Original Article

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RELATION OF TUMOUR THICKNESS WITH LYMPH NODE METASTASIS IN ORAL SQUAMOUS CELL CARCINOMA

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ABSTRACT

Objective: To measure the tumour thickness in oral squamous cell carcinoma (OSCC) and to establish relationship with metastasis in the cervical lymph nodes.

Study design: Descriptive study.

Place and study duration: Department of Histopathology, Armed Forces Institute of Pathology (AFIP), Rawalpindi, 6 months (Feb - July 2010).

Materials and Methods: Thirty cases of neck dissection for oral squamous cell carcinoma were included in the study. The tumour thickness was measured in all cases and total number of involved lymph nodes was documented. Comparison was made between the tumour thickness and the involved lymph nodes.

Results: The mean age of the patients was 54±11.5 years. Male to female ratio was 1.5:1. The cases were taken from different oral sites, tongue being the most prominent of all (36%). Majority (63.3%) of patients had tumour metastasis in the cervical lymph nodes. The mean tumour thickness of cases with neck node metastasis was 9.9 mm. Significant relationship was observed between tumour thickness of ≥5mm increases the chances of cervical lymph node metastases (p<0.001), hence it should be considered as an important prognostic indicator.

Conclusion: Importance of tumour thickness cannot be neglected as it is an important prognosticator. A cut off size of ≥5 mm could be used to predict the cervical lymph node metastasis in an oral SCC patient.

Keywords: Lymph node metastasis, Oral cavity, Oral squamous cell caricinoma (OSCC), Tumour thickness.

INTRODUCTION

Oral squamous cell carcinoma (OSCC) is considered to be amongst the most prevalent life threatening malignancies in the world. Prognosis of an oral SCC patient depends upon different stages of the disease but 81% of these patients have a one year survival rate where as the five years survival rates are reported to be 48% to 56%[1].

Mortality and morbidity rates of OSCC remain unwavered despite all the advancement in the field of oncology and surgery. The final outcome of an oral SCC patient depends upon various prognostic factors like age, tumour thickness and its depth of invasion in the underlying connective tissue, sentinel and cervical lymph node metastasis, its extra capsular spread and many other predictive indicators[2,3].

The OSCC is characterized by high potential for local invasiveness and distant metastasis. The metastasis is first to sentinel and then to other cervical lymph nodes which has an increased impact on patient's survival rate. Studies have been carried out worldwide to show the important prognostic factors of survival among which correlation between the increasing tumour thickness and an increased risk of cervical metastasis presents a problem[3,4].

The OSCC patients are treated surgically by intra oral excision of the primary tumour with neck dissection depending upon the staging of the tumour alone. Tumour thickness is considered to be a more reliable feature, as many studies have shown that the risk of metastasis and spread to cervical lymph nodes increases with increase in tumour thickness. Previously this relation of tumour thickness and the metastasis to cervical lymph nodes was studied by many authors[1,4-7]. The results from these studies have been conflicting due to lack

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of comparable groups and no standardized measurement techniques[5].

Considering this, a study was designed to see the relationship of tumor thickness in OSCC with cervical lymph node metastasis.

MATERIAL AND METHODS

It was a descriptive study done on neck dissection specimen resected for OSCC in the department of Histopathology, Armed Forces Institute of Pathology. The study period was six months from Feb to July 2010.

A total of thirty patients of OSCC with their neck dissection samples were selected. The data on gender, age and site was extracted from the clinical forms provided with the samples. Gross examination was carried out and the tumour size was measured macroscopically.

Inclusion and exclusion criteria laid down for the specimen selection was that all the neck dissection specimen for OSCC were included in the study. Specimens which were autolysed, or had extremely sloughed off bases of the tumour were excluded from the series. For sampling technique, non probability and purposive sampling was selected. In order to analyze the results, different quantitative variables including age, thickness of tumour and number of involved lymph nodes were measured. Qualitative variables included gender and site of tumour. Mean and standard deviation (SD) were calculated for quantitative variables while frequency and percentages were calculated for qualitative variables. Chi Square test was applied in order to evaluate the statistically significant correlation between the incidence of lymph node metastasis and the OSCC tumour thickness. A *p*-value of less than 0.05 was considered statistically significant.

Tumour was cut in a bread loafing pattern and the section showing maximum tumour involvement was taken in the cassette. If the tumour was greater than 3 cm, the respective section was cut into 2 and then embedded. The first section was taken from the surface of the tumour to the midpoint. The second section was taken from the midpoint to the bottom of the tumour. In case of larger tumours, more than 2 sections were taken. The neck dissection specimens were carefully evaluated for the presence of lymph nodes. Especially, the sentinel lymph nodes were recovered first followed by the rest of the cervical lymph nodes. Then the total number of lymph nodes recovered were noted.

All the obtained lymph nodes and sections were dissected and fixed. The blocks were made which were cut using microtome into the sections of 4-5µm thickness. They were then stained with heamatoxylin and eosin for examination. The prepared slides were first analyzed for the primary tumour and lymph node metastasis. Then digital images of the primary tumour were fed into the computer for precise measurement of the tumour thickness using software, Image J. The tumour depth was measured taking the tumour surface as a starting reference point to the maximum depth of tumour invasion. A value of ≥ 5 mm was considered to be significant as it was established in an Indian study and since no local study had been carried out, this value was taken as an ideal value[5].

For the statistical analysis data was entered in statistical package (SPSS version 16) in order to analyse all quantitative analysis (mean and standard deviation) and qualitative variables (frequency and percentages).

RESULTS

The total number of cases was thirty. The age of the patients ranged from 25-78 years with a mean age of 53.98±11.58 years. In total, 18 patients were male and 12 were female with male to female ratio of 1.5:1. Different oral sites were included in the study which is depicted in figure.

From a total sample size of 30 patients, 19 (63.3%) had tumour metastasis in the cervical lymph nodes whereas 11 (36.6%) had no nodal metastasis. The mean tumour thickness of those cases with neck node metastasis was 9.9±3.1 mm and the mean thickness of cases without neck metastases was 5.6±3.23 mm.

Significant relation between tumour thickness and lymph node metastasis was observed as shown in table.

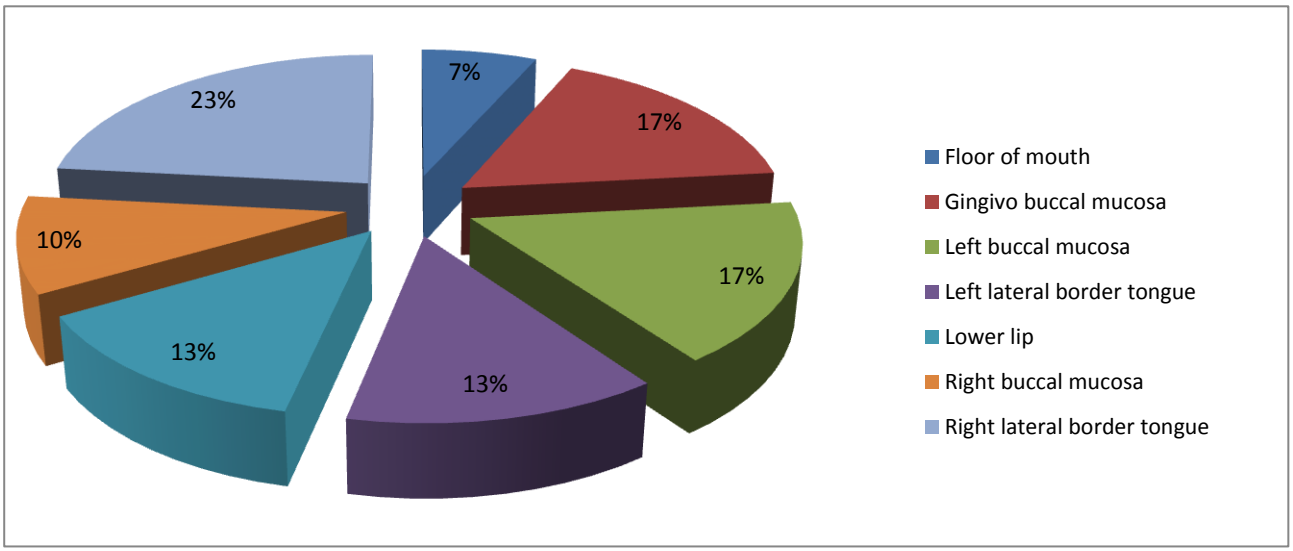

Figure: Distribution of squamous cell carcinomas according to site (n = 30)

Table: Relationship of tumor thikness and lymph made metastasis.

Thickness in mm	Metastasis present	Metastasis absent
<5mm	0 (0%)	6 (55.6%)
≥ 5mm	19(100%)	5 (45.4%)

p- Value < 0.001

DISCUSSION

Many authors have supported the fact that tumour thickness of OSCC is an important prognosticator for the occurrence of subclinical and clinical metastasis. The only problem that presents a challenge is the varying data and different cut off tumour thickness values.

According to this study, tumour thickness is defined as the distance measured from the surface of the tumour including the keratin to the point of maximum invasion in the underlying connective tissue stroma. In cases of ulcerated tumours, base of the ulcer serves as the reference point. Depth of invasion is considered as a synonym for tumour thickness.

Many studies have used the terms "depth of invasion" and "tumour thickness" synonymously whereas, few studies like the one carried out by Moore *et al* defined tumour thickness and depth of invasion as two different entities. According to them, depth of invasion means the extent of cancer growth into the tissue beneath an epithelial surface. He defined tumour thickness as the entire tumour mass[8].

Our study took thickness from either the tumour surface or from the base of the ulcer. Giacomarra *et al* affirmed that tumour thickness is commonly used as a synonym of depth of invasion and indicates the part of tumour situated under the line of basal membrane[9]. So, in comparison, the tumour measuring methods are different.

Another study done by Suzuki *et al* in Japan defined tumour thickness and depth of invasion as two separate terms. According to Suzuki's study, definition of tumour thickness is similar to ours and depth of invasion is defined as a distance from theoretically reconstructed normal mucosal line to the deepest portion of invasion. The only difference between the two definitions is the reference points taken in the epithelium. In our study, we considered the two terms as one hence eliminating any doubt about these entities[10].

For cup shaped ulcerated SCC of lower lip, Cooper and Frierson made several radially oriented measurements. Out of all these measurements, the largest one was taken into consideration[11]. Our study contradicted this measurement since for ulcerated tumours, thickness was measured from the base of the ulcer to the maximum tumour invasive island.

Even though in our study, the mean tumour thickness for patients with neck node metastasis came out to be 9.9 mm, this value has been biased towards higher side owing to a fewer samples with larger thickness measurements. However, it has been found that most of these cases have a cut off value of 5 mm. This value of 5 mm was found to be significant to predict the cervical lymph node metastasis as no case with lesser thickness had nodal metastasis. Similar results were found in an Indian study conducted by Kane. Out of 48 OSCC cases, 25% patients had metastatic disease. He took a cut off value of 5 mm or more to be significant histopathological predictor of neck node metastasis[6].

In an Australian study carried out by Wallwork, a sample size of 53 patients of SCC of the floor of the mouth was studied. The mean tumour thickness in the patients with lymph node metastasis was 14.6 mm and those without metastasis were 8.6 mm. The mean tumour thickness of cases with lymph node metastatic deposits was significantly greater than the others. A cutoff value of tumour thickness was taken which was 7.5 mm. It was shown that tumours equal or greater than 7.5 mm presented a risk towards cervical metastasis[5]. Our study varies slightly from the cutoff value. These variations may arise owing to smaller sample size of 30 in our conducted study.

O'Brien conducted a study on 145 stage I and II OSCC patients which were grouped according to their various sites. Overall, 55 patients had pathologic node involvement at some time in their disease. The mean thicknesses of different sites were taken. A median tumour thickness value for all sites was taken which was 4 mm. It was seen that prognosis changed significantly at a cut-off of 4 mm with local control, nodal disease, and survival rates of 91%, 8%, and 100%, respectively, for tumours <4 mm compared with 84%, 48%, and 74% for those 4 mm or more. Our study showed nearly similar results, which was also conducted on SCC from five different oral cavity sites. We found that tumours ≥ 5mm proposed greatest threat to patient's survival along with cervical metastasis[7].

A Spanish study carried out by Gonzalez-Moles on tongue SCC showed that the 5 year survival rate of patients with a tumour thickness ≤ 3mm was 85.7% which is higher than the 58% five year survival rates of patients with a thickness of 4-7 mm. Hence a wide thickness range was given in this study rather than a significant and specific value in contrast to our study[12].

A study conducted by O-Charoenrat in London showed very similar results to our studies. A total of 50 patients having early tongue SCC were selected as a study group and it was seen that patients with tumours exceeding 5 mm thickness showed a metastatic rate of 64%. Whereas, those tumours which were less than 5 mm, the incidence of cervical nodal metastasis was only 16%[13].

However, in contrast to our study, authors like Sheahan and Kligerman extended their research and linked tumour thickness to local recurrence rates in OSCC patients[14,15].

Similarly, many studies linked the tumour thickness not to the nodal metastasis but to survival of the patients, whereas our study concentrated purely on nodal metastasis[8,16].

Our conducted study was heterogeneous and included all the OSCCs. Many studies limited themselves on selection of certain sites rather than the whole oral cavity. The most commonly studied site was tongue as seen in research conducted by Veness, Gonzalez-Moles, Fukano, Fakih, and O-Charoenrat *et al*[12,13,16-18].

Despite all the different values, most of the study groups along with our study agreed on the point that one thickness is an important prognosticator for a patient of oral squamous cell carcinoma along with a predictor of cervical lymph node metastasis.

CONCLUSION

Tumour thickness is a well accepted prognostic indicator as this has been established by many studies world over including this study. Relationship of tumour thickness to lymph node metastasis was found to be

significant as shown by this study. Differences of results worldwide may be attributed to different measurement techniques and sample size, leading to different results and cut off values. This study is being conducted for the first time in our set up, thus it can be taken as pilot study and research area is open for future studies.

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