

Optimization of Sentinel Lymph Node Detection and Clinical Analysis in Carcinoma Breast

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Abstract:

Introduction: The Sentinel lymph node biopsy is a good alternative for the nodal staging in breast cancer. Sentinel lymph node biopsy is the first node in the regional nodal basin that drains a primary tumor and reflects the tumor status of the entire nodal basin. Sentinel lymph node biopsy is a reliable method. The technology is evolving rapidly but no standardization has yet been established and there is no agreement on how many nodes must be submitted for study.

Objective: To analyze and evaluate the micro-metastasis in Carcinoma Breast, with the aid of Sentinel lymph node biopsy, in different early malignant breast lesions using 1% isosulphan blue; Study design: Prospective study; Place and Duration of study: Department of General Surgery & Department of Pathology, S.V. Medical College, Tirupati from January 2018 to June 2019 (18 months)

Material & Method: Among 140 simple mastectomy cases – 118 cases identified as early T1, T2 and T3 (without palpable lymph nodes) stages of operable carcinoma breast. The correlation of patients' age, sex, tumor size, Histological type, Grade is done with Sentinel Lymph node dissection by pre-operative injection of 1% Isosulphan blue. Mastectomy along with Sentinel Lymph node dissection is done and subjected for routine Histopathological examination. Univariate and Multivariate analysis were applied.

Results: In 118 cases the procedure was performed. Sentinel Lymph node is positive in 67.79%. Majority of cases reported over Right side (61.01%). Common location of Breast lump is outer and upper quadrant (88.98%). The Mean size of the Breast lump is 3.42 x 2.91 cms. Most of the tumors were in T1 stage (36.44%). Single node (sentinel lymph node) was noted in 88.13%; two nodes in 5.93%; three nodes in 3.38%; four nodes in 2.5% of cases. Ductal Carcinoma Insitu is the most common primary lesion i.e., in 65% of cases.

Conclusion: Sentinel Lymph node dissection is an effective and potential alternative to routine axillary lymph node dissection in order to predict and stratify the prognostic information in various types of breast carcinomas, with the help of 1% Isosulphan blue dye, which is free of dangerous side effects.

Key words: Biopsy, Breast cancer, Isosulphan blue, Metastasis, Sentinel Lymph node.

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I. Introduction

Sentinel Lymph Node is first lymph node or Echelon lymph node on the direct lymphatic drainage pathway of a tumor. Sentinel Lymph Node evaluation is a major breakthrough in diagnosis, staging and management of carcinoma breast. It overcomes the difficulty of diagnosis of carcinoma breast in early stage and ensures the best status of cure of the future impending lesion¹. Sentinel Lymph Node gained its importance, when in past times there were no accurate non-invasive techniques to assess the axillary status; clinical assessment in associated with high degree of false negative rate¹. In 1977 Canabas coined the term "SENTINEL LYMPH NODE" and statement was depicted that, "If Sentinel Lymph Node is negative for deposits then, no further resection is necessary"². Morton et al³ (1992) developed and first published the Sentinel Lymph node dissection technique for stage I Cutaneous Melanoma. Guenther et al⁴ (1997) successfully identified the Sentinel Lymph node dissection. Kolleret al⁵ (1998) documented the Sentinel Lymph node experience by using Methylene blue dye technique. Guiliano et al^{6,7} (1994) attempted lymphatic mapping in 174 patients. In the initial stages, the identification of the Sentinel Lymph node was 65% and false negative occurred. But in later study the procedure was associated with 100% accuracy. Edge et al^{8,9} (1997 and 2000) reviewed more than 3000 early stage breast cancer patients and Sentinel Lymph node dissection was done. Cody et al¹⁰ (1998)

documented that this technology predicts the axillary status in 98% of all patients, and in 95% of node positive patients.

Isolation of Sentinel Lymph Node negative for deposits obviates the utmost need of Axillary Lymph Node Dissection (ALND) and clearance, thus the patient is spared of its potential side effects. The technology is evolving rapidly but no standardization has yet been established and there is no agreement on how many nodes must be submitted for study. Kennedy et al¹¹ stated that two sentinel lymph nodes accurately stages the axillary status in the breast cancer. Cody¹⁰ stated that Sentinel lymph node biopsy reliably predicts the axillary status in 98% of all patients and in 95% of those; with node positive. It is a minimally invasive method for determining the status of regional lymph nodes in patients with clinically node negative invasive breast cancer. This technique is also used for *Ductal carcinoma insitu Grade III*. Various studies stated that Sentinel lymph node biopsy with multiple serial sections and Immunohistochemistry (IHC) improves and increases the sensitivity for identifying the nodal micro metastasis. The sentinel node is identified intraoperatively by lymphatic mapping by using a vital blue dye and/or a radioactive tracer. The technique is of great value as it avoids unnecessary axillary toilet and its side effects. The Sentinel lymph node biopsy is also preferable in patients with preoperative palpable nodes or ultrasound guided Fine needle aspiration cytology is non-diagnostic^{8,9}.

The Sentinel Lymph Node identification technique is feasible and is well accepted because of its advantages – Simple, Safe, Inexpensive and cost effective, Decreases the surgical morbidity, Early detection of the disease in disease free axilla, Improves the standard of life in primary carcinoma breast patients^{6,7}.

The present study was carried out to clinically, evaluate various types of Breast carcinoma in relation to Sentinel Lymph Node status, by analyzing the efficacy of 1% Isosulphan blue dye in present scenario.

II. Materials And Methods

In the present study, the procedure of localization was employed in 118 cases. Of the 118 cases 117 were females and 1 male patient were included. Study was conducted in Dept. of Pathology & Dept. of General Surgery, S.V. Medical College, Tirupati from January 2018 to June 2019 (18 months) patients with unifocal breast carcinoma diagnosed by means of Fine Needle Aspiration Cytology (FNAC) or Lumpectomy without distant metastases were included in the study. Thorough clinical, physical, general and systemic (Breast and Axillary lymph nodes and other lymph nodes) examination was performed in all patients.

The inclusion criteria: - Patients who had undergone mastectomy with axillary clearance for unifocal breast carcinoma; size of tumor upto 5 cms and T3 cases, where lymph nodes were not palpable. Sentinel Lymph Node, localization was done and 2-3 lymph nodes were removed. The exclusion criteria: - Multicentric Breast carcinoma; Patients with previous history of carcinoma breast or axillary clearance; patients undergoing or has already taken chemo or radiotherapy for the same. At the time of surgery, 3-5 ml of Isosulfan blue dye (Lymphazurin) is injected into the breast parenchyma. The dye is injected laterally, adjacent to the breast mass and below the subcutaneous fat, to avoid tattooing the overlying skin. If the primary tumor has already been excised, the dye is injected into the wall of the biopsy cavity. If the primary tumor is not palpable, dye is injected through a needle inserted under mammographic guidance for tumor localization. For 5-7 minutes after dye injection, the breast is gently compressed to enhance lymph flow. A transverse incision is then made just below the hair bearing area in the axilla. The amount of dye injected and the interval between dye injection and skin incision increase with the distance of the tumor from the axillary drainage basin. Blunt dissection is performed to identify the dye – filled lymphatic tract. This tract is then followed proximally and distally to a blue stained sentinel node. Normal Axillary dissection is performed, with a small incision based on the normal surgical anatomy of the axilla and lymph nodes in the axilla. The dark blue stained track is followed which a lymphatic is draining the lymph nodes, this track is followed till end. A globular dark stained firm non-elastic mass is palpated in the axillary pad of fat, which is ligated and excised. In the positively stained lymph nodes sectioning is performed and Hematoxylin and Eosin staining procedure is performed on three thin sections of paraffin block and these sections are thoroughly examined to know the status of the lymph node. Serial deeper sections were made and reserved for Immunohistochemistry profiling.

III. Results

A total of 210 cases were analyzed by Fine Needle Aspiration Cytology. There were 376 cases of Lumpectomy and Mastectomy. Among 376 lesions 233 were of Benign and 143 were Malignant. In 118 Malignant lesions, Sentinel Lymph Node Dissection was performed.

The commonest Benign lesion noticed was Fibroadenoma (178 cases) giving a percentage of 47.34% among the total breast lesions. The commonest Malignant lesion noticed was Ductal carcinoma in situ (69 cases), giving a percentage of 18.35% among the total breast lesions. The second common malignant lesion was Invasive duct cell carcinoma (49 cases) giving a percentage of 13.03%. The third common malignant lesion noticed was Lobular carcinoma in situ (22 cases) giving a percentage of 5.85%.

In 118 malignant breast lesions clinically the axillary nodes were not palpable. The Sentinel Lymph nodal mapping was done in 118 cases (31.38%). Intraductal carcinoma (DCIS) was the commonest lesion, with 52 (44.06%) cases positivity of Micrometastasis in Sentinel Lymph Node Dissection. The next common lesions were Invasive duct cell carcinoma and Lobular carcinoma in situ in 13 (11.01%) and 12 (10.16%) cases with Sentinel Lymph node dissection positivity. Among 118 various malignant lesions 80 cases showed Sentinel Lymph node dissection positivity giving a percentage of 67.79%, 38 cases of breast lesion showed Sentinel Lymph node negativity giving a percentage of 32.30%. Among 118 malignant lesions, Intra ductal carcinoma was noticed in 69 cases (58.47%). 52 cases (44.06%) show Sentinel Lymph node positivity and 17 cases (14.40%) showed Reactive hyperplasia.

Among 24 cases of Invasive duct cell carcinoma Sentinel Lymph node was positive in 13 cases (11.01%) and 11 cases (9.32%) showed Reactive hyperplasia. (Rest of 25 cases were with palpable lymph nodes)

Among 22 cases (18.64%) of Lobular Carcinoma In situ, the Micrometastasis in Sentinel Lymph node is noticed in 12 cases (10.16%) and 10 cases (8.47%) showed Reactive Hyperplasia. There were 2 cases (1.69%) of Medullary Carcinoma and 1 case (0.84%) of Mucinous carcinoma which showed Sentinel Lymph Node positivity. Among the 118 cases, 72 (61.01%) of cases had cancer in Right Breast and 46 (38.98%) of cases in the Left Breast. The Average mass size of lump on Clinical Examination was 3.42 x 2.91 cms (**Mean- 2.96 cms**). Among the 118 cases, 105 cases (88.98%) show tumor in the Upper and Outer Quadrant of the Breast, and 13 cases (11.01%) show tumor in the Lower and Inner ; Central Quadrants. According to the clinical staging 43 cases (36.44%) were of T1 Stage, 67 cases (56.77%) were of T2 Stage and 8 cases (6.7%) were of T3 stage with impalpable lymph nodes.

IV. Discussion

Axillary Lymph Node Dissection (ALND) is considered to be a reliable method of evaluating the nodal status. Histologically negative nodes will not have any therapeutic benefit from ALND and as such, one is challenged with potential morbidity of the procedure⁶. In present era, the potential need of ALND is under chaos as about 75% of Axillary nodes in the dissected cases are free of disease. The status of Axillary lymph nodes is a very important prognostic indicator and directs subsequent adjuvant therapy for patient with any type of Breast cancer. Levels I and II ALND is standard method for surgical evaluation of axilla.

Lymphatic mapping a technique initially devised to aid in treatment of Melanoma, has gained enormous momentum in treatment of Carcinoma Breast., since the first published Carcinoma Breast multi-center study in 1998. It has emerged as minimally invasive alternative to ALND. The pathological analysis of the SLND differs from that of standard ALND. As in ALND, each node is bisected and evaluated by means of Hematoxylin and Eosin stains. In SLN analysis, multiple thin cut sections of each node are examined by means of Hematoxylin and Eosin and Immunohistochemistry stains, resulting in higher probability of deriving the micro metastatic disease. Thus, SLN is highly accurate technique for identifying axillary metastasis in all variants of Carcinoma Breast. Success rate increases with competent hands. Of all the dyes used by most of the researchers, 1% Isosulphan blue is recommended as the best agent for lymphatic mapping – as it quickly enters the lymphatic channels and is readily visualized in the vessels with minimal diffusion into soft tissues^{6,7,12} and is devoid of any dangerous side effects. Methylene blue has a poor lymphatic uptake and fluorescent dyes have been used and they have got property to leak into interstitial tissue.

The clinical parameters studied by various researchers have been evaluated in present study in correlation to previous studies as follows:-

In the present study the frequency of the lump on the Right side in 72 cases (61.01%) and Left side in 46 (38.98%). Tumors in right breast in 52.6% and tumors in left breast in 47.4%. Our study correlated with SadiaHameedet al¹³ (2007). Frequency of Tumor in upper and outer quadrant in 105 cases (88.9%) and in other quadrants in 13 cases (11.1%). SadiaHameedet al¹³ (2007) documented that frequency in outer upper quadrant was 66% and in other quadrants they range from 7-10%. According to clinical staging, in present study 43 (36.44%) were of T1 stage; 67 (56.77%) were of T2 stage and 8 (6.7%) were of T3 stage without any palpable lymph nodes. In a similar study carried out by SadiaHameed et al.,¹³ (2007) T1 – 30 (37.5%); T2 – 50 (62.5%) were observed. Mean size of Breast lump 3.42 x 2.91 cms with a range of 1-5 cms, observed in present study. In a study done by SadiaHameedet al¹³, the mean size is 3.39 x 2.82cms with a range of 1-5 cms. Leung et al¹⁴ (2007) documented that the percentage of metastasis is more in T2 clinical stage; the same was noticed in the present study. Khalid I. Al Shibli et al¹⁵ (2005) documented the number of lymph nodes received and examined for carcinoma breast, in majority of cases single stained node was identified which is a similar observation in the present study. The incidence of Ductal carcinoma in situ is more and incidence of Lobular carcinoma in situ is less in the study conducted by Khalid I. Al – Shibli et al¹⁵ (2005) and the same observation was evident in present study.

Thus, the clinical relation is made out with all the positive Sentinel Lymph Node cases with the aid of 1% Isosulphan blue dye, because of its good visualization and least possible side effects, the more advantageous features is it – being simple technique and less costly, last but never the least is – its high success rate.

V. Conclusion

In our series using only Blue dye only has gathered enormous information regarding Sentinel Lymph Node with best results thus – technique is considered to be accurate. Even though there are some controversies beeping around the technical, clinical and pathological aspects of Sentinel Lymph node mapping, Sentinel Lymph Node Biopsy is now regarded as accurate alternative to routine level I & II ALND for patients with Breast cancer. The sensitivity of Intro operative examination of SLN is tumor size dependent and efficacy of surgeon cause zero false negativity. Thus, it’s now time for the rapidly evolving technology for the potentiation and standardization of the technique and analysis of SLNB, to submit a non-controversial environment regarding Sentinel Lymph Node – A BOON FOR PATIENTS WITH EARLY BREAST CARCINOMA.

Table:1. Age wise distribution of Malignant lesions

Sl.no	Lesion	Age wise distribution of lesions in Biopsy specimens (age in years)							Total
		0-10	11-20	21-30	31-40	41-50	51-60	>60	
1.	Intra ductal carcinoma	-	2	13	27	14	13	-	69
2.	Lobular Carcinoma In situ	-	-	5	7	6	4	-	22
3.	Invasive Duct cell carcinoma	-	-	2	8	14	18	7	49
4.	Medullary	-	-	-	-	-	1	1	2
5.	Mucinous	-	-	-	-	-	1 (male)	-	1
	Total	-	2	20	42	34	37	8	143
	Grand Total (Benign + Malignant)								376

Table: 2.Distribution of lesions according to age and positivity for SLND

Sl.no	Lesion	Age of the patients (in years) and behavior of SLN															
		0-10		11-20		21-30		31-40		41-50		51-60		>60		Total	
		+	-	+	-	+	-	+	-	+	-	+	-	+	-	+	-
1.	Intraductal Carcinoma	-	-	2	-	8	5	21	6	12	2	9	4	-	-	52	17
2.	Lobular carcinoma In situ	-	-	-	-	3	2	4	3	3	3	2	2	-	-	12	10
3.	Invasive Duct cell carcinoma	-	-	-	-	1	1	3	2	4	3	4	2	1	3	13	11
4.	Medullary	-	-	-	-	-	-	-	-	-	-	1	-	1	-	2	-
5.	Mucinous	-	-	-	-	-	-	-	-	-	-	1	-	-	-	1	-
	Total	-	-	2	-	12	8	28	11	19	8	17	8	2	3	80	38

Table: 3. Distribution of lesions according to age and side of involvement

Sl.no	Lesion	Age of the patients and Side of involvement of the lesion														Total	
		0-10		11-20		21-30		31-40		41-50		51-60		>60		R	L
		R	L	R	L	R	L	R	L	R	L	R	L	R	L		
1.	Intraductal Carcinoma	-	-	2	-	10	3	17	10	8	6	7	6	-	-	44	25
2.	Lobular carcinoma In situ	-	-	-	-	3	2	4	3	3	3	1	-	-	13	9	
3.	Invasive Duct cell carcinoma	-	-	-	-	1	1	2	3	4	3	4	2	3	1	14	10
4.	Medullary	-	-	-	-	-	-	-	-	-	-	1	1	-	1	1	
5.	Mucinous	-	-	-	-	-	-	-	-	-	-	1	-	-	1	1	
	Total	-	-	2	-	14	6	23	16	15	12	14	11	4	1	72	46

Table: 4.Stage related study of Sentinel Lymph node

Study	No. of Cases	Stage distribution
Guenther ⁴	46	T1 – T3
Fant ¹⁶	46	T1 –T2
Naik ¹⁷	210	T1 – T3
Jeruss ¹⁸	73	T1 – T4
Fan ¹⁹	38	T1 – T3
Sadia Hameed ¹³	95	T1 – T2
Present Study	118	T1 – T3

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