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Evaluation of Neck Node Metastasis from Oral Cancer in an Indian Population: A Comparative Pilot Study

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Abstract

Introduction: Cervical node metastasis in oral cancer is an indicator of advanced disease. It is therefore important to evaluate neck node involvement as a predictor of progression and treatment planning.

Materials & Methods: Eleven patients with age range between 38 to 63 years (median age 54 years) undergoing neck dissection simultaneously with the resection of primary intraoral squamous cell carcinoma formed the basis of the present study. A pre-operative assessment of neck by clinical examination, ultrasonography and computed tomography scan was done, which was then compared to the histopathological assessment. The histopathological examination formed the reference.

Results: The percentage of sensitivity by clinical examination was 46%. The percentage of sensitivity by ultrasonogram was 69%. The percentage of sensitivity by computed tomography (CT scan) was 85%. These were against the histopathological examination.

Conclusion: The study reported an error of almost 50%

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for the clinical examination alone. The margin of error decreases when combining ultrasonography or CT scan in the examination. However, in the existing economic condition in India, even the use of CT scan can be prohibitive. Nevertheless, it is advised to combine other diagnostic modalities during the clinical examination of cervical metastasis.

Key words: cancer, cervical metastasis, nodal metastasis, squamous cell carcinoma, ultrasound and CT scan in oral cancer.

Introduction

Oral cancer is the sixth most common cancer in the world and is largely preventable (1,2). It accounts for approximately 4% of all cancers and 2% of all cancer deaths world-wide (3). In India it is the commonest malignant neoplasm, accounting for 20-30% of all cancers. Globally, tobacco consumption in all its various forms is the commonest etiological risk factor for the subsequent development of oral cancer (4-6). In developing countries the use of tobacco and/or the areca (betel) nut produces chronic, potentially malignant lesions from which the majority of oral cancers arise (7). Cervical node involvement in head and neck cancer has always been indicative of advanced disease. The cases in India present with advanced lesions with variable involvement of neck nodes especially in the lower socio-economic group. The status of the cervical nodes is the single most important prognostic indicator of survival for patients with oral cancer (8) since the development of nodal metastases halves the 5-year survival rate (9). In this context it is imperative to diagnose nodal involvement in planning any therapeutic modality. However, two recent studies have demonstrated that clinical examination of the neck is imprecise because there was a false negative rate of between 27% and 34%, and a false positive rate of between 31% and 40% (10,11).

The importance of identifying and eliminating nodal disease was recognized as early as 1898 by Henry Butlin (12). Kalins and co-workers in 1977 quoted a five year survival rate of 75% for neck nodes, which fell to 49% if one node was involved and 13% if multiple nodes were involved (13). Subsequent studies had showed almost similar results (14). In 1986 Spiro and co-workers conducted studies to correlate tumor size and thickness to nodal metastasis and survival (15).

There is therefore a need to combine clinical evaluation with radiological and other modalities of non-invasive diagnosis to accurately predict cervical nodal involvement in oral squamous cell carcinoma. In this study we tried to:

- 1. Evaluate the accuracy and reliability of clinical examination in detecting cervical lymph node metastases in oral squamous cell carcinoma using histopathological examination as the reference.
- 2. Evaluate the role of ultra-sonogram (USG) and computer tomography (CT scan) in detection of cervical lymph node metastases in oral squamous cell carcinoma.
- 3. Determine the best diagnostic aid, if any in pre-surgical diagnosis of cervical lymph node metastases in the setting of limited resources.

Material and Methods

Eleven patients underwent neck dissection along with the resection of primary intra-oral squamous cell carcinoma formed the basis of the present study. For the purpose of study only the tobacco and alcohol related cases were

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included because these are the most commonly implicated etiologies for squamous cell carcinoma. Patients with local or systemic infections were excluded lest there were false positive cervical findings (Table 1).

Patients No. 5 and 6 currently had no deleterious habits but had a history of tobacco or alcohol consumption many years ago. The eleven patients comprised eight males and three females. Their age range was 38 - 63 years (median 54 years). Diagnosis of squamous cell carcinoma had been confirmed by incisional biopsy of the primary tumor. None of the patients had pre-operative radiotherapy or chemotherapy. Ethical approval was obtained from the Health and disability ethic committee of the institution for the study.

Pre-operative assessment of neck by clinical examination

A detailed history was obtained and careful clinical examination of the neck for metastatic nodes was assessed according to the different levels. The system established by the Sloan-Kettering Memorial Group for assessing cervical nodal regions has been used here for classification. The case history and the clinical examination were recorded in the proforma specially prepared for the study. TNM staging of all cases was also done on the basis of clinical examination of the neck. An informed consent was obtained prior to the surgery. The clinical examination was done by the same experienced maxillofacial surgeon every time to avoid examiner bias.

Minitab 15 was used to statistically analyze the data.

Preoperative assessment of neck by ultrasonogram

Ultrasonogram was performed using 7.5 to 10 MHZ linear probe B-mode real time imaging ultra sound machine [Wipro logic (400pro)] in all patients. The criteria used for ultra sound staging and diagnosis of cervical lymphadenopathy included:

1. Size: more than 10mm. 2. Shape: rounded is more likely to be malignant. 3. Necrosis: central necrosis of the node. 4. Extra capsular spread: An irregular border on USG. 5. Echogenicity: The more hypoechogenic the node, the greater the likelihood of malignant changes. Based on the echogenicity the findings were classified as: A) Hyperechoic: Echo increased relative to the adjacent tissue. B) Isoechoic: Same as the adjacent tissue. C) Hypoechoic: Decreased with the adjacent tissue. D) Anechoic: no reflection or just the whole degree of passing through the tissue. The assessment was always done by the same experienced sonologist.

Table 1: Demographic data of patients							
Pt. No	Age / Sex	Habits	Medical History	TNM Staging	Site of Lesion	Surgery & Reconstruction	
1	55 / M	Smoking beedi for 40 yrs.	Stomach ulcer	T ₂ N _{2B} Mx	Right post palatal region.	Right side maxillectomy and Radical neck dissection.	
2	52 / M	Smoking beedi & consumes alcohol or 25 yrs.	-	T ₄ N ₃ Mx	Floor of the mouth.	Resection of the floor of the mouth with marginal mandibulectomy, right side radical neck dissection and left side functional neck dissection.	
3	54 / M	Betel nut & tobacco chewing for 20 yrs.	Hypertension	T ₂ N _{3B} Mx	Left buccal mucosa involving mandibular alveolus.	Left hemimandibulectomy, Radical neck dissection and Pectoralis major flap reconstruction.	
4	55 / M	Smoking cigars for 40 yrs.	-	T ₄ N ₀ Mx	Left buccal mucosa and alveolus.	Left hemimandibulectomy and Radical neck dissection.	
5	50 / F	Currently no habits	-	T ₄ N ₀ Mx	Left side palatal region extending into the sinus.	Left side maxillectomy with floor of the orbit and posterior wall of sinus and Radical neck dissection and Reconstruction with temporalis flap.	
6	45 / F	Currently no habits	-	T ₄ N _{2B} Mx	Left side palatal region.	Left side mandibulectomy, Radical neck dissection and Reconstruction with temporalis flap.	
7	55 / F	Tobacco chewing for 30 yrs.	-	T ₄ N ₀ Mx	Left buccal mucosa extending into the mandible from I to III molar.	Left hemimandibulectomy and Radical neck dissection.	
8	53 / M	Betel nut & tobacco chewing and alcohol consumption for 40 yrs.	-	T ₄ N ₀ Mx	Left posterior mandibular alveolus up to retromolar trigone.	Left hemimandibulectomy and Radical neck dissection.	
9	38 / M	Smoking beedi and alcohol consumption for 20 yrs.	-	T ₄ N _{3B} Mx	Floor of the mouth extending along the ventral portion of the tongue.	Anterior segmental mandibulectomy, resection of anterior 1/3rd of tongue with Right side radical neck dissection and left functional neck dissection and Reconstruction with right Pectoralis major flap.	
10	63 / M	Betel nut & tobacco chewing for 40 yrs.	-	T ₄ N ₀ Mx	Left mandibular alveolus and buccal vestibule.	Left hemimandibulectomy and Radical neck dissection.	
11	55 / M	Tobacco chewing for 40 yrs & smoking for 25 yrs.	Known diabetic for 10 yrs.	T ₄ N _{2B} Mx	Left retromolar trigone involving up to the maxillary tuberosity.	Left hemimandibulectomy, Left posterior maxillectomy, Radical neck dissection and Reconstruction with forehead flap.	

Preoperative assessment of neck by CT scans

All patients were examined with a CT scanner, type -

Spiral CT with upgraded 4th generation scanner (Wipro-GE CTe model). The scanning was done no more than 3 weeks

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before the surgery. Both the ultrasound and the CT scan were done preferably within 24 hours of each other. Each patient received intravenous injection of contrast medium to enhance the attenuation of lymph nodes with that of the normal adjacent tissue. The IV contrast medium used was Uro scan – 76 (Diatrizoate meglumine and diatrizoate sodium injection USP). The dosage given intravenously was 1mg/kg of body weight. An axial section of 5mm thickness from the base of the skull to the root of the neck was used in this study. The criteria used to detect cervical lymphadenopathy were nodes larger than 1cm and central necrosis. The assessment was always done by the same experienced radiologist

Surgical Procedure of Radical Neck Dissection

Eleven patients were operated for 13 necks (2 patients had bilateral neck dissection one side radical neck dissection and the other side functional neck dissection). Two patients had a functional neck dissection done on the opposite side. A brief outline of the procedure was as follows: An apron incision was outlined and marked in the neck extending from the midline anteriorly and coursing down up to the level of the clavicle and going upwards and backwards to the mastoid process. After careful dissection and hemostasis the lymph nodes and associated structures in each level were identified and dissected. Care was taken to get the specimen in 'one piece.' The surgery was done by an experienced maxillofacial surgeon whose primary interest was in cancer surgery. Level VI was not dissected because the lymph node levels removed are based on the location of the primary tumor because of the predictable clinical patterns of cervical lymphatic metastasis from head and neck cancer. The levels were finally demarcated by colored tags to delineate the different levels. The specimens were transported in 10% buffered formalin to the pathology department.

Pathological assessment of metastatic status

The tagged neck specimens were submitted to the Department of Pathology where all gross dissections and histological assessments were made by a single pathologist. Lymph nodes were identified by visual inspection and palpation and were dissected out from the fixed gross specimen in each of the five anatomic levels. All nodes were measured and processed routinely. Initial histological assessment was made on a single hilar section with examination of step serial sections in selected nodes. If the nodes were positive, then the extent of replacement of the nodal architecture by metastatic deposit was further evaluated for each level. The examination was performed

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by an experienced oral pathologist.

All clinicians were blinded to the others' reports before their assessment.

Results

The percentage of sensitivity by clinical examination was 46%. The percentage of sensitivity by ultrasonogram was 69%. The percentage of sensitivity by computed tomography was 85%.

The percentage of nodal involvement was as follows:

Level I - 69.23 Level II - 38.46 Level III - 23.07 Level IV - 7.60 Level V - 0.00

Discussion

This study was done to evaluate the relative sensitivity of cervical neck nodes by clinical examination, ultrasonography and CT scan with reference to post-operative staged neck histopathology.

Various non-invasive diagnostic techniques have been employed to enhance the sensitivity and specificity for neck nodes (16-20). They include ultrasonography, CT scan, MRI, PET scan and lymphoscintigraphy. There is a unanimous agreement on the usefulness of ultrasonography and CT scan. However they do not match up to the desired levels of sensitivity and specificities with the post-operative histopathology. Preoperative CT/MRI imaging may not improve the accuracy of clinical examination as many occult nodal metastases are only detectable by thorough post-resection histological examination [11].

Lymph nodes at different levels with all four different evaluation criteria were tabulated in Table 2. The findings in Table 2 were evaluated for percentage sensitivity. In thirteen necks, clinical evaluation produced only six concurrences at all levels with histopathology making it an average sensitivity of only 46%. Significantly there was one false positive node (a reactive inflammatory node). On the other hand ultrasonography gave nine concurrences and CT scan gave eleven concurrences giving both the techniques an accuracy percentage of 69% and 85% respectively. After eliminating false positives there is an accuracy of 77% and 85%. Table 2 was also used to evaluate node involvement at different levels as reflected in Table 4.

While our results more or less matched with other published literature, there were some differences (21-24). As all lesions were T4 it was not possible to corroborate lesion size with neck node involvement. The significance of this study is that the clinical evaluation of 46% sensitivity was

Patient no.	Level	Clinical examination	Ultrasonogram	Computed to- mography	Histopathological examination
				подгарну	
	Ι	2	1	1	1
	II	1	2	2	2
	III	1	1	0	1
	IV	0	0	0	0
	V	0	0	0	0
Right Side	Ι	1	3	3	4
	II	0	0	0	4
	III	1	0	0	3
	IV	0	0	0	0
	V	0	0	0	0
Left Side	Ι	1	1	1	1
	Π	0	0	0	0
	III	0	0	0	0
	IV	0	0	0	0
	V	0	0	0	0
;	Ι	1	2	0	1
	II	1	0	0	0
	III	0	0	0	0
	IV	0	0	0	0
	V	0	0	0	0
ŀ	Ι	1	0	0	0
	Π	0	0	0	0
	III	0	0	0	0
	IV	0	0	0	0
	V	0	0	0	0
	Ι	1	0	0	0
	II	0	0	0	0
	III	0	0	0	0
	IV	0	0	0	0
	V	0	0	0	0
;	Ι	2	1	2	2
	II	0	0	0	0
	III	0	0	0	0
	IV	0	0	0	0

	V	0	0	0	0
7	Ι	1	1	1	1
	II	0	0	0	0
	III	0	0	0	0
	IV	0	0	0	0
	V	0	0	0	0
8	Ι	1	1	2	3
	II	0	3	2	1
	III	0	0	0	0
	IV	0	0	0	0
	V	0	0	0	0
9 Right Side	Ι	1	1	1	1
	II	0	1	1	1
	III	0	1	0	1
	IV	0	0	0	0
	V	0	0	0	0
9 Left Side	Ι	1	0	0	1
	II	0	2	0	0
	III	0	0	1	0
	IV	0	0	0	0
	V	0	0	0	0
10	Ι	1	2	2	2
	II	0	0	0	0
	III	0	0	0	0
	IV	0	0	0	0
	V	0	0	0	0
11	Ι	2	3	2	3
	II	0	1	1	0
	III	1	2	2	1
	IV	1	2	1	3
	V	0	0	0	0

Table 3: Percentage of Sensitivity in Thirteen Necks with Histopathology as a Guideline							
Methode of Evalu- ation	False Positive	False negative	Concurrence	%			
Clinical Examina- tion	1	6	6	46%			
Ultrasonogram	1	3	9	69%			
Computed Tomog- raphy	0	2	11	85%			

Table 4: Nodal Involvement at Different Levels for Thirteen Necks							
Patient #	Level I	Level II	Level III	Level IV	Level V		
1	Х	Х	Х	-	-		
2 Right Side	Х	Х	-	-	-		
2 Left Side	Х	-	-	-	-		
3	Х	Х	-	-	-		
4	-	-	-	-	-		
5	-	-	-	-	-		
6	Х	-	-	-	-		
7	Х	-	-	-	-		
8	Х	Х	-	-	-		
9 Right Side	Х	Х	Х	-	-		
9 Left Side	Х	-	-	-	_		
10	Х	-	-	-	_		
11	Х	_	Х	Х	-		

way below the pre-operative evaluations in other studies that showed a clinical accuracy of 60% - 75% in comparison with histopathology [Table 3].

On the other hand ultrasonography and CT scan were consistent with other published studies (75% - 85%) for sensitivity and specificity [24]. Level I, II and III were the most involved. Levels IV was involved only in one case. Level V involvement was not seen at all [Table 4]. This seems to be inconsistent with other western literature, though it is for occult primary (25).

Many criteria for detecting lymph nodes with CT and

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US have been put forth (17,18,22,26-28). However, some are uncommon. US detected varying appearances of the echogenic lymph node hilum and the surrounding hypoechoic cortex have been shown to be helpful in distinguishing malignant from benign normal sized nodes. This was similar to other findings (16).

Since CT scan is more highly sensitive we suggest that size and central necrosis can be considered reliable criteria in detecting positive nodes. However, central necrosis was not found in our cases. We agree with other findings that a size of 10mm and above for the level 1 and descending for the other levels signify positive nodes (29,30).

Margins of error with clinical, ultrasonography and CT studies were still significant and there is still room for improvement. In expert hands techniques like FNAC with ultrasonography have accuracy of nearly 100% specificity and sensitivity on a node to node basis, but cannot be employed for full screening of neck (31). PET scan, SPECT and MRI are expensive and were not included in the study. To conclude, cervical node metastasis in oral cancer is an indicator of advanced disease. It is therefore important to evaluate neck node involvement as a predictor of progression and treatment planning. In the existing economic condition in India, even the use of CT scan can be prohibitive. Ultrasonography while being not very accurate, is a financially reasonable tool to detect neck nodes. All patients were routinely followed-up but their survival data is beyond the scope of this present study. The option of no imaging especially in the setting of limited resources should be weighed against the potential morbidities if the patient is scheduled for an elective radical neck dissection. The merit of such an evidenced-based practice requires a well controlled randomized controlled trial.

The limitation of clinical evaluation is evident in our study and it is urged that clinical examination should be supplemented with diagnostic tools like CT scan and ultrasonography. MRI and other advanced techniques were not evaluated in our study but could be used in a more economically sound environment.

In the light of lack of evidence of involvement of Level IV and Level V in our cases, the anatomic and biologic variations of tumors need to be assessed strongly here. Our study revealed that these levels were never significantly involved in 13 necks dissected, even though all cases were in advanced stages.

This is a pilot study but a more thorough multi-centre study would perhaps give more information on the behavior of these tumors in different races.

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