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RESEARCH

Cervical lymph node metastasis in oral squamous carcinoma preoperative assessment and histopathology after neck dissection

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Abstract
Background The presence or absence of nodal metastasis has a great impact on the prognosis and survival of patients with head and neck cancer. The risk of occult metastasis is related to the method by which the lymph nodes are evaluated. It is possible to reduce the risk of undiagnosed metastasis with accurate imaging techniques and thus probably reduce the number of elective neck treatments.
Aims and objectives To assess the accuracy of clinical palpation, CT Scan, Ultrasound and Ultrasound guided FNAC in prediction of lymph node metastasis in oral squamous cell carcinoma so that a suitable surgical neck dissection can be carried out.
Methods Ten patients with oral squamous cell carcinoma who underwent 10 neck dissections (4 RND, 6 SOND) were included. All the patients underwent examination of neck pre operatively by palpation, Computed Tomography with contrast, Ultrasound and Ultrasound guided FNAC for no detection. The findings were correlated with the results of histopathologic examination of the neck specimen. The results were obtained after statistical analysis.
Results Six neck dissection specimens showed metastatic lymph node involvement in postoperative histopathology. Lymph node involvement was identified preoperatively by palpation in 7 necks, CT in 3 necks, US in 9 necks and US-FNAC was positive in 4 cases. The palpation showed 83% sensitivity, 50% specificity. CT showed sensitivity of 50%, specificity of 100%, US showed sensitivity of 100%, specificity of 25% and US-FNAC showed sensitivity of 67%, specificity of 100%.
Conclusion The palpation, CT Scan and US are equally accurate but the US-FNAC is the most accurate technique in assessing metastasis in lymph nodes in patients with oral squamous cell carcinoma.

Keywords Oral squamous cell carcinoma · Occult metastasis · Computed tomography · Ultrasound · Fine needle aspiration cytology

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Introduction

Oral cancer is the sixth most common cause of cancer related death in the world. The global incidence of cancers of the oral cavity, pharynx account for 363,000 annual new cases worldwide and almost 200,000 deaths [1,2,3]. Most oral cancers are squamous cell carcinomas because most of the risk factors affect the most superficial layers of the mucosa and gingiva. The presence or absence of nodal metastasis has a great impact on the prognosis and survival of patients with head and neck cancer. Nodal metastasis to one side decreases the survival by 50%, while bilateral metastasis decreases survival by a further 25% [4,5,6,7].

The risk of occult metastasis that is higher than 20% is the most important indication for elective neck treatment. The risk of occult metastasis is related to the method by which the lymph nodes are evaluated. It is possible to reduce the risk of undiagnosed metastasis with accurate imaging techniques [8]. Various tools for the staging of lymph nodes are palpation, CT (Computed Tomography), MRI (Magnetic Resonance Imaging), US (Ultrasonography), FNAC (Fine Needle Aspiration Cytology) and PET (Positron Emission Tomography).

The purpose of this prospective study was to evaluate the accuracy of clinical

Fig. 1 CT scan of neck showing an enlarged submandibular lymph node

Fig. 2 Ultrasonography of neck showing a submandibular lymph node with central necrosis

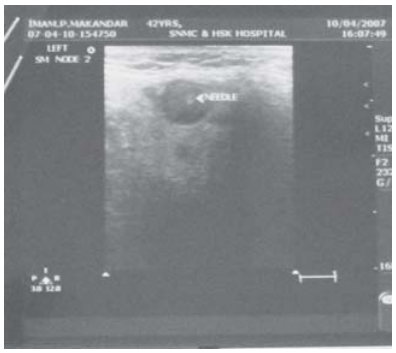

Fig. 3 A lymph node showing the needle tip within the node during US-FNAC

palpation, CT Scan, US and US-FNAC (Ultrasound guided FNAC) in detection of metastatic lymphnodes in oral squamous cell carcinoma by correlating these results with postoperative histopathology after neck dissection.

Methodology

Ten patients reporting to Department of Oral and Maxillofacial Surgery, PMNM Dental College and Hospital, Bagalkot with squamous cell carcinoma of oral cavity requiring surgical treatment were included in the study. Patients who have undergone radiotherapy and chemotherapy and patients with inoperable disease were excluded. The site of primary tumour was lower buccogingival sulcus in 8 (80%) patients and buccal mucosa in 2 (20%) patients. The distribution of pretherapeutic tumour dimensions according to the UICC classification was T4N1Mo in 8 cases and T4N0M0 in 2 cases. The examination of neck was carried out by palpation, CT scan and Ultrasound. Ultrasound guided FNAC was carried out for the nodes detected by Ultrasound. The results were later confirmed by detailed histopathological examination of the subsequent surgically resected specimen.

Palpation

The criteria to consider node as metastatic on palpation was a firm to hard fixed node more than 10 mm in size.

Computed tomography

All the patients were examined by CT of neck from the base of the skull to the clavicle with 5mm sections contiguously subsequent to the injection of non ionic contrast material.

The criteria used to define a node as metastatic in our study were [5] (Fig. 1) nodes with minimal axial diameter >11 mm or nodes with central hypodensity and peripheral rim enhancement or conglomeration of three or more lymph nodes.

Ultrasound

Ultrasound examination of the neck on both the sides was carried out with high frequency (7MHz-10MHz) linear transducer.

The criteria used to define a node as metastatic in ultrasound were [4,5] (Fig. 2) node with short axis diameter >8 mm, round in shape, with central hypoechogenecity, with loss of hilus, presence of necrosis, with irregular margin suggesting extracapsular spread and roundness index (L/S Long Axis/ Short Axis Ratio) =/< 2 were considered malignant.

Ultrasound – FNAC: US-FNAC was taken from enlarged lymph nodes suspected clinically and detected on Ultrasound. Nodal aspirate was obtained using 23 gauge needle and 5ml syringe under US guidance (Fig. 3). All patients tolerated US –FNAC well without any

The sensitivity, specificity, predictive values and accuracy were calculated as follows.

Sensitivity determines how well positive lymph nodes are diagnosed by a particular method.

$$\text{Sensitivity} = \frac{\text{True positive}}{\text{True positive} + \text{False negative}}$$

Specificity determines how well positive nodes are distinguished from non-affected nodes by a particular method

$$\text{Specificity} = \frac{\text{True negative}}{\text{True negative} + \text{False positive}}$$

Accuracy determines how well a method functions

$$\text{Accuracy} = \frac{\text{True positive} + \text{True negative}}{\text{Total}}$$

Positive predictive value determines the probability of a node with a positive diagnostic result being actually positive

$$\text{Positive predictive value} = \frac{\text{True positive}}{\text{True positive} + \text{False positive}}$$

Negative predictive value determines the probability of a node with a negative diagnostic result being actually unaffected

$$\text{Negative predictive value} = \frac{\text{True negative}}{\text{True negative} + \text{False negative}}$$

Table 1 Comparison of palpation with histopathologic examination

Investigation	Findings	Histopathologic examination	
		Positive	Negative
Palpation	Positive	True positive (n=5)	False positive (n=2)
	Negative	False negative (n=1)	True negative (n=2)

Table 2 Comparison of computed tomography with histopathologic examination

Investigation	Findings	Histopathologic examination	
		Positive	Negative
Computed Tomography	Positive	True positive (n=3)	False positive (n=0)
	Negative	False negative (n=3)	True negative (n=4)

Table 3 Comparison of ultrasound with histopathologic examination

Investigation	Findings	Histopathologic examination	
		Positive	Negative
Ultrasound Examination	Positive	True positive (n=6)	False positive (n=3)
	Negative	False negative (n=0)	True negative (n=1)

Table 4 Comparison of US-FNAC with histopathologic examination

Investigation	Findings	Histopathologic examination	
		Positive	Negative
US-FNAC	Positive	True positive (n=4)	False positive (n=0)
	Negative	False negative (n=2)	True negative (n=4)

Table 5 Sensitivity, Specificity, Accuracy, Positive, Negative predictive and 'P' Values of methods used

Statistical test	Palpation	Computed tomography	Ultrasound examination	Fine needle aspiration cytology
Sensitivity (%)	83	50	100	67
Specificity (%)	50	100	25	100
Positive predictive value (%)	71	100	67	100
Negative predictive value (%)	67	57	100	67
Accuracy (%)	70	70	70	80
'p' Value *	0.22	0.08	0.15	0.03

*Fisher's exact test

complications such as ecchymosis or hematoma.

All the patients underwent unilateral neck dissection. SOND (Supraomohyoid Neck Dissection) was performed in N0 cases and MRND (Modified Radical Neck Dissection) was done in N+ cases. In our study in SOND was done in 5 patients and MRND in 5 patients. Wide excision of the tumour was carried out and mandible was addressed by hemimandibulectomy in 8 cases and marginal mandibulectomy with reconstruction using temporomyofacial flap in 2 cases. The resected neck specimens were oriented anatomically; levels marked and sent for histopathologic examination. Palpation, CT, US and US-FNAC findings were compared with histopathologic findings. Diagnostic validity tests for different methods to assess the lymph node metastasis were performed. The results were presented in terms of sensitivity, specificity, predictive values and accuracy. Fisher's Exact Test was used to assess the value of each screening method. A 'p' value of 0.05 or less was considered for statistical significance.

Results

Histopathologic examination was the gold standard for comparing these methods. On final histopathologic examination out of 10 neck specimens six contained metastatic deposits. Out of 7 positive necks on palpation 5 had metastasis on histopathologic examination. 2 were false positive. Out of 3 negative necks on palpation one neck was positive on histopathologic examination giving one false negative result.

All the 3 positive cases on CT were confirmed by histopathology. Out of 7 negative cases on CT 3 were positive on histopathological examination giving false negative results in 3 cases.

Out of these 9 positive necks on US 6 were proved positive on histopathological examination. The negative neck on US was negative on histopathologic examination also. On US guided FNAC examination, all 4 positive cases had metastasis on histopathologic examination. Out of 6 negative cases, 2 showed metastasis on histopathologic examination giving false negative results in 2 cases.

The results of the neck histopathology and the results of the imaging studies were considered per neck side and are presented in Table 1 to 4. The results of the statistical analysis are presented in Table 5. Using Fisher's Exact Test, the 'P' value for palpation, CT, US and US-FNAC is 0.22, 0.08, 0.15 and 0.03 respectively. US-FNAC is the only test showing statistical significance in our study.

Discussion

Lymphatic metastasis is the most important mechanism in the spread of head and neck squamous cell carcinomas. The rate of metastasis probably reflects the aggressiveness of the primary tumour and is an important prognosticator [10]. Accurate radiologic imaging could potentially allow for a more conservative approach regarding management of the neck if the risk of occult metastatic disease could be reduced to 20% [11].

Clinical palpation is the first line method in evaluating metastatic cervical lymphadenopathy. In our study palpation results are comparable to various studies where they have got a sensitivity of 79.5% and 92.30% respectively [5,12]. The high sensitivity of palpation is attributable to the use of only physical characteristics such as size and consistency. The reactive lymph

nodes can also achieve the same dimensions as metastatic nodes and so false positive results are inevitable. The accuracy of 70% for palpation in our study can be comparable to previous studies [12,14,15,16] but it ranged from 60–86% in the literature reported [5,7,11,13].

CT has been used to determine neck metastasis in carcinoma of head and neck since 1981. Today there is some controversy about its usefulness. Criteria for assessing neck lymph nodes vary with many authors. Van den Brekel et al. in 1990 proposed the radiologic criteria in CT for assessing cervical metastasis in patients with primary SCC of head and neck. Based on their study we used a size criteria of 11mm, rim enhancement and central necrosis which is similar to the criteria suggested by Sarvanan K et al. in 2002 [5]. Our CT results are comparable to previous studies [11,14]. Considering the similar criteria Sarvanan K et al. in 2002 have got a sensitivity of 95.65%, specificity of 66.65% and accuracy of 92.30%. In their study the conglomeration and central necrosis had a sensitivity and specificity of 100% thus increasing the accuracy of CT. But in our study none of the cases showed conglomeration or necrosis. So this indicates rim enhancement and necrosis are the highly specific indicators of metastasis [5]. Though necrosis is a reliable criterion, it is unfortunately quite rare in small nodes. Although very small irregularities in contrast enhancement are present in many lymph nodes, it is very difficult to distinguish these small irregularities from artifacts or anatomic irregularities. So size of nodes plays an important role in assessing their nature [10]. The accuracy of 70% for CT in our study can be compared to previous studies [11,12,15]. The accuracy for CT ranges from 68%–92.30% in the literature [5,7,12,14,15].

CT is capable of imaging the neck in any plane. Resolution and depiction of tissues in deeper planes is superior in CT. CT can show the primary tumour with its local extensions and documentation is possible. Disadvantages of CT are its cost, radiation. It is an invasive technique due to injection of contrast. The older people may find it difficult to lay down for longer time [17,18].

US has got the highest sensitivity of 100% and lowest specificity of 25% in our study indicating that US can detect more number of cases but lacks the ability to confirm those cases. The detection of more number of lymph nodes however inevitably leads to a lower specificity and as the differentiation between reactive and metastatic is based on morphologic criteria, this leads to low specificity [17]. The accuracy of ultrasound in our study can be compared to previous studies conducted where they got the accuracy of 70%, 72.7% and 72.2% respectively [14,15,19]. The results of our study show that the accuracy of US alone never exceeds 70% as any rise in sensitivity is always accompanied by a decrease in specificity [13,19]. In reported literature the accuracy of US ranges from 67–95% [5,7,13,16]. Advantages of US over other imaging techniques are it is economical, widely available and well tolerated by the patient, absence of radiation, lack of need for a contrast medium and ability to easy on-screen node measurements. It is the only available imaging technique that can be used for frequent routine follow-up. It has disadvantages like primary tumour is seen infrequently and documentation of the finding is also a problem [9,10,18].

Differentiation between benign and metastatic nodes is not possible as far as ultrasound examination, CT and magnetic resonance imaging are concerned. Although several criteria have been developed for this purpose, specificity of all imaging modalities is low. The major advantage of US is that it is, unlike CT can easily be combined with FNAC. This procedure takes only a few minutes for each node, while aspiration under guidance of CT is time consuming and costly [16]. With the introduction of US–FNAC the high sensitivity of US can be combined with the high specificity of cytologic examination [17].

The findings of US-FNAC in our study can be compared to the previous studies [11,13,14,19]. In our study the sensitivity of US –FNAC is lower than palpation and US alone which can be correlated with other studies reported in the literature [11,14]. The specificity of US-FNAC is similar to that of previous studies [10,13,14,17]. To increase the sensitivity of US-FNAC that is to detect more number of cases, the false negative results should be low. So to get a less number of false negative results the selection of the correct node to aspirate is very important. A thorough knowledge of the lymph drainage pathways in the neck is necessary. As a simple guide enlarged nodes in level III, IV and V are always suspicious for metastasis. Reactively enlarged nodes occur more frequently in level I and II [19].

Using fisher's exact test US-FNAC ($p=0.03$) has reached statistical significance in terms of predicting neck metastasis compared to palpation ($p=0.22$), CT ($p=0.08$) and US ($p=0.15$) alone. To reach a statistical significance 'p' value should be equal to or less than 0.05 according to Fisher's exact test.

In our study CT showed lowest sensitivity of 50% which is similar to a study conducted by Feinmesser et al. in 1987 who got a sensitivity of 59.6%. So CT will enable the correct diagnosis of metastatic neck disease in only 50% of the cases with proved pathologic disease. Palpation has better sensitivity and predictive values than CT. It seems clear that CT offers no advantage over physical examination in correctly diagnosing the presence of neck metastasis. Results of CT will confirm the physical findings in a large percentage of necks with positive metastatic disease [20].

Though the specificity of US is lower than other methods it has highest sensitivity that is it can detect more number of positive cases and high negative predictive value indicating that, probability of predicting a negative node as actually negative is high. To reliably select patients who do not need elective treatment, criteria with a high negative predictive value should be chosen. To obtain this high negative predictive value, the number of false negative results should be as low as possible [21]. So accordingly US has got the highest negative predictive value. CT is a two dimensional reconstruction of the anatomy if a single scan picture is viewed. But US allows a multidirectional scanning by using different angulations of the transducer. This may be the reason why US showed a higher sensitivity than CT. This problem may be approached by using thin slices in CT investigation [9].

In our study 3 patients with nodal metastasis were missed by CT and 2 were missed by US-FNAC. US-FNAC and CT missed 2 of the same cases. The main error incurred by CT and US-FNAC was false negative results which were high. Therefore sensitivity of CT (50%) and US-FNAC (67%) is low. This shows that they fail to detect more number of cases. Reasons for CT inaccuracy may be erroneous interpretation of scan and presence of microscopic disease in nodes below the threshold detection for CT. US-FNAC inaccuracy could have been operator error in visualizing a malignant node or sampling errors in which the wrong node or the wrong part of an involved node was assessed by FNAC [14].

Various researchers have reported on difficulties with US-FNAC from lesions with a diameter of less than 4–5mm. Marco Knappe et al. say that though they have successfully aspirated nodes with a diameter of 3mm the lower limit for consistent results is 4mm. In our study the smallest node which we aspirated was 4mm. We found difficulty in aspirating the 4mm node and also the aspirate collected was very less and has given false negative results. So we would like to conclude that the nodes less than 5mm are difficult to aspirate and may give false negative results. Factors influencing the size limit for reproducible aspirates are patient compliance, needle size, resolution of the ultrasonographic image and criteria for cellularity of the biopsy specimen laid down by the cytopathologist [22,23].

Since the early days of aspiration biopsy, implantation of tumour cells along the needle tract has been of concern. There is experimental evidence of tumour cells spreading to the puncture site, needle tract and possibly even into blood and lymph secondary to the aspiration biopsy. Clinical implications in the form of local or distant metastasis have not been reported. Although seeding of tumour cells along the needle tract has been reported with tru-cut needles, this is a rare finding and has never occurred with thin aspiration needles [13,22].

Possible complications of FNAC include hematoma formation, hemorrhages, nerve damage and infection. Vasovagal reaction, fainting and seizures have been observed as rare complications [22]. In our study this technique was well tolerated by the patients without any complications.

The advantage of US and US guided FNAC over CT are the low cost of US, more convenient in elderly and/or dyspneic patients. FNAC is less invasive procedure than the administration of intravenous contrast material in CT. If it is performed by an experienced examiner it is proved to be quick (10–20min) and safe (no complications) technique, causing only moderate discomfort to the patient. It can usually be repeated during patients' follow-up visits. This is extremely important for patients who do not undergo elective neck dissection and it ensures early detection of regional recurrence in the neck [13,14,17].

The major advancement in the staging and management of oral cancer is the sentinel lymph node biopsy. This technique accurately stages the regional lymphatics based on the status of the first echelon nodes in the lymphatic basin draining the primary tumour site while limiting morbidity caused by unnecessary lymph node dissection. If this technique is proved to be more valid and practical it may replace the other investigational modalities in the assessment of neck metastasis [24].

Conclusion

In our study the sensitivity of CT was less compared to other modalities and accuracy was comparable to palpation and US. Taking into consideration disadvantages of CT like radiation, injection of contrast and is expensive in our socioeconomic status it is not a feasible technique to advice in each and every patient.

In our study none of the considered diagnostic methods show high sensitivity and specificity individually, so we can get this by combining the methods. Thus from our study of 10 patients we would like to conclude that by combining the ability of US to detect more number of positive cases (high sensitivity) and ability of FNAC in confirming the cases (high specificity). Ultrasound examination combined with fine needle aspiration cytology is the most accurate method for assessment of neck in oral squamous cell carcinoma. Experience and skill of the ultrasonographer and cytopathologist are prerequisites for good results. So along with the routine clinical examination of the neck US guided FNAC should be carried out preoperatively in all the patients. If in case, the staging of primary tumour is done by CT then at the same time neck also can be examined for nodal assessment by CT along with US-FNAC.

Our study is too small to come into final conclusion. So further study is required before its utility can be accurately assessed in the evaluation of lymph node metastasis for surgical management of neck.

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