

ABSTRACT

INTRODUCTION

Oral carcinogenesis is a complex process involving multiple genetic damages. Molecular changes at the tumour invasive front have been recognized to provide insight into the aggressiveness of a tumour and hence prognosis. This study aimed to describe the demographic and clinicopathological characteristics of oral squamous cell carcinoma (OSCC) as well as the expression of several molecules, Ki-67, p53, MDM-2 and Bcl-2, in this area from various sites and their relationship with certain demographic (age, sex and gender) and clinicopathological parameters (TNM staging, Broder's classification and pattern of invasion).

MATERIALS AND METHODS

Forty five biopsy OSCC samples with sufficient connective tissues were collected for the study. Expression of Ki-67, p53, MDM-2 and Bcl-2 was investigated using immunohistochemical method. Expression of markers was captured with an image analyzer for assessment. Statistical significance was carried out using chi square tests (Pearson's and Fisher's exact) and Mann-Whitney U for categorical and continuous data.

RESULTS

Twenty five male and 20 female with a mean age of 59.0 years (\pm 11.90) were included in the study. Most subjects were Indian (68.9%) followed by the Chinese (22.2%) and Malay (8.9%). A majority of cases were in Stage III and IV (74.54%) and were moderately differentiated tumours (55.6%). Expression of Ki-67 was observed in 28 cases (62.2%), p53 in 35 cases (77.8%), MDM-2 in 44 cases (97.8%) and Bcl-2 in 2 cases (4.4%) at the tumour invasive front. Ki-67 and p53 shared similar pattern of expression;

immunoreactivity was observed mainly in the nuclei of basal (progenitor compartment), suprabasal (maturation compartment) layers of the tumour epithelium and also in the invading tumour islands. MDM-2 also exhibited similar pattern of expression, in addition to that, immunoreactivity was also observed in all layers of the tumour epithelium. Bcl-2 immunoreactivity was confined to the cytoplasmic of cells in the basal (progenitor compartment) and suprabasal (maturation compartment) layers of the tumour epithelium at the tumour invasive front. There is no significant relationship between the expression of markers and parameters investigated.

CONCLUSION

The expression of Ki-67, p53, MDM-2 and Bcl-2 might not serve as candidate markers for prognosis and to predict the course of the disease. Nevertheless, the overexpression of MDM-2 and Bcl-2 indicates that they may be involved in the mechanism for oral carcinogenesis.

RECOMMENDATIONS

Patients with good clinical data and follow up are the best candidates for future studies. Assessment of Ki-67 should be continued to shed light on its role in prognosis. Mechanism of p53 protein stabilization should be looked into via mutational analysis besides MDM-2 overexpression. Future study involving Bcl-2 should also include Bax in order to determine the role of the ratio of Bax/Bcl-2 in oral carcinogenesis.

ACKNOWLEDGEMENT

I would like to express my deepest gratitude to the following persons:

- Professor Dr Rosnah Bt Mohd Zain. My supervisor. Thank you for continuous teaching and insight into the histopathology of oral cancer.
- Cancer Research Initiatives Foundation (CARIF). Special thanks to my advisor, Dr Cheong Sok Ching for your teaching and technical help in molecular biology despite your very busy schedule. Also to all the staffs at CARIF who had helped me tremendously during the project; Dr Soo-Hwang Teo, Ms Sharifah, Ms Yoon Sook Yee, Ms Amyza, Ms Kue Peng Lim.
- Deans and Deputy Deans of Dental Faculty, UM. Especially Prof Dr Nasruddin Jaafar for allowing me to take time off from my busy schedule at BRU to finish my master degree.
- Staffs at the Department of Oral Pathology, Oral Medicine and Periodontology especially Prof Siar CH, Assoc Prof Dr Khoo SP, Prof Tara, Dr Zuraiza and Dr Nurshaline. Also to the staffs at the Oral Pathology Diagnostic Laboratory; Mrs Rusnani, Mrs Nurul, Mrs Khoo, En Hassan.
- Staffs at the Oral Cancer Research Coordinating Center (OCRCC). Thanks to Mrs Nabillah, Mr Koh, Pn Sutati.
- Dr Marhazlinda Jamaludin from Informatics Unit for her statistical input.
- Staffs at Bahagian Rawatan Utama (BRU). Dr Raja Rozita, Dr Haslinda Ramli, Dr Chuan KS, Dr Firdaus, Pn. Suzana, Pn Ani, En. Azman and En. Ramli for your kind support and encouragement.
- All the staffs in every department whom I have worked closely with.
- Institut Pengurusan Penyelidikan dan Perundingan, UM for the short term grant Vote F0211/2003A in sponsoring this project.
- My family and friends for waiting so very patiently for me to finish the study.