

## COMPARISON OF HISTOPATHOLOGICAL FEATURES OF SYNCHRONOUS AND SINGLE PRIMARY ORAL SQUAMOUS CELL CARCINOMAS

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### Introduction

Synchronous second primary tumours (SPT) were defined as tumours occurring simultaneously or within one month after the patient's first tumour (Liao et al., 2007). Many authors have described the occurrence of second primary squamous cell carcinoma (SCC) of the upper aerodigestive tract. Although field cancerization was first described in oral squamous cell carcinomas (OSCCs), only a very few studies have concentrated on second primary SCC occurring in the oral cavity (Liao et al., 2007). Even those very few studies in the English literature that compared second primary OSCCs with single primary OSCCs have not analyzed the histopathological differences between the two groups. Therefore, the aim of the present study was to compare the histopathological features of synchronous second primary OSCCs with single primary OSCCs.

### Patients and Methods

Surgical histopathological reports of patients with OSCCs, diagnosed at the Department of Oral Pathology, Faculty of Dental Sciences, University of Peradaeniya from 1995 to 2009 were retrospectively reviewed. Twenty eight

patients with synchronous primary OSCCs were identified according to the criteria defined by Moertel et al, 1961. The criteria include; (A) all the tumours had to be histologically malignant; (B) all had to be distinct masses, separated by normal tissue (at least 2cm); and (C) the possibility that the tumours could be metastatic had to be histologically excluded. The age and sex matched control group of single primary OSCC patients was randomly selected using SPSS 13.0 for windows software (SPSS, Inc., Chicago, IL, USA). Two synchronous lesions were assigned as synchronous-1 and synchronous-2 randomly. The histopathological differences between two synchronous tumours and also between synchronous and single primary OSCCs were investigated.

Chi-square test and Fisher's exact test for the sub-groups were carried out to evaluate the significance of the histological parameters between groups. Statistical analysis was performed using SPSS 13.0 software for Windows. For all tests, a p value of < 0.05 was considered significant.

## Results

The male to female ratio in the synchronous OSCC population was 3:1 (21:7). The mean age at diagnosis of tumours was 65 years. (Male: 67, Female: 61). No significant difference was found with regards to any of the histological features among synchronous OSCCs.

Significantly a higher number of abnormal mitoses was found in the single primary group ( $p < 0.05$ ) compared with the synchronous group. Tumour induced stroma (TIS) was evident in 14(50%) single primary OSCCs while only 3(10.7%) synchronous OSCCs were positive for TIS. This showed a strong statistical significance with  $p$  values of 0.011 and 0.001 respectively.

In the present study, 7 (25%) single primary OSCC patients were positive for lymph node metastasis, where as only one synchronous OSCC patient was positive for lymph node metastasis ( $p$  value = 0.051). Out of 7 single primary OSCC patients who had lymph node metastasis, 5 showed Extracapsular Invasion (ECI). Interestingly none of the synchronous OSCC patients had ECI ( $p$  value = 0.051).

Synchronous OSCCs (means: synchronous 1 = 2.16 mm, synchronous 2 = 2.46 mm) showed a significantly less depth of invasion in comparison to single primary OSCCs (mean = 3.82 mm). This was statistically significant ( $P=0.001$ ) (one way ANOVA). At the average critical thickness for oral tumours i.e. 4mm (Woolgar, 2006), only 3(10.7%) and 2(7.1%) synchronous OSCCs showed

depth of invasion  $> 4$  mm where 12 (42.9%) single primary OSCCs showed a depth  $> 4$ mm ( $p < 0.05$ ). To support the above finding, significantly higher number (85.7%) of single primary OSCCs have invaded the deep corium and muscle, whilst 39.3% synchronous OSCCs remained in the superficial corium. A significant difference was not found with regard to the degree of differentiation, keratinization, pattern of invasion, host response, number of mitoses, perineural invasion and vascular invasion.

## Discussion

According to the results of our study, synchronous second primary tumours are less aggressive forms histologically with low depth of invasion, less frequent abnormal mitoses and tumour induced stroma when compared with the single primary OSCCs. This finding was supported by the fact that only one synchronous case showed nodal metastasis in comparison to 7(25%) cases in single primary OSCCs. However, according to the various studies on second primary OSCCs the onset of SPTs decreases the 5 year survival by 30% as compared to those with only a single tumour (Liao et al., 2007).

These findings raise the question of whether the synchronous OSCCs behave in a different way clinically despite their less aggressive histological features or some unproven factors that affect the survival of patients. Early presentation for treatment when they have multiple lesions rather than a single lesion is a possible explanation for the low depth of invasion showed in synchronous



OSCCs. In addition, the verrucous lesions, probably of PVL origin are also considered as less aggressive forms histologically, at least in early stages. Therefore, this highlights the importance of further studies in this context to assess other possible parameters which can affect the survival of synchronous OSCC patients to arrive at a conclusion on their behaviour.

### **Conclusion**

This study indicates that synchronous OSCCs display more favourable histological prognostic features such as significantly low depth of invasion, lack of lymph node metastasis, less frequent abnormal mitosis and reduced tumour induced stroma than single primary OSCCs.

### **References**

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