Methods of Investigating Metastatic Lymph Nodes in Head and Neck Cancer

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ABSTRACT

When dealing with patients who have head and neck cancer - squamous cell carcinoma and have clinically N0 neck disease it is very difficult to assess the real extension of the malignant process. This is why several techniques are currently in use to determine the actual TNM classification for each patient in order to apply best suited therapy management. Up until today the staging of the neck has been done by using a combination of the physical exam and conventional imaging studies. Recent studies and research have tried to determine whether the use of sentinel lymph node biopsy is a more reliable tool in predicting occult metastasis in cancer patients with clinically N0 neck disease. There are no guidelines in this matter and as such the use of the sentinel lymph node detection technique is yet to be used on a routine basis. The authors are trying to assess the benefits of different paraclinical investigation regarding the improvement of over-all survival rates in patients with T1/T2 squamous cell carcinoma of the head and neck and N0 neck disease.

Keywords: clinically N0 neck disease, conventional imaging, sentinel lymph node

INTRODUCTION

Cancer represents the second cause of death after cardiovascular disease, and this is one of the main points of view by which we need to guide our medical journey. Cell biology of cancer, the uncontrolled growth of abnormal cells along with the malfunction of the apoptosis regulation confirm that neoplasia is a genetic determined disease based on the inbalance of the activation of oncogenes and the inactivation of the tumor suppressor genes. Those patients who are afflicted by such a malignancy have a poor quality of life especially when faced with late stage neoplasia. The possibility of early detection and treatment of the head and neck cancer shows a great potential for improving the quality of life for these cancer patients and a better prognosis(1). Occult metastasis is the main reason for this plan for detecting the tumor spread which is not al-
ways a simple thing to do. The task the treating clinician has to face is an essential one because it is known that the presence of lymph node invasion drops the percentage of survival rate with as much as 50 points, making this one of the most important prognosis factors for the squamous cell carcinoma of the head and neck. Because of this poor prognosis baseline in patients with occult metastasis in the lymph nodes all the clinicians should take into consideration the presence of micrometastasis, which is present in head and neck cancer in 10 to 30% (2).

Sentinel lymph node biopsy is a new concept that was introduced in clinical practice in 1977 by Cabanas and suffered improvement ever since it was widely used in breast cancer from 1990. Penile cancer and melanoma are two other diseases that used this sentinel lymph node biopsy protocols. In 1981 Shah proposed a simplified classification for lymph node levels in head and neck region that has been used since then by the Memorial Cancer Center Sloan-Kettering in New-York. There is a simple approach that made this classification possible in terms of anatomical landmarks.

Many classifications have been used in clinical practice but the reference guide lines were set by the American Joint Comitee in Cancer (AJCC) and the American Academy of Head and Neck Surgery (AAO-HNS). This classification establishes six levels of lymph node sites and an additional seventh level in the upper mediastinum. This last level does not take into consideration the cervical region of the cervical region in which lymph nodes are located but which is highly connected to the invasion patterns of cancer of the upper aero-digestive pathways.

Several lymph node levels are also divided into A and B in order to have a more accurate description of the anatomical spaces in relation to the invasion pattern.

**Description of the lymph node levels:**

**Level I** – limits: the body of the mandible, anterior and posterior bellies of the ipsilateral digastric muscle, anterior belly of the contralateral digastric muscle;

– divisions: submental group (Ia), submandibular group (Ib).

**Level II** – limits: upper third of the internal jugular vein, posterior border of the SCM muscle, stylohyoid muscle;

– divisions: anterior to the spinal accessory nerve are part of level (IIA), posterior to the nerve are located in level (IIB).

**Level III** – limits: carotid bifurcation, cricothyroid membrane, posterior border of the SCM muscle, sternohyoid muscle;

**Level IV** – limits: lower jugular group, omohyoid muscle, clavicle, posterior border of the SCM muscle, sternohyoid muscle;

**Level V** – limits: posterior neck triangle which includes the spinal accessory, transverse cervical, and supraclavicular lymph node sites.

**Level VI** - limits: lymph nodes in the anterior compartment of the neck, hyoid, supraclavicular notch.

Lymph nodes are subject to assessment when establishing the stage of the disease in the TNM system. TNM system is tributary to clinical exams and imaging studies and need to be classified in one of the N staging categories.

**N (node) staging in the TNM system:**

**NX:** Regional lymph nodes cannot be assessed.

**N0:** No regional lymph node metastasis is observed.

**N1:** Metastasis is observed in a single ipsilateral lymph node, measuring 3 cm or less in greatest dimension.

**N2a:** Metastasis in a single ipsilateral lymph node is observed and measures more than 3 cm but less than 6 cm in greatest dimension.

**N2b:** Metastasis is found in multiple ipsilateral lymph nodes; none of the nodes measure greater than 6 cm in their greatest dimension.

**N2c:** Metastasis in bilateral or contralateral nodes is observed; no nodes are larger than 6 cm in their greatest dimension.

**N3:** Metastasis is observed in a lymph node that measures greater than 6 cm in its greatest dimension.

**IMAGING STUDIES**

Head and neck patients usually undergo a series of investigations that include ultrasonography, computed axial tomography (CT) and magnetic resonance imaging (MRI). Because of less than 100% accuracy for each of the methods depicted above there is a need for a better investigation.

Sentinel lymph node biopsy comes as a new detection method for occult metastasis with
not so much increased morbidity in order to plan a better therapy management of the head and neck cancer patients. The goal is to determine which patients have true-negative (specificity) and true-positive (sensitivity) neck disease. This is the basics for establishing which patients need neck dissection or external beam radiotherapy and those who do not.

Imaging studies have been compared to the classical palpation of the cervical lymph nodes and sensitivity and specificity were determined for all the techniques used in the diagnosis protocol. After assessing data from this study we found that palpation is not adequate for conclusive N staging due to the fact that micrometastases can occur in less than 10 mm lymph nodes. The size of the lymph nodes and the neoplasia markers in a lymph node (central necrosis and extracapsular spread) is subject to interpretation in the clinical context for each patient thus making this technique less than perfect.

Ultrasound

In our study we found ultrasonography to have a sensitivity of 81% and specificity of 88%. When comparing this investigation to histological findings we found the accuracy of the method to be as high as 81%. Because of this we consider ultrasound to be superior to clinical palpation for detecting lymph nodes and metastases. There are certain advantages for using the ultrasound investigation such as low cost, non-invasive technique, reproducible, suited for follow-up.

The landmarks for invaded lymph nodes are poorly defined borders, central necrosis, parafuid collections and the alteration of the signal over the lymph node sites. In addition to the characterisation of the lymph nodes we can assess the relation with the surrounding tissues such as invasion of the arteries and veins of the neck.

The main problem that rises from this imaging study is that the borderline sized lymph nodes are not conclusively determined in terms of structure. This is the argument for using additional exams performed by the ultrasound physician such as fine-needle aspiration. This invasive method has not been used in our study thus making ultrasonography subject to improvement, yet to be established.

Computed axial tomography (CT scans)

The use of CT scans is acknowledged by all the clinicians that deal with head and neck lymph node pathology (3). The addition of contrast media, digital reconstruction, temporal and spatial high resolution images and the fine-cut images have made a reliable tool for physicians to use. All these improvements allowed physicians to evaluate smaller lymph nodes and thus leading to a decrease in the incidence of occult cervical metastases. Having been introduced in 1998 multiple spiral CT imaging has the ability to determine the composition of a large volume of tissue in a very little amount of time and the possibility of 3D reconstruction (4).

According to the methods advantages there have been set a number of criteria for a lymph node to be considered invaded. As previously discussed central necrosis is the main argument for tumor invasion in a lymph node. The size of the node is of at most importance as several researchers established a direct correlation between a 10 to 15 mm lymph node and the tumor spread. It is considered that a lymph node of 10 mm or above is a borderline situation, but if it were to visualise at least 3 lymph nodes at the same site this is consistent data for tumor invasion. The relation with the surrounding tissue is also important to consistently say that a lymph node is invaded as long as the dissection planes between relevant tissues are lost (5,6). The boundaries of the lymph node levels were easily established thus making it easy for the radiologists to determine the large lymph nodes tumor involvement. Som et al. proposed a an imaging-based classification which has not been adopted by all the clinicians (7).

Magnetic resonance imaging (MRI)

When using magnetic resonance imaging in head and neck cancer patients it is easy to assess the anatomical structure of the soft tissue but when trying to determine the sensitivity and specificity for MRI scanning we came to a surprising finding. The specificity for this method was found to be 89% and the sensitivity was determined to be 44%. The low rate of determining true-positive cases because of the poor findings in lymph node architecture is the main reason for us not to advise clinicians to use MRI over CT scanning. In spite of this the assessment of soft tissue regions such as the orophar-
METHODS OF INVESTIGATING METASTATIC LYMPH NODES IN HEAD AND NECK CANCER

Cancer patients in early T1 and T2 stages are those who will benefit most from detecting invaded lymph nodes as this is the situation the lead to a decrease in the survival rates to as much as 50%. The right surgical indication leads to the succes of the multimodal oncological treatment for cancer patients. There is a reasonable conduct in a surgical patient that is the principle of precaution, this meaning in doing no harm to the patient but good. Extended surgery when unwanted can lead to the decrease in over-all survival rates. This means that lymph node invasion patterns need to be correctly assessed in order to plan a correct multimodal approach.

Sentinel lymph node proved to be a reliable tool in establishing further therapy techniques on lymph node basin. We found the method to have maximum specificity and a very high accuracy rate. Although we find the method to be extremely reliable there are no guidelines for it.

Imaging studies have been used for a long time now in order to evaluate the involvement of regional lymph nodes. CT scanning is still the imaging study to be regulary used when stagging head and neck cancer patients but not in an absolute manner. Several other techniques like Positron Emission Tomography (PET), PET-CT and PET-like imaging studies play an important role in stagging a cancer patient. The combination between PET and CT is considered to have better predictive values than regular imaging studies but are yet to be assessed.

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CONCLUSIONS

Sentinel lymph node detection

Sentinel lymph node detection has been referred to by Alex and Krag in 1996 when they established a correlation between the involvement of primary drainage site of lymph flow and the implication of other regional basins. This lead to further research in the field of labeling and identifying tumor invaded lymph nodes(8). Sentinel lymph node biopsy had a sensitivity of 85% and a specificity of 100% with an accuracy rate of 92%. There were some false-negative results because of the lymph pathways that drain the lymph flow towards the contralateral side. On the other hand there were no false-positive results because we admit that when finding a positive lymph node this is because there is evidence of local and regional tumor spread. This argument sets the need of performing sentinel lymph node biopsy in order to determine the need for extended neck dissection and external beam radiotherapy.

REFERENCES