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CASE SERIES

Preliminary experience of reverse lymphatic mapping technique using indocyanine green dye lymphangiography and patent blue dye in melanoma patients undergoing sentinel lymph node biopsies: a case series

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Summary
Sentinel lymph node (SLN) biopsy is essential for staging and treatment planning in melanoma, but access to standard techniques such as preoperative radiotracer injection may be limited in resource-constrained settings. We describe a novel technique combining patent blue dye with indocyanine green (ICG)-guided reverse lymphatic mapping to identify SLN in lower extremity melanoma. This method offers a feasible alternative when radioactive isotope injection devices are unavailable. Three patients underwent this technique with successful localisation of SLN and no complications.
Keywords: melanoma, sentinel lymph node biopsy, indocyanine green, patent blue, reverse lymphatic mapping

Case reports

Case 1

An 86-year-old female patient presented with progressive gangrene in the left big toe over several months. Debridement and incisional biopsy revealed melanoma of the acral lentiginous subtype. The melanoma lesion measured 2.6 cm in diameter, with Breslow thickness greater than 4 mm. A fluorodeoxyglucose (FDG)-positron emission tomography (PET) scan indicated no distant metastasis.

A left inguinal sentinel lymph node (SLN) biopsy was performed before the wide excision of the primary lesion, using a combination of patent blue dye and indocyanine green (ICG) reverse lymphatic mapping, as described. Prior to surgery, 0.5 ml of patent blue dye was intradermally injected at each of four points around the melanoma lesion in the lower extremity, for a total of 2 ml (Figure 1A). Subsequently, local massage for about 10 minutes is performed at the injected site to facilitate the penetration of the patent blue injection into the tissues and lymphatic systems. During the waiting period for the diffusion of patent blue dye, 1–2 ml of ICG is intradermally injected at three to four sites on the affected side, approximately 3–4 cm above the inguinal ligament, as illustrated (Figure 1B). This aims to demonstrate the lymphatic pathways. The pathway can be seen and drawn via fluorescence image (Figure 2A and B).

Once sufficient time had passed for the action of patent blue dye, about 60 minutes, an incision was made in the inguinal area, approximately 1 cm below the inguinal ligament, for SLN biopsy. By observing the direction of local lymphatic imaging with ICG, the lymphatic pathway becomes visible. Combining this information with the discolouration effect caused by the diffusion of patent blue dye permitted localisation of the discoloured SLN (Figure 2C). A total of 5 SLN stained with patent blue dye and ICG dye were extracted.

After completion of the SLN biopsy, a wide excision of the melanoma lesion was performed with a 2 cm safety

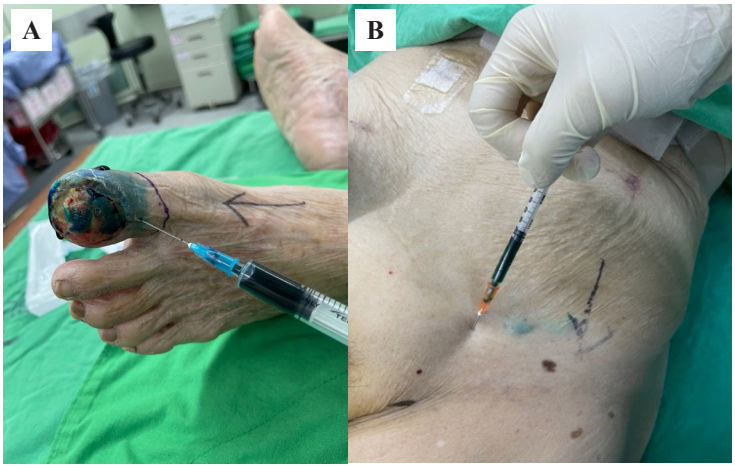

Figure 1: (A) Patent blue dye injection; (B) ICG injection

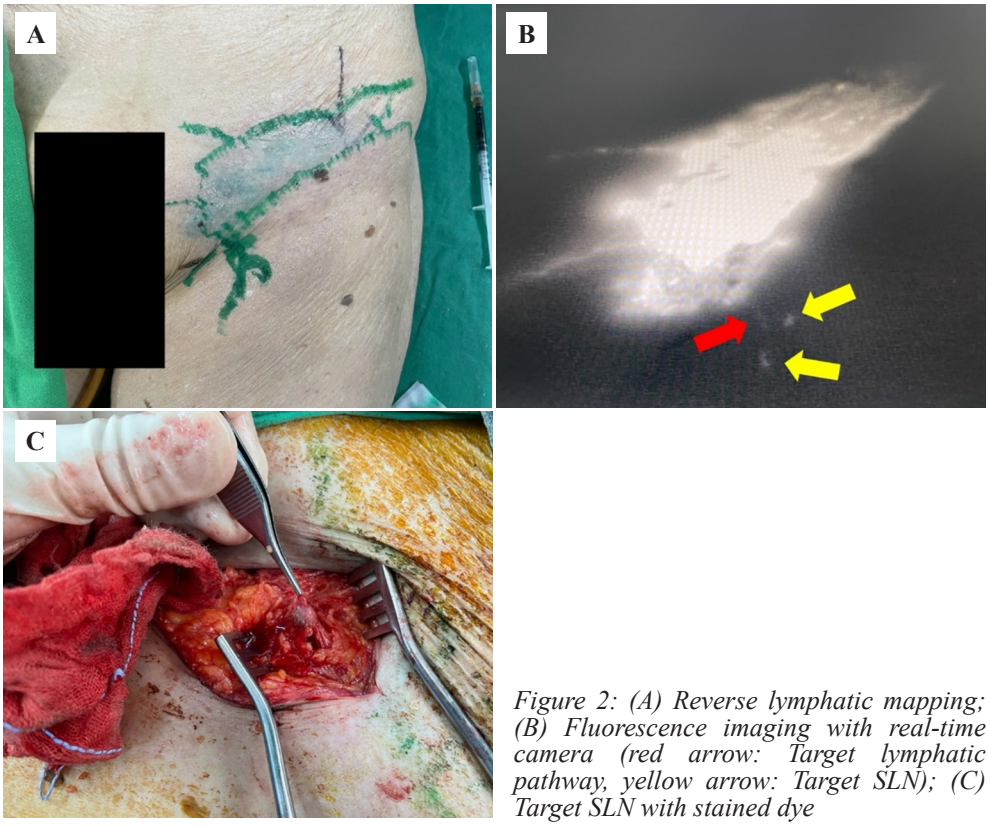

Figure 2: (A) Reverse lymphatic mapping; (B) Fluorescence imaging with real-time camera (red arrow: Target lymphatic pathway, yellow arrow: Target SLN); (C) Target SLN with stained dye

margin, based on a Breslow thickness of greater than 4 mm, and confirmed by intraoperative frozen section. In this case, amputation of the hallux was performed for oncologic safety. The entire procedure took two and a half hours.

Case 2

A 68-year-old female patient with a history of arrhythmia presented with sudden black spots on her left heel. Incisional biopsy revealed melanoma of the superficial spreading subtype. PET/CT showed no distant metastasis but intense FDG uptake only in the left heel region. The melanoma lesion measured 1.2 cm in diameter, with a Breslow thickness between 1 and 2 mm. A wide excision of the left heel lesion with a 2 cm safety margin, along with a left inguinal SLN biopsy were performed using the same mapping protocol as above. A total of 6 SLN were harvested, and the entire procedure took 3 hours.

Case 3

A 78-year-old female patient presented with a brownish nodule on the plantar aspect of the right foot. An incisional biopsy revealed the nodular subtype of melanoma. Systemic evaluation revealed no evidence of distant metastasis. The melanoma lesion measured 1.1 cm in diameter, with a Breslow thickness of greater than 4 mm. A wide excision with a 2 cm margin for the right plantar foot lesion, extending deep to the plantar fascia, was scheduled, along with wound reconstruction using a dermal substitute and a right inguinal SLN biopsy. A total of 5 SLN were extracted, and the entire procedure took two and a half hours.

In all three surgical cases, including the intraoperative delivery of frozen pathology slides, the elapsed time did not exceed 3 hours. Fluorescence imaging was performed with the real-time camera during SLN biopsy and high localisation rate of lymph nodes has been found in our experience. Postoperatively, all patients recovered well with no complications observed, and subsequent treatments proceeded as planned.
(Table I)

Discussion

The SLN biopsy plays a crucial role in the detection and treatment strategy for melanoma nodal metastases. Common techniques include preoperative injection of nuclear medicine for localisation, intraoperative use of patent blue dye injection, and the assistance of ICG in detecting sentinel lymph nodes, all serving as auxiliary methods for sentinel lymph node excision surgery.[1,2,3] However, not all hospitals are equipped with sophisticated radioactive isotope detective devices. Therefore, optimising the use of limited resources for the most accurate sentinel lymph node biopsy becomes paramount.

Similar to the combined use of patent blue dye injection and ICG to enhance the accuracy of SLN excision in breast

Table I: Summary of clinical information of 3 cases

	F/86	F/68	F/78
Underlying disease	HTN, DM, colon cancer	arrhythmia	HTN, DM
Melanoma appearance	gangrene with ulcer	black spots	brownish nodule
Clinical symptoms	wound pain	N	sting pain
Site of melanoma	left big toe	left heel	left heel
Size in cm	2.6 cm	1.2 cm	2.0 cm
Intraoperative frozen section	+	+	+
Operation time (hour)	2.5	3.0	2.5
Number of SLN biopsy	5	6	5
Complication	N/A	N/A	N/A

cancer patients[4] and the use of reverse lymphatic mapping with ICG in SLN biopsy surgery or vascularised lymph node transfer surgery for breast cancer patients,[5,6] these methods can also be employed in patients with melanoma for SLN biopsy surgery.

This approach allows patients to undergo surgery without the necessity of being in a large medical centre, eliminating the inconvenience of transfers and the long wait for surgery scheduling.[7]

Furthermore, both patent blue and ICG are readily available, cost-effective, and easy to use dyes.[8,9] During the surgical process, the prolonged diffusion of dye agents in the lymphatic system requires a skilled surgeon for assessment, and relying on a single dye agent may lead to challenging judgments. The key difference between our novel method and injecting only one dye at the melanoma lesion is the distance the dye travels along the lymphatic pathway. Intradermal injection of ICG at the inguinal region on the affected side produces reverse lymphatic pathway imaging from the proximal to the distal body. On the other hand, injecting ICG at the melanoma lesion generates a lymphatic pathway imaging from the distal to proximal body. The reverse lymphatic mapping pathway to the target SLN is shorter, significantly saving time. Combined with the staining effect of patent blue dye injection, this approach allows for a rapid identification of the targeted SLN.

The approach proposed in this study, combining patent blue dye with ICG dye to assist in reverse lymphatic pathway imaging, not only achieves accurate results in sentinel lymph node excision but also minimises the time required. However, this method is limited by a small number of cases, and further exploration with more cases is needed to investigate parameter settings and effects for improved prognosis.

To our knowledge, reverse lymphatic mapping has not previously been reported in melanoma patients for sentinel node identification. While the conventional dual technique with radiocolloid and blue dye remains the gold standard, access to radiocolloids is limited in some institutions. Our preliminary experience suggests that combining ICG-guided reverse mapping with patent blue dye is a feasible alternative in such settings. Although the total operative time in our cases may be longer due to frozen section assessment and concomitant reconstruction, the use of ICG clearly shortened the localisation process by providing rapid and reliable visualisation of the lymphatic pathway.

Our preliminary experience indicates that ICG-guided reverse lymphatic mapping combined with patent blue dye is a feasible alternative for SLN biopsy in melanoma patients when radiocolloids are unavailable. This technique enables rapid and reliable lymphatic visualisation, facilitating accurate node localisation. Further studies with larger cohorts and direct comparisons to the conventional dual mapping method are needed to confirm its efficacy.

Conflict of interest

The authors declare no conflict of interest.

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Ethical approval

This study was approved by the Institutional Review Board of China Medical University Hospital (Approval No. CMUH113-REC3-037).

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