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ORIGINAL ARTICLE

THE ROLE OF SENTINEL LYMPH NODE BIOPSY (SLNB) IN THE MANAGEMENT OF DIFFERENTIATED THYROID CANCER

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Abstract

Aim: The aim of this work was to evaluate the concept of Sentinel Lymph Node Biopsy (SLNB) in the management of thyroid cancer as regards feasibility and its impact on the decision-making.

Methods: The study included 45 patients with differentiated thyroid cancer. At operation the thyroid tumour was exposed, 1.0% isosulfan blue dye was injected into it. When the dye stained a lymph node, the latter was marked and labeled as the sentinel lymph node (SLN). Total thyroidectomy and bilateral central neck dissection was then completed. The tumour and the nodes were examined histologically.

Results: SLNs were detected in 24 patients (60%). All of them showed single stained nodes. All SLNs were level VI. All were located on the same side of the tumour, inferior to the location of the inferior thyroid artery. Eighteen (75%) SLNs were invaded by malignant tissue. The remaining 6 SLNs (25%) were free of malignancy. This was confirmed by immunohistochemical staining.

Conclusion: According to the findings of the study, Sentinel Lymph Node (SLN) detection is a feasible technique. When successful, it is also a reliable one.

Keywords: Papillary carcinoma, early detection, metastases.

INTRODUCTION

Sentinel lymph node detection has become a recognized practice in detecting early lymph node spread of some cancers, including malignant melanoma and carcinoma of the breast.[1] This has stimulated researchers to explore the potentials of applying this principle to other common cancers. Papillary thyroid cancer, being one of the common cancers that usually affects young females, is suitable for that purpose.[2-4] A big percentage of patients with this tumour will have lymph node metastasis when they first present to the surgeon. Many of these metastases might be occult at the time of diagnosis. Sentinel lymph node might help identifying such occult metastasis; thus allowing them to be treated by node dissection at the same time as the primary tumour.[2] Moreover, patients with no nodal metastasis might be spared unnecessary radio-active iodine therapy. Lymph nodes of the neck are usually divided into “areas”.

(Fig. 1) shows the 6 areas of lymph nodes. The aim of this work was to evaluate the concept of SLNB in the management of thyroid cancer as regards feasibility and its impact on the decision-making.

Fig 1. Shows the six levels of cervical lymph nodes.

PATIENTS AND METHODS

The study included 45 consecutive patients diagnosed as differentiated thyroid cancer by clinical examination and/or fine needle aspiration cytology (FNAC). The study was approved by the Ethical Committee of the Faculty of Medicine, University of Alexandria, Egypt. Exclusion criteria included previous neck surgery, pregnancy and known hypersensitivity to the dye used. An informed consent was obtained from all the patients.

Peroperative workup included history taking, clinical examination, relevant laboratory investigations, including thyroid hormone assay, and ultrasonography of the neck with special emphasis on the thyroid focal lesion and cervical lymph nodes. FNAC was attempted in all patients.

All patients were then subjected to operation. A systematized surgical approach was adopted for the purpose of the study: this started by collar incision, development of sub-platysmal skin flaps and separation of strap muscles in the midline. This was followed by exposure of the thyroid gland, identification of the thyroid tumour; injection of the dye into the tumour, waiting for the dye to reach the lymph nodes, identifying the stained node, labeling it as the sentinel node (SLN), performing total thyroidectomy and bilateral central neck dissection.

The injection was given using a tuberculin syringe, 0.1 to 0.8 mL (average, 0.5 mL) of 1.0% isosulfan blue dye (Bell Venue Labs Inc, Bedford, Ohio). The needle was introduced precisely into the tumour. This was done immediately after exposure of the thyroid gland, before any further dissection into the thyroid bed to avoid disturbing the lymphatics (Fig. 2). The central neck area was then dissected to search for stained lymph node(s), which was labeled as SLN.

The resected specimen was fixed by formaldehyde, stained with hematoxylin and eosin and examined with light microscopy. If the SLN was found to be free of malignant deposits, it was further examined by immunohistochemical staining. The immune stain used was mouse monoclonal antibody for high molecular weight cytokeratin (clone 34 & E12, ready to use, Dakocytomation). The immune staining procedure was carried out using Acidic Biotin Peroxidase Complex Amplification System (Neomarkers, Ferment CA, USA) as described in the kit manual. The immune peroxidase reaction was visualized by liquid DAB chromogen (Diaminobenzoid).

When SLN is not detected, there will be NO reporting of result, i.e., as if SLN was never used. When a SLN is detected: true negative result is where SLN is free from metastases AND all other lymph nodes are also free from metastases. False negative is when SLN is free while other lymph nodes harbor metastases. True positive is when SLN is having metastases. There should not be a "false positive" result as SLN affection per se is metastasis.

Statistical analysis: Descriptive statistics were used to analyze demographic data. Sensitivity, specificity and predictive value of the SLN were calculated. The histopathological report of the excised specimen was considered the criterion standard.

RESULTS

This study included 45 patients, 19 were male (42.2%) and 26 female (57.8%). The mean age was 44.09±16.94 years.

Three patients showed hyperthyroid hormonal profile. The remaining 42 patients were euthyroid.

Ultrasound examination (US) of the thyroid gland revealed a dominant nodule on the right side in 9 patients (20%), on the left side in 23 patients (51.11%) and bilaterally enlarged asymmetrical goiter in 11 patients (24.44%). Three patients showed lymphadenopathy on US examination. They were excluded from the study.

The size of the tumour in thyroid ranged from 7 to 32 mm with a mean of 14.3+/-11.4 mm.

FNAC was attempted in all patients. It was successful in 38 patients (84.44%). It showed a papillary lesion in 21 patients (46.67%), atypical cells in 3 patients (6.67%), Hürthle cell tumour in 3 patients (6.67%) and was inconclusive in 12 patients (26.67%).

At operation, two patients (4.44%) showed enlarged lateral neck nodes. They were also excluded from the study. They were treated by total thyroidectomy and lateral functional neck dissection.

The remaining 40 patients (100%) showed no lymphadenopathy. They constituted the population of

this study. Those patients were subjected to intra-tumoural dye injection to detect SLNs. SLNs were detectable in 24 patients (60%). All of them showed single stained nodes. All SLNs were level VI paratracheal or pretracheal LNs. All were located on the same side of the tumour, inferior to the location of the inferior thyroid artery (Fig. 3). The dye reached the SLN within 1 to 2 minutes after the injection. Sixteen patients failed to show stained nodes in the central neck (40%) (Fig. 4). It was noted that parathyroid glands were not stained by the dye (Fig. 5). Finally, all patients underwent bilateral central neck dissection.

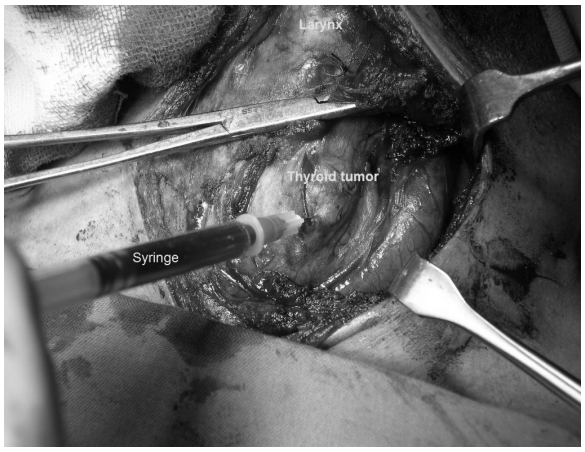

Fig 2. Isosulfan blue dye being injected into the tumour.

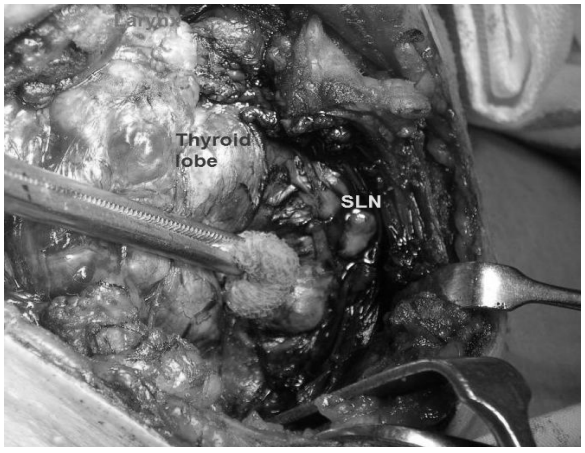

Fig 3. Successful detection of a stained lymph node after dye injection.

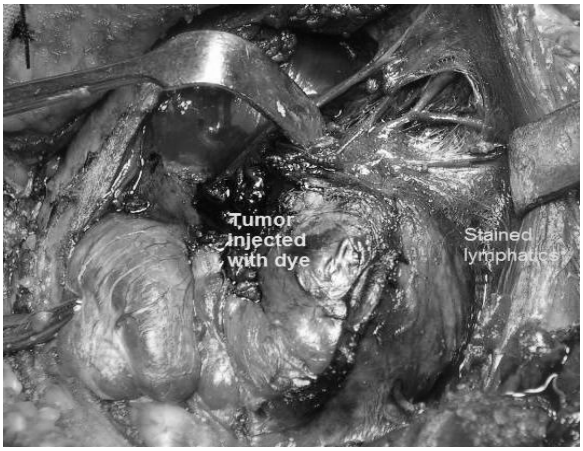

Fig 4. Stained lymphatics of the thyroid gland, but still no visible S.

Fig 5. Parathyroid gland not taking the stain.

Postoperatively, one patient (2.5%) had a temporary concussion of the right recurrent laryngeal nerve (RLN), one patient (2.5%) had seroma. Both resolved spontaneously.

Histopathological examination of the submitted glands showed that all patients had malignant tumours. Thirty six of them (90%) were papillary carcinoma, while two (5%) were Hürthle cell tumour. Examination of level VI specimens submitted from the 16 patients who did not show a stained SLN found no nodal metastases in any of them. Eighteen (75%) of the 24 SLNs submitted were invaded by malignant tissue. The remaining 6 SLNs (25%) were free of malignancy. This was confirmed by immunohistochemical staining which confirmed the absence of micrometastases.

All patients were followed up for one year. One patient (2.5%) developed node metastasis in level II 4 months after his surgery. He was one of the patients who had shown SLN that was positive for malignancy. He was subjected to functional neck dissection.

According to the findings of the study, SLN had a sensitivity, specificity and predictive values of 100% each.

DISCUSSION

Papillary thyroid cancer (PTC) associated with lymph node metastases have been associated with an increased incidence of locoregional recurrence.[5-9]

In 1977, Cabanas 10 discovered the sentinel lymph node (SLN). Morton et al in 1992[11] reported the usefulness of sentinel lymph node biopsy using vital blue dye for malignant melanoma. Keleman et al[2] as well as others have described the utilization of a vital dye technique for identification of the sentinel node in thyroid cancer patients.[3,4,6,12-14]

Haigh et al reported 33 patients who underwent SLN biopsy using a dye technique. Sentinel nodes were identified in 16/17 patients (94%).[13]

Dixon et al carried out SLN biopsy on 40 patients. Sentinel node(s) were identified in 10 of 12 patients (83%). The false negative rate was 20%.[12]

Pelizzio et al carried out SLN biopsy on 29 N0 patients with preoperative cytological diagnoses of papillary thyroid cancer. The vital dye utilized in his study was Patent Blue Dye V. The sentinel node was identified in 22 of 29 patients (76%). The location of the sentinel node was in the central compartment in 19 patients (86%) and in the lateral compartment in 3 patients (14%). When identified, the sentinel node accurately predicted the disease status of the neck in all patients.[4]

In Japan, Fukui et al[14] carried out sentinel lymph node biopsy (SLNBX) using the dye technique on 22 patients with papillary carcinoma. The vital dye utilized in this study was methylene blue. All study patients underwent central compartment and lateral compartment dissection. Sentinel nodes were identified in 21 of 22 patients (95%) and they accurately predicted the disease status of the neck in 19 of 21 patients (90%). There were 2 false negatives in this series.

Tsugawa[15] compared the incidence of malignancy in SLN as compared to that of nodes harvested during a radical neck dissection. He found that 23 (57.5%) of 40 SLNs were involved by cancer metastases in overall patients. On the other hand, only 132 (11.4%) of 1160 non-sentinel lymph nodes were involved. The incidence of metastatic nodes in sentinel lymph nodes was significantly higher than that in non-sentinel lymph nodes ($P < 0.0001$). He also reported that the sentinel lymph nodes contained cancer metastases by H&E staining in 16 (59%) of the 27 patients with identified sentinel lymph nodes. All the patients had metastases in other cervical nodes. Three (11%) of the 27 cases were falsely negative, i.e., no tumor was identified in the sentinel lymph nodes, but at least one non-sentinel lymph node had metastasis. Consequently, a diagnostic accuracy of 89%, a sensitivity of 84%, and a specificity of 100% were achieved in the diagnosis of cervical lymph node metastasis.

In this study SLN was detectable in 24 patients (60%). All of them showed single stained node in the central compartment (level VI) paratracheal or pretracheal LNs. All sentinel nodes were located on the same side of the tumour. They were all located inferior to the inferior thyroid artery (Fig. 3). Eighteen (75%) of the 24 SLNs submitted were invaded by malignant tissue. The remaining 6 SLNs (25%) were free of malignancy.

Schreiber et al reported the usefulness of using immunohistochemical staining for detecting micrometastasis in SLN.[16] Arch-Ferrer et al[6] carried out SLNBX on 22 patients using a dye technique. They demonstrated that staining the sentinel node with low molecular weight cytokerratins improved the detection of micrometastatic disease.

Following their experience, in the current study, SLNs that were negative for malignancy on H&E staining were further examined by immunohistochemical staining using cytokeratin.[20] No micrometastases were found.

Lateral neck dissection was not performed in the current study and, therefore, SLN outside the central compartment were not detectable. We realized that a modified lymph node dissection would have been the ideal criterion standard, but we were not able to justify a modified lymph node dissection in patients without gross evidence of lymph node enlargement. During the period of follow up, none of the patients who had negative SLN, showed lateral neck adenopathy.

Similar policy has been adopted by other authors: Haigh et al.[13] did not perform neck dissection to all their patients; neither did Dixon et al[4] who used radioactive iodine scan in some of their patients to scan for lateral neck nodes.

The blue dye technique remains to be a simple, quick and inexpensive.[14-17] It does not require any sophisticated equipment. It also has the advantage of being able to detect nodes in close proximity to the thyroid gland.[18-21]

The current practice is to perform bilateral central neck dissection for all patients with papillary carcinoma. This adds to the operative time and morbidity. In a clinical setting, when a SLN is detected, examined and was free from metastases, the patient will not have central neck dissection. He will not need postoperative watchful follow-up for lateral neck nodal metastases. A second potential use of SLN sampling would be to avoid[131] I ablation[6]

Haigh et al reported that blue dye uptake by the parathyroid glands led to the gland being mistakenly removed as a sentinel lymph node[13] This complication when utilizing the dye technique to carry out SLNBX on

thyroid cancer patients has also been described by Dixon et al.[4]

Parathyroid glands were not stained by the dye in the current study (Fig. 5). It might be that parathyroid glands take the dye only through the venous channels rather that the lymph. Injection strictly to the tumour would therefore avoid this complication.

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