductal carcinoma with tumor cells in nests H&E 400x, Figure 3: shows medullary patterns with tumor cells in syncytial sheets & lymphocytic infiltration H&E 200x

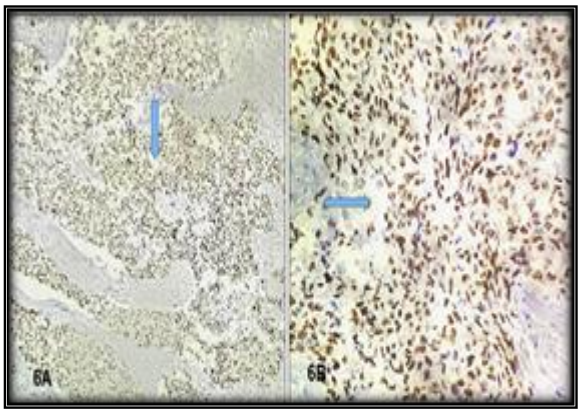

Figure 6: TRPS1 positivity invasive
A. Trps1: nuclear staining in the tumors cells:100x
B. Trps1: nuclear staining in the tumors cells: 400x

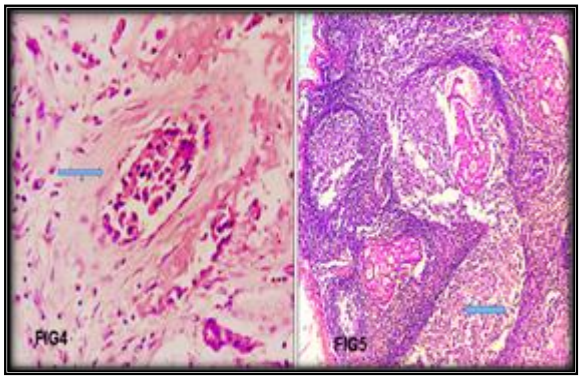

Figure 4: shows lymphovascular invasion H&E 400x, Figure 5: shows lymph node with metastatic deposits H&E 100x

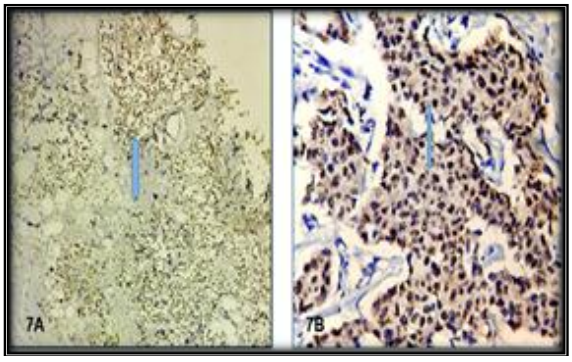

Figure 7: GATA3 positivity, A. Gata3: positive nuclear staining in >5% of tumor cells : 100x, B. Gata3: positive nuclear staining in >5% of tumor cells : 400x

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DISCUSSION

TNBC is classified into 6 tumor-specific subtypes by gene expression profiling, including basal-like 1, basal-like 2, immunomodulatory, mesenchymal, mesenchymal stem-like, and luminal AR subtypes.[6] Most TNBCs are basal types of IBCs.

TRPS1 is a breast lineage biomarker and is highly expressed in both ER luminal and TN/basal types of breast carcinoma, as shown in previous studies.[7] On the contrary, GATA3 involves breast luminal differentiation and is a luminal cell marker, mainly expressed in luminal A and B types of IBC, but not in TN/basal-like IBC.[8] Therefore the sensitivity of TRPS1 I TNBC is better than that of GATA3 because more than 90%of TNBCs are positive for TRPS1 and almost all GATA3 negative TNBCs are positive for TRPS1.

In the present study, 8 out of 15 cases (53%) were more than 50 years, which is in contrast to the study done by Elaiffy et al, [1] in which all 70[100%] cases were>50 yrs., and 9[60%] cases showed left breast involvement, which is in contrast to the study done by Elaiffy et al,[1] i.e., 37[53%] cases.

In the present study, 8 [53%] cases showed the size of the tumor to be >5cms which is in contrast to the study done by Elaiffy et al,[1] in which 53[75.7%] cases showed < 2 cm. Ten [67%] cases showed invasive carcinoma NST(fig 2) which is in contrast to the study done by Elaiffy et al i.e, 31[45%] cases and 9 [63%] cases showed grade 3, which in contrast to the study done by Elaiffy et al,[1] i.e, 25[35.7%]cases. Two cases (14%) showed medullary carcinoma (fig 3) which was in contrast to the study done by Joshua W Lui et al [10], i.e.,49 cases(2.5%).

In our study, a p-value of TRPS1 is 0.00008 which is in contrast to the study done by Nadia E. Elafify et al,[1] and Ai et al[constituting p=0.0000 and p=,0.0001 respectively. TRPS1 sensitivity is 80%, which is in contrast to the study done by Nadia E. Elafify et al,[1] Lennarte et al,[3] and Ai et al,[2] which are 93%,77%, and 86% respectively.

In the present study, GATA 3 sensitivity is 42%which is in contrast to the study done by Nadia E. Elafify et al,[1] Lennartz et al,[3] & Ai et al,[2] constituting 80%,55%, and 51% respectively.

In the present study,7(47%) out of 15 cases showed lymphovascular invasion(fig 4) which is in contrast to the study done by Nadia E. Elafify et al,[1] i.e, 44 cases(62.9%).out of 15 cases in the present study,8 (53%)cases showed N0,2(13%) cases showed N1,2 (13%) showed N2(lymph node metastasis) [Figure 5], 3 (20%) cases showed N3 which is in contrast to the study done by Nadia E. Elafify et al,[1] i.e,29 cases(41.4%) showed N0,10(14.3%)cases showed N1,17 cases (24.3%) showed N2,15 cases(20%) showed N3.

TRPS1 has a diagnostic sensitivity of 100% in TNBC and is higher than the sensitivity of TNBCs that are positive for GATA3. In addition to a much higher diagnostic sensitivity in detecting TNBC, TRPS1 is a more robust immunostaining marker than GATA3, with diffuse and strong nuclear staining in most of the positive cases. In contrast, GATA3-positive cases tend to show intermediate to weak nuclear staining.[9]

In our study, TRPS1(fig 6) showed diffuse positivity in (12/15) cases which are 80%, GATA3 [Figure 7] was positive in (10/15 cases) at 67% whereas in the study done by Terrance J.Lynn et al,[9] s TRPS1 positivity (35/35) was 100% and GATA 3 positivity(27/35) was 77%.

In a total of 15 cases of TNBCs with data on TRPS1 expression, 12 cases (80%) were TRPS1 positive for the remaining 3 cases (20%) were negative. GATA3 was positive in 10 cases (67%), so an additional 2 cases were positive for TRPS1.

Three cases were negative for both breast markers. They were grade 3 with necrosis, less differentiated, and more aggressive. We should be aware of the lack of expression for breast-specific markers.

In our study, TRPS1 is a more highly sensitive marker than GATA3 which is similar to the study conducted by, Di Ai et al.[2]

CONCLUSION

The study demonstrates that TRPS1 is a highly reliable marker to confirm breast primary in triple-negative carcinomas of the breast, surpassing the current widely used GATA3. Given its performance, TRPS1 could be considered a vital marker to confirm breast primary nodal metastasis of unknown origin.

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