

# 根據前哨淋巴結摘除術治療之肢端小痣性黑色素瘤 台灣首例報告

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## First Report of Acral Lentiginous Melanoma Treated According to Result of Sentinel Lymph Node Biopsy in Taiwan

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A 40-year-old female with pigmented lesion on left index fingernail for decades came to our clinic due to recent pigmentation change on her nail. An incisional biopsy was done which revealed melanoma with 1.2mm thickness. Contemplating on the need of complete lymph node dissection and the use of interferon as an adjuvant therapy, we arranged preoperative lymphoscintigraphy which revealed dominant radio tracer uptake at axilla. Sentinel lymph node biopsy was done through the assistance of handheld gamma probe. Since the sentinel node revealed no malignant cell, resection of the primary lesion was done. No further treatment was suggested except regular follow-up at our clinic. (*Dermatol Sinica* 19 : 282-287, 2001)

*Key words:* Melanoma, Sentinel lymph node, Complete lymph node dissection, Interferon, Lymphoscintigraphy

一位四十歲女性因其左手食指指甲數十年的色素病灶近來產生變化而至門診就醫。實施切片檢查為厚度1.2公釐的黑色素細胞癌。因計劃根除性淋巴結摘除及以干擾素做輔助治療，我們安排了術前淋巴閃爍檢查，並於腋下發現多數放射性追蹤劑。經手持探測器輔助，完成前哨淋巴結摘除。由於前哨淋巴結未發現惡性細胞，故將原始病灶予以切除。除定期門診追蹤外，並不建議更進一步的治療。(中華皮誌19 : 282-287, 2001)

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## INTRODUCTION

Although cutaneous melanoma is becoming an ever more common disease, the management for this fatal cancer still poses a challenge to medical professionals.<sup>1</sup> For years, appropriate surgery is the only standard treatment for melanoma. Though the efficacy of elective lymph node dissection (ELND) has been debated over the last decade, long-term follow-up of the patients has shown that survival was better for patients with microscopic nodal disease found at elective dissection than for those who did not have a node dissection until they developed gross nodal disease.<sup>2</sup> In 1992, Morton et al. developed sentinel lymph node biopsy in order to evaluate the status of lymph node metastasis.<sup>3</sup> Using this method, the status of nodal involvement can be determined without undergoing complete lymph node dissection, which has numerous associated morbidities.<sup>3,4</sup> In addition, with the result published by Eastern Cooperative Oncology Group (ECOG), a new light has shed on the treatment of cutaneous melanoma. According to this study, the prognosis of melanoma patients with nodal involvement can be significantly improved by the use of interferon alpha. Here, we present a 40-year-old woman with acral lentiginous melanoma. A therapeutic approach was devised based on current advances in the management of melanoma.

## CASE REPORT

A 40-year-old female office worker with no known underlying disease came to our clinic due to increased pigmentation on her left index fingernail. She has pigmented fingernail over left index finger since childhood. For decades, the pigmentation has been stationary. Four months prior to the office visit, onycholysis over left index finger was noticed; while no obvious change in pigmentation was noted. Subsequently, the woman removed fingernail of left index finger by herself. After a few days, several vesicles were seen on the naked nail bed, and some pigmented macules were noticed.

At our clinic, a careful documentation of

the lesion was done which include: part of the left index fingernail was removed revealing naked nail bed with minute vesicles; the remaining part contained inky black colored nail (Fig. 1A). The volar surface of the fingertip showed multiple irregular brownish macules with ill-defined border (Fig. 1B). Under the impression of acral lentiginous melanoma, an incisional biopsy was done at our clinic that revealed melanoma 1.2mm in thickness (Fig. 2). Subsequently, the patient was admitted for further management. A complete physical examination and general survey for systemic metastasis-including chest x-rays, abdominal sonography, whole body bone scan, and lymphoscintigraphy-was done which revealed no remarkable finding except dominant radio tracer up-take at left axillary lymph node. A sentinel lymph node biopsy, complete technical details described by Albertini *et al*,<sup>5</sup> was then performed after injection of the <sup>99m</sup>Tc Technetium-radiolabeled sulfur colloid with the aid of gamma probe. Since this is the first report of sentinel lymph node biopsy in Taiwanese melanoma patient, the procedure will be summarized below. Briefly, approximately 400  $\mu$ Ci of technetium sulfur colloid was injected intradermally around the primary melanoma. Preoperative lymphoscintigraphy was done after injection. Axillary sentinel node was identified according to this image study (Fig. 3). Sentinel node biopsy was then performed in the operation room. A hand-held gamma probe (neoprobe 2000) was used to identify the area of greatest activity in counts per second (Fig. 4A). The gamma probe was moved from the primary lesion site to axilla at a speed of 1 second per centimeter to detect "hot spot," which has a radioactivity greater than 150% over background. On our patient, the radio signal at primary site was 4230 and the signal at axilla was 1325; while the background radioactivity was under 10. The single node containing the majority of the radio signal was removed (Fig. 4B), and the microscopic finding of this node revealed reactive hyperplasia with no malignant cells. Amputation of left index finger's distal

phalanx was then performed. The microscopic examination of the specimen demonstrated surgical margin greater than 1cm free of malignant cells. The patient was discharged from our hospital four days after surgery. Since neither clinical nor pathological examination showed metastasis, no further treatment measure was arranged; however, regular outpatient clinic follow up was suggested.

## DISCUSSION

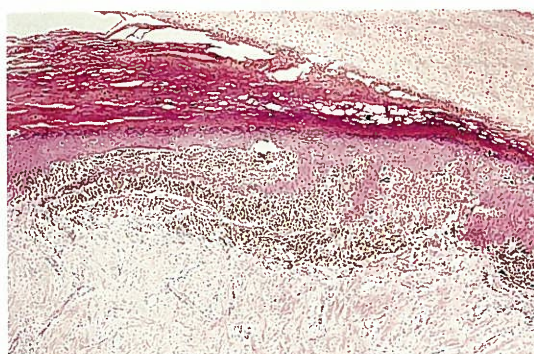
Despite numerous new therapeutic avenues for management of melanoma, there is no consensus on the treatment of melanoma except total excision of early stage tumor. Melanoma remains to be a deadly disease; at least 20% of people diagnosed with melanoma will experience advanced disease and die within 5 years of diagnosis.<sup>6</sup> In 1995, ECOG published results that altered the conventional approach to the management of early stage melanoma. According to ECOG 1684, interferon alpha-2b therapy is especially effective for patients with lymph node metastasis: The 5-year relapse-free survival rate improved 66%, and the overall 5-year survival rate improved 40%. No significant benefit was demonstrated for patients with no nodal involvement.<sup>7</sup> Thus, the status of lymph node involvement became an invaluable information which may direct the clinician's therapeutic approach. The classical method of lymph node evaluation encompassed ELND; however, this method entails considerable side effects-including lymphedema, seroma, delayed wound healing, and stiffness.<sup>8</sup> Nevertheless, according to the results from long-term follow-up of World Health Organization's randomized trial, ELND has demonstrated increased survival for patients with microscopic nodal disease found at elective dissection than for those who did not have a node dissection until they developed gross nodal disease.<sup>2</sup> Thus, lymph node dissection may benefit melanoma patients with subclinical lymph node metastasis. In 1992, Morton et al. described a method for selective intraoperative lymphatic mapping which locates the first draining node from the

cutaneous melanoma.<sup>3</sup> This node, termed sentinel node, is able to provide accurate and reliable information about the nodal involvement of the entire lymphatic basin.<sup>3-4</sup> Since occult regional lymph node metastasis occurs in less than 5% of patients with melanomas thinner than 1mm while patients with thickness between 1 and 4 mm have an occult metastasis rate of 20 to 40%, sentinel lymph node biopsy has become a standard procedure for melanoma patients with tumor thickness greater than 1mm in many cancer centers.<sup>9</sup>

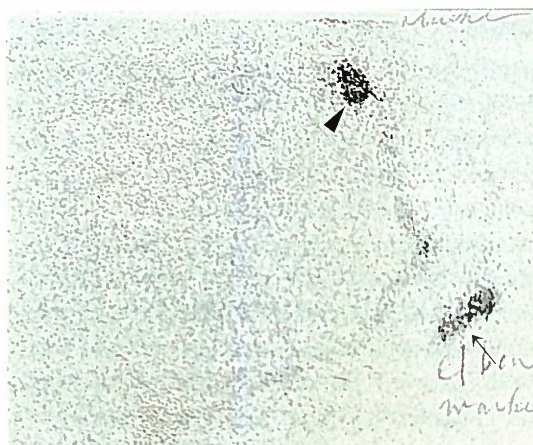
The initial sentinel lymph node biopsy reported by Morton *et al.*<sup>3</sup> showed remarkable accuracy in predicting nodal metastasis, demonstrating a false negative rate of less than 1%. Briefly, the technique involves injecting a blue dye around melanoma lesion circumferentially which rapidly diffused into the lymphatics. A skin flap was elevated and the dye stained lymphatic channel leading from the primary tumor was identified. Then by dissecting along the lymphatic channels, the first draining node was removed for evaluation. Drawbacks to Morton's original method are perceivable.<sup>10</sup> First, there is significant learning curve for surgeons associated with this difficult and tedious procedure of raising skin flaps and dissecting dye stained lymphatic duct. Second, the postoperative complications of this flap raising technique include serious morbidity, such as wound edge necrosis and seroma. The use of preoperative lymphoscintigraphy and intraoperative gamma probe have obviated the aforementioned problems. Through these new techniques, the location of sentinel node can be determined prior to the skin incision, and thus, strenuous skin flapping and lymphatic dissecting can be eliminated along with their concurrent morbidities. The hardest part of sentinel lymph node biopsy is locating the appropriate node. With the use of radio-tracers, this procedure can be successfully performed in over 95% of patients as compared to Morton's original method which has a failure rate of up to 20%.<sup>11</sup> This improvement has made sentinel lymph node biopsy a more acceptable examination.



**Fig. 1**  
(A) Part of fingernail was removed revealing naked nail bed; the remaining part contained inky black colored nail. Periungual pigmented macules were present. (B) Volar surface of the same finger showed multiple irregular brownish macules with ill-defined border.



**Fig. 2**  
Melanoma cells distributed over epidermis and upper dermis. (H & E stain, x400)



**Fig. 3**  
Preoperative lymphoscintigraphy showing sentinel lymph node over axilla. (arrow head) An elbow marker (arrow) was placed as reference.

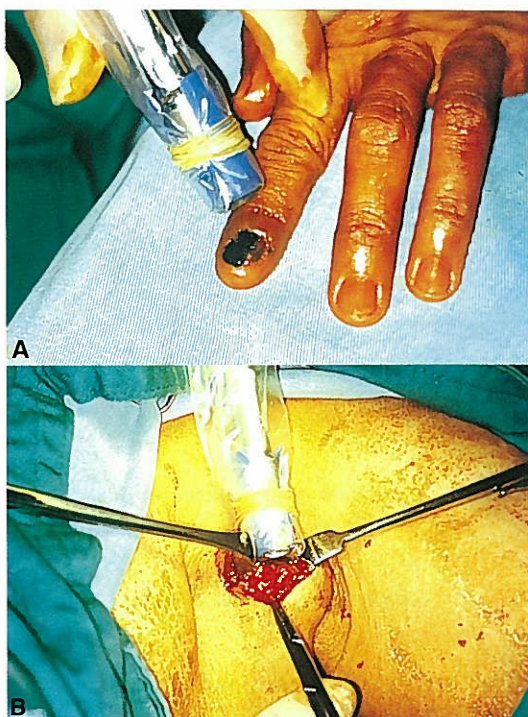
As the technique of intraoperative radiolymphoscintigraphy is refined, standard criteria for defining a hot spot will be needed. To the best of our knowledge, only Alex *et al.*<sup>10</sup> and Albertini *et al.*<sup>5</sup> have report such criteria. While Alex *et al.*<sup>10</sup> defined hot spot as lymph node having a ratio of three times that of background, Albertini *et al.* proposed a ratio of greater than one point five times background. Clearly, a more definite quantitative ratio is needed for the establishment of a standard protocol.

It is a well-known fact that the prevalence of melanoma differs between different ethnic groups. In contrast to Western countries which nodular melanoma has the highest prevalence, acral lentiginous melanoma is the type that poses greatest threat to Asian population. Through personal communication with Dr. Kuniaki Ohara of Toranomon Hospital in Tokyo, Japan, it is confirmed that Japanese dermatologists have been advocating the use of sentinel lymph node biopsy on melanoma patients for years. In their experience, this method is accurate and reliable for evaluating lymph node status. However, more data need to be gathered before a quantitative analysis can be given.

Here, we have reported a patient with acral lentiginous melanoma. After the diagnosis was

confirmed by incisional biopsy, we have taken the necessary steps-including preoperative lymphoscintigraphy and sentinel lymph node biopsy-in order to plan future treatment for this patient. Since sentinel node showed no evidence of metastasis, no further treatment was arranged for this patient except surgical intervention. The extent of surgical margin was in accordance with the recommendations published by Tseng *et al.*<sup>12</sup> However, if the sentinel node revealed positive finding, complete lymph node dissection would have been performed and the option of implementing adjuvant therapy would have been discussed with the patient. To our best knowledge, sentinel lymph node biopsy has never been performed for melanoma patients in Taiwan, though it has been a common procedure for management of breast cancer patients in several medical centers. Perhaps, the difficulty of the procedure has prevented the wide acceptance of this examination; or perhaps, the practicing dermatologists have overlooked the value of sentinel node biopsy. On the other hand, recent review by Otley *et al.*<sup>13</sup> holds a different opinion. According to the review, conflicting data have been published since the report of ECOG 1684, and there is no randomized, controlled data supporting the use of sentinel lymph node biopsy in the management of melanoma. However, Otley agrees that sentinel lymph node biopsy and systemic interferon are promising modalities in the management of melanoma. Therefore, with the development of new techniques and evidences supporting the value of sentinel node evaluation, these modalities should be made available to melanoma patients.

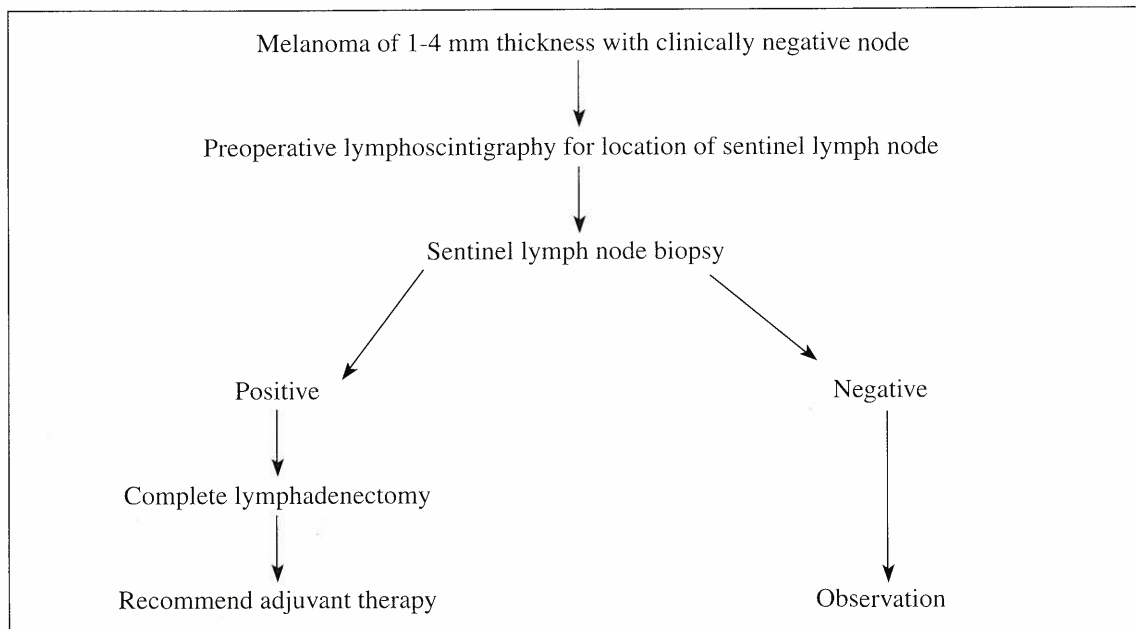
In conclusion, a patient with melanoma greater than 1 mm in thickness and no clinical evidence of metastasis should be recommended for sentinel lymph node biopsy. Those with lymph node involvement should undergo complete lymph node dissection; the results of the ECOG 1684 and related studies should be made available, so that the patients may come to an informed decision about adjuvant treatment for their melanoma (Fig. 5).



**Fig. 4**  
(A) Hand held gamma probe was used to detect radioactivity at primary lesion site. (B) After identification of hot spot, a 3cm incision was made to remove sentinel lymph node.

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**Fig. 5** Current algorithm for management of melanoma patient with lesion greater than 1mm and no clinical evidence of metastasis at Kaohsiung Medical University Hospital.

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