Clinicopathological Profile of Metastatic Cervical Lymph Nodes - A Descriptive Study in a Tertiary Care Centre

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Abstract
The single most important factor determining the survival of patients with head and neck malignancy is the presence or absence of metastatic disease in the neck. clinicopathological profile of metastatic lymph nodes were conducted in the department of surgery, Medical College, Kozhikkode for a three years. Thirty nine cases of head and neck malignancy having either clinically evident cervical metastasis or those with a high chance of occult metastasis were selected. Twenty six of 39(66.7%) were male with male to female ratio 2.1. The mean age was 58.7(10.7) years. Most of the patients in this study belonged to 61-70 year group. The most common site of the primary lesion was at the anterior tongue(41%). Twenty one (53.8%) patients was at stage II, followed by 11(28.2%) patients in the stage III. The most common symptom was ulcer of the oral cavity(60%) followed by neck swelling in 15%. Cervical nodes were pathologically positive for metastasis in twenty one of the thirty nine cases (53.8%) of these seven were unilateral and four were bilateral. The commonest presenting feature was ulcer in the mouth followed by neck swelling,pain in the mouth, difficulty in swallowing, change in voice and ankyloglossia. The present study revealed most of the lesion were of ulcerative type.

Introduction
The single most important factor determining the survival of patients with head and neck malignancy is the presence or absence of metastatic disease in the neck1. Unfortunately medical opinion is divided on various aspects of metastatic neck disease.2 Controversies remain in assessment of neck disease, the prophylactic treatment of metastatic nodes, place of radical neck dissection as opposed to modified radical neck dissection and the role of radiotherapy3. Accurate determination of a neck node requires exacting clinical examination combined with considered use of appropriate supportive investigational diagnostic techniques4. Clinical examination of neck lacks strict objectivity being affected by various factors like the thickness of patient’s neck skin, the amount of subcutaneous fat and the width obscured by the sternomastoid muscle5. But the potential benefits of clinical examination far outweigh these drawbacks and it still remains as the most important method of assessing regional lymph nodes6. Impact of various aspects of primary disease in determining the neck metastasis is of utmost importance. A consensus needs to be reached on
which ones are the more important determinants of metastasis; so that appropriate management of the neck can be planned. Since its first description by George Washington Crile in 1906, classical radical neck dissection has undergone an increasing number of modifications. It has now come to selective neck dissection in which only those lymph node groups are removed that are more likely to contain metastatic deposits from the concerned primary. But its rationale and indications remain controversial. Many critics view it as only a staging procedure; with the need for a more comprehensive dissection if obvious metastatic nodes are present on histological examination. The objective of this study was to describe the clinicopathological profile of metastatic lymph nodes.

Materials and Methods
This is a descriptive study conducted in the department of surgery, Medical College, Kozhikode during 2007 to 2010. Patients were recruited into the study only after the approval of the protocol by the research and ethics committee in the institution. Only those patients giving informed consent were recruited to the study. In addition, we conducted the study conforming to declaration of Helsinki in all phases of the study. This particular study was a part of a larger study comparing the diagnostic accuracy of clinical, sonological and histopathological examination of metastatic lymph node in the neck.

A total of thirty nine patients with head and neck malignancy having either clinically evident cervical metastasis or those with a high chance of occult metastasis admitted in various wards of department of surgery and radiotherapy were included in the study. They were treated with wide local excision of the primary combined with neck dissection with or without reconstruction of the primary area. All consecutive patients satisfying the inclusion and exclusion criteria were included in the study. We included only patients above the age of 13. Those patients with history of preoperative radiotherapy were excluded from the study. Moreover we excluded those patients with recurrent swelling and previous neck dissection. A formal sample size calculation was done.

Thirty nine cases of head and neck malignancy having either clinically evident cervical metastasis or those with a high chance of occult metastasis were selected. Proper history was elicited and clinical examination was performed. Neck examination was carried out standing behind the patient. Using both the hands, each side of the slightly flexed neck was palpated simultaneously in a sequential manner starting from the submental and submandibular triangles, then the neck anterior to the sternomastoid passing from above downwards, the suprACLavicular fossa, then upwards into the posterior triangle and forwards across the sternomastoids to the nodes of the anterior triangle which are palpated a second time. Ultrasound examination was done in the N0 neck and in cases were deeper structure fixity was suspected. CT scan was carried out as indicated as per the standard treatment protocol.

The patients were then posted for surgery. After the neck dissection the specimen was cut according to the level of lymph nodes. The specimen were fixed in 10% buffered formalin and sent for histopathology examination where they were embedded in paraffin wax. Similarly the specimen of the primary lesions were fixed and sent. Tissue sections were stained with haematoxylin-eosin. The primary lesions were studied for the type and grade of malignancy and the presence or absence of perineural or lymphovascular invasion. Lymph nodes were studied for the presence or absence of metastasis and extracapsular spread.

All data were taken in a well designed case report form. All these data were abstracted into an excel based database and then analyzed.

All data were analyzed with Epiinfo 6.0 software and R statistical software. Contiguous data were summarized with mean and standard deviation or median and interquartile range depending on the distribution of the data. All categorical data were summarized with percentages and number.
Results
Of the patients included in this study, 26 of 39 (66.7%) were male with a male to female ratio 2.1. The mean age was 58.7 (10.7) years. Most of the patients in this study belonged to the 61-70 year group. The most common site of the primary lesion was at the anterior tongue (41%) as shown in the figure 1.

Figure 1: site of primary lesion.

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Table 1: baseline characteristics of the patients

| Variables     | N=39 |
|---------------|------|
| Age           | 58.7 (10.7) |
| Sex:          |      |
| Female        | 13 (33.3%) |
| Male          | 26 (66.7%) |
| site:         |      |
| Buccal mucosa | 7 (17.9%) |
| Floor of mouth| 5 (12.8%) |
| Lower alveolus| 8 (20.5%) |
| Retromolartrigone | 2 (5.13%) |
| Supraglottis  | 1 (2.56%) |
| Anterior tongue| 16 (41.0%) |

Thirty three of the thirty nine patients (84.6%) had clinically palpable cervical node; while six (15.4%) were clinically node negative. Among the clinically positive group thirty (91%) had unilateral cervical metastasis, while three (9%) had bilateral cervical metastasis. The most common lymph node level affected was level Ib (51.2%) followed by II (34.9%) whereas the least commonly affected were level IV and V (2.3%) as shown in table 2. Analysis of stage of neck nodes revealed that most patients were in the N1 stage (18/39) 46.1%, twelve were N2, six were N0 and only three were N3.

Analysis of morphology of the primary lesion revealed that in most cases it was ulcerative (51.2%), it was ulcer proliferative in 38.5% and proliferative in 10.3%. In 58.9% (23/39) of the cases the primary lesion was T2, while in 30.8% (12/39) it was T4. Two patients each were having T1 and T3 tumors.

Ultrasound of the neck was done in ten patients. All the six patients with N0 neck clinically were found to be N0 after ultrasound examination also. All the six patients with N0 neck clinically were found to be N0 after ultrasound examination also. In one patient with clinically N3 unilateral node, ultrasound detected nodes on the opposite side, while in another patient with N3 node, ultrasound detected multiple nodes on the same side. One of the two patients with N1 neck in whom ultrasound was done had multiple nodes on the same side while in the other ultrasound confirmed the clinical finding of single unilateral node. All the thirty nine cases were squamous cell carcinoma of...
which twenty (51.3%) were moderately differentiated, sixteen (41.0%) were well differentiated and only three (7.7%) were poorly differentiated. Lymphovascular invasion was present in four (10.3%) cases while it was absent in the rest thirty five (89.7%).

Figure 2: stage of disease grouped by histopathology

\begin{figure}
\centering
\includegraphics[width=0.5\textwidth]{stage.png}
\caption{Barplot of 'stage' by 'hpr'}
\end{figure}

Cervical nodes were pathologically positive for metastasis in twenty one of the thirty nine cases (53.8%) of these seven were unilateral and four were bilateral and were N0 and only three were N3. Most common level of node affected by metastasis was level II which was positive in seventeen neck dissections (75%) either singly or in combination with nodes at other levels. This was followed by level Ib which was positive in twelve neck dissections. The least affected was level Ia which was involved in only four cases. In no case metastasis bypassed level I, II or III to involve level IV or V. Extracapsular involvement was present in seven of the twenty one pathologically positive neck dissections while it was absent in the rest. Five of the six clinically negative neck were negative pathologically also, while the other patient with T2 tongue lesion had metastasis at level Ib and II. Nine of the eighteen N1 and four of the twelve clinically N2 patients were pathologically negative for metastasis. But all the clinically N3 were pathologically positive.

**Discussion and Conclusion**

Undetected nodal metastasis is the commonest cause of treatment failure in head and neck cancer. Hence, regional control of nodal metastasis in the neck is an important factor in predicting the clinical course and outcome of the patient with head and neck malignancy (Hibbert et al., 1983)\textsuperscript{21}. The oral cavity has a rich lymphatic drainage. Palpable nodes on presentation reduces the survival by about one half\textsuperscript{46}. In the present study thirty eight out of the total thirty nine patients had primary malignancy in the oral cavity.

There is a progressive increase in the incidence of cancer with age, with the elderly showing a much increased rate of susceptibility\textsuperscript{11}. This is believed to be related to a protracted conditioning period that is associated with environmental factors, especially tobacco chewing or smoking. The present study also reflects the same pattern with maximum cases in the sixth and seventh decade and a mean age of 58.7 years. Shah et al., (1990)\textsuperscript{40} found the mean age to be 60 years in patients with oral cancer\textsuperscript{12,13}. The mean age of patients presenting with oral cancer in Kerala was found to be 57.8 years by Sankaranarayanan et al., (1992)\textsuperscript{36} in an earlier study\textsuperscript{14}.

As evident from table, the incidence of oral cancer in this study is more among males, the male female ratio being 2:1. The results are comparable with previous studies. Hamner et al., (1986)\textsuperscript{20} found the male female ratio of oral cancer to be 2:1\textsuperscript{15}. Studies by Cherian et al., (1991)\textsuperscript{9} and Sankaranarayanan et al., (1992)\textsuperscript{36} also showed a higher incidence in males\textsuperscript{16}. This is probably due to males being more habituated to tobacco chewing, smoking and alcohol consumption when compared to women.

Most of the patients with oral cancer present with ulcer. However, a few present with a metastatic node in the neck with no complaints related to the oral cavity\textsuperscript{11}. 

#mdcc-moderately differentiated SCC, pdssc-poorly differentiated SCC, wdscc-widely differentiated SCC
In the present study too, the commonest presenting feature was ulcer in the mouth followed by neck swelling. Pain in the mouth, difficulty in swallowing, change in voice and ankyloglossia were the other symptoms with which the patients presented.

Brunn et al., (1976)6 showed the average delay between the start of symptom and treatment to be 10.5 months17. In present study, the duration of symptoms ranged from one month to three years with a mean duration of 7.67 months. This reduction in the mean duration reflects increased awareness about this health problem among the population of our state.

Smoking and alcohol are the two most strongly implicated factors in the aetiology of oral cancer18,19. The increased incidence of oral cancer in some parts of our country is related to the habit of pan chewing and reverse smoking prevalent in those parts20.

The present study also reflects a similar epidemiological pattern with 66% of the people addicted to smoking, pan chewing or alcohol.

In oral cancer, majority of the nodes on presentation or which develop subsequently, are ipsilateral and are confined to the submandibualr or upper and mid jugular groups. Contralateral or bilateral nodes are more likely in lesions which are close to the midline e.g. in the floor of the mouth and/or dorsum of the tongue11, 39, 41.

Metastatic disease in the lower neck may occur in the absence of obvious disease higher in the neck; particularly with primary tongue lesions21.Woolgar et al., 199753).

In the present study the most common lymph node level affected on clinical examination was found to be level Ib followed by level II and the least commonly affected were level IV and V. This finding is similar to that reported in world literature.

Various studies have shown tongue to be the most common site of oral cancer followed by floor of mouth and lower alveolus11.

In the present study too the most common site of primary lesion was anterior tongue followed by lower alveolus, buccal mucosa, floor of mouth and retromolartrigone, in the decreasing order of frequency.

The vast majority of mouth cancers are both ulcerative and infiltrative; exophytictumours are less common22. In this study too most of the lesion were of ulcerative type.

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