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ORIGINAL ARTICLE

The Feasibility of Sentinel Lymph Node Biopsy with a Multidisciplinary Cooperative Team Approach for the Management of Koreans with Cutaneous Malignant Melanoma

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Background: The regional lymph nodal status is the most powerful independent predictor of survival for patients with clinical N0 primary cutaneous malignant melanoma. **Objective:** We wanted to evaluate the feasibility and morbidity of the sentinel lymph node biopsy (SLNB) staging using a multidisciplinary team approach, in cooperation with other surgical departments, at a university hospital setting. **Methods:** Twenty two patients with cutaneous melanoma and who were treated at Kyungpook National University Hospital were included in this study. They all received SLNB, which was done by the Departments of Dermatology and General Surgery. We evaluated the feasibility and side effects of SLNB. **Results:** Pathologically-positive sentinel nodes were found in 7 of the 22 cases (31.8%) and all 7 patients were consequently upstaged. The whole process involved in SLNB was well tolerated by nearly all the patients, with only mild and transient complications being observed. **Conclusion:** We suggest that in a Korean setting, utilizing SLNB with a multi-disciplinary team approach is a technically feasible procedure that is able to detect occult nodal metastasis with low morbidity rates in patients with cutaneous malignant melanoma. **(Ann Dermatol 22(1) 26～34, 2010)**

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Malignant melanoma, Multidisciplinary approach, Sentinel lymph node, Sentinel lymph node biopsy

INTRODUCTION

Primary cutaneous malignant melanoma was thought to be a disease of Western countries due to its fairly low incidence rate in Asian countries. Yet the incidence of malignant cutaneous melanoma has increased 3-fold worldwide since the early 1970s[1]. It is significant that the incidence of melanoma has shown steady increments in countries such as Korea, Japan and China, although these increments are not as high as those in Western countries[2,3]. As the incidence rate is also increasing among Asians, the importance of making an early, accurate diagnosis and the proper management of malignant melanoma according to accurate staging has been emphasized. Among the main prognostic factors for primary melanoma of the skin, the status of the regional nodes, and particularly the number and burden of metastatic lymph nodes, is the most important prognostic factor. Various methods to detect micro- or macroscopic nodal metastasis have been investigated and scrutinized. The traditional method was to remove all the regional lymph nodes that drained the tumor and search for evidence of metastasis. However, this elective lymph node dissection incurs some risky and troublesome complications such as chronic lymphedema, nerve injury, deep vein thrombosis and

thrombophlebitis. More importantly, only 20% of melanoma patients are diagnosed as having metastasis in the nodes that are harvested through elective dissection surgery[4]. Biopsy of the first draining lymph node, the so called sentinel lymph node biopsy (SLNB), has permitted selective lymph node assessments for regional metastasis. SLNB shows a relatively high accuracy rate of 99.1% by using blue dye plus a radiocolloid in regards to lymphatic mapping. This method is known to be useful, and especially for thin melanoma for accurate staging and to determine the postoperative adjuvant treatments.

SLNB is based on the hypothesis that hematogenous spreading follows lymphatic spreading, although there is some controversy about this[5]. Lymphatic drainage from the primary tumor follows an orderly progression through the afferent lymphatic vessels into the SLN(s) before flowing into the non-SLN(s) in the regional lymphatic basin[6,7]. It is generally thought that lymphatic metastasis does not create skip metastasis and consequently, the occurrence of negative results on SLNB means there is no metastasis of the regional nodal basin containing the SLN(s)[8]. For the SLNB technique, lymphoscintigraphy detects the SLN and biopsy of this node allows for accurate pathologic staging, and this makes it possible to achieve higher accuracy for melanoma staging than the accuracy of just the clinical staging in the era before SLNB. This procedure provides a direction for the appropriate management of melanoma, for example, deciding on whether or not to use adjuvant therapy.

In Korea, several reports regarding SLNB in the treatment of cutaneous malignant melanoma have been published[9,10]. However, SLNB is not yet extensively performed in Korea, unlike that in western countries. This report focuses on the feasibility and morbidity of performing SLNB for patients with primary cutaneous melanoma, and particularly with the cooperation of the Departments of Dermatology, General Surgery and other departments in a university hospital setting.

MATERIALS AND METHODS

Patient selection

From March 2006 to February 2009, 54 patients were diagnosed as having primary cutaneous malignant melanoma in Kyungpook National University Hospital. In this group, 22 patients with cutaneous melanoma thicker than 1.01 mm (Breslow thickness) and no nodal and distant metastasis as assessed clinicoradiologically were enrolled in a prospective study at the Departments of Dermatology and General Surgery. The patients with melanoma thinner than 1.0 mm, but who had high risk factors like histopathological ulceration (T1b) or definite evidence of extensive regression were also enrolled in the study. One of the most important preoperative evaluations, PET-CT, was performed for all the patients to ensure that they had no distant metastasis.

Patients and methods

1) Patients (Table 1)

The clinicopathological characteristics, including the gender and age of the patients, the location of tumor, Breslow's thickness and the laboratory and radiologic findings were evaluated. SLNB was conducted in 22 patients after the surgical procedure. Comparisons between the clinical staging and histopathological staging of the patients were evaluated.

2) Lymphoscintigraphy and sentinel lymph node biopsy

The detailed accounts for the SLNB procedure are provided as follows (Fig. 1). The patients underwent lymphoscintigraphy on the day or the day prior to the surgery in order to identify all the basins at risk and the SLN, as well as any possible interval nodes. A single dose of radioactive contrast (Tc^{99m}) in normal saline was injected intradermally around the biopsy site with a 27-Gauge needle at two to four points, depending on the size of the cutaneous melanoma. Dynamic imaging, with using a low energy high resolution collimeter to visualize the lymph flow, was initiated immediately after tracer administration, and the imaging was continued for 20 min. Static scintigrams were subsequently acquired. A radioactive flood source was used to outline the body contour. Another set of static images was taken 2 hr later. All the possible lymph drainage regions were imaged (Fig. 1A). In regards to melanoma that was located in the upper extremities, with the exception of the lower extremities and trunk, an intradermal injection of 1～2 ml methylene blue was added just before draping the operation site, in addition to lymphoscintigraphy, to facilitate the detection of SLNs in the rather sophisticated axillary vault. With the patient positioned on the operating table, external counting with using a hand-held γ-probe was repeated to confirm the location of the SLN prior to the procedure (Fig. 1B). Different anesthetic methods were applied according to the site of the primary lesion. In regards to the groin area, local anesthesia alone was sufficient for SLNB, but SLNB was conducted in the axillary area under general anesthesia due to risk of intolerable pain during local anesthesia. In the case of primary melanoma lesions in the lower extremity, SLNB was done by dermatologists, but SLNB was done by general surgeons in the case of primary lesion in the upper extremity. After the skin

Table 1. The clinical and histopathological information of the melanoma patients and the staging

Patient No.	Gender/Age (yr)	Primary tumor			SLN status		AJCC staging		
		Primary site	Thickness (mm)	Pathologic type	SLN site (number)	SLN microscopic status	Clinical stage	Pathologic stage	Up staging (+/−)
1	F/64	Rt. sole	9.1	ALM	Rt. femoral LN (1)	+	IIB (T4aN0M0)	IIIC (T4aN1M0)	+
2	M/42	Rt. 4th toe	1.21	ALM	Rt. popliteal LN (1)	−	IB (T2aN0M0)	IB (T2aN0M0)	−
3	F/75	Rt. 3rd finger	4.01	NM	Rt. axillary LN (1)	−	IIB (T4aN0M0)	IIB (T4aN0M0)	−
4	M/42	Rt. heel	5.1	ALM	Rt. femoral LN (1)	+	IIC (T4bN0M0)	IIIC (T4bN1M0)	+
5	M/69	Lt. sole	2.5	ALM	Lt. femoral LN (1)	−	IIA (T3aN0M0)	IIA (T3aN0M0)	−
6	M/51	Lt. sole	4.52	ALM	Lt. femoral LN (1)	+	IIC (T4bN0M0)	IIIB (T4bN1M0)	+
7	F/59	Rt. upper arm	1.1	SSM	Rt. axillary LN (1)	−	IB (T2aN0M0)	IB (T2aN0M0)	−
8	M/70	Upper back	3.5	NM	Lt. axillary LN (1)	+	IIC (T4bN0M0)	IIIC (T4bN2M0)	+
9	M/65	Lt. 4th finger nail	2	ALM	Lt. axillary LN (1)	−	IB (T2aN0M0)	IB (T2aN0M0)	−
10	M/54	Lt. sole	4.1	ALM	Lt. femoral LN (2)	+	IIB (T4aN0M0)	IIIA (T4aN1M0)	+
11	F/58	Lt. thumb	1.5	ALM	Lt. axillary LN (1)	−	IB (T2aN0M0)	IB (T2aN0M0)	−
12	M/54	Lt. sole	3.8	ALM	Lt. popliteal LN (1)	−	IIB (T3bN0M0)	IIB (T3bN0M0)	−
13	F/37	Rt. thumb	2.22	ALM	Rt. axillary LN (1)	−	IIA (T3aN0M0)	IIA (T3aN0M0)	−
14	F/39	Lt. sole	1.54	ALM	Lt. femoral LN (1)	−	IIB (T3bN0M0)	IIB (T3bN0M0)	−
15	M/40	Lower back	1.82	NM	Lt. femoral LN (1)	+	IB (T2aN0M0)	IIIA (T3aN1M0)	+
16	F/79	Rt. 2nd toe	3.6	ALM	Rt. femoral LN (1)	−	IIB (T3bN0M0)	IIB (T3bN0M0)	−
17	M/84	Rt. sole	1.5	ALM	Lt. femoral LN (1)	−	IIA (T2bN0M0)	IIA (T2bN0M0)	−
18	F/64	Lt. heel	2	ALM	Lt. femoral LN (1)	−	IB (T2aN0M0)	IB (T2aN0M0)	−
19	M/72	Rt. thumb	2.2	ALM	Rt. axillary LN (1)	−	IB (T2aN0M0)	IB (T2aN0M0)	−
20	M/84	Rt. heel	3.5	ALM	Rt. femoral LN (1)	−	IIIA (T4aN1M0)	IIIA(T4aN1M0)	−
21	F/64	Rt. toe nail	5	ALM	Rt. femoral LN (1)	−	IIB (T4aN0M0)	IIB (T4aN0M0)	−
22	M/42	Rt. thumb	2.5	ALM	Rt. axillary LN (1)	+	IB (T2aN0M0)	IIIA (T2aN1M0)	+

SLN: sentinel lymph node, ALM: acral lentiginous melanoma, NM: nodular melanoma, SSM: superficial spreading melanoma.

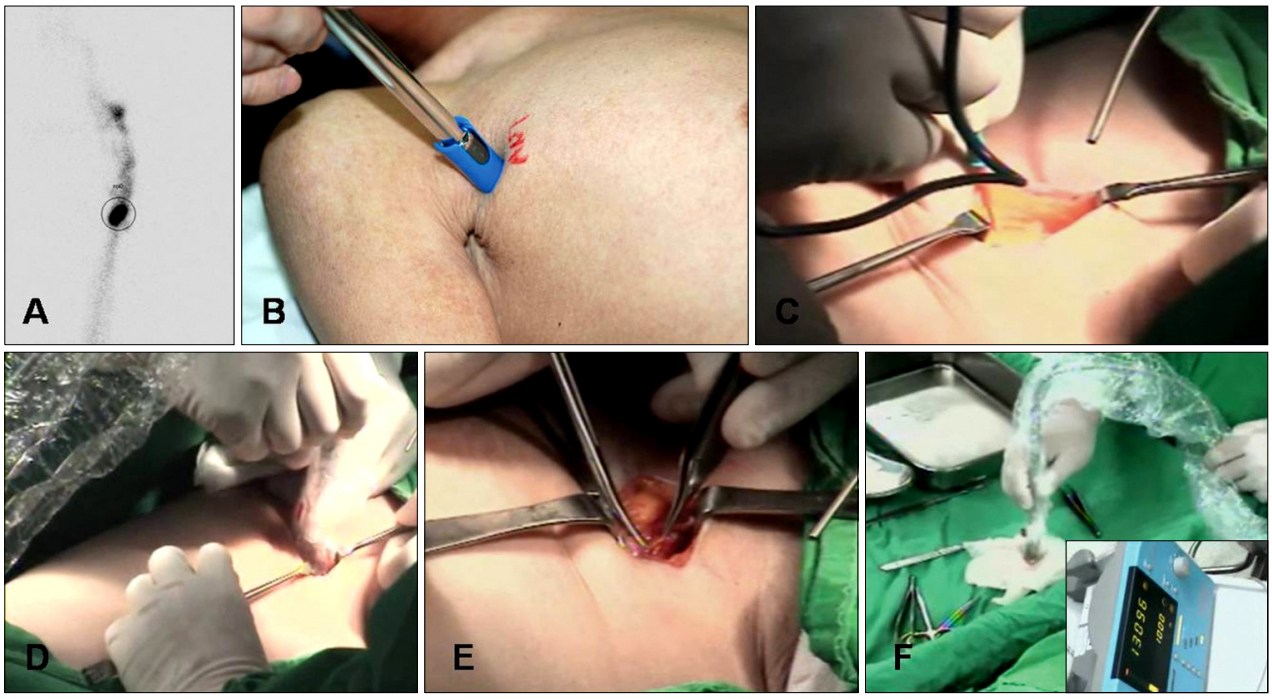

Fig. 1. (A) The lymphoscintigram obtained from a patient who recently underwent surgery for cutaneous melanoma on the left sole: Lymph flows toward a single sentinel node in the left groin area (circle). (B) External γ-probe counting: approximation of the location of the SLN(s). (C) Incision (2～4 cm) on the skin & subcutis of the axilla. (D) Surgical dissection is guided by a hand-held γ detection probe and/or combined with blue dye in the axilla. (E) Harvesting SLN(s) & measuring their radioactivity. (F) Confirmation of no more significant radioactivity except the SLN(s). The excised SLN showed high radioactivity (inset).

incision (3～5 cm) was completed (Fig. 1C), surgical dissection was guided by a hand-held gamma detection probe to investigate the blue-stained afferent lymphatic vessels that led to hot and/or blue-stained SLN(s) (Fig. 1D). The hot node, which definitely had higher radioactivity compared to the surrounding lymph nodes, was regarded as the SLN. Hot nodes were usually identified in comparison to the background radioactivity, which is defined as the average count rates of the surrounding non-SLNs, as well as that of the lymph node basin. Any lymph node for which the counting rate was more than 10% of the radioactivity at the hottest node in the basin was considered as an additional SLN and it was harvested (Fig. 1E). This procedure was performed in all the lymphatic draining basins that were identified by preoperative lymphoscintigraphy. Once the SLN has been identified, harvested and measured again for radioactivity, the probe was used to search the harvested bed to ensure that there were no residual nodes with meaningful radioactivity (i.e., a SLN) (Fig. 1F). After confirming no meaningful radioactivity by the probe, a primary layered closure was conducted on the biopsy site. The complications or side effects that developed after the SLNB were also evaluated.

3) Histopathological examination

The specimen preparation methods were also different according to the site of the primary lesion (i.e., permanent preparation for the lesion of the lower extremity and the frozen section for that of the upper extremity).

The collected SLN(s) from the lower extremity were used for hematoxylin-eosin (H&E) staining and immunohistochemistry, (i.e., S-100 and HMB-45 through the usual formalin fixation) to ascertain the metastasis of malignant cells. If metastasis was present in the permanent section of the SLN, then a complete dissection of the draining basin was conducted a few days later. In contrast, a SLN from the upper extremity, in regard to the frozen sectioning, was immediately sent intraoperatively to the Department of Pathology to ascertain the presence of malignant cells. If metastasis was present in the frozen section, then a complete dissection of the draining basin was immediately conducted. However, if malignant cells were not present, then primary closure was done on the biopsied site. Thereafter, the excised SLNs were again stained for H&E, S-100 and HMB-45, through usual formalin fixation, in order to ascertain the presence of metastasis by malignant cells.

RESULTS

Clinicopathological characteristics

Of the 22 patients who underwent SLNB, 13 were males (59.1%), 9 were females (40.9%) and their ages ranged from 37～84 years (average age: 59.5 years). The location of primary melanoma was almost always on the extremities; for the total 22 cases, there were 13 cases (59.1%) on the foot (sole, heel, toe, toe nail), 6 cases (27.3%) on the hand, 2 (9.2%) on the back and 1 (4.5%) on the upper arm. The clinicopathologic classification included 18 acral lentiginous melanomas (81.8%), 3 nodular melanomas (13.7%) and 1 superficial spreading melanoma (4.5%). A histopathological evaluation of the initial punch/incision biopsy or postoperative specimens revealed that the tumor depths were 1.10 to 9.10 mm. They included 7 cases of T2a (1.01～2.00 mm, no ulceration), 1 case of T2b (1.01～2.00 mm, with ulceration), 3 cases of T3a (2.01～4.00 mm, no ulceration), 3 cases of T3b (2.01～4.00 mm, with ulceration), 5 cases of T4a (>4.00 mm, no ulceration) and 3 cases of T4b (>4.00 mm, with ulceration).

There weren't any palpable lymph nodes on the physical examinations and no abnormal findings on the preoperative laboratory tests (i.e., CBC, renal function test, liver function test, urinalysis, hepatitis viral marker, VDRL, HIV antibody test and the basic radiological evaluation, chest X-ray and EKG).

Lymphoscintigraphy and sentinel lymph node biopsy

For all 22 patients, 23 SLNs were identified at the preoperative lymphangiography stage, and these were all located in the local lymph node basin. As 2 SLNs were detected in 1 case, a total of 23 SLNs were harvested and he underwent a histopathological evaluation for the detection of micrometastasis. Most of the SLNs were located in the ipsilateral axillary lymph node for the upper extremity lesions as well as in the ipsilateral femoral lymph node for the lower extremity lesions. In regards to the 2 back lesions, a SLN of the upper back melanoma was found in the ipsilateral axillary lymph node, and that of the lower back melanoma was found in the ipsilateral femoral lymph node.

The SLNs were pathologically tumor-positive in 7 out of the 22 patients (31.8%) (Fig. 2). All the patients who exhibited micrometastasis in the SLN showed pathologic upstaging (Fig. 3). These 7 patients showed upstaging: 2 patients from stage IB (T2aN0M0) to IIIA (T3aN1M0), 1 patient from stage IIB (T4aN0M0) to IIIA (T4aN1M0), 1 patient from stage IIB (T4aN0M0) to IIIC (T4bN2M0), 2 patients from IIC (T4bN0M0) to IIIC (T4bN1M0) and 1 patient from IIC (T4bN0M0) to IIIB (T4bN1M0).

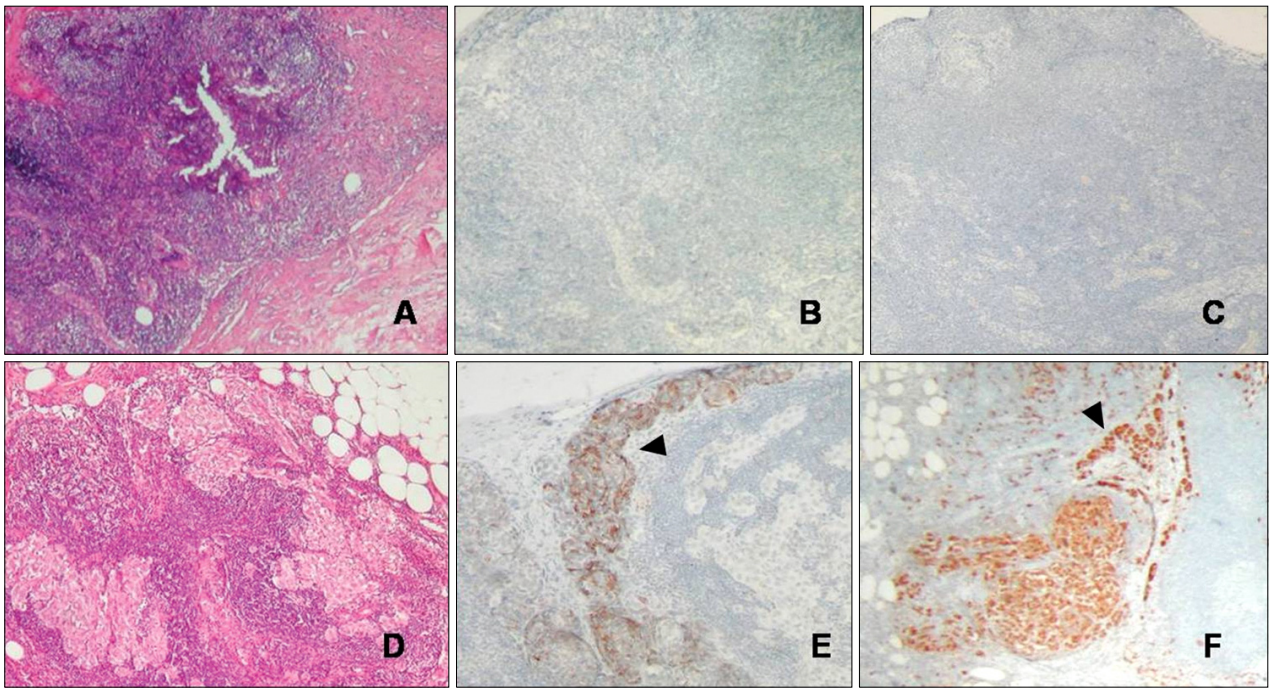

Fig. 2. Histopathological examination of the sentinel lymph node biopsy specimen showing a negative result in case 2 (A: H&E, ×100, B: HMB45, ×100, C: S-100, ×100) and micrometastasis (arrowhead) in case 4 (D: H&E, ×100, E: HMB45, ×100, F: S-100, ×100).

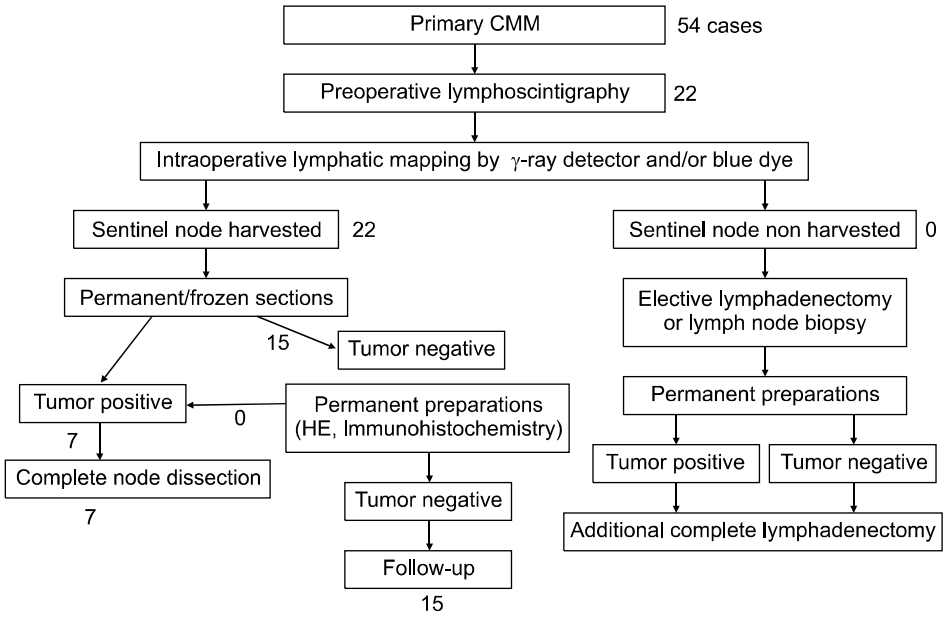

Fig. 3. The algorithm of the procedure and the result of SLNB in 22 melanoma patients at our hospital.

After SLNB, the patients having melanoma in their toes and/or fingers underwent excision with a safety margin and/or amputation, as suggested by the NIH guidelines[11]. Patients with positive SLN(s) underwent complete lymph node dissection procedures. In regards to regular follow-up, 2 patients exhibited local and distant metastasis, and both showed positive SLNB results. In addition, 1 patient (case 4, IIIC) whose primary lesion was on the right heel revealed multiple metastases on the internal organs and bones with respect to the PET-CT conducted 3 months after the operation, and this patient was referred to the Department of Hematology-Oncology for treatment. In spite of treatment, his disease spread over his whole body and he died after 6 months. The other patient (case 8, IIIC) who had a primary lesion on the upper back exhibited local lesion recurrence on the skin close to the primary lesion, so a local excision was again conducted. During regular follow-ups, a solitary asymptomatic nodule was discovered to have developed on the chest, which turned out to be metastatic malignant melanoma. A wide local excision was then conducted. He has continued to regularly visit the Department of Dermatology and Hematology-Oncology until the present time, 18 months after treatment was initiated.

There were neither intolerable significant complications nor side effects after SLNB in most patients. After SLNB, 4 patients complained of neurologic symptoms such as a tingling sensation and dysthesia on the biopsied site, but the symptoms improved over time. Additionally, local pain at the nodal biopsy was reported by 3 patients, and mild hematoma developed in one patient, but these problems all gradually disappeared. The pigmentation on the methylene blue injection site usually persisted for 2～3 weeks, but this remained for several months only in one patient. Any other complications, such as wound infections or persistent bleeding, were not revealed.

DISCUSSION

There is a widespread international agreement that the introduction of the SLNB procedure has been the most important advance over the past 25 years for the management of melanoma. With its introduction in the early 1990s, more accurate staging of patients with melanoma was achieved and a more rational approach became possible for the management of melanoma patients who present with clinically uninvolved regional lymph nodes[12]. SLNB is currently applied in patients with other malignant cancers, such as squamous cell carcinoma of the head and neck[13], breast cancer[14] and cervical cancer[15], in addition to those patients with cutaneous melanoma.

There is still debate regarding SLNB as to its prognostic aspects, but SLNB is meaningful for accurate staging. The 'watch-and-wait policy' was previously applied to melanoma patients with clinically-negative lymph nodes and who underwent wide excision of the primary melanoma with a 1 or 2 cm margin according to the Breslow thickness. When lymph nodes became palpable during follow-up procedures, then therapeutic lymph node dissection was performed[16,17]. Yet recently, if SLNB detects positive node(s), then a complete lymph node dissection is performed.

SLN is known to be the first lymph node that drains a tumor. The English word "sentinel" is used to describe a specific lymph node that drains a particular area, and this node appears as the "sentinel lymph node" when the nodes receiving direct lymphatic drainage are identified by vital dye staining. Although many researchers had recognized the sentinel node concept, the potential surgical application of lymphatic mapping and SLNB was not fully appreciated until the report by Morton et al.[7].

Generally speaking, SLNB is based on the concept that lymphatic drainage from the primary tumor follows an orderly progression through afferent lymphatic vessels into the SLN(s) before flowing into the non-sentinel nodes in the regional lymphatic basin, rather than the hematogenous spread of tumor[6,7]. Lymphatic metastasis also shows "skip metastasis", so negative results for the SLNB means metastasis does not exist with respect to the regional lymph nodes[8]. SLNB has several advantage: 1) it generally has a high success rate (86～100%), 2) an accurate pathological diagnosis is achieved in comparison to elective lymph node dissection and 3) it is less invasive than complete lymph node dissection, so there are fewer complications i.e., chronic lymphedema, nerve injury, deep vein thrombosis and thrombophlebitis[9,10,12]. Most of all, it facilitates an early accurate diagnosis of the regional lymph nodal status in order to achieve an early diagnosis with respect to postoperative chemotherapy or adjuvant therapy. However, some studies have insisted that the possibility of hematogenous spread before lymphatic metastasis and the development of skip metastasis cannot be completely ruled out. In fact, about 2% of patients show false-negative results because of a skip metastasis[6]. However, in spite of different suggestions, SLNB generally facilitates accurate pathological staging and it helps determine further management[7,8].

A generally accepted indication for SLNB is cutaneous melanoma thicker than 1.0 mm for the Breslow thickness, due to the increased positivity according to the tumor thickness[4]. However, SLNB is also recommended for patients who are clinically node-negative with melanoma thinner than 1.0 mm and who have high risk factors such as histopathological assessed ulceration and evidence of extensive tumor regression[4]. However, performing SLNB in patients with melanoma more than 4 mm in thickness is still indisputable. One reason for this, with respect to a tumor with over 4 mm thickness, is the rate of detecting metastasis is quite high, up to 75%, so the likelihood of pre-existing nodal metastasis is also high. In a 26 month follow-up study by Sumner et al.[18], the difference of the recurrence rates between the sentinel node positive and negative melanoma patients with thicker melanoma was found to be insignificant. In other words, for a tumor that is over 4 mm thick, it is highly possible that cancer cells have already metastasize via hematogenous spread, so the sentinel nodal status does not significantly affect the prognosis[18]. However, Cherpelis et al.[16] reported that in regards to a tumor thickness of over 3 mm, the difference in the 3 year disease-free survival for the positive and negative SLNB patients showed statistically meaningful results (73% vs 37%). Though SLNB still has debatable factors, it is true that SLNB has enabled more accurate pathologic staging, and so patients could avoid unnecessary treatment such as elective lymph node dissection.

There are a few variations for detecting the SLN intraoperatively or preoperatively. One is the method using lymphangiography and the injection of a vital blue-dye technique alone[19], Another method is to first intradermally inject radiocontrast to the peritumoral areas and then perform γ-probe-guided SLNB[20,21]. The last procedure incorporates a mix of these two methods. The success rate of lymphoscintigraphy for SLN identification is usually approximately 98%, whereas the use of the vital blue-dye technique alone has a 75～80% rate of detection[19]. The addition of blue dye improves the radioguided identification of SLNs to a 98～99% success rate, and especially if the SLN is diffusely metastatic[19]. In our hospital, selective methods of discrimination were used in regards to SLNB. First, in order to detect the SLN, the patients who had a primary lesion on the lower extremities were examined using the γ-probe alone because the SLNs were in the groin area in most of the cases. In contrast, for the patients who had a primary lesion on the upper extremities, after all the SLNs were confirmed by γ-probing, an intradermal injection of 1～2 ml methylene blue was added because the lymph nodes in the axillary area were more complicated in structure. In order to detect SLN(s) easier, a combination of two methods was used in the patients with upper extremity lesions. Second, the lower extremity lesions were operated on by a dermatologist. In contrast, the upper extremity lesion surgery was conducted by general surgeons so that an immediate procedure of complete lymph node dissection could be done for the case with positive metastasis seen on the frozen section. Third, SLNB was done under local anesthesia for the patients with metastatic nodes in the groin area, but the patients with metastatic nodes in the axillary area were put under general anesthesia due to intolerable pain and the complicated structure of axilla. Last, with respect to the pathological preparation of the biopsied nodes, if the SLN(s) was in the lower extremity, then permanent fixation of the SLN(s) was done to ascertain the metastasis of malignant cells, and then

complete lymph node dissection was quickly done later by another general surgeon if positive metastasis was confirmed. If the SLN(s) was in the upper extremity, then the frozen section was immediately sent intraoperatively to the Department of Pathology in order to avoid the repetition of unnecessary general anesthesia at the time of SLNB and a complete node dissection. So, if positivity of metastasis was confirmed, then complete lymph node dissection was immediately conducted. In our hospital, various specialists are placed under one roof, and our multidisciplinary cooperative team approach is different from the prior SLNB technique in that a dermatologist plays a key role in controlling the whole process of all the departments. So, the multidisciplinary approach was an efficient, cost-effective way to care for patients with melanoma and it allows treatment by various specialists working and communicating with each other. Although this approach is considered superior to a single consultation with an individual specialist, there are still some limitations. First of all, patients often become confused after seeing several specialists with conflicting opinions. Second, the major disadvantage to this approach is that it is time-consuming for both physicians and patients, making this approach impractical in the setting of a private hospital.

The location of the SLN may be variable according to the primary lesion, as primary lesions in nearly the same location may reveal a differently located SLN. It is crucial to confirm the location of the SLN through lymphoscintigraphy. In this study, for the cases of the primary lesion in the upper extremity (i.e., palm, finger, finger nail etc.), an ipsilateral axillary node was the SLN. On the contrary, if the primary lesion was in lower extremity, i.e., sole, toe, toe nail etc., then the SLN was the ipsilaterally located femoral node. Among the 13 patients whose primary lesion was located in the lower extremity, 2 patients showed a SLN in the popliteal lymph nodes. In addition, for the 2 patients whose primary lesion on the back showed a differently-located SLN as compared to each other, one patient with melanoma on the left upper back exhibited a SLN in the ipsilateral axillary node and the other patient with melanoma on the left lower back exhibited an ipsilateral femoral node as the SLN.

Considering that the purpose of the SLNB is to pathologically confirm microscopic metastasis, there had been various attempts to improve the detection rate[22]. To do this, serial sections of the specimen, H&E staining, immunohistochemical staining with S-100 and HMB-45 and sometimes RT-PCR are conducted, and these methods are carried out differently by various hospitals[19,23]. In this study, in order to detect micrometastasis, 2～3 sections of H&E staining (according to the size of specimen), 1 section for S-100 and 1 section for HMB-45 were examined in all the excised SLNs specimens, and this confirmed that the SLNs were positive in 7 patients. The interest in detecting occult metastasis in sentinel nodes has prompted researchers to explore the most sensitive tools available, including primary cell culture and an amplification of the mRNA of specific biologic markers by RT-PCR. In principle, these techniques can detect even a few or single isolated metastatic cells among 1～10 million normal cells. This is extremely high sensitivity as compared with a detection limit of approximately 1 malignant cell in 10,000 for conventional H&E staining and 1 malignant cell in 100,000 for immunohistochemistry. Despite the high sensitivity of the RT-PCR method, we didn't perform this procedure because of the relatively high false-positive rate[19].

The common complications after SLNB are edema, tenderness and infection of the operation site. Most of the patients included in this study did not show any significant complications or side effects. Although bluish pigmentation on the methylene blue injection site appeared for all the patients, it usually disappeared in 2～3 weeks. However, in one patient, it remained until several months after the operation. After that, about 1 ml of methylene blue in one finger was used, and thereafter no similar side effects developed.

The learning curve regarding SLNB reflects the time required to form a team of specialists in Nuclear Medicine, Surgery Pathology and Dermatology. Although some controversy exists about the number of procedures that a team must complete to qualify as a routine performer of lymphatic mapping in patients with cutaneous melanoma, we think Morton's suggestion of 30～50 procedures is advisable, and this is considerably fewer than the 60～80 procedures considered necessary for the lymphatic mapping in patients with breast cancer. It is also believed that the learning phase will be shorter if some or all of the team members have prior experience with intraoperative lymphatic mapping in other clinical applications (primarily breast cancer). Due to these reasons, a cooperative team approach was created for SLNB of cutaneous melanoma with respect to the breast cancer team. The multidisciplinary team for SLNB in melanoma patients must meet 2 important performance requirements to be considered as having completed their learning phase: The SLN must be successfully identified in at least 97% of patients, and metastasis must be found in the sentinel node of between 12% and 20% of the patients whose melanoma is thicker than 1 mm[19]. In this study, SLNs were identified in 100% of the cases, and metastasis was found in 31.8% of the

SLNs, so SLNB was a comparatively good modality with sufficient reliability.

This cooperative team approach has successfully identified SLNs with low morbidity rates. It is concluded that SLNB, within a multidisciplinary approach, is necessary for the accurate staging of malignant melanoma in order to direct the appropriate management of Korean melanoma patients.

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