SSR Institute of International Journal of Life Sciences
ISSN (O): 2581-8740 | ISSN (P): 2581-8732
Sachdeva *et al.*, 2025
doi: 10.21276/SSR-IIJLS.2025.11.1.36

Original Article

open access

Correlation of Calretinin Immunostaining with Molecular Subtypes and Clinicopathological Parameters in Breast Carcinoma

Vartika Sachdeva[1]*, Karan Chhabra[2], Swati chhabra[3], Anuradha Kusum[4], Neena Chauhan[5], Sunil Saini[6]

[1]Senior Resident, Department of Pathology, GB Pant Hospital GIPMER, New Delhi, India
[2]Associate Consultant, Department of Gastroenterology, Fortis Hospital, Shalimar Bagh, New Delhi, India
[3]Principal, SKS College of Pharmacy, Kurukshetra, India
[4]Professor and Head, Department of Pathology, Himalayan Institute of Medical Sciences, Dehradun, Uttarakhand, India
[5]Professor, Department of Pathology, Himalayan Institute of Medical Sciences, Dehradun, Uttarakhand, India
[6]Professor, Department of Surgery, Himalayan Institute of Medical Sciences, Dehradun, Uttarakhand, India

***Address for Correspondence:** Dr. Vartika Sachdeva, Senior Resident, Department of Pathology, GB Pant Hospital GIPMER, New Delhi, India
E-mail: drvartikasachdeva19@gmail.com

Received: 06 Aug 2024/ Revised: 05 Oct 2024/ Accepted: 08 Dec 2024

ABSTRACT

Background: Breast cancer is one of the most predominant malignancies worldwide, with diverse molecular subtypes influencing prognosis and treatment approaches. This study evaluated Calretinin expression in invasive breast carcinoma and its correlation with molecular subtypes and clinicopathological parameters.

Methods: This study was an observational, cross-sectional study at the Himalayan Institute of Medical Sciences, where tissue samples from 96 patients were analyzed through histopathological and immunohistochemical evaluation. Calretinin expression was assessed using a scoring system based on nuclear and/or cytoplasmic staining intensity and the percentage of positive tumor cells.

Results: The results exposed significant variation in Calretinin expression across different molecular subtypes (p=0.000). Luminal A and HER2-enriched subtypes showed predominantly low expression, whereas Triple Negative Breast Cancer showed the highest levels, with 71% of cases demonstrating moderate-to-high expression. A significant correlation was also observed between Calretinin expression and histological tumor grade (p =0.000), with high expression levels more frequently associated with Grade III tumors.

Conclusion: Calretinin could serve as a possible biomarker for aggressive breast cancer subtypes, predominantly TNBC. Its association with high tumor grade and proliferation indices designates a possible role in tumor progression, the importance of its prognostic and diagnostic significance. Additional studies are required to establish its potential use in therapeutic decision-making.

Key-words: Calretinin, Immunohistochemistry, Molecular Subtypes, Triple Negative Breast Cancer, Biomarker, Prognostic Marker, Histopathology

INTRODUCTION

Breast cancer is a malignant neoplasm originating from the epithelial cells of the breast and stands as the most frequently diagnosed cancer among women globally. The disease represents a serious public health issue, owing to its growing incidence and high mortality rates. The development of breast cancer involves a multifactorial etiology, shaped by the interaction of environmental exposures, lifestyle practices, and hereditary predispositions [1,2]. Among genetic contributors, mutations in the BRCA1 and BRCA2 genes are particularly significant, substantially elevating the risk of breast cancer development. A strong correlation has also been found between family history and breast cancer risk, as individuals with affected relatives face a heightened likelihood of diagnosis [3]. I addition to

How to cite this article
Sachdeva V, Chhabra K, Chhabra S, Kusum A, Chauhan N, et al. Correlation of Calretinin Immunostaining with Molecular Subtypes and Clinicopathological Parameters in Breast Carcinoma. SSR Inst Int J Life Sci., 2025; 11(1): 6858-6865.

Access this article online
https://iijls.com/

crossref doi: 10.21276/SSR-IIJLS.2025.11.1.36

hereditary factors, several modifiable risk factors—such as advancing age, smoking, obesity, and alcohol intake—have been recognized as influential in breast cancer pathogenesis [4].

Social disparities further compound challenges related to breast cancer diagnosis and management, especially among marginalized populations. Studies have revealed that awareness about breast cancer risk factors and early detection measures is considerably lower in certain groups, notably Black and African-American communities. Persistent myths, including the misconception that breast cancer predominantly affects white women, lead to delayed screenings and treatments, contributing to poorer outcomes [2]. Therefore, targeted public health campaigns focusing on education and awareness are critical to lowering breast cancer incidence and improving prognosis within these underserved populations [2,5].

Additionally, demographic changes and urbanization trends have fueled a rise in breast cancer incidence in low- and middle-income countries. Contributing factors include shifting reproductive behaviors, evolving dietary habits, and increased life expectancy, all of which have been linked to greater susceptibility to the disease in these regions [5].

Breast cancer is categorized into several molecular subtypes that hold significant prognostic and therapeutic implications. The primary subtypes include Luminal A, Luminal B, HER2-enriched, and Triple-negative breast cancer (TNBC), each defined by distinct biological features that affect clinical outcomes and treatment strategies [6,7]. Luminal A tumors, characterized by estrogen receptor (ER) and/or progesterone receptor (PR) positivity along with low HER2 expression, are the least aggressive and are highly responsive to endocrine therapy, correlating with better survival rates [6,8]. Luminal B tumors, while also hormone receptor-positive, exhibit higher proliferation rates and a poorer prognosis compared to Luminal A, with reduced sensitivity to hormone therapies [7].

HER2-enriched breast cancers demonstrate HER2 protein overexpression and are associated with a more aggressive clinical course. Despite this, targeted therapies such as trastuzumab (Herceptin) have markedly improved the outcomes for patients with HER2-positive tumors, although these tumors continue to present a lower survival rate than Luminal subtypes [9,10].

Triple-negative breast cancer, lacking ER, PR, and HER2 expression, remains the most aggressive and therapeutically challenging subtype. TNBC is more commonly diagnosed in younger women and is marked by an increased propensity for metastasis and a poor overall prognosis. Current treatments are largely limited to chemotherapy, although emerging research is focused on advancing immunotherapies and novel targeted agents to improve TNBC management [7,8].

Molecular subtyping not only guides treatment decisions but also provides valuable prognostic information. Consistent evidence suggests that hormone receptor-positive tumors carry a more favorable outlook compared to triple-negative cancers [6-10].

Recent research has explored the potential of calretinin, a calcium-binding protein of the S100 family, as a biomarker for breast cancer, particularly within aggressive basal-like subtypes. Hou et al. identified a significant association between elevated calretinin expression and poor prognosis in basal-like breast carcinomas [11]. Similarly, Jones et al. found calretinin positivity in approximately 67% of basal-like tumors [13]. Furthermore, Jassim et al. reported that high calretinin expression correlates with elevated Ki-67 levels, reinforcing its link to increased tumor proliferation and aggressiveness [12].

Although calretinin expression is more prevalent in basal-like breast cancers, studies report varied overall expression rates in breast cancer patients, ranging from 14.5% to 32% [13]. While calretinin shows promise as a diagnostic and prognostic marker, its known expression in other malignancies, such as mesotheliomas, necessitates careful pathological evaluation to ensure diagnostic accuracy [14].

MATERIALS AND METHODS

Research Design- This observational, cross-sectional study was conducted in the Department of Pathology at the Himalayan Institute of Medical Sciences, Swami Rama Himalayan University, Dehradun. The study aimed to assess Calretinin expression in cases of invasive breast carcinoma diagnosed at the institution. Conducted over one year, it included all eligible cases. Ethical approval was obtained from the Institutional Ethics Committee, and written informed consent was secured from all

doi: 10.21276/SSR-IIJLS.2025.11.1.36

participants. A significant difference determined the sample size of 96 to ensure adequate analytical power. Physical examination, clinical data from local and systemic examinations, and radiological observations were documented using a structured case reporting form. The study analysed excisional biopsies and mastectomy specimens submitted by referring surgeons. The samples were fixed in 10% buffered formalin to maintain morphological integrity. Smaller biopsy specimens were fixed overnight, while larger mastectomy specimens required fixation for up to three days, depending on size. Specimen grossing followed standard departmental protocols, including sectioning of tumor tissue, surgical margins, and lymph nodes. Gross findings were recorded before tissue processing.

Tissue processing was done using an automated tissue processor. Samples underwent dehydration through graded alcohols, clearing in xylene, and paraffin embedding. Paraffin blocks were prepared, and sections of 4-5 µm thickness were cut using a microtome. Sections were stained with hematoxylin and eosin to evaluate the morphological features of invasive breast carcinoma. Immunohistochemical analysis was performed for Calretinin, ER, PR, Ki67, and Her-2 neu markers. The staining process involved deparaffinization, antigen retrieval using a microwave technique, blocking of endogenous peroxidase activity, and incubation with primary monoclonal antibodies. A polymer-based detection system with horseradish peroxidase was used for signal amplification, with 3,3'-diaminobenzidine tetrahydrochloride as the chromogen. Counterstaining was done with hematoxylin, followed by dehydration, clearing, and mounting in DPX. Calretinin immunostaining was assessed based on nuclear and/or cytoplasmic staining. A combined scoring system considered the percentage of positive tumor cells and staining intensity. The final score ranged from 0 to 9, with higher scores indicating stronger expression. Cases were classified into low expression (score 0-2) and high expression (score 3-9) groups based on staining intensity and distribution.

Inclusion Criteria

- All diagnosed patients with invasive breast carcinoma at the institution were included in the study.

Exclusion Criteria

- Benign or in situ/intraductal breast carcinoma was diagnosed in patients.
- Chemotherapy or radiotherapy patients diagnosed with the study were excluded.

Statistical Analysis- Statistical analysis was conducted using SPSS software (version 23) and Microsoft Excel. The collected data were analyzed and presented through tables, bar charts, and pie diagrams. Categorical variables were expressed as frequencies, while continuous variables were represented as mean ± standard deviation or median, as appropriate. The significance of categorical variables was evaluated using Pearson's chi-square test, with a $p<0.05$ considered statistically significant. These statistical methods were used to identify key relationships and trends in Calretinin expression and its correlation with various clinicopathological parameters.

RESULTS

The breast-related conditions are most common in middle-aged individuals, with the highest prevalence in the 41-50 age group (34%), followed by the 61-70 age group (20%). The occurrence decreases suggestively in older individuals, with only 2% of cases in patients above 80. The majority of patients (88%) presented with a lump as their only complaint, while 9% had both pain and a lump, and 3% qualified a lump with nipple discharge. Most breast lumps are painless, which may delay early detection without regular screening. Regarding the location of breast lumps, the upper outer quadrant was the most affected (47%), followed by the upper inner quadrant (20%). The lower outer and inner quadrants accounted for 17% and 12% of cases, respectively, while the sub-areolar region and cases involving all quadrants were the least frequent. The prevalence of lumps in the upper outer quadrant parallels known breast cancer patterns, as this region contains a higher concentration of glandular tissue (Table 1).

In Grade I tumours, the majority (60%) had a Calretinin score of 3-6, with 20% each in scores 0 and 1-2, and no cases in the highest category (7-9). Grade II tumours had a broader distribution, with the highest proportion (39%) in the 1-2 score range, followed by 33% in score 0, 18% in 3-6, and 10% in 7-9. Grade III tumours showed a comparatively even spread, with 44% in scores 1-2, 33%

doi: 10.21276/SSR-IIJLS.2025.11.1.36

in 3-6, 11% in score 0, and 11% in 7-9. Overall, most cases (39%) fell within the 1-2 score range, followed by 30% in score 0, 22% in 3-6, and 9% in 7-9. The significant differences in p (0.000) correlation between histological grade and Calretinin expression represent that Calretinin levels vary significantly across tumour grades (Table 2).

Table 1: Age Distribution, Symptoms, and Quadrant Involvement in the pattern of Breast Lump

Age group (years)	Number of Patients	Percentage (%)
31 - 40	19	9%
41- 50	33	34%
51 - 60	18	18%
61 - 70	20	20%
71 - 80	4	4%
>80	2	2%
Total	96	100%
Complaint		
Pain and Lump	9	9%
Lump and Nipple discharge	3	3%
Lump only	84	88%
Total	96	100
Quadrant of the breast		
Upper Outer	45	47
Upper Inner	19	20
Lower Outer	17	17
Lower Inner	11	12
Sub-aerolar	1	1
All quadrants	3	3
Total	96	100

Table 2: Comparison between Calretinin Expression and Grade

Grade	Calretinin					
	Score 0	Score 1-2	Score 3-6	Score 7-9	Total	p-value
Grade I	1 (20%)	1 (20%)	3 (60%)	0 (0%)	5	P=0.000
Grade II	27 (33%)	32 (39%)	15 (18%)	8 (10%)	82	
Grade III	1 (11%)	4 (44%)	3 (33%)	1 (11%)	9	
Total	29 (30%)	37 (39%)	21 (22%)	9 (9%)	96	

The analysis of Calretinin expression across different molecular classifications of breast cancer exposes significant differences, as indicated by the ANOVA test (F=12.2, p=0.000). Calretinin expression is predominantly low in Luminal A and HER2 Neu subtypes, with 86% and 88% of cases, showing low expression scores (0-2), and no cases showing high expression (7-9). Luminal B shows a to some extent higher Calretinin expression, with 30% of cases falling into the moderate-to-high category (3-9), though high expression remains rare (3%). In difference, Triple Negative Breast Cancer proves a distinct pattern, with 71% of cases showing moderate-to-high Calretinin expression, including 38% with high expression. This significant association proposes that Calretinin is more often expressed in TNBC than other subtypes. The statistical significance of these results supports the potential role of Calretinin as a biomarker for TNBC, which could have diagnostic or therapeutic inferences in this aggressive breast cancer subtype (Table 3).

doi: 10.21276/SSR-IIJLS.2025.11.1.36

Table 3: Comparison between Calretinin Expression and Molecular classification

	Calretinin					
Molecular classification	**Score 0**	**Score 1-2**	**Score 3-6**	**Score 7-9**	**Grand Total**	**p-value**
Luminal A	8 (36%)	11 (50%)	3 (14%)	0 (0%)	22	ANOVA test F=12.2 p-value=0.000 (S)
Luminal B	7 (24%)	13 (44%)	8 (27%)	1 (3%)	29	
HER 2 NEU type	9 (38%)	12 (50%)	3 (13%)	0 (0%)	24	
Triple-negative	5 (24%)	1 (5%)	7 (33%)	8 (38%)	21	
Total	29 (30%)	37 (39%)	16 (17%)	9 (9%)	96	

DISCUSSION

Calretinin expression in breast carcinoma has been studied, and there are significant correlations found between calretinin immunostaining and other molecular subtypes of the cancer. Calretinin, being a calcium-binding protein, is a candidate biomarker, most notably for aggressive forms of tumor, like basal-like subtype breast cancer. One of the key observations is that high expression levels of calretinin occur predominantly in basal-like breast cancers, which are poor prognosis and aggressive. No calretinin immunoreactivity was detected in invasive lobular, cribriform, or tubular carcinomas—subtypes that are frequently estrogen receptor-positive and of less aggressive potential Taliano *et al.* Conversely, calretinin was highly expressed in high-grade invasive ductal carcinomas, particularly in basal-like phenotypes where it was associated with poor clinical outcomes [15].

Also, in concurrence with these findings, Venugopal et al. explained that 68.4% of the basal-like subtype were highly positive for the expression of calretinin, concurring with increased levels of Ki-67, a proliferation marker. Such concurrence suggests that high levels of calretinin can serve as a marker of an aggressive clinical course. In their study, they observed that individual molecular subtypes had heterogeneous calretinin expression patterns, with the basal subtype having significantly higher positivity compared to other types [16].

Powell *et al.* also provided evidence to support these observations, with calretinin staining positivity in breast carcinomas varying significantly by subtype, and at 15% overall expression in breast carcinomas and up to 67% in basal-like cases. This is in support of the hypothesis that calretinin may be a valuable marker for identifying aggressive tumor types that would need more aggressive treatment interventions [17].

Finally, Aboobacker and Saldanha's study resonated with the same views, highlighting the role of calretinin in the discrimination of breast cancer subtypes. They reported no correlation between patient age and calretinin expression, highlighting its possible dependence on molecular properties over demographic properties. The results of this study on calretinin expression in breast carcinoma agree with and are an extension of previous research in the same area. Calretinin expression is highly correlated with some molecular subtypes of breast carcinoma, particularly the basal-like subtype, which is well known for its aggressive clinical characteristics. Moreover, the previous studies, for example, Aboobacker and Saldanha's research, indicated the quite low frequency of calretinin expression in breast carcinoma overall, with the positivity of calretinin showing in groups between 14.5% to 32% [1].

The studies conducted by Venugopal et al. proved that the high 68.4% of basal-like carcinomas had outstanding calretinin positivity, consistent with earlier studies exhibiting the same pattern Venugopal *et al.* [16]. For instance, Taliano *et al.* [15] also observed that elevated calretinin expression was predominantly observed in cases within the basal-like phenotype, under the assertion that calretinin is an aggressive tumor behavior biomarker [18-21]. In contrast, certain subtypes, particularly invasive lobular, tubular, and cribriform carcinomas, were noted to be consistently negative for calretinin. This is in line with findings by Sasaki *et al.* [19] who stated that such subtypes tend to be of low grade and tend to be estrogen receptor-positive, highlighting the feeling that calretinin is capable of differentiating between less virulent and more virulent subtypes of breast cancer. The reality that calretinin is present in high proportions in basal-like tumors suggests a specific

doi: 10.21276/SSR-IIJLS.2025.11.1.36

pathogenic role that can aid clinicians in prognosis estimation and treatment modalities [19].

Breast carcinoma research has clarified important associations between calretinin expression and many clinicopathological parameters, and these can have significant prognostic implications. Expression of calretinin is predominantly identified by aggressive histopathological characteristics of tumors, specifically with certain molecular subtypes of breast carcinoma, including the basal-like subtype [20].

One of the important among them is that calretinin expression and basal-like subtype of breast carcinoma have a strong correlation. Studies have shown that approximately 68.4% of basal-like cases presented with high calretinin expression [21]. This subtype is characteristically known for its aggressiveness, and the high level of calretinin expression statistically reflects higher proliferation indices, such as Ki-67 [17,20]. High calretinin levels may thus be a marker for a more aggressive presentation of the disease, which is of prognostic significance, with patients having calretinin-positive tumors having potentially worse overall survival [21].

Moreover, Vuoto *et al.* [22] also underlined the fact that intense expression of calretinin had a strong correlation with poor overall survival, particularly among basal-like patients of breast cancer. It is to be compared to other less aggressive types and identifies calretinin as a potential prognosticator. In addition, the study by Aboobacker and Saldanha reported that over half of the calretinin-positive individuals did not show estrogen receptor (ER) expression, adding to the evidence pointing towards calretinin in aggressive tumor features more usually associated with unfavorable hormonal receptor status [22]. This lack of ER expression, though statistically not significant, is in line with previous findings attributing the absence of hormone receptors to more aggressive disease phenotypes [23].

Besides, clinicopathological features such as the stage and grade of the tumor were also examined. Generally, more aggressive tumors have higher calretinin expression, and this implies that calretinin may be a great marker for clinicians to assess tumor aggressiveness and therefore tailor treatment. The fact that the expression of calretinin has been found to correlate with poor hormonal receptors and higher tumor grades implies a poor prognosis in tumor-positive patients [24].

CONCLUSIONS

This study establishes a significant association between Calretinin expression and breast cancer molecular subtypes, with the uppermost levels observed in Triple Negative Breast Cancer cases. In addition, a strong correlation between Calretinin expression and higher tumor grades recommends its potential role as a marker of aggressive tumor behavior. Given the statistical significance of these results, Calretinin may serve as a valuable biomarker for prognosis and therapeutic directing, chiefly in aggressive breast cancer subtypes. However, additional large-scale studies are needed to validate its clinical utility in guiding treatment approaches.

CONTRIBUTION OF AUTHORS

Research concept- Vartika Sachdeva
Research design- Karan Chhabra
Supervision- Anuradha Kusum
Materials- Swati chhabra
Data collection- Vartika Sachdeva
Data Analysis and Interpretation- Neena Chauhan
Literature search- Neena Chauhan
Writing Article- Vartika Sachdeva
Critical Review- Sunil Saini
Article Editing- Sunil Saini
Final Approval- Neena Chauhan

REFERENCES

[1] Aboobacker K, Saldanha P. Expression of mesothelial marker calretinin in breast cancer. Int J Innov Res Med Sci., 2019; 4: 21-31. doi: 10.23958/ijirms/vol04-i01/550.

[2] Allah M, Omar M, Youssef S. Evaluation of claudin-1 and ki-67 in different molecular subtypes of breast ductal carcinoma: immunohistochemical study. Med J Cairo Univ., 2019; 87: 517-26. doi: 10.21608/mjcu.2019.52416.

[3] Arafah M, Arain S, Raddaoui E, Tulba A, Alkhawaja F, Shedoukhy A. Molecular subtyping of mammary Paget's disease using immunohistochemistry. Saudi Med J., 2019; 40(5): 440-46. doi: 10.15537/smj.2019.5.23967.

[4] Arjmandzadeh E, Binesh F. Determination of relative frequency of calretinin expression in patients with breast cancer in Yazd, Iran. Chin J Med Res., 2020; 3(2): 37-40. doi: 10.37515/cjmr.091x.3202.

[5] Askan G, Basturk O. Expression of calretinin, marker of mesothelial differentiation, in pancreatic ductal adenocarcinoma: A potential diagnostic pitfall. Turk J Pathol., 2021; 37(2): 1-15. doi: 10.5146/tjpath.2020.01519.

[6] Chen CJ, Hang JF, Chen YA, Lin SJ, Chiu HM, et al. The diagnostic utility of trichorhinophalangeal syndrome type 1 immunohistochemistry for metastatic breast carcinoma in effusion cytology specimens. Cancer Cytopathol., 2023; 131(4): 226-33. doi: 10.1002/cncy.22663

[7] Dijkshoorn AB, van Stralen HE, Sloots M, Schagen SB, Visser-Meily JM, et al. Prevalence of cognitive impairment and change in patients with breast cancer: a systematic review of longitudinal studies. Psycho-Oncol., 2021; 30(5): 635-48.

[8] Franzoi MA, Agostinetto E, Perachino M, Del Mastro L, et al. Evidence-based approaches for the management of side-effects of adjuvant endocrine therapy in patients with breast cancer. Lancet Oncol., 2021; 22(7): 3-13.

[9] Gupta P, Naresh N, Agarwal L, Namdev S. Comparison of molecular subtypes of carcinoma of the breast in two different age groups: a single institution experience. Cureus, 2018; doi: 10.7759/cureus.2834.

[10] Hansini M, Ganapathy H. Expression of calretinin in carcinoma breast in correlation with various histological and molecular subtypes. J Pharm Res Int., 2021: 1-11.

[11] Hou L, Qiu M, Chen M, Li F, Li J, et al. The association between molecular type and prognosis of patients with stage IV breast cancer: an observational study based on SEER database. Gland Surg., 2021; 10(6): 1889-98. doi: 10.21037/gs-21-32.

[12] Jassim M, Premalata CS, Okaly GV, Srinivas C. Tall cell carcinoma with reverse polarity of breast: report of a case with unique morphologic and molecular features. Turk J Pathol., 2021; 37(2): 175-83. doi: 10.5146/tjpath.2020.01511.

[13] Lee S, Chang J, Shin S, Chu A, Yi A, et al. Imaging features of breast cancers on digital breast tomosynthesis according to molecular subtype: association with breast cancer detection. Br J Radiol., 2017; 90: 20170470. doi: 10.1259/bjr.20170470.

[14] Jones C, Maben J, Jack R, Davies E, Forbes L, et al. A systematic review of barriers to early presentation and diagnosis with breast cancer among black women. BMJ Open, 2014; 4(2): 10-12. doi: 10.1136/bmjopen-2013-004076.

[15] Taliano RJ, Lu S, Singh K, Mangray S, Tavares R, Noble L, Resnick MB, Yakirevich E. Calretinin expression in high-grade invasive ductal carcinoma of the breast is associated with basal-like subtype and unfavorable prognosis. Human pathol., 2013; 44(12) :2743-50.

[16] Venugopal S, Sundaram S. Calretinin expression in molecular subtypes of invasive carcinoma breast. Int J Res Med Sci., 2020; 8(4):14-98.

[17] Powell AA, Talasaz AH, Zhang H, Coram MA, Reddy A, Deng G, Telli ML, Advani RH, Carlson RW, Mollick JA, Sheth S. Single cell profiling of circulating tumor cells: transcriptional heterogeneity and diversity from breast cancer cell lines. PloS one. 2012; 7(5):33-788.

[18] Powell G, Roché H, Roche W. Expression of calretinin by breast carcinoma and the potential for misdiagnosis of mesothelioma. Histopathol., 2011; 59: 950-56. doi: 10.1111/j.1365-2559.2011.04031.x.

[19] Sasaki E, Iwakoshi A, Satake T, Nakajima K, et al. The diagnostic utility of IDH2 R172 immunohistochemistry in tall cell carcinoma with reversed polarity of the breast. Appl Immunohistochem Mol Morphol., 2022; 30: 654-61.

[20] Qi Y, Cheng H, Wang Y, Chen Z. Revealing the precise role of calretinin neurons in epilepsy: we are on the way. Neurosci Bull., 2022; 38(2): 209-22. doi: 10.1007/s12264-021-00753-1

[21] Ramathuba D, Ratshirumbi C, Mashamba T. Knowledge, attitudes and practices toward breast cancer screening in a rural South African community. Curationis., 2015; 38: 1. doi: 10.4102/curationis.v38i1.1172.

[22] Vuoto H, García A, Candás G, Zimmermann A, Uriburu J, et al. Bilateral breast carcinoma: clinical characteristics and its impact on survival. Breast J., 2010; 16(6): 625-32. doi: 10.1111/j.1524-4741.2010.00976.x.

[23] Wang G, Zhu H, Bi S. Pathological features and prognosis of different molecular subtypes of breast cancer. Mol Med Rep., 2012; 6(4): 779-82. doi: 10.3892/mmr.2012.981.

doi: 10.21276/SSR-IIJLS.2025.11.1.36

[24]Yoshino R, Nakatsubo M, Ujiie N, Kitada M. Breast cancer with biomarker reversal during the course of treatment: a case report. J Surg Case Rep., 2024; 2024(6): rjae432. doi: 10.1093/jscr/rjae432.