Sentinel lymph node biopsy in N0 neck of upper aero-digestive tract Squamous cell carcinoma

ESSAY

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By

Ahmed Salah El-Din Ali

Under supervision of

Prof.Dr./Mohamed Magdy Samir

Professor Of Otorhinolaryngology

Faculty of Medicine – Ain Shams University

Dr./ Ossama Hassan Mahmoud

Assistant Professor of Otorhinolaryngology

Faculty of Medicine – Ain Shams University

Dr./ Mohamed Shehata Taha

Assistant Consultant of Otorhinolaryngology

Ain shams university hospitals

Faculty of Medicine

Ain Shams University

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List of abbreviations

- (18F-FDG PET) 18F-Fluorodeoxyglucose positron emission tomography .
- (ACOSOG) American College of Surgeons Oncology Group
- (AE1/AE3) pancytokeratin antibodies
- (cGRPP) current good radiopharmacy practice
- (cN0) clinical node negative
- (cN+) clinical node positive
- (CT) computed tomography
- (cT1/2) clinical T1/2
- (DW) Diffusion weighted
- (EANM) European Association of Nuclear Medicine
- (ECAD) E-Cadherin
- (ECS) extracapsular spread
- (END) elective neck dissections
- (ENI) elective neck irradiation
- (H&E) Hematoxylin-Eosin
-(HNC) Head and neck cancers
-(HNSCC) head and neck squamous cell carcinoma
- (HSA) human serum albumin
- (ICG) indocyanine green

- (IFP) interstitial fluid pressure

-(IHC) immunohistochemistry

-(IR) infra red

- (IRS) Intensity Reactivity Score

- (L/T ratio) longitudinal / transverse diameters ratio

-(LSG) lymphoscintigraphy

-(MBq) megabecquerel

- (MIP) maximum intensity projection

- (MR) magnetic resonance

- (MRI) magnetic resonance imaging

- (N0) clinically negative neck

- (N+) clinically positive neck

-(NDII) neck dissection impairment index

-(NIR) near-infrared

- (NPC) nasopharyngeal carcinoma

- (OCSCC) oral cavity squamous cell carcinoma

- (OCT) optimal cutting temperature.

- (OSCC) oral/ oropharyngeal squamous cell carcinoma

- (OSNA) one step nucleic acid

- (pN+) pathological node positive

- (PP) percentage of positive cells

-(QRT–PCR) quantitative real-time polymerase chain reaction

- (SCC) squamous cell carcinomas

- (SENT) Sentinel Node European Trial

- (SI) staining intensity

- (SLN) sentinel lymph node

- (SLNB) sentinel lymph node biopsy

- (SNB) Sentinel node biopsy

- (SND) selective neck dissection

- (SPECT) single photon emission computed tomography

- (SSS) step serial section

- (STDs) soft tissue deposits

- (Tc99) technetium-99

- (TC-SC) Technetium 99-labelled sulfa colloid

- (TNM system) tumor, node and metastasis system

- (US) ultrasound

- (USgFNAC) ultrasound guided fine needle aspiration cytology

- (VEGF-C) vascular endothelial growth factor C

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AHMED SALAH EL-DIN

Introduction

Head and neck cancers (HNC) are dominated by squamous cell carcinomas originated from the epithelium of the upper aerodiagestive tract. The initial route of metastases is, in most cases, via lymphatics to the regional nodes of the neck. The presence of cervical metastases (N1-N3) is the most important prognostic factor in head and neck cancer patients, reducing the survival to 50% compared with patients without nodal involvement (N0). **(1)**

Accurate staging at the time of diagnosis is critical for selection of the appropriate treatment strategy. Unfortunately, at the time of initial diagnosis more than 50% of patients already present with regional nodal metastases or even distant metastases.**(2)** A single tumor-containing node will upstage tumors to at least stage 3, irrespective of primary tumor size. **(3)**

The clinically negative (N0) neck is defined by its absence of palpable or radiographically suspicious lymph nodes. **(4)**

The management of N+ head and neck squamous cell carcinoma (HNSCC) is relatively clear-cut . By contrast, the investigation and treatment of patients with clinically N0 disease is controversial . Most institutions electively treat the neck with surgery or radiotherapy because the risk of occult metastases is over 20%, even though it will be unnecessary in the majority of cases. **(5)**

The problem of identifying microscopic nodal disease is exemplified by the patient who has a primary tumor in the head and neck, but no metastatic cervical adenopathy evident on clinical , computed tomography (CT) and magnetic resonance (MR) examinations (N0 neck by tumor, node and metastasis TNM system). **(6)**

Morphologic imaging with computed tomography and/or magnetic resonance imaging (MRI) assess the aerodigestive tract to provide information about primary tumor size, infiltration, involvement of surrounding structures and regional nodal involvement. **(2)**

Use of 18F-Fluorodeoxyglucose positron emission tomo-graphy (18F-FDG PET) in head and neck cancer compared to CT indicates that positron emission tomography has a higher sensitivity and specificity for staging cancer. The main drawback of 18F-FDG PET alone is the limitation with respect to lesion localization.**(2)**

The combined use of these modalities has proven efficacious for cases with diseased nodes larger than 1 cm. They all remain ineffective for the assessment of occult disease (tumor-containing nodes < 1 cm in size), because microscopic metastases of the lymphatics cannot be identified with imaging studies. **(3)**

By definition, the sentinel lymph node (SLN) is the first draining lymph node to receive lymphatic drainage from a primary tumor of a specific site . In case of lymphatic spread, the lymphatic drain will first pass to the SLN. All following nodes may be reached only subsequently by the disease. **(7)**

Lymphoscintigraphic localization of the sentinel lymph node in combination with ultrasound guided fine needle aspiration cytology (USgFNAC) offers the possibility of detecting occult metastatic disease in patients staged as N0. However, the potential inability of the method to puncture small sentinel nodes and incidental aspiration of micrometastatic material within a node strongly limit the negative predictive value of this method. Thus, it does not seem to be an alternative to biopsy of the SLN. **(8)**

Some authors have suggested that patients with negative results using the most accurate imaging studies, such as CT or PET-CT, could be candidates to a wait-and-see policy. **(9)**

It should be kept in mind that the stage at which recurrences are detected is also dependent on the means and intensity of follow-up and may well determine the salvage rates. Salvage surgery was successful in only 24% of patients who presented later with neck metastasis. **(10)**

Finally, although all these strategies have attempted to avoid unnecessary neck dissections, the number of negative elective neck dissections (END) could still be as high as 80%.**(9)**

The amount and quality of information currently available does not offer a definitive answer to the question of the prognostic effect of elective neck dissection. Furthermore, the recent introduction of sentinel lymph node biopsy in the diagnosis and treatment of head and neck cancer, has brought back the old question regarding the clinical usefulness of elective neck dissection. **(9)**

Sentinel node biopsy (SNB) is an alternative to elective neck dissection for the management of T1/T2 N0 oral and oro-pharyngeal squamous cell carcinomas and is also finding application to head and neck cancer at other sites. The main clinical aim of sentinel node biopsy is to achieve better staging and there is now evidence that the procedure reduces morbidity **(11) .** In recent studies using radiotracers, the diagnostic accuracy and the localization rate reaches almost 100%. **(12)**

Aim of the work :

This work aims at reviewing the literature for the role of sentinel lymph node biopsy in achieving more accurate staging in **N**0 neck of upper aero-digestive tract squamous cell carcinoma , to avoide false negative results or overtreatment and hence reduce neck dissection- associated morbidity .

Cervical Lymph Node Groups

The patterns of spread of cancer from various primary sites in the head and neck to the cervical lymph nodes have been documented by retrospective analysis of large series of patients undergoing neck dissection. The nodal groups at risk for involvement are widespread throughout the neck, extending from the mandible and skull base superiorly to the clavicle inferiorly and from the posterior triangle of the neck laterally to the midline viscera and then to the contralateral side of the neck. It is now recommended that the lymph node groups in the neck be categorized according to the level system originally described by the Memorial Sloan-Kettering Group (Fig. 1). **(13)**

Division of Neck Levels By Sublevels

The 2001 report of the American Head and Neck Society's Neck Dissection Committee recommended the use of sublevels for defining selected lymph node groups within levels I, II, and V on the basis of the biologic significance, independent of the larger zone in which they lay. These are outlined in (Fig. 1) as sublevels IA (submental nodes), IB (submandibular nodes), IIA and IIB (together composing the upper jugular nodes), VA (spinal accessory nodes), and VB (transverse cervical and supraclavicular nodes). The boundaries for each of these sublevels are defined in Table 1. **(13)**

(Table 1.) Lymph Node Groups Found within the Six Neck Levels and the Six Sublevels.

Lymph Node Group	Description
Submental (sublevel I_A)	Lymph nodes within the triangular boundary of the anterior belly of the digastric muscles and the hyoid bone; these nodes are at the greatest risk of harboring metastases from cancers arising from the floor of the mouth, anterior oral tongue, anterior mandibular alveolar ridge, and lower lip (see Fig.1).