Assessment of Cervical Lymph Nodes in Squamous Cell Carcinoma of the Head and Neck

Magdy Eisa Saafan^{1*}, Ahmed Samy Elguindy¹, Mahmoud Fouad Abdel-Aziz¹, Ahmed Abdel-Rahman Younes¹, Osama Amin Albirmawy¹, Mahmoud Mandour¹ and Khalid El-Shafey²

¹Department of Otolaryngology and Head & Neck Surgery, Tanta Faculty of Medicine and University Hospitals, Egypt

²Department of Radiology, Tanta Faculty of Medicine and University Hospitals, Egypt

Abstract

Background: The most important prognostic factor in squamous cell carcinoma of the head and neck is the presence or absence of clinically involved neck nodes. The presence of metastases in a lymph node is said to reduce the 5-years survival rate by about 50%. The appropriate diagnosis of the presence of metastatic node is very important for the management of squamous cell carcinoma of the head and neck. The aim of this work is to study the status of cervical lymph nodes in known cases of squamous cell carcinoma in the head and neck and their relation to the primary site.

Methods: This study was carried out on 100 consecutive patients with a histologically proven non-cutaneous Head and Neck Squamous Cell Carcinoma (HNSCC). Every patient was subjected to clinical examination for cervical lymph nodes, CT scan on the neck with intravenous contrast and gray scale ultrasound scanning on the neck.

Results: Clinical palpation for cervical lymph nodes had a sensitivity of 71.43%, specificity 75.86% and accuracy 72.7%. CT scan was better than clinical palpation. The sensitivity for CT was 82.9%, while the specificity was 89.66% and the accuracy was 84.85%. Ultrasound scanning was found to be the best modality in assessment of metastases in cervical lymph nodes. The sensitivity was 97.1%, the specificity was 93% and the accuracy was 95.96%. The positive predictive value for Ultrasound scanning was 97.1% and the negative predictive value was 93%.

Conclusion: CT and ultrasound scanning increase the accuracy of lymph node detection. Although CT is better than clinical palpation, it is also considered inferior to ultrasound scanning in this aspect. Besides, ultrasound scanning is cheaper and with no hazards of radiation exposure.

Keywords: Metastases; Neck; Lymph node; Ultra sonar; Malignancy; CT

Introduction

Squamous cell carcinoma is the most common malignant tumor in the head and neck region [1]. Lymphatic spread is the most important mechanism in the spread of the head and neck squamous cell carcinomas [2]. The rate of metastases to cervical lymph nodes probably reflects the aggressiveness of the primary tumor. The presence of metastases in a lymph node is said to reduce the 5-year survival rate by about 50% [3].

Lymph nodes of the neck have been classified into 7 levels. The spread of carcinoma to these levels is probably predictable according to the site of the primary [4].

The appropriate staging of cervical lymph nodes is very important in the management of any head and neck primary carcinoma. Clinical palpation of cervical lymph nodes has many false negative and false positive results [5,6]. It was said to be existed in 20 – 40% of cases [7,8]. Computed tomography has improved the accuracy of diagnosis of cervical metastase [9,10]. It has disadvantages of being expensive and with hazards of radiation exposure [11,12]. Ultrasound scanning has improved the overall accuracy of diagnosis of cervical metastases [13]. It is a cheap and highly reliable method without hazards of radiation exposure [14,15].

Materials and Methods

A total of one hundred consecutive patients with a histologically proven non-cutaneous Head and Neck Squamous Cell Carcinoma (HNSCC), were chosen from patients admitted to the Department of Otolaryngology, Head and Neck Surgery, Tanta University Hospitals, between January 2007 and April 2009.

Each patient was subjected to full history taking, then a complete head and neck examination was performed stressing the site of the previously diagnosed cancer. Nasopharyngeal examination was performed using the 0 and 30 degrees telescopes. In oral cancers, mobility of the tongue, the condition of the floor of the mouth and retromolar trigone was evaluated. For hypopharyngeal and laryngeal cancers, rigid telescopic examination, using the 90 degrees telescope was used. Flexible rhinolaryngoscopy was used especially for patients with a strong gag reflex.

Metastatic workout was performed with whole body CT scan. Patients with distant metastasis, patients with previous radiotherapy and patients having previous neck resections other than skin lesions were excluded from the study.

Palpation of the neck was done thoroughly; first from the back, then from the front of the neck, after exposing the neck down to the level of the clavicle bilaterally to determine the presence or absence of enlarged cervical lymph node. The lymph nodes were assigned using the leveling system adopted by Memorial Sloan Kettering Cancer

***Corresponding author:** Magdy Eisa Saafan, Department of Otolaryngology and Head & Neck Surgery, Tanta Faculty of Medicine and University Hospitals, 61 Kafr Esam Street, El Nadi Square, Tanta, Egypt, E-mail: eisamagdy@hotmail.com

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Center and approved by the American Joint Committee on Cancer (AJCC) 1997 [9-11,16]. The site, size and consistency of the enlarged cervical nodes were reported.

CT examination was performed with a spiral CT Toshiba[®] Xvision/GX scanner (3.5 KHU). Sixty ml of 76% intravenous contrast (urographin) were given as a bolus for all patients. Contiguous axial CT sections (5/5-mm) were taken from the base of the skull to the level of the clavicles. The lymph nodes were assigned similar levels to that of the clinical examination. We followed the criteria proposed by Sarvanan et al. [17] for CT assessment of the lymph nodes based on the minimal axial diameter of the node as follows: a size of 11 mm or greater in the transverse plane was considered as a metastatic node. Central hypodensity with peripheral rim enhancement suggestive of necrosis or conglomeration of three or more lymph nodes in the drainage region of the primary tumor were also taken as metastatic lymph nodes.

High resolution ultrasonography on the neck was done by a high resolution real time B-mode (General Electric)[®] ultrasound machine with a linear transducer of 7.5 MHz frequency. We followed the ratio of long to short axis diameters (L/S) or (L/T) as proposed by Steinkamp et al. [18]. This ratio assesses the shape of the lymph node. The nodes were classified according to their L/S ratio into 2 classes: L/S ≥ 2 (oval) and L/T < 2 (round). Malignant lymph nodes tend to be round.

Patients with clinical and radiological criteria of malignant metastatic cervical adenopathy were subjected to fine needle aspiration cytology of the suspected nodes, which was ultrasound guided in some patients. Besides, the histopathologic data of specimens removed surgically were analyzed.

Ultimately, clinical, CT and sonographic data as well as histopathologic data from the surgically treated subjects were available as our database. Statistical analysis was performed using the sensitivity, specificity, accuracy, Positive Predictive Value (PPV) and Negative Predictive Value (NPV).

Results

This study included one hundred consecutive patients with non-cutaneous head and neck squamous cell carcinoma (HNSCC), 64 (64%) of these patients were males and 36 (36%) were females, ranging

in age from 35 to 76 years, with an average of 59 years. One patient died and was missed in the follow up, so the study was completed with 99 patients. Laryngeal carcinoma (32%) was the commonest cancer in our population, followed by hypopharyngeal carcinoma (22%), nasopharyngeal carcinoma (15%) and oral cancers (15%).

Results of clinical, CT and ultrasound examination of cervical lymph nodes were also correlated with the cytological findings and the histopathologic results of 25 neck dissections performed in the management plan of some patients of this group. They confirmed the results based on cytologic examination as shown in Tables 1-3 respectively. All nodes with conglomeration or central necrosis (CT criteria): were cytologically positive. The sensitivity and the positive predictive value for conglomeration and central necrosis in CT are 100%. To study the pattern of spread of malignant disease to the neck nodes, we correlated nodal stage, with the primary site and T-stage as shown in Table 4 and Figures 1-3. We found that 85% of the glottis carcinomas have N₀ nodal stage.

Discussion

Lymphatic spread is the most important mechanism in the spread of head and neck squamous cell carcinomas. The rate of metastases probably reflects the aggressiveness of the primary tumor, and is an important prognostic factor [3].

This work included 100 patients with non-cutaneous head and neck squamous cell carcinoma. Most of our patients were in the 6th decade. Our series showed male predominance. Laryngeal carcinoma followed by hypopharyngeal carcinoma was the most common cancers in our series.

In our series, clinical palpation provided false positive results of about 12.3% and false negative results of about 47.6%. The sensitivity of clinical palpation in our series was 71.43%; the specificity was 75.86%, while the accuracy was 72%. These figures are in accordance with most reported series for the results of clinical palpation [19].

On the other hand, CT scanning in our series demonstrated a sensitivity of 82.9%, a specificity of 89.66%, and an accuracy of 84.85%. Ultrasound scanning provided the highest sensitivity (97.1%), specificity (93%), and accuracy (95.96%) for detecting metastatic cervical lymph nodes in our patients.

	Cytological +ve	Cytological -ve	Total
Clinically +ve	50	7	57
Clinically -ve	20	22	42
Total	70	29	99

Table 1: Correlation between clinical examination and cytological findings.

Sensitivity	= 71.43%
Specificity	= 75.86%
Accuracy	= 72.7%
Positive predictive value	= 87.7%
Negative predictive value	= 52.4%

	Cytological +ve	Cytological -ve	Total
CT +ve	58	3	61
CT -ve	12	26	38
Total	70	29	99

Table 2: Correlation between computed tomography (CT) scan and cytological findings.

Sensitivity	= 82.9%
Specificity	= 89.66%
Accuracy	= 84.85%
Positive predictive value	= 95%
Negative predictive value	= 68.4%

	Cytological +ve	Cytological -ve	Total
US +ve	68	2	70
US -ve	2	27	29
Total	70	29	99

Table 3: Correlation between ultrasonography (US) scan and cytological findings.

Sensitivity	= 97.1%
Specificity	= 93%
Accuracy	= 95.96%
Positive predictive value	= 97.1%
Negative predictive value	= 93%

Primary site	T-Stage	N ₀ (%)	N ₁ (%)	N _{2,3} (%)
Larynx (n=32)	T ₁	60	20	20
	T ₂	56	18	26
	T ₃	39	17	44
	T ₄	40	13	47
Hypopharynx (n=22)	T ₁ *	-	-	-
	T ₂	28	26	46
	T ₃	16	22	62
	T ₄	20	14	66
Nasopharynx (n=15)	T ₁	0	25	75
	T ₂	25	25	50
	T ₃	25	-	75
	T ₄	33.3	-	66.7
Lips & oral cavity (n=15)	T ₁	80	20	0
	T ₂	66	35	-
	T ₃	50	25	25
	T ₄	33.3	33.3	33.4
Oropharynx (n=13)	T ₁	33	67	-
	T ₂	25	25	50
	T ₃	33	-	67
	T ₄	-	33	67
Paranasal sinuses (n=2)	T ₁ *	-	-	-
	T ₂	-	-	-
	T ₃	100	0	0
	T ₄	0	100	0
Parotid gland (n=13)	T ₁ *	-	-	-
	T ₂ *	-	-	-
	T ₃ *	-	-	-
	T ₄	0	0	100

Table 4: The probability of cervical metastases (N) related to primary (T) staging in our series.

Figure 1a: Two axial CT scans of a patient with left supraglottic primary cancer showing no cervical metastases.

Figure 1b: Ultrasound scan of the same patient showing left level II metastatic lymph node (L/S ratio <2).

The reported incidence of false positive clinical examination of the neck in patients with squamous cell carcinoma of the oral cavity

and oropharynx ranged between 10% to 33% [16,17]. Clinically occult cervical nodal disease is occurring in 15%-40% of patients undergoing elective neck dissection for cancer arising in this area [16].

Size is the most commonly used CT criterion for differentiating benign from malignant lymph nodes. This is based on the assumption that the larger the node, the greater the probability of metastatic involvement when one is examining a homogenous well-defined node [20].

Geetha et al. [19] reported sensitivity for CT scan 50% and specificity 100%, while they reported sensitivity 83% and specificity 50%, for physical examination. In an earlier study by Sönmez [21],

Figure1c: A photo of the operative specimen of the same patient (total laryngectomy with left lateral selective neck dissection).

Figure 2a: Axial CT of a patient with right tonsillar carcinoma showing right level II metastatic lymph node.

Figure 2b: Ultrasound scanning of the same patient showing metastatic right submandibular (level Ib) lymph node (L/S <2).

Figure 3a: Coronal CT scan showing left nasopharyngeal carcinoma.

Figure 3b: Axial CT scan of the same patient showing left level II metastatic lymph node with central necrosis.

Figure 3c: Ultrasound scan of the previous patient showing the left level II metastatic lymph node (L/S ratio <2).

Figure 3d: Ultrasound scan of the previous patient showing left level V metastatic lymph nodes (L/S ratio <2).

authors have reported sensitivity 95% and a specificity 47% for CT scan, while a sensitivity 86% and a specificity 84% were reported for physical examination.

Curtin et al. [22] evaluated the sensitivity and specificity of different size criteria for HNSCC metastatic disease and found that a 1-cm size cutoff in the largest axial diameter achieved 88% sensitivity and 39% specificity, whereas a 1.5-cm cutoff resulted in 56% sensitivity and 84% specificity. More recently, Geetha et al. [19] have used RECIST 1.1 (Response Evaluation Criteria in Solid Tumors) by measuring lymph nodes in the short axis on axial images. They reported that nodes ≥ 15 mm are pathologically enlarged and measurable, and lymph nodes measuring 10–15 mm in short axis are reportable as pathologic non target sites.

In our series the sensitivity of central nodal necrosis and conglomeration criteria was 100% with no false positive results. These results go in accordance with the observations made by Van den Brekel [23] and Sarvanan et al. [17]. Sarvanan et al. [17] suggested that the presence of central necrosis was the most specific sign of metastatic

lymphadenopathy. They reported 100% sensitivity and specificity for central nodal necrosis criteria.

Ultrasonography is an alternative imaging modality which is considered an accurate and reliable method of evaluating neck metastases. The staging of the carcinoma of the head and neck is an important goal of head and neck imaging using ultrasonography [5]. Griffith et al. [24] showed that the addition of neck ultrasonography to staging by clinical and CT criteria resulted in a change in TNM staging in 22% of patients in their study. They suggested that more accurate preoperative staging with neck ultrasonography allows a more consistent selection of patients for different treatment protocols.

In our series, we have chosen the criterion of L/S (longitudinal/short axis) ratio for differentiation between benign and malignant nodes. Kim et al. [25] found that there was no significant difference between benign and malignant nodes in terms of their largest diameter, but, there was marked difference in terms of their L/S (L/T) ratio (or shape) which can be assessed without limitations only with ultrasound scanning. Since metastasis causes lymph node enlargement by malignant cell proliferation it alters the normal ovoid shape of the lymph node to a more spherical form, while benign processes tend to maintain the oval shape of the lymph node, in which enlargement occurs by benign lymphoid cell proliferation. The tendency of benign nodes to be “oval” ($L/S > 2$) and malignant nodes to be “round” ($L/S < 2$) has also been reported by other observers [5,19].

Our results agree with the results of most previous studies, which have taken the L/S ratio as criteria of differentiation between benign and malignant lymphadenopathy. In our series, we have reported a sensitivity of 71.43% and a specificity of 75.86% for palpation of lymph nodes. A sensitivity of 82.9% and a specificity of 89.66% for CT scanning and a sensitivity of 97.1% and a specificity of 93% for ultrasound scanning. Steinkamp et al. [18] reported 95% sensitivity of the L/S ratio as well as a specificity of 95% compared with 37% for the long axis method and 86% for the transverse diameter method. They noted the decrease of false positive results from 63% to 5% using the L/S ratio. Sarvanan et al. [17] have showed similar sensitivity (94.44%) and higher specificity (100%) than that reported by Steinkamp et al. [18].

In 1993, John et al. [26] reported sensitivity of 62%, specificity of 80% and accuracy of 81% for palpation in the upper neck, while reported sensitivity of 44%, specificity of 67% and accuracy of 67% for ultrasonography in the upper neck. They reported sensitivity and specificity of 100% for palpation and ultrasonography in the midneck with 95% accuracy for both methods. They reported that in the posterior triangle, sensitivity for palpation was 38% and for ultrasonography 60%. The specificity for palpation was 64% and for ultrasonography 85%; and accuracy was 57% for palpation and 67% for ultrasonography. In a more recent study, Sureshkannan et al. [5] presented a sensitivity of 85.7% and a specificity of 90% for ultrasound scanning, while the clinical examination presented sensitivity 68.7% and specificity 87.5%. Geetha et al. [19] reported the sensitivity in detection of cervical lymph nodes to be 83% for palpation and 100% for ultrasound scanning.

Ultrasound scanning has an advantage of being a simple non-invasive maneuver with no hazards of exposure to radiation. Moreover, ultra-sonography can detect lymphadenopathy in presence of severe postoperative scarring or post radiotherapy thickening of the soft tissues of the neck [16]. Ultrasonography appears to be the best modality for assessing carotid artery invasion. Ultrasonography can be considered a valuable diagnostic measurement for cancer tongue. By providing a three dimensional view of the tumor, it is more accurate

than palpation in detecting spread of tumor across the midline, to the base of the tongue and floor of the mouth. The tumor is predominately hypoechoic. It is difficult to differentiate fibrosis from tumors and also to detect very superficial lesions.

Other study suggests that ultrasound combined with ultrasound guided fine needle aspiration cytology is a reliable, safe and simple method in staging head and neck malignancies and may be useful in the follow up of the patients. Van den Brekel et al. [27] has reported a specificity of 100% for ultrasound guided fine needle aspiration cytology. They Showed that sonography guided fine needle aspiration cytology often ensures detection of neck recurrences at an early stage.

Conclusion

From this work, it is concluded that we should not rely solely on clinical examination; other diagnostic modalities should be considered. CT and ultrasound scanning increase the accuracy of lymph node detection. Although CT is better than clinical palpation, it is also considered inferior to ultrasound scanning in this aspect. Besides, ultrasound scanning is cheaper and with no hazards of radiation exposure.

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