IS THE PATTERN OF INVASION A RELIABLE PREDICTOR OF METASTASIS OF ORAL CANCER?

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ABSTRACT

Although oral cancer accounts for over 35% of all the cancers in our patients, there is no reliable way to predict prognosis. Various studies have shown different relationship of histological features to prognosis, but the results are not conclusive. Arrangement of cells at the advancing front of the tumour may play a significant role in predicting prognosis. Metastasis is considered as a key clinical and histological parameter, which decides the outcome of a given patient. Therefore the aim of this study was to compare the relationship between the pattern of invasion and metastasis.

Fifty cases of oral squamous cell carcinoma which have been excised with the neck lymph nodes, received at the Department of Oral Pathology, Faculty of Dental Sciences, University of Peradeniya from July 1999 to August 2000, were selected for this study. Pattern of invasion has been graded as type 1,2,3, and 4 according to the arrangement of tumour cells at the advancing front.

Statistical analysis showed metastasis of 22% in type 2, 50% in type 3, and 71% in type 4 oral squamous cell carcinoma patients. These results were statistically significant and the p value was $0.001 < p < 0.01$.

In conclusion, pattern of invasion is a reliable predictor for metastasis of oral squamous cell carcinoma. Therefore this histological parameter may be of use in planning treatment of oral Squamous cell carcinoma.

INTRODUCTION

The incidence of oral squamous cell carcinoma is increasing world-wide (Blot, Devesa and McLaughlin, 1994; Macfarlane, Sharp and Porte, 1996). This is the commonest malignancy in South Asia and it accounts for over 35% of all cancers of Sri Lankan patients. The high incidence of the disease in this part of the world is due to the habit of betal chewing.

Despite the advances in treatment options at a global scale, mortality still remains high with an overall five year survival rate of 53% (American Cancer Society, 1997). Survival rate of cancer patients in Sri Lanka may even be less than the above figure due to various reasons such as unavailability of refined treatment options and the late presentation of such patients to clinicians. Therefore, the five year survival rate of local patients may be around 25% which is the accepted figure for late presentations.

Although oral cancer is the commonest malignancy in Sri Lanka the survival rate of patients is not satisfactory. Therefore it is an extreme necessity for the researchers to critically look at this problem in terms of improving prognosis of oral squamous cell carcinoma. It is an accepted fact that a cancer showing metastasis has a poor prognosis. This raises an important question whether one can identify the cancers which have the likely potential for metastasis. If there is a method to solve the above problem the surgeons are in a better position when the treatment plan is established to decide the extent of the surgery and other adjuant treatment modalities

There are numerous studies which have tried to show the relationship between various histopathological parameters and prognosis (Anneroth, Hansen and Silverman, 1987; Broaders, 1941). Consequent researches have questioned the validity and specially the practicality of most of the grading systems. Other prognostic predictors especially molecular markers have proved to be imprecise for routine use (Bryne, Nielsen and Koppang, 1991). As oral cancer is the commonest cancer in Sri Lanka, a simple system which can be used in routine diagnosis to predict the prognosis of a given cancer is needed. Pattern of invasion at the advancing front of the tumour has been shown to correlate more accurately with survival (Yamamoto, Miyakawa and Kohama, 1984; Bryne, Koppang and Lilleng, 1992).

There are no studies carried out in Sri Lanka in order to assess the histological parameters in relation to prognosis of oral cancer. Therefore the aim of our study is to analyse the relationship between the pattern of invasion and metastasis of oral cancers in Sri Lankan patients.

MATERIALS AND METHODS

Excision specimens of fifty cases of oral squamous cell carcinoma together with cervical block dissections were selected from the Department of Oral Pathology, Faculty of Dental Sciences, University of Peradeniya for the present study. The sample which was selected represented patients from different districts of the country. All the specimens were formalin fixed and embedded in paraffin wax. On average 8-10 haemotoxylin and eosin stained sections were prepared from all fifty cases. Histological analysis was performed in order to study the pattern of invasion at the advancing front of the tumour. The lymph nodes which were identified from the neck in each case were assessed for the evidence of metastasis. Each case was histologically examined using a light microscope available for routine diagnosis in the department. The cases which did not include adequate advancing front were excluded from the study. The invasive front of the tumour was graded into four types based on the arrangement of tumour cells as follows (Fig. 1).

Type I	Large cohesive islands of tumour
Type II	Small islands of tumour
Type III	Thin strands of tumour
Type IV	Dyscohesive individual tumour cells

A pilot study was carried out by the investigators in order to get familiarised with the various histological patterns at the advancing front. When grading the type of invasion the worst score was recorded for the cases which showed more than one pattern. Presence or absence of metastasis were given the scores 0 and 1 respectively (Fig. 2).
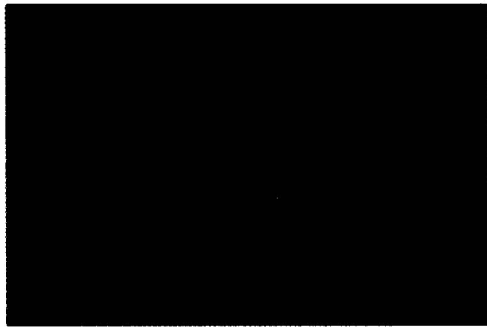
Statistical analysis was performed in order to assess the relationship between pattern of invasion and metastasis using chi-square test.
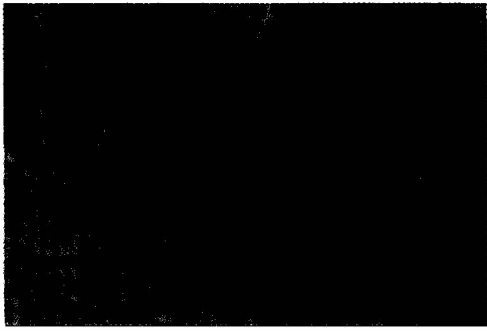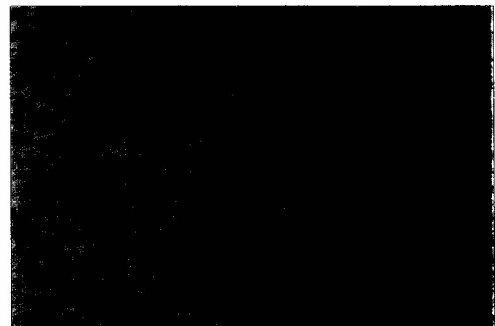

Type I

Type II

Type III

Type IV

Fig. 1. Four types of pattern of invasion of squamous cell carcinoma used in the study
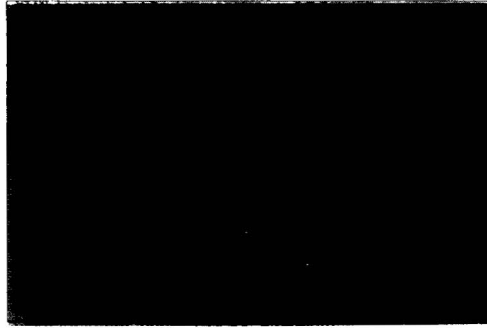
Fig. 2. Lymph node showing metastatic squamous cell carcinoma

RESULTS

After a detailed histological assessment all fifty cases were categorised in to four types depending on the pattern of invasion at the advancing front. There was only a single case of Type I. The highest number of cases belonged to Type IV (Table).

Table 1. Number of cases showing metastasis according to the pattern of invasion.

Pattern of invasion	I		II		III		IV	
	No	%						
Metastasis (1)	O	0	4	22.2	5	50	15	71.3
No metastasis (0)	1	00	14	77.8	5	50	6	28.7
Total	1		18		10		21	

As there were inadequate cases of Type I, the chi-squared test could not be applied there. Therefore Type I had to be excluded from further statistical analysis. The chi-squared test results of other types were as follows:

X^2- 9.324 (chi-Square value)
Df - 2 (degree of freedom)

Chi-square test showed that results were highly significant ($0.001 < p < 0.01$).
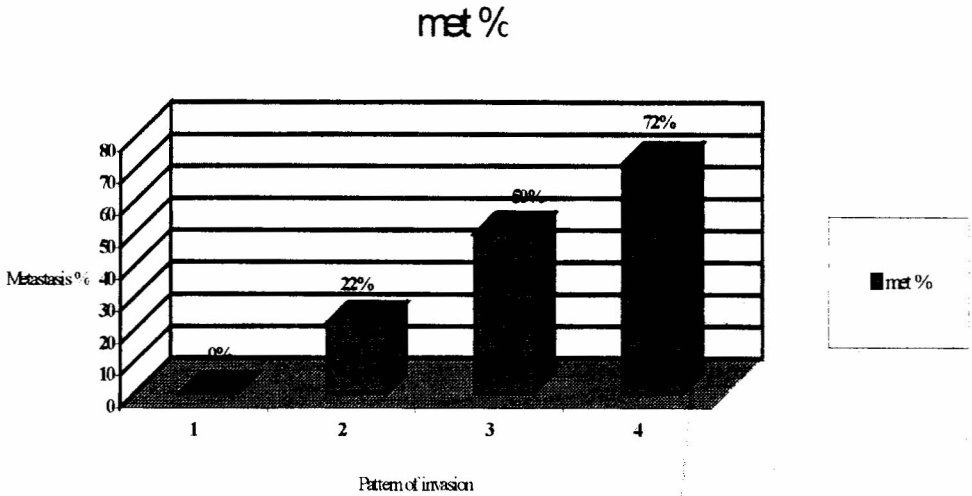
met %

Fig. 3. Graph showing the relationship between pattern of invasion and metastasis.

DISCUSSION

The study of prognostic markers of oral squamous cell carcinoma is an area of research that has been studied extensively world wide. The features that various scientists investigated include both cellular and molecular features of cancer (Bryne, Nielsen and Coppang, 1991; Broders, 1941; Anneroth, Hansen and Silverman 1986; Holm et al, 1982). Broders system which was originally devised for lip cancer, is simple and most widely used, but it is a poorly predictive system for metastasis and survival (Cade, Lee, 1957). Consequently, a large number of complex grading systems has been described (Anneroth, Hansen and Silverman, 1987 and 1984; Bryne, Koppang and Lileng, 1989; Jakobsson et al, 1973).

It is accepted that there is no reliable and reproducible prognostic predictor of oral cancer despite the extensive research that has been carried out on this subject. A few studies in the recent past (Odell et al, 1994; Bryne, 1998) has shown that there is a relationship between the pattern of invasion and prognosis. Further, it is a more reliable histological feature in terms of reproducibility. The Pathologist and surgeons need to have a marker that can be applied to predict the prognosis of their patients as oral squamous carcinoma is the commonest cancer in Sri Lanka. Our results clearly showed that there is a statistically significant relationship between the pattern of invasion and metastasis. The results are similar to the previous studies carried out on the pattern of invasion (Odell et al, 1994). Identification of cancers which have a metastatic potential will certainly help the clinician to plan the treatment accordingly. However, a further study using a larger sample is needed before recommending the investigated histological parameter as a definitive predictive indicator. In the present study, especially with regards to Type 1, the statistical analysis was not possible as the sample size was small. Although there are no metastatic cases in Type 1, certainly some cancers of this group will end up in lymph nodes. The pattern Type IV, which shows individual tumour cells at the invasive front, metastasises to lymph nodes more than any other pattern, at a rate of

three out of four cancers. The possible explanation for the high percentage of metastasis in this group could be due to the fact that individual tumour cells, when they are in isolation, can invade the extra cellular matrix and lymphatics/blood vessels more easily than a solid island of tumour. If this is the case, the clinicians would be in a position to alter their treatment according to the biopsy report, specially on the invasive front. However, as discussed earlier, this histological parameter should be further investigated with a larger sample before implementation.

As this is an ongoing research carried out by us, this study will be extended to investigate some other histological parameters, which may have a significant relationship with prognosis such as host response, level of differentiation, and the depth of invasion.

In conclusion, our study shows the validity and reliability of the relationship between pattern of invasion and metastasis. Therefore, the clinicians should be encouraged to take deep incisional biopsies including the invasive front in order to allow the proper assessment of the pattern of invasion by the Pathologist. Further studies are indicated to confirm the results of this study with a much larger sample and also to investigate other histological parameters. It is suggested that this histologial parameter could be of much use to clinicians to plan the treatment for oral cancer patients in Sri Lanka and to achieve a better survival rate for oral cancer victims.

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