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Original Research Article

The accuracy of USG and USG guided FNAC axilla in predicting nodal metastasis in a clinically lymph node negative cancer breast patient

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ABSTRACT

Background: Breast malignancies are the second most common cause of cancer-related mortality among women. As the size of the primary breast cancer increases, some cancer cells are shed into cellular spaces and transported via the lymphatic network of the breast to the regional lymph nodes, especially the axillary lymph nodes. Objective of the study was to determine the accuracy of USG and US-FNAC in detecting lymph node metastasis in a clinically lymph node negative CA Breast patient.
Methods: This prospective study was conducted on 40 consecutive patients with biopsy proven breast cancer with clinically negative axilla, who had attending the OPD or IPD in our department of surgery, Swaroop Rani Nehru Hospital, Allahabad, during the period of 2014 to 2015. All of these patients were planned to undergo surgery (breast conservation or modified radical mastectomy with axillary clearance).
Results: Sensitivity of the study = 97.77%, specificity = 25%, positive predictive value =92.01%, negative predictive value =50%, diagnostic accuracy =90%.
Conclusions: Using axillary ultrasound and selective US-FNAC is a rapid, non-morbid method of staging the axilla in newly diagnosed breast cancer patients and should become a routine part of patient care because it can spare many patients particularly those who are undergoing axillary dissection.

Keywords: Axillary lymph node, CA Breast, US-FNAC

INTRODUCTION

Breast malignancies are the second most common cause of cancer-related mortality among women. As the size of the primary breast cancer increases, some cancer cells are shed into cellular spaces and transported via the lymphatic network of the breast to the regional lymph nodes, especially the axillary lymph nodes. Cancer cells may grow through the lymph node capsule and fix to contiguous structures in the axilla, including the chest wall. Typically, axillary lymph nodes are involved sequentially from the low (level I) to the central (level II) to the apical (level III) lymph node groups. Approximately 95% of the women who die of breast cancer have distant metastases, and traditionally the most important prognostic correlate of disease-free and overall survival was axillary lymph node status. Women with node-negative disease had less than a 30% risk of recurrence, compared with as much as a 75% risk for women with node-positive disease.[1,2]

The status of axillary lymph node metastasis, in addition to being the most important prognostic factor in this group of patients, has a critical place in the management

of this disease. For many years, axillary lymph node dissection (ALND) was the choice of method for axillary nodal evaluation which reliably staged and effectively treated metastatic lymph node involvement. However, for those cases that had no nodal involvement ALND gave no advantage and sometimes was associated with significant complications such as lymphedema, wound infections, stiffness, shoulder weakness, pain and numbness of the affected arm. Afterwards, the concept of sentinel lymph node biopsy (SLNB) was developed.[3]

This method has been shown to be a valuable tool in determining whether the cancer has spread from its original site and for axillary staging. It has proven to be an effective alternative to ALND. Those patients whose SLNB is disease-free require no further treatment and are spared from unnecessary axillary surgery. Despite its wide acceptance for practice, SLNB has some drawbacks; it is a slow and meticulous process for surgeons in the operating room, requires the administration of radioisotopes to patients, and needs multiple microscopic sections for final histological examination. Also SLNB is not available in all centres and is not cost effective.

An ultrasound examination is recommended by previous studies to detect suspicious involved axillary lymph nodes. High resolution ultrasound, which establishes structural features of lymph nodes and structural changes suggesting malignant involvement, is being increasingly accepted as an appropriate non-invasive method. In addition to imaging, fine needle aspiration cytology (FNAC) is a minimally invasive intervention that establishes the cytological features of image-suspicious lymph nodes.[4]

In this respect, ultrasound-guided fine needle aspiration (US-FNA) is a suggested technique for axillary lymph node staging. However, US-FNA is not as sensitive as SLNB and its false-negative rate is too high to entirely replace SLNB. Patients with negative findings at US-FNA will still need to undergo SLNB for evaluation of the axilla. Additionally, FNA is more operator dependent compared with other methods such as the core-needle biopsy (CNB). The reported rate of insufficient cytological material following US-FNA is 0%-54%. Until now, the findings of ALND or its alternative method, SLNB, have been used as the gold standard for axillary staging in breast cancer cases that have clinically negative axilla. However, if nodal positivity can be proven pre-operatively, it helps diagnosing one-stage axillary clearance and SLNB can be avoided. In addition, it may also have an impact on the decisions to offer neoadjuvant therapy and breast reconstruction.[5]

Therefore, it is helpful for both the patient and surgeon to establish a simple pre-operative method in patients with metastatic lymph nodes who could directly undergo an axillary dissection and eliminate the need to search for the sentinel lymph node. The aim of this study is to evaluate the clinical usefulness of axillary ultrasonogram and US guided FNAC in diagnosing axillary nodal metastasis in cases with breast cancer.

METHODS

This prospective study was conducted on 40 consecutive patients with biopsy proven breast cancer with clinically negative axilla, who had attending the OPD or IPD in our department of surgery, Swaroop Rani Nehru Hospital, Allahabad, during the period of 2014 to 2015. All the patients with history & clinical examination suggestive of carcinoma breast (CA Breast) and who will undergo intervention in the S.R.N. Hospital were included in the study. All of these patients were planned to undergo surgery (breast conservation or modified radical mastectomy with axillary clearance). Approval by the institutional ethics committee was obtained and patients were entered prospectively into the study protocol after signing an informed consent. The patients underwent a detailed clinical examination and baseline haematological investigations.

Selection criteria

All the symptomatic Patients, who were able to understand & follow study related advices, and to understand and give consent for the study and were histologically proven CA Breast were included in the study, whereas patients with serious life threatening medical illness or underwent radiotherapy initially who were unable to understand and give consent were excluded from the study. All these patients were subjected to preoperative ultrasonography (USG) of the axilla to determine the presence of nodes which were sonographically suspicious of malignancy.

Table 1: Correlation of USG guided FNAC with histopathological result.

	HPE by ALND	
USG guided FNAC	Positive	Negative
Positive	35	3
Negative	1	1

The descriptors which were considered are:

Suspicious

Size more than 10mm; B. absence of fatty hilum; C. hypoechoic internal echo; D. circular shape; E. sharply demarcated border compared with surrounding fatty tissue; F. asymmetric cortical thickening or eccentric lobulations of hypoechoic cortical rim.

Benign

If lymph node showed Longitudinal axis/Diameter (L/D) ratio >1.5, with fatty hilum present and hyperechoic cortex

Indeterminate

If L/D ratio <1.5 or >1.5 with absence of fatty hilum or hypoechoic cortex

US Guided FNA procedure

- In supine position, US guided FNA done with 22G needle attached to a 10 ml syringe.
- Smears prepared from the aspirate and air-dried.
- Cytology results were reported as satisfactory for cytologic evaluation, negative for malignancy; positive for malignancy; or insufficient for diagnosis.

Findings were noted with regard to the level and number of suspicious nodes. The details of descriptors characterizing findings of suspicious nodes in each case were also noted. These nodes were marked on the skin with an indelible marker and depth from the skin surface was also noted. At the time of surgery, after mobilization of the axillary tail of breast, these nodes were taken out from the axillary fat pad separately with their localization being guided by skin marking. In obese patients with abundant axillary fat it was difficult initially to locate the node, but with experience we overcame the problem. After sampling of these suspicious nodes, axillary dissection was completed along with surgery for the primary lesion.

Lymph nodes dissected out of the axilla were subjected to histopathological examination for metastatic disease. Based on the correlation of USG and histopathologic (HPE) findings, diagnostic accuracy of US guided axillary node sampling (UGANS) was calculated.

Table 2: ALND – Histopathological result.

ALND - Presence of Mets	No of patients
Positive for mets	36
Negative for mets	4

RESULTS

Present study was conducted in SRN Hospital, Allahabad, Uttar Pradesh, India. Total of 40 patients were included in study.

Number of true positive =35 No of False Positive =3
Number of true negative =1 No of False Negative =1

Using statistical equations A the final diagnosis from histopathological examination, the following statistics were generated

Sensitivity of the study = 35/(35+1) x 100 = 97.77%
Specificity of the study = 1/(1+3)x100= 25%

Positive predictive value (PPV) of the study = 35/(35+3)x100=92.01%

Negative predictive value (NPV) of the study = 1/(1+1)x100=50%

Diagnostic accuracy of the study = (35+1)/(35+1+3+1)x100=90%

DISCUSSION

In present study conducted among 40 patients, USG detected lymph nodes in all 40 patients. Lymph nodes were evaluated for specific USG characteristics like L/D ratio, presence or absence of fatty hilum and for echogenicity and any morphological changes in cortex (notching, distortion). In present study True positive cases were 35, True negative 1, false positive cases are 3 and false negative 1.

The sensitivity, specificity, positive predictive value and negative predictive value of USG of axilla in correlation with histo-pathology was found to be 97.77%, 25%, 92.01% and 50%. These results can be compared to study conducted by Jain SA, et al, they conducted study on 57 patients with proven breast malignancy.[1] They underwent ultrasound of axilla and USG guided FNAC preoperatively. They found out that out of 164 lymph nodes, USG labelled 52 lymph nodes as normal (benign) and 112 abnormal (indeterminate+suspicious) Out of 52 normal lymph nodes on USG 43 were true negative on FNAC and out of 112 abnormal Lymph nodes 106 were found true positive on FNAC, with Sensitivity=92.2%, Specificity=87.8%, NPV =82.7%, PPV=94.6%.

Feng Y, et al also compared the efficacy of physical examination (PE), ultrasound (US), and US combined with fine-needle cytology (US-FNAC) in evaluation of node status before SLNB for breast cancer patients.[2] They performed a retrospective study of 3,781 breast cancer patients and calculated the sensitivity, specificity, PPV, NPV, and accuracy for PE, US, and US-FNAC, respectively. Abnormal axillary nodes under US were detected in 1,152 cases, among which 821 were proven to have positive nodes by FNAC. The positive FNAC results enabled 11.7% of cN0 (clinically lymph node negative) patients (373/3,175) to avoid unnecessary SLNB. All 331 cases with abnormal US but negative FNAC results, and the 2,629 cases with normal US underwent SLNB procedure for nodal staging, and metastatic nodes were identified in 745 patients. The sensitivity of PE was 32.2%, with a specificity of 95.5%, a PPV of 83.5%, a NPV of 65%, and an accuracy of 69.3%. The sensitivity, specificity, PPV, NPV, and accuracy of axillary US alone were 58.6, 89.4, 79.6, 75.3, and 76.7%, respectively. Combining axillary US with FNAC resulted in sensitivity, specificity, PPV, NPV, and accuracy of 52.4, 100, 100, 74.8, and 80.3%, respectively.

Another study by Ahn HS, Kim SM, et al conducted study on 220 patients with breast cancer who underwent preoperative or pre-chemotherapy sonography for

axillary staging, 52 patients who underwent US-FNAC and CNB for cortical thickening or a compressed hilum of lymph nodes on sonography were prospectively enrolled.[3] Sonography and FNAC/CNB findings were compared with final pathologic results from SLNB or ALND. Result was, the PPV of axillary sonography was 54%, the sensitivity and specificity of FNAC were 73% and 100%, respectively, and those of CNB were 77% and 100%.

Alkuwari, et al in their study found The PPV and NPV of FNAC of axillary lymph nodes for metastatic breast carcinoma were 1.00 and 0.60, respectively.[4] The overall sensitivity of axillary lymph node FNA in all the cases studied was 65% and the specificity was 100%. The sensitivity of FNA was lower in the sentinel lymph node group than in the full lymph node dissection group (16% vs 88%, respectively), which was believed to be attributable to the small size of the metastatic foci in the sentinel lymph node group (median, 0.25 cm). All false-negative FNAs, with the exception of 1 case, were believed to be the result of sampling error.

Holwitt DM, et al reviewed 256 patients with clinically node-negative breast cancer. Axillary ultrasound (AUS)-guided FNAC/CNB was compared to histopathology to determine sensitivity, specificity, NPV and PPV.[5] AUS-FNACC/CNB and final pathology were positive in 72/256 patients (28%). In 125/256 cases (49%), the AUS and final pathology were negative. Two of 110 patients had a false positive FNAC (1.8%); both received neoadjuvant chemotherapy. Nine patients (8%) had a false negative FNAC/CNB; the median size of lymph node metastasis was 3 mm. The sensitivity and specificity of AUS-FNACC/CNB was 71% and 99%, with a NPV of 84% and PPV of 97%.

Verbanck J, et al the value of axillary sonography in 144 consecutive patients was prospectively studied.[6] Abnormal lymph nodes were demonstrated in 72 axillae, only half (36 of 72) of which were clinically detected. In comparison with intraoperative findings in 47 patients with breast carcinoma, the sensitivity of sonography in detecting malignant nodes was 92%, the specificity 95%, and the PPV and NPV 96% and 91%, respectively. Krishnamurthy, et al conducted study in 103 patients and found the overall sensitivity of US-FNAC was 86.4%, the specificity was 100%, the diagnostic accuracy was 79.0%, the PPV was 100%, and the NPV was 67%.[7]

In another study by Kuenen-Boumeester V, et al evaluated the material of 183 US-FNACs of non-palpable axillary lymph nodes of primary breast cancer patients.[8] The cytological results were compared with the final histological diagnosis. US-FNAC detected metastases in 44% (37/85) of histologically node-positive patients, in 20% of the total patient population studied. These percentages are likely to be higher when women with palpable nodes are included. Cytologically false-negative and false-positive nodes were seen in 28 (15%) and three cases (1.6%), respectively. Interestingly 25% (n=7) of the false-negative nodes, revealed micro-metastases on postoperative histology. The sensitivity was 57%, the specificity 96%.

CONCLUSION

In this study USG alone showed the accuracy of 86.5% which was improved to 90.9% by adding US-FNAC. USG of axilla in correlation with US-FNA showed the sensitivity, specificity, PPV and NPV of 97.77%, 25%, 92.01%, and 50% respectively. The diagnostic accuracy of USG and US-FNAC is 90%. On correlation of specific USG characteristics with US-FNA, the sonographic feature most predictive of malignancy was absence of fatty hilum, Hypoechoic cortex was the next best predictor followed by L/D ratio. The ability of USG to detect more suspicious lymph nodes increased with increasing tumour size. In conclusion, only those patients who showed benign or indeterminate features of lymph nodes on USG and had negative US-FNA of suspicious lymph node will require SLNB as the staging procedure. Rest of the patients who showed definite features of lymph node involvement on USG and positive US-FNA may undergo ALND directly as a part of primary breast surgery, thus saving time and also avoiding the morbidities associated with SLNB. UGANS sampling has high rate of diagnostic accuracy and could be a valuable tool for evaluation of axillary metastasis in early breast cancer in low resource settings. When nodes are not identified at all, then chances of metastasis are minimal. Higher experience with the technique may decrease the rate of failure. Availability of Intra-operative USG for assessment of lymph nodes may prove to be a helpful tool for sampling of suspicious nodes. Conclusively, using axillary ultrasound and selective US-FNAC is a rapid, non-morbid method of staging the axilla in newly diagnosed breast cancer patients and should become a routine part of patient care because it can spare many patients particularly those who are undergoing axillary dissection. US-FNAC can be considered in patients with locally advanced breast carcinoma for whom neoadjuvant chemotherapy is planned even if the lymph nodes appear normal.

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