Principles of sentinel lymph node identification: background and clinical implications

Alistair J. Cochran
Richard Essner
D. Michael Rose
Edwin C. Glass

Abstract The management of clinically negative regional lymph nodes in early-stage melanoma has been controversial for many years. While some advocate wide excision of the primary with elective node dissection (ELND), others recommend excision of the primary alone and therapeutic node dissection (TLND) for recurrences in the nodal basin. ELND is based on the concept that metastases occur by passage of the tumor from the primary to the regional nodes and distant sites, in which case early dissection of regional nodes will disrupt metastatic progression and prevent the spread of disease. Advocates of the “wait and watch” approach suggest that regional node metastases are markers for disease progression and that distant disease can occur without node metastases. Four randomized prospective studies comparing ELND and TLND have not demonstrated overall survival advantage for ELND, but suggest that patients with early regional metastases may benefit from ELND. As an alternative, Morton et al., from UCLA and the John Wayne Cancer Institute, devised intraoperative lymphatic mapping and sentinel lymphadenectomy (LM/SL). These minimally invasive operative procedures allow identification of the first and key (sentinel) lymph node (SN). The technique accurately maps the lymphatics by lymphoscintigraphy, and vital blue dye leads the surgeon to the SN. The pathologist then concentrates on seeking metastases in the nodes most likely to contain metastases. Patients with tumor-positive SN undergo completion lymph node dissection (CLND), while those without SN metastases avoid the complications and costs associated with this procedure. Morton et al., in a report on their initial experience of LM/SL, performed CLND in all cases regardless of SN tumor status and demonstrated the precise staging capacity of the procedure. Since this initial report, numerous studies have validated the accuracy and low morbidity of the procedure. Each center must master a learning phase. The procedure is dependent on the close cooperation of nuclear medicine physicians, surgeons, and pathologists. While LM/SL is now almost standard practice in the US, the results of clinical trials are awaited to determine whether LM/SL can replace ELND and TLND in the management of early-stage melanoma.

Key words Cutaneous melanoma · Regional lymph nodes · Sentinel lymph node(s) · Sentinel node dissection · Occult tumor cells · Lymphoscintigraphy
Introduction

The surgical management of regional nodes in early-stage melanoma has been controversial for over 100 years. In 1892, Snow [1] advocated wide excision and elective lymph node dissection (ELND) to control lymphatic permeation of metastases. Arguments in favor of ELND include better survival of patients with clinically negative, histologically positive lymph nodes relative to patients with clinically apparent metastases to the regional nodes [2, 3, 4, 5, 6,7]. An argument against ELND is that if all high-risk melanoma patients are subjected to ELND, 70–80% will undergo, unnecessarily, a morbid surgical procedure with a small possibility of operation-associated death. Retrospective studies suggest a survival benefit for ELND, yet the benefit of removing clinically normal nodes has not been proved by randomized prospective studies [8, 9, 10, 11,12]. Procedure cost, morbidity, and the low yield of tumorous nodes have led to a sharp reduction in the routine use of ELND, although tumor status of the nodes is important for determining prognosis and the need for adjuvant therapy [13,14].

Detection of occult regional node (see [35,41]) metastases has been improved by intraoperative lymphatic mapping and sentinel lymphadenectomy (LM/SL) [15]. This technique maps the direct lymphatic path from the primary to the regional nodes and permits selective excision of the first (“sentinel”) lymph node(s) (SN) [15,16]. Because the SN is the likely site of early metastatic tumor, focused pathologic examination permits the accurate staging of regional nodes. LM/SL is an accurate and sensitive technique for detecting regional metastases with minimal morbidity and expense.

Technical aspects and results

Technical details

LM/SL is a highly technical procedure and requires the close cooperation of nuclear medicine physicians, surgeons, and pathologists. The procedure has three steps: (1) preoperative cutaneous lymphoscintigraphy, (2) intraoperative LM/SL, and (3) detailed pathologic analysis of the SN.

Cutaneous lymphoscintigraphy

LM/SL is preceded by preoperative cutaneous lymphoscintigraphy. Robinson et al. [17] reported the use of intradermal injections of colloidal gold to document lymphatic pathways from truncal melanoma. This study confirmed that both dual and unexpected lymphatic drainage patterns are common [18,19]. Cutaneous lymphoscintigraphy has now been refined to permit the identification of lymphatic drainage patterns and the site of each SN (Fig. 1). In the US, lymphoscintigraphy is performed using technetium-99m (99mTc) sulfur colloid (SC) or albumin colloid (AC) or 99mTc human serum albumin (HSA) injected intradermally [up to 18 MBq (0.5 mCi) radiopharmaceutical] into the four quadrants around either a primary or a biopsy scar. The skin is gently kneaded to aid passage of the radiopharmaceutical through the lymphatics, and a scintillation camera documents lymphatic drainage from the primary to the regional nodes. The skin overlying the SN is marked. Because of variations in the transit time of radiopharmaceuticals, dynamic images are required to differentiate SN from non-SN. Body outlines are marked on the images to locate and orientate the SN. The surgeon must have these films for reference in the operating room.

SN can be identified 1–30 min after injection (depending on the agent and the distance of primary to regional nodes). After 4 h, SN can no longer be differentiated from non-SN [20]. We now perform lymphoscintigraphy on the day of surgery to allow the same dose of radiopharmaceutical to be used for intraoperative SN identification [21]. Lymphoscintigraphy accurately determines the node basin at risk for metastases and is particularly helpful for tumors with ambiguous lymph drainage [22] on the head and neck or on the torso.

Fig. 1 Cutaneous lymphoscintigraphy for a scalp primary melanoma. A total of 18 MBq of filtered 99mTc SC was injected intradermally around the biopsy site. Approximately 15 min later, several parotid and cervical lymph nodes are visualized and marked on the patient’s skin. The body outline is provided to assist the surgeon with the orientation of the image.