Topographic and histopathological analysis of neck nodes in patients with laryngeal carcinoma

Thesis submitted for the partial fulfillment of the M.D degree in Otolaryngology

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2011

جامعة القاهرة / كلية الطب
الدراسات العليا

محضر
اجتماع لجنة الحكم على الرسالة المقدمة من
الطبيب/ أحمد محمود أحمد البطاوى
توطئة للحصول على درجةالدكتواره
في جراحة الاذن والانف والحنجرة
تحت عنوان

باللغة الانجليزية:

Topographic and histopathological analysis of neck nodes in patients with laryngeal carcinoma

اللغة العربية:

التحليل الطبوجرافى والهستوباثولوجى لغدد الرقبة في مرضى سرطان الحنجرة

بناء على موافقة الجامعة بتاريخ ٩/ ١ /2013 تم تشكيل لجنة الفحص والمناقشة للرسالة المذكورة أعلاه على النحو التالى :

1- أ.د / هشام أحمد محمد نجم — عن المشرفين
2- أ.د./بدر الدين مصطفى بدر الدين — ممتحن داخلى
3- ا. د/ لؤى سمير الشرقاوى — ممتحن داخلى

بعد فحص الرسالة بواسطة كل عضو منفرداً وكتابة تقارير منفردة لكل منهم انعقدت اللجنة مجتمعة بتاريخ يوم الموافق١٠/ ١/ 2012 الساعة 12 صباحا بمبنى العيادة الخارجية باقسام الاذن والانف والحنجرة وذلك لمناقشة الطالب في جلسة علنية في موضوع الرسالة والنتائج التى توصل إليها وكذلك الأسس العلمية التى قام عليها البحث.

قرار اللجنة: .....
قـــبول الـــرسالـــــة
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توقيعات أعضاء اللجنة

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Abstract

Objectives*:** Metastatic neck disease is the most important factor in the spread of head and neck squamous cell carcinoma (SCC) from primary sites, the presence of neck metastasis is known to reduce survival by 50%. ***Aim of the study: determining the incidence and topography of nodal micrometastasis in laryngeal carcinoma and to correlate nodal micrometastasis with site and stage of the primary tumor, nodal stage, and gross morphological and microscopic aspects of the primary tumor. ***Methods*:** 30 patients with clinically N_0 nodal stage laryngeal carcinoma who underwent surgery for the treatment of the primary tumor and the possible occult cervical lymph node metastasis, the lymph node levels were labeled intra-operatively for differentiation between levels and were sent separately for histopathological examination using routine H&E staining and cytokeratin antibody staining. ***Results:*** the incidence of cervical lymph node macrometastasis was 30% (9/30) and the incidence of micrometastasis was 26.7% (8/30), the overall occult metastasis increased to 53.8% (7/13) for glottic tumors, 50% (6/12) for supraglottic tumors and 40% (2/5) for transglottic tumors. ***Conclusions:*** The routine sectioning and examination for metastasis can result in as many as 30% false negative results, so we have to combine cytokeratin staining together with the routine H&E staining. Selective neck dissection has to be done also with T_3 glottic carcinoma due to high incidence of metastasis. If neck dissection is performed, en-bloc resection is very important due to the incidence of lymphatic emboli.

Keywords: cervical metastasis – micrometastasis - cytokeratin staining – laryngeal carcinoma – lymphatic emboli.

Acknowledgments

*Thanks to **ALLAH** (The most merciful & powerful) for completing this work.*

*I would like to express my sincere thanks and supreme gratitude to **Prof.** Dr. **Hesham Negm,** professor of otorhinolaryngology, Cairo University for his valuable time and advices he offered me through the preparation of this work.*

*I would like to stress on the great and honest conscious of Prof. Dr. **Mohamed Mosleh**, Assist. Professor of Otorhinolaryngology, Faculty of Medicine, Cairo University who is actually the key for this work. Actually, I could not be able to finish this study without his help and support. His ethics and experience will be always my guide.*

*I am also too much grateful to **Dr. Hesham Fathy,** Lecturer of otorhinolaryngology, Faculty of Medicine, Cairo University for his active participation and guidance throughout the preparation of the work.*

*My special gratitude to **Dr. Amal Hareedy,** Lecturer of Pathology, Faculty of Medicine, Cairo University who was very welcoming and appreciating to my work. She expended lots of time and effort in preparing the material for this study.*

I am also greatly indebted to all my family members for their active support and encouragement.

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Abbreviations & what they stand for:

AAOHNS: American Academy of Otolaryngology-Head and Neck Surgery.

AJCC: American Joint Committee on Cancer.

CK: cytokeratin.

CT: Computed tomography.

ECM: extracellular matrix.

FDG: ^{18}F fluorodeoxyglucose.

FNAC: fine-needle aspiration cytology.

H&E: hematoxylin and eosin.

HNSCC: head and neck squamous cell carcinoma.

HPV: Human papilloma virus.

IARC: the International Agency for Research on Cancer.

ICA: internal carotid artery.

IFP: interstitial fluid pressure.

IFV: interstitial fluid volume.

IJV: internal jugular vein.

ITCs: isolated tumor cells.

LECs: lymphatic endothelial cells.

MND: modified neck dissection.

MRI: magnetic resonance imaging.

PET: Positron emission tomography.

RLN: regional lymph nodes.

RND: Radical neck dissection.

SAN: spinal accessory nerve.

SCC: squamous cell carcinoma.

SCM: sternocleidomastoid.

SLN; sentinel lymph node.

SNB: Sentinel node biopsy.

SND: selective neck dissection.

UICC: International Union against Cancer.

WHO: the World Health Organization.

Aim of the work

This study will determine the incidence and topography of nodal micro-metastasis in laryngeal carcinoma and to correlate nodal micro-metastasis with site and stage of the primary tumor, nodal stage, and gross morphological and microscopic aspects of the primary tumor.

Review of literature

Introduction & historical background

Approximately 300 lymph nodes are located in the head and neck, and they comprise 30% of the total 800 lymph nodes in the human body. ***In 1880, Kocher and Uber*** reported the detrimental effect of neck metastasis in patients with head and neck cancer. ***In 1906, Crile*** reported his experience with 132 neck dissections. The advent of functional neck dissections, aimed at reducing morbidity and maintaining function, was made possible with the further advancement of understanding of the lymphatic spread in the 1960s ***(Bocca et al., 1980)***.

Metastatic neck disease is the most important factor in the spread of head and neck squamous cell carcinoma (SCC) from primary sites. Cervical metastasis has a tremendous impact on the prognosis in patients with carcinomas of the head and neck. The presence of neck metastasis is known to reduce survival by 50%, and the frequency of such spread is greater than 20% for most squamous cell carcinomas (SCCAs). The presence of extra capsular spread further halves the chances of cure. The survival rate is less than 5% in patients who previously underwent surgery and have a recurrent metastasis in the neck. Therefore, control of the neck is one of the most important aspects in the successful management of these particular tumors ***(Shah, 1990; March et al., 2010)***.

Because clinical palpation is not sufficiently sensitive to detect cervical nodal metastasis, C.T, MRI, and positron emission tomography imaging are useful, however, they have a limited power for detection of metastasis less than 1cm in diameter. Histopathology remains the gold

standard method for detection of metastatic lymph nodes ***(Barrera et al., 2003)***.

The traditional histopathological approach for examination of regional lymph nodes entails removal of a longitudinal section from the middle of each of those nodes, which of necessity represents an incomplete partial of the entire node ***(Devaney et al., 2000)***.

Furthermore, histopathology is usually performed on a limited number of 3-4 mm thickness sections from each lymph node. However, because micrometastasis consists of tumor deposits measuring less than 2 mm in diameter, they can be easily missed on routine light microscopy ***(Hermanek et al., 1999; Genden et al., 2003)***.

Three pathological categories of occult nodal metastasis were delineated; isolated tumor cells, micro-metastasis and macro-metastasis ***(Stoeckli et al., 2002)***.

For bringing uniformity to their project, it was suggested that the following definition could be adopted for nodal metastasis in head and neck squamous cell carcinoma; a micrometastasis measures greater than 0.2 mm but less than 2 mm in diameter and smaller deposits were designated as isolated tumor cells and both were subdivided into those detected by light microscopy, immune-histochemistry or molecular methods ***(Devaney et al., 2007)***.

The main potential problem relates to the question of the existence of any demonstrated use of these attempts at discovering increasingly smaller metastatic deposits in head and neck squamous cell carcinoma patients ***(Devaney et al., 2007)***.

Several reports have suggested that there may be indeed some prognostic values in identifying patients with nodal micrometastasis and that their presence conveys additional information for treatment of head and neck cancer patients ***(Colnot et al., 2004; Yamazaki et al., 2005)***.

Predictive factors of cervical metastasis are primary site, primary tumor size, degree of differentiation of tumor, perineural invasion, perivascular invasion, inflammatory response, and tumor DNA content (ploidy) ***(Bocca et al., 1980)***.

It is for this reason, that although nodal micrometastasis may not be routinely sought in the case of patients with head and neck cancer, they certainly should be a target of the study research settings ***(Devaney et al., 2007).***

Anatomical and pathological considerations

Extensive knowledge of the lymphatic drainage pathways and the topography of the draining lymph node system is an essential requirement for understanding the lymphogenic distribution of inflammatory and malignant processes ***(Werner 2001; Werner et al., 2001).***

The lymphatic drainage of the mucosal surfaces and other tissues of the head and neck is directed to the lymph nodes located within the fibroadipose tissue that lies between the investing (superficial) layer of the deep fascia superficially and the visceral and prevertebral layers underneath. In this space, these lymph nodes tend to be aggregated around certain neural and vascular structures such as the internal jugular vein, spinal accessory nerve, and transverse cervical artery ***(Francis et al, 2008).***