Original Article

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Impact of Sentinel Lymph Node Biopsy on Outcome of Extremity Melanoma: A Retrospective Single Centre Experience

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Abstract

Background: Since the introduction of sentinel lymph node biopsy (SLNB), its use as a standard of care for patients with clinically node negative cutaneous melanoma remains controversial in India. We wished to evaluate our experience of SLNB for extremity melanoma.

Methods: This is a retrospective study which was done at our centre from 2013 – 2020 by the Plastic surgery team. From 2013 to 2020, 44 patients (30 mens and 14 womens) with non -metastatic melanoma underwent SLNB.

Result: From 2013 to 2020, 44 patients (30 mens and 14 womens) with non-metastatic melanoma underwent SLNB. The mean age was 56 +/− 16 (16 to 86). Positive sentinel nodes were identified in 12/44 (27%) patients. Single SLN was harvested in 67% of our cases, the mean number of SLN harvested was 1.5 +/− 1 in our study.

Conclusion: Our data confirm previous studies and support the clinical usefulness of SLNB as a reliable and accurate staging method in patients with cutaneous melanoma. However, the benefit of additional CLND in patients with positive SLN remains controversial.

Keywords: Melanoma; Sentinel lymph node.

INTRODUCTION

Sentinel lymph node biopsy (SLNB) was introduced in 1992[1], since then it has become a staple in melanoma care in most of the melanoma centres around the world but it is yet to become a part of mainstream treatment in India. The main short term aim of SLNB is the early identification of patients with occult nodal metastasis, who might require Completion lymph node dissection (CLND). The long term aim is to provide a more accurate basis for formulating a prognosis. Further more, the presence or absence of occult disease in the sentinel lymph node (SLN) is critical for accurate AJCC[5] staging and decisions regarding planning of adjuvant therapy and in deciding follow up.

There are two trials which were conducted Multicentre Selective Lymphadenectomy Trials (MSLT I and II). MSLT-I[2] concluded that there is no survival benefit when comparing patients with cutaneous melanoma who under went Wide excision + SLNB followed by CLND if SLNB was positive to patients who were only kept on follow up without CLND. The results of MSLT-II[3] showed that CLND had no consequence on the overall survival compared with patients who were kept

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on close follow up and delayed CLND. Despite the results of MSLT – I, II CLND is practiced in mostcentres in India.

The incidence of melanoma is less frequent in the Indian sub continent and till now there are no Indian studies reporting the experience of SLNB. We present our 8 years consecutive clinical experience of performing SLNB for cutaneous melanoma. We evaluated the outcome of patients in terms of disease progression and mortality based on the SLNB result.

MATERIALS AND METHODS

This is a retrospective study which was done at our centre from 2013–2020. SLNB has been performed for cutaneous melanoma in our centre by the Plastic surgery team since 2013.

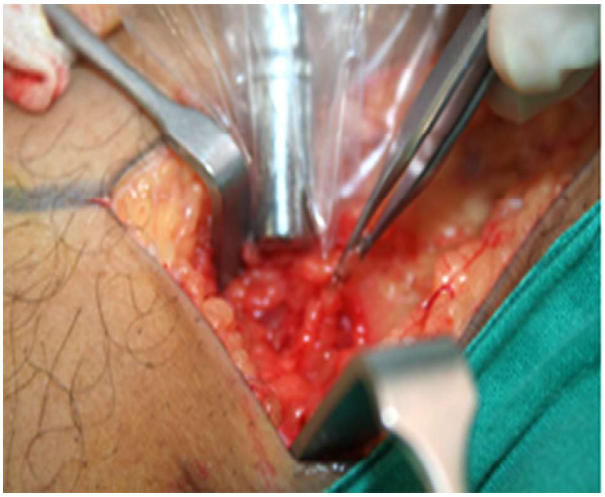

Fig. 1: Hand held Gamma camera being used to identify Sentinel node intraoperatively



Fig. 3: Confirmation Ex Vivo

From 2013 to 2020, 44 patients (30 mens and 14 womens) with non-metastatic melanoma under went SLNB. Inclusion criteria included all patients with a primary cutaneous melanoma without clinical evidence of metastasis who under went SLNB. Follow up period ranged from 12 to 64 months (Mean 42 months). Patients with head and neck CM and those with clinical or radiological evidence of regional nodal metastasis were excluded.

Patients were selected and each clinical data was obtained from the Online hospital medical records system. The following data were collected: epidemiological criteria (sex, age), histological criteria, clinical features, SLN status (positive or negative), results of CLND and evolution criteria (relapse and survival).

SLNB PROCEDURE

Preoperative lymphoscintigraphy was done in all patients wherein we injected technetium Tc 99m labelled sulphur colloid intradermally around the lesion.



Fig. 2: Geiger counter

Gamma camera was used and the SLNs were visualized and the site of SLN was marked by the Nuclear medicine team. Surgery took place the same day. The SLN was identified intra-operatively using a hand heldgamma probe. (Fig. 1-3). After SLN harvesting, the radioactive count was measured using the gamma probe. The background count of the wound bed was then measured to ensure that all radioactive nodes have been removed. The specimen was sent for Histopathological evaluation.

FOLLOW-UP

Patients were followed up in an outpatient setting by clinical examination post-operatively on a 4 monthly basis for the first 1 year then 6 monthly for the next year and every year for the next 3 years. In addition, periodic assessment in the form of CT thorax was done to rule out any metastatic spread. PET CT was considered if the patient showed evidence of regional nodal spread on clinical or radiological examination. Tumour progression and survival status were gathered from the hospital clinical data and by directly contacting the patient from the information available in hospital records.

RESULTS

From 2013 to 2020, 44 patients (30 men and 14 women) with non-metastatic melanoma underwent SLNB. The mean age was 56 (16 to 86). Positive sentinel nodes were identified in 12/44 (27%) patients. Single SLN was harvested in 67% of our cases, the mean number of SLN harvested was 1.5 in our study.

All the patients with positive SLN were offered completion lymph node dissection, 11 of 12 patients under went additional CLND. One patient refused further surgical intervention. None of them had any relapse in the operated site. 3/12 patients had further pathologically positive lymph nodes. Of the patients with positive SLN, all were offered adjuvant therapy but none of them agreed, possibly because of the high costsinvolved.

Patients were followed up for a period ranging from 12 months to 64 months, with a mean follow up period of 42 months. Of the patients who were SLN positive (12/44), 9/12 (75%) developed progressive disease, 2/12 (17%) have remained disease free, 1 patient died in the postoperative period because of an adverse cardiac event post inguinal block dissection. Among the SLN positive group the mean time for detection of progressive disease was 18 months. 2 patients developed In transit / Satellite nodules, 2 patients developed Pelvic nodal disease detected via radiological imaging, 2 patients developed lung metastases, 2 developed brain metastases and 1 patient was detected to have peritoneal disease.

Table 1. Age distribution of patients who underwent Sentinel node biopsy for Extremity melanoma at our centre

Age Distribution	Number
21-30	1
31-40	2
41-50	9
51-60	12 (27%)
61-70	10
71-80	8
81-90	2

Table 2 . Association between tumor thickness and sentinel lymph node positivity.

T Stage	SLN +(12)	SLN - (32)
T1	-	2(6%)
T2	-	7(21%)
T3	2 (17%)	14(43%)
T4	10 (83%)	9(28%)

Table 3. Association between ulceration and sentinel lymph node positivity.

Ulceration	SLN +	SLN -
Yes	11(91%)	21(65%)
No	1(9%)	11(35%)

In the SLN negative group 24/32(75%) patients have remained disease free till date, 8/32 (25%) patients developed progressive disease. Out of these 3 (9%) patients developed in transit /satellite lesions. 4 (12%) patients developed nodal recurrence which constituted the false negative percentage of our series. 1 patient developed lung metastasis. The mean time for development of Nodal recurrence was 32 months. 3/4 patients with subsequent nodal recurrence underwent completion lymph node dissection. 1 patient refused further surgery and all patients who underwent CLND went on to develop distal metastases.

The overall cohort mortality rate was 27 % (12 / 44). The mortality rate was significantly higher in the SLN positive group than in the SLN negative group (75% versus 9.3%), The 3-year overall survival (OS) rate was 73 % for all patients, but was significantly higher for SLN negative patients as compared to SLN positive patients. The 3-year disease free survival (DFS) rate was 43.6% for all patients, but was significantly higher in SLN negative patients than in SLN positive patients.

Complications of SLN biopsy were seen in 36% (16/44) of patients. The complications which were noted were seroma (8/44) which was the commonest complication, cellulitis and surgical site infection. Post-operative complications of additional CLND were observed in 42% of patients (6/14), which included skin necrosis, seroma,

cellulitis and lymphodema.

DISCUSSION

Despite the small number of patients in our cohort, our results confirm previous studies on SLN analysis in melanoma, in terms of SLN identification rate (100%), percentage of SLN positive patients (27%) and percentage of additional positive on CLND (25%).[6-9,20] We also observed a significant association between positive SLN and primary tumour thickness and microscopic ulceration (Table 1-3). Although only one SLN was harvested in 67% of our cases, the mean number of SLN harvested was 1.5 in our study which is similar to those found by previous studies.[10,20] SLNB has contributed to the selection of earlier CLND in patients without nodal disease by detecting microscopic positive SLN. Complete lymph node dissection (CLND) has been a vital in the treatment of melanoma patients with a positive SNB for quite some time now. And the same was being followed in our institute till recently. The underlying idea behind performing CLND is to preventing systemic spreadand attain accurate staging. But recent data has brought this policy into question. Two Randomised controlled trials have been published the MSLT-2 (Multicentre Selective Lymphadenectomy Trial) and DeCOG (German Dermatologic Cooperative Oncology Group Selective Lymphadenectomy)[4] comparing the effectiveness of CLND with observation after positive SNB. DeCOG had patients within the age group of 18-75, and patients with tumor thickness < 1mm were excluded. DeCOG study did not find any differences in survival in between the groups. In MSLT-2 SLNB positive patients were randomly allotted to either CLND group or observation group and CLND was done only in patients with nodal recurrence. The local disease control rate was improved in the immediate CLND group compared with observation but there was no difference in survival. There has been a meta analyses by Delgados[11] which included four RCTs, comparing immediate CLND with observation/delayed CLND there was no survival benefit from CLND. In the clinical scenario, it is difficult to decide which patients should undergo CLND or not. Considering the new age of adjuvant treatment, both Combiad[12] and Check Mate 23813 trials included patients who were stage III and IV, with patients required to undergo CLND before randomly allotting them to systemic treatment or placebo. It was unclear if there is a benefit with CLND compared with observation in combination with adjuvant treatment such as BRAF/MEK inhibition or PD-1 inhibition. In the case of a positive SNB, it is extremely vital to discuss all options with the patient and to openly discuss the possible benefits and risks associated with the procedure. Furthermore, if there is nodal recurrence without signs of distant metastases CLND can be offered. Our overall survival rates (34% and 82% for SLN positive and negative patients, respectively) were similar to previous prognostic values of SLN analysis[14] when followed by additional CLND.

The frequency of post-operative complications (infection and lymphocele) observed in our study was more or less similar to other studies in terms of morbidity.[15]

Even though our patients are counselled for adjuvant therapy no patient has opted for the newer line of agents on a long term and most have defaulted, We discussed this with patients and the reason was because of the prohibitive cost. There are some adjuvant therapy regimens which are recommended after complete removal of stage III / IV lesions which have been approved since 2015 based on results of a few randomized trials which have shown some improvement in disease free survival with systemic agents.[16-18] According to latest data those patients who are SLNB positive and tumour thickness is 1mm or more should now be considered for adjuvant therapy, and a few trials have shown a decrease in recurrence rate in patients by up to 50%,[16-18] but these trials needed CLND to be done prior to starting adjuvant treatment. But as two RCT's have now shown that there is no survival benefit after a CLND, many institutes including ours has stopped doing CLND after a positive SLNB [3,4].The main benefit of CLND seems to be that of prevention of local recurrence. In comparison adjuvant therapy might improve distal as well as local DFS. With modern immunological drugs, adjuvant therapy has now been shown to improve DFS in stage III patients after completere section and. In a study by Farrow et al[19] where they analysed different studies, they observed no difference in the DFS of patients who had received adjuvant therapy after only SLNB without CLND and and those who underwent CLND .

In conclusion the main benefit of this study was in understanding the prognostic value of SLNB in terms of relapse and survival. The usefulness of CLND excision is still a subject of debate due to the high percentage of normal results after final histopathology and the morbidity associated with surgery. All recent evidence shows that newer adjuvant drugs, although prohibitive by costs, have a significant role to play and we are trying to recruit

and study response in our patients in the future.

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