Original Article

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Role of Nipple Discharge Cytology in Predicting NAC Involvement in Carcinoma Breast

Sumanashree Mallappa[1]*, Nimisha Sharma[1], Uma sharma[1], Arti Khatri[1] and Vimal Bhandari[2]

[1]Department of pathology, VMMC & Safdarjung hospital, New Delhi, India
[2]Department of surgery, VMMC & Safdarjung , Hospital, New Delhi, India

ABSTRACT

Introduction: Cancer of the breast in women is a major health burden worldwide. It is the most common cause of cancer among women in both high-resource and low-resource settings, and is responsible for over one million of the estimated 10 million neoplasms diagnosed worldwide each year in both sexes. Limited number of studies have addressed the optimal surgical management of patients with breast carcinoma associated with benign or pathologic nipple discharge

Methods: Thirteen breast carcinoma cases with nipple discharge were studied. Nipple discharge cytology was studied using giemsa method. Later all the mastectomy specimens were inked and sectioned from medial to lateral into no greater than 1 cm thick tissue sections and grossly examined. Extensive sampling of nipple areola was followed taking 12 sections from each nipple areolar complex.

Thirteen breast carcinoma cases without nipple discharge were chosen as control and also grossed and examined for nipple areolar involvement

Result: In our study, there were 13 cases with nipple discharge. Out of which, 10 cases were having benign cytologic findings and 3 cases showed malignant cytologic findings

Spss statistical software was used which showed no association between presence of nipple discharge and nipple areolar involvement also it showed no association between malignant nipple discharge cytologic findings and nipple areolar involvement

Conclusions: Nipple discharge itself has no association with nipple areolar involvement and should not deter a clinician from nipple sparing mastectomy if other factors are conducive. Careful patient selection can be done in cases with malignant nipple discharge cytologic findings, if negative margins could be achieved and appropriate adjuvant therapy given. Further studies are needed to study the role of nipple discharge cytology in conservative mastectomy procedures

Keywords: *Nipple Discharge Cytology, Nipple Areolar Complex, Breast Carcinoma, Conservative Mastectomy*

Introduction:

Cancer of the breast in women is a major health burden worldwide. It is the most common cause of cancer among women in both high-resource and low-resource settings, and is responsible for over one million of the estimated 10 million neoplasms diagnosed worldwide each year in both sexes[1]

There have been many studies conducted to study the predictive factors associated with nipple areolar involvement in carcinoma breast. One of the factors least studied is the nipple discharge and its role as a factor in influencing nipple areolar involvement in breast carcinoma. This can further influence the oncological safety of nipple areolar sparing mastectomy procedures.

Nipple discharge fluid cytology is a simple non-invasive method to study cells exfoliated into the ductal system of the breast [2]

The availability of nipple discharge fluid in normal non-lactating women however varies with age, race, menstrual history, menopausal status and presence or absence of breast disease[2] The discharge seen may be serous, mucinous, bloody, greenish. Significant nipple discharges in ductal conditions are spontaneous with the exception of Fibrocystic changes and Duct ectasia.[3]

A variety of benign and malignant ductal conditions may cause nipple discharge, including duct ectasia, fibrocystic breast changes, intraductal papilloma, intraductal carcinoma, and invasive (usually papillary) ductal carcinoma[3]

The proportion of breast carcinoma cases associated with nipple discharge ranges from 1.6% to 13%.[4] Nipple discharge is traditionally regarded a sign of breast cancer, incidence of breast cancer in nipple discharge patients is 5-12%.[5]

Limited number of studies have addressed the optimal surgical management of patients with breast carcinoma associated with benign or pathologic nipple discharge.[4]

Present study was undertaken to know the role of nipple discharge as a predictive factor in nipple areolar involvement in carcinoma breast and its corresponding implications on nipple sparing mastectomies

Materials and Methods

Aims and objectives

1. Cytological examination of nipple discharge.
2. To know the correlation between presence of nipple discharge and nipple areolar involvement in carcinoma breast

To know to correlation between malignant cytologic findings in nipple discharge and nipple areolar involvement in carcinoma breast.

The study was carried out in Department of Pathology, Vardhman Mahavir Medical College and Safdarjung Hospital, New Delhi.

Thirteen breast carcinoma cases with nipple discharge were studied. Nipple discharge cytology was studied using giemsa method. Later all the mastectomy specimens were inked and sectioned from medial to lateral into no greater than 1 cm thick tissue sections and grossly examined. Extensive sampling of nipple areola was followed taking 12 sections from each nipple areolar complex.

Thirteen breast carcinoma cases without nipple discharge were chosen as control and also grossed and examined for nipple areolar involvement .

Result

All the 13 cases of nipple discharge had associated breast mass.

- Of the 13 cases-
- 6/13 cases showed greenish discharge
- 2/13 cases showed sero-sanguineous discharge
- 1/13 case had clear discharge
- 2/13 cases showed sanguineous discharge
- 2/13 cases showed serous discharge.

2 cases with serosanguinous discharge and 1 case with clear discharge showed malignant cytologic changes.(fig-3) Out of 13 cases-(fig1-4) 11/13 cases showed unilateral breast carcinomas. Out of these 11 cases, 3/11 cases showed bilateral nipple discharge and 9/11 cases showed unilateral nipple discharge laterality corresponding to that of laterality of breast carcinoma. 2/13 cases showed bilateral breast carcinomas and both cases showed bilateral nipple discharges. Among the cases with malignant cytologic findings- 1 case had bilateral discharge and 2 cases had unilateral discharges.

In our study, there were 13 cases with nipple discharge. Out of which, 10 cases were having benign cytologic findings and 3 cases showed malignant cytologic findings(table-1)

Correlation between presence of nipple discharge and NAC involvement(table-2)

The chi- square statistic - 2.4762. The p- value - 0.115582. The result is not significant at p<.05

Correlation between nipple discharge findings and NAC involvement(table-3)

The chi-square statistic - 0.6603. The p-value - 416448. This result is not significant at p<.05.

Tables 1: Cytologic findings of nipple discharge

Benign	Malignant	Total
10	3	13

Table 2: Nipple discharge cases and NAC involvement Correlation between presence of nipple discharge and NAC involvement(table-2)

	NAC involvement present	NAC involvement absent	Total
Nipple discharge present	8	5	13
Nipple discharge absent(control cases)	4	9	13
Total	**12**	**14**	**26**

The chi- square statistic is 2.4762. The p- value is 0.115582. The result is not significant at p<.05

Table 3: Correlation between nipple discharge findings and NAC involvement(table-3).

Nipple discharge findings	Number of cases with NAC involvement	Number of cases without NAC involvement	Total number of cases
Benign	4	6	10
Malignant	2	1	3
Total number of cases	**6**	**7**	**13**

The chi-square statistic is 0.6603. The p-value is .416448. This result is not significant at p<.05.

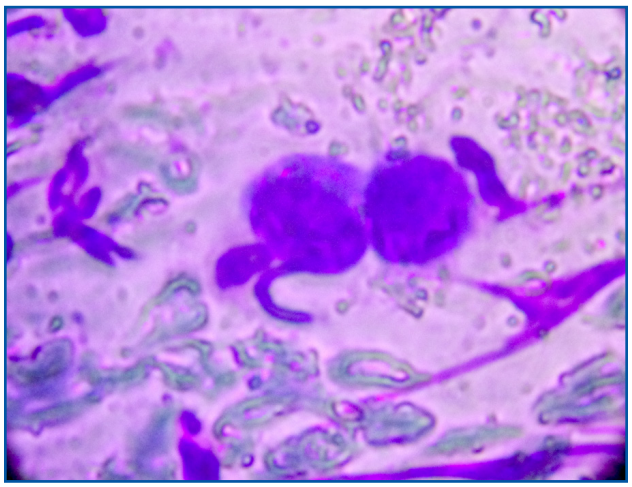

Fig. 1: Giemsa Stained Smear Showing Malignant Cells in the Nipple Discharge H/E=400X.

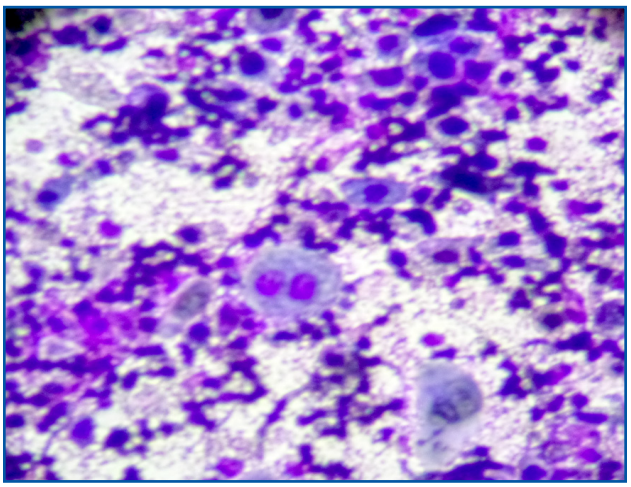

Fig. 2: Giemsa Stained Smear Showing Atypical Cells in Nipple Discharge, H/E=400X.

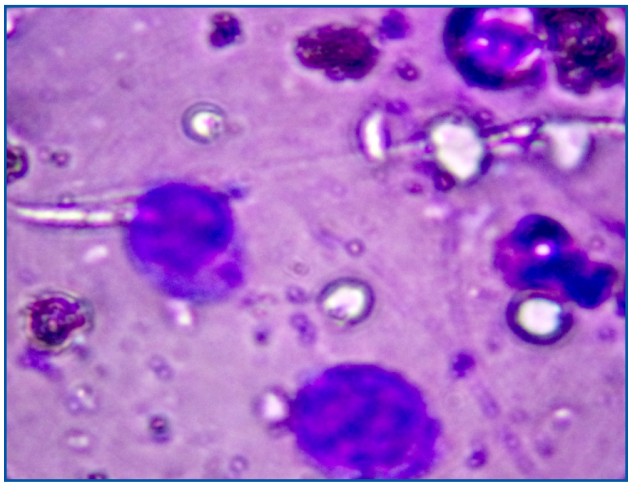

Fig. 3: Giemsa Stained Smear Showing Presence of Scattered Malignant Cells in Nipple Discharge, H/E=400X .

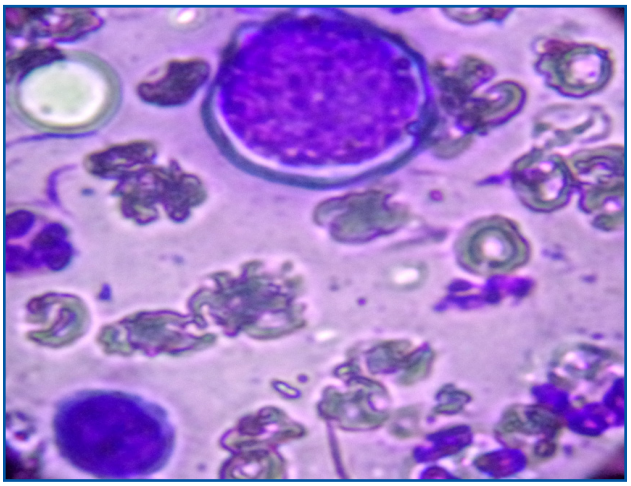

Fig. 4: Giemsa Stained Smear Showing Malignant Cell in Nipple Discharge, H/E=400X.

Discussion

Performance of conservative procedure necessitates the knowledge of frequency with which the nipple areola complex is involved in carcinoma of breast[6] Reported rates of neoplastic involvement of NAC by various studies range from 0% to 58%[6-21]. The proportion of breast carcinoma cases associated with nipple discharge ranges from 1.6% to 13%.[4]

The role of breast-conserving surgery (BCS) in patients with breast carcinoma associated with pathologic nipple discharge has not been clearly defined.[4]

The discharge may be clear serous, green, mucinous, bloody or green-black. A variety of benign and malignant ductal conditions can cause nipple discharge, including ductal ectasia, fibrocystic breast changes, intraductal papilloma, intraductal carcinoma and invasive ductal carcinoma.[3]

Nipple discharge that is clear, serous, serosanguinous (pink), or bloody is associated with an increased risk of carcinoma. An increased risk of carcinoma has also been reported in women in whom nipple discharge is associated with a palpable mass or related imaging abnormality.[22]

Nipple discharge that is bilateral and non-spontaneous and that emanates from multiple ducts after breast manipulation or stimulation is classified as benign. Nipple discharge that is unilateral, from a single duct, spontaneous, and persistent is classified as "pathologic," because it is associated with an increased risk of an underlying pathologic process.[22]

Because there is a theoretic concern that the risk of nipple-areola complex (NAC) involvement may be greater for patients with breast carcinoma with associated nipple discharge than for those without nipple discharge, the role

of breast-conserving surgery (BCS) in patients with breast carcinoma associated with pathologic nipple discharge has not been clearly defined.[4]

Few studies have addressed the clinicopathological characteristics and optimal surgical management of breast carcinoma with nipple discharge.[23]

According to Cabioglu N et al, there is a theoretic concern that the risk of nipple-areola complex (NAC) involvement may be greater for patients with breast carcinoma with associated nipple discharge than for those without nipple discharge[4]

Cabioglu N and Krishnamurthi S et al conducted a study to determine the feasibility of breast conserving surgery for breast carcinoma patients with nipple discharge. The medical records of patients who presented with pathologic nipple discharge and underwent diagnostic or curative surgery between January 1990 and December 2002 were retrospectively reviewed.[4]

A total of 188 patients presented with nipple discharge during the study period. Of those, 47 had breast carcinoma. One patient had metachronous bilateral nipple discharge associated with malignant disease. Therefore, medical records associated with a total of 48 cases were reviewed. Twenty-four patients were ultimately treated with mastectomy. Twenty-four patients were ultimately treated with BCS with or without adjuvant radiotherapy.[4]

By the results they got they concluded that, Patients with breast carcinoma accompanied by nipple discharge presented primarily with early-stage breast carcinoma associated with DCIS. Occult NAC involvement was not an uncommon finding in patients with early-stage breast carcinoma. Nonetheless, BCS can be performed safely if negative margins are achieved and if appropriate adjuvant radiotherapy or systemic therapy is administered.[4]

Pang BS et al conducted a study to determine the clinicopathological characteristics of breast carcinoma that presents with nipple discharge and the feasibility of breast conservation for these patients. They retrospectively reviewed the medical records of the patients with breast carcinoma who presented with nipple discharge and who also underwent curative surgery at Korea Cancer Center Hospital between January 1999 and December 2003.[23]

They concluded by saying that, 23 of 37 (62%) women with breast carcinoma associated with nipple discharge and who also underwent mastectomy had no evidence of extensive disease. They suggested that breast conservation can be done for these patients with performing careful patient selection and appropriate adjuvant therapy.[23]

Cabioglu N et al conducted a study to identify patient and nipple discharge characteristics associated with the diagnosis of breast cancer and to determine the utility of mammography, sonography, ductography and cytology in surgical decision making, in patients presenting with pathologic nipple discharge. Medical records of all patients who presented with nipple discharge at their institution between August 1993 and September 2000 were reviewed. Patient and nipple-discharge characteristics and findings on imaging studies and cytologic examination were analyzed[22.]

Their study suggest that cytology might be useful if combined with other findings, but that it is not by itself sufficient for discriminating between patients with pathologic discharge with and without malignancy. That is, cytologic analysis of nipple discharge specimens will not likely change the diagnostic[22.]

They concluded that, Discrimination between patients with nipple discharge who do and do not require operation can sometimes be complex and should be based on history, physical examination, and imaging studies (including ductography in cases with suspicious nipple-discharge characteristics).[22]

Krishnamurthy S et al observed that the probability of detecting malignant cells in nipple discharge fluid is dependent on the extent of ductal carcinoma in situ (DCIS) and nipple involvement by DCIS. Nipple discharge fluid is not a sensitive marker for invasive carcinoma of the breast.[2] The significance of the cytologic findings in nipple discharge fluid can be known by correlating the findings with the histopathological changes in the underlying breast tissue. Atypical cytology in nipple discharge fluid is usually associated with papillary lesions in the underlying breast.[2] In our study 3 out of 13 cases of nipple discharge showed malignant cytologic findings (table-1, fig-1-4)

Out of three cases with malignant cytologic findings , 2 cases has serosanguinous discharge and one case had clear discharge, findings supported few earlier studies[3,22.]

We studied if there was any association between the presence of nipple discharge and nipple areolar involvement,

8 cases out of 13 cases with nipple discharge showed NAC involvement and 4 cases out of 13 control cases(breast carcinoma cases without nipple discharge) showed NAC involvement. The chi- square statistic was calculated at $p< 0.05$, p value was 0.1155.

The result was not significant showing no association between presence of nipple discharge and NAC involvement.

Our findings supported few earlier studies which showed that presence of nipple discharge as such may not increase the risk of nipple areolar involvement [2,4,22].

We also studied if there was any association between the malignant cytologic findings and nipple areolar involvement,

There were 13 cases with nipple discharge in our study, out of which 6 showed NAC involvement. 4 cases out of 10 with benign nipple discharge showed NAC involvement. 2 cases out of malignant nipple discharge showed NAC involvement. Chi-square statistic at $p < 0.05$ was not significant showing that there was no correlation between cytologic findings of nipple discharge and NAC involvement.

Study found no significant association between malignant cytologic findings and nipple areolar involvement supporting few previous studies[2,4,22].

Conclusion

Nipple discharge itself has no association with nipple areolar involvement and should not deter a clinician from nipple sparing mastectomy if other factors are conducive. Careful patient selection can be done in cases with malignant nipple discharge cytologic findings, if negative margins could be achieved and appropriate adjuvant therapy given. Further studies are needed to study the role of nipple discharge cytology in conservative mastectomy procedures.

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***Corresponding author:**
Dr Sumanashree Mallappa, Malayashree nilaya, 2 cross, 1B Main, Nagarbhavi village, Bangalore 560072 INDIA
Email: kusumadallisumana@gmail.com

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