International Poster Journal IPJ of Dentistry and Oral Medicine

Int Poster J Dent Oral Med 2006, Vol 8 No 02, Poster 317

An Immunohistochemical Study of p53 in Oral Epithelial Dysplasia and Squamous Cell Carcinoma

Language: English

Authors:
Dr Mei Siang Ma, Armed Forces Dental Centre, Kem Kementah, Jalan Padang Tembak, Kuala Lumpur, Malaysia

Date/Event/Venue:
6-11 September 2004
12th International Congress on Oral Pathology and Medicine
The Faculty of Odontology, Complutense University of Madrid, Spain

Introduction

Squamous cell carcinoma accounts for more than 90 % of all carcinomas in the oral cavity. It is well acknowledged that carcinogenesis is a multi-steps process in which carcinogens induce genetic damage in certain cells and if these cells are not identified by DNA repairing mechanism, selective growth advantage may develop and form a tumour[1].
Despite advances in etiology and epidemiology, the exact mechanisms involved in oral carcinogenesis remain unknown. Results of current researches suggest that p53 mutation may play a role in the development of oral squamous cell carcinoma2. p53 can sense damage DNA and invoke a protective response either by blocking the cell cycle or inducing cell apoptosis[3,4]. Loss of this function of the gene can lead to propagation of genetic imperfect cells and development of cancer.

Material and Methods

66 consecutive formalin fixed paraffin embedded blocks which were diagnosed by oral pathologist as SCC or keratoses with or without dysplasia were retrieved from the histopathology laboratory file of Leeds Dental Institute. Specimens with epithelium dysplasia were classified into mild, moderate and severe according to World Health Organization (WHO) classification. There were 11 hyperkeratosis without dysplasia; 11 hyperkeratosis with mild dysplasia; 11 hyperkeratosis with moderate dysplasia; 10 hyperkeratosis with severe dysplasia and 13 SCCs. Ten normal mucosa were included to serve as controls of the study.
Specimens from patients who have been treated with radiotherapy were excluded from the study. Standard immunohsitochemistry staining procedure was carried out by using Mouse anti-p53 monoclonal antibody (Chemicon International Inc MAB-4054 USA) with a dilution of 1/50. Negative and positive controls were included in the staining procedure.

Results

All the normal mucosa and 11 hyperkeratosis without dysplasia show negative staining with p53 antibody. Only one (9%) keratosis with mild dysplasia scored positive. For moderate dysplasia, three (27%) stain positive, whereas 30% of keratosis with severe dysplasia stained positive. In five of the margins studied, one (20%) has positive reactivity. In the 13 SCCs studied, 10 (77%) have positive staining. The percentage of positive lesions increases with the severity of epithelium dysplasia with the highest score in SCC (figure 1).

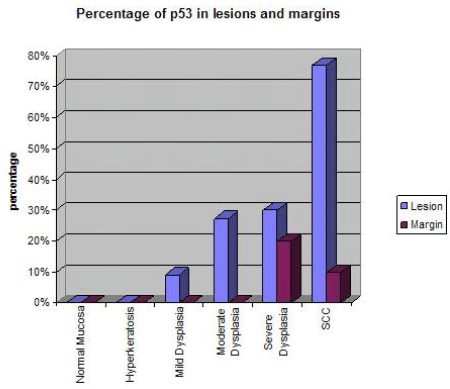


Figure 1: percentage of p53 positivity in lesions and margin

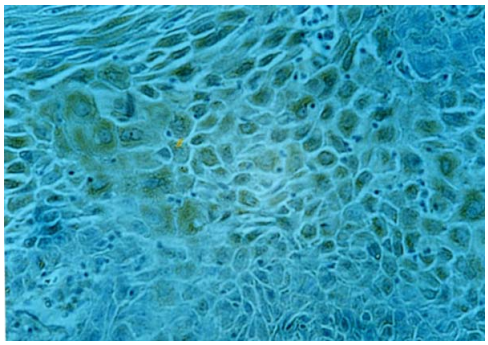


Figure 2: Positive p53 staining demonstrated in the cytoplasm of epithelial cells.

Conclusions

Many investigators found that the grade of epithelium dysplasia is unreliable as the only indicator in predicting cancer development. Moreover, the histological grading of epithelial dysplasia is subjected to individual experience even among senior pathologist. Therefore, a method which can accurately predict the potential malignant transformation of premaglinant lesion is needed for the surgeons to plan the treatments for patients.

Kantola et al.[6] noticed a poorer prognosis on SCC of tongue without overexpression of p53 proteins. However, study by Karpranos et al.[6] shows p53 expression was not significantly related to the prognosis of head and neck cancer.

The result of present study is in accordance with study by Kikegawa[5], Girod et al.[7], and Shintani et al.[8], in which the percentage of p53 overexpression in oral preneoplastic and neoplastic lesions is related to the degree of epithelium dysplasia and loss of differentiation of SCC.

p53 positivity has been reported in 34 to 81% of OSCC[9,10]. In contrast, reports regarding p53 positivity in normal oral mucosa are controversial, it was detected in some studies[11] but not in others[8,9] with a range of 0 to 58 %.

In our study, p53 could not be detected in 23 % of SCC, suggesting that p53 mutation is not essential for tumour transformation.

In summary, the need to interpret the results of p53 overexpression by immunohistochemistry techniques with cautious cannot be overemphasized since this depends greatly on stabilization and half-life of point mutated p53.

Literature

1. Field JK. The role of oncogenes and tumour-suppresser genes in the aetiology of oral, head and neck squamous cell carcinoma. J R Soc Med 1995; 88: 35P-39P.
2. Werner G & Summerlin DJ. The relationship of p53 and human papillomavirus in oral carcinoma in-situ. (abstract) Oral Surg Oral Med Oral Pathol Oral radiolol & Endo 1996; 82(2).
3. Lane DP. p53, guardian of the genome. Nature 1992; 358: 15-16.
4. Lane DP. A death in the life of p53. Nature 1993; 358: 15-16.
5. Kantola S, Parikka M, Jokinen K, Hyrynkangs K, Soini Y, Alho OP, Salo T. Prognostic factors in tongue cancer - relative importance of demographic, clinical and histopathological factors. Br J Cancer 2000; 83(5): 614-9.
6. Karpranos N, Stathopoulos GP, Manolopoulos L et al. p53, p21 and p27 protein expression in head and neck cancer and their prognostic value. Anticancer Res 2001; 21(1B): 521-8.
7. Girod SC, Krueger G, Pape HD. p53 and Ki67 expression in preneoplastic and neoplastic lesions of the oral mucosa. In J Oral Maxillofac Surg 1993; 22: 285-288.
8. Shintani S, Yoshihama Y, Emilio ER, Matsumura T. Overexpression of p53 is an early event in the tumourigenesis of oral squamous cell carcinomas. Anticancer Res 1995; 15: 305-308.
9. Sulkowska M, Falmuski W, Chyczewski L, Sulkowski S. Evaluation of p53 nad bcl-2 oncoprotein expression in precancerous lesions of the oral cavity. Neopalsma 2001; 48(2): 94-8.
10. Lavieille JP, Bramilla E, Riva-Livieille C, Reyt E, Charachon R, Bramilla C. Immunohistochemical detection of p53 protein in preneoplastic lesions and squamous cell carcinoma of the head and neck. Acta Otholaryngol 1995; 115: 334-339.
11. Nakanishi Y, Noguchi M, Matsuno Y. P53 expression in multicentric squamous cell carcinoma and surrounding squamous epithelium of the upper aerodigestive tract. Cancer 1995; 75: 1657-1662.

This Poster was submitted by Dr Mei Siang Ma.

Correspondence address:
Dr Mei Siang Ma
Armed Forces Dental Centre
Kem Kementah
Jalan Padang Tembak
50634 Kuala Lumpur
Malaysia

Poster Faksimile:

AN IMMUNOHISTOCHEMICAL STUDY OF P53 IN ORAL EPITHELIUM DYSPLASIA AND SQUAMOUS CELL CARCINOMA

Mei Siang Ma

BDS(Malaya) MDentSci(Leeds) FDS RCS(Eng)

Malaysian Armed Forces Dental Center
Kem KEMENTAH
Jalan Padang Tembak
50634 KUALA LUMPUR, Malaysia
Tel: +603 2071 2146 Fax: +603 2698 0505 email: lianama@time.net.my

ABSTRACT

Squamous cell carcinoma (SCC) is the commonest cancer in the mouth. Multiple risk factors, including smoking, alcohol consumption, irradiation, viruses infection and chronic irritation are thought to be responsible for the formation of oral squamous cell carcinoma. Although SCC can develop through precancerous stages manifested as various degrees of epithelial dysplasia, this is not always the case. p53 is the commonest mutated gene in human cancers. Mis-sense mutation of the gene or complexing of the protein with viral or cellular proteins prolongs its half-life and leads to its detection by immunohistochemistry. This study was designed with the aim of demonstrating any possible relationship between p53 and oral squamous cell carcinoma immunohistochemically. A total of 66 specimens from the oral cavity (10 normal mucosa, 11 hyperkeratosis without dysplasia, 11 mild dysplasia, 11 moderate dysplasia, 10 severe dysplasia and 13 SCC) were examined for the presence of p53. The results show p53 was not expressed in normal mucosa, but was found with increasing frequency in increasingly severe dysplasia and SCC. In conclusion, this study shows p53 mutation is common in oral squamous cell carcinoma and probably occurs early in the multisteps of oral carcinogenesis.

INTRODUCTION

- Squamous cell carcinoma accounts for more than 90 % of all carcinomas in the oral cavity. It is well acknowledged that carcinogenesis is a multi-steps process in which carcinogens induce genetic damage in certain cells and if these cells are not identified by DNA repairing mechanism, selective growth advantage may develop and form a tumour[1].
- Despite advances in etiology and epidemiology, the exact mechanisms involved in oral carcinogenesis remain unknown. Results of current researches suggest that p53 mutation may play a role in the development of oral squamous cell carcinoma[2]. p53 can sense damage DNA and invoke a protective response either by blocking the cell cycle or inducing cell apoptosis[3,4]. Loss of this function of the gene can lead to propagation of genetic imperfect cells and development of cancer.

MATERIAL AND METHODS

- 66 consecutive formalin fixed paraffin embedded blocks which were diagnosed by oral pathologist as SCC or keratoses with or without dysplasia were retrieved from the histopathology laboratory file of Leeds Dental Institute. Specimens with epithelium dysplasia were classified into mild, moderate and severe according to World Health Organization (WHO) classification. There were 11 hyperkeratosis without dysplasia; 11 hyperkeratosis with mild dysplasia; 11 hyperkeratosis with moderate dysplasia; 10 hyperkeratosis with severe dysplasia and 13 SCCs. Ten normal mucosa were included to serve as controls of the study.
- Specimens from patients who have been treated with radiotherapy were excluded from the study. Standard immunohisitochemistry staining procedure was carried out by using Mouse anti-p53 monoclonal antibody (Chemicon International Inc MAB-4054 USA) with a dilution of 1/50. Negative and positive controls were included in the staining procedure.

RESULTS

- All the normal mucosa and 11 hyperkeratosis without dysplasia show negative staining with p53 antibody. Only one (9%) keratosis with mild dysplasia scored positive. For moderate dysplasia, three (27%) stain positive, whereas 30% of keratosis with severe dysplasia stained positive. In five of the margins studied, one (20%) has positive reactivity. In the 13 SCCs studied, 10 (77%) have positive staining. The percentage of positive lesions increases with the severity of epithelium dysplasia with the highest score in SCC (figure 1).

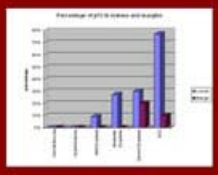
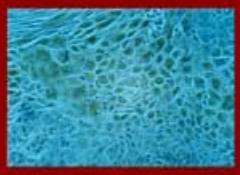


Figure 1 percentage of p53 positivity in lesions and margin



Positive p53 staining demonstrated in the cytoplasm of epithelial cells

DISCUSSION

- Many investigators found that the grade of epithelium dysplasia is unreliable as the only indicator in predicting cancer development. Moreover, the histological grading of epithelial dysplasia is subjected to individual experience even among senior pathologist. Therefore, a method which can accurately predict the potential malignant transformation of premaglinant lesion is needed for the surgeons to plan the treatments for patients.
- Kantola et al.[6] noticed a poorer prognosis on SCC of tongue without overexpression of p53 proteins. However, study by Karpranos et al.[6] shows p53 expression was not significantly related to the prognosis of head and neck cancer.
- The result of present study is in accordance with study by Kikegawa[5], Girod et al.[7], and Shintani et al.[8], in which the percentage of p53 overexpression in oral preneoplastic and neoplastic lesions is related to the degree of epithelium dysplasia and loss of differentiation of SCC.
- p53 positivity has been reported in 34 to 81% of OSCC[9,10]. In contrast, reports regarding p53 positivity in normal oral mucosa are controversial, it was detected in some studies[11] but not in others[8,9] with a range of 0 to 58 %.
- In our study, p53 could not be detected in 23 % of SCC, suggesting that p53 mutation is not essential for tumour transformation
- In summary, the need to interpret the results of p53 overexpression by immunohistochemistry techniques with cautious cannot be overemphasized since this depends greatly on stabilization and half-life of point mutated p53.

REFERENCES

1. Field JK. The role of oncogenes and tumour-suppresser genes in the aetiology of oral, head and neck squamous cell carcinoma. J R Soc Med 1995; 88: 35P-39P.
2. Werner G & Summerlin DJ. The relationship of p53 and human papillomavirus in oral carcinoma in-situ. (abstract) Oral Surg Oral Med Oral Pathol Oral radiolol & Endo 1996; 82(2).
3. Lane DP. p53, guardian of the genome. Nature 1992; 358: 15-16.
4. Lane DP. A death in the life of p53. Nature 1993; 358: 15-16.
5. Kantola S, Parikka M, Jokinen K, Hyrynkangs K, Soini Y, Alho OP, Salo T. Prognostic factors in tongue cancer – relative importance of demographic, clinical and histopathological factors. Br J Cancer 2000; 83(5): 614-9.
6. Karpranos N, Stathopoulos GP, Manolopoulos L et al. p53, p21 and p27 protein expression in head and neck cancer and their prognostic value. Anticancer Res 2001; 21(1B): 521-8.
7. Girod SC, Krueger G, Pape HD. p53 and Ki67 expression in preneoplastic and neoplastic lesions of the oral mucosa. Int J Oral Maxillofac Surg 1993; 22: 285-288.
8. Shintani S, Yoshihama Y, Emilio ER, Matsumura T. Overexpression of p53 is an early event in the tumourigenesis of oral squamous cell carcinomas. Anticancer Res 1995; 15: 305-308.
9. Sulkowska M, Falmuski W, Chyczewski L, Sulkowski S. Evaluation of p53 nad bcl-2 oncoprotein expression in precancerous lesions of the oral cavity. Neoplasma 2001; 48(2): 94-8.
10. Lavieille JP, Bramilla E, Riva-Liviciille C, Reyt E, Charachon R, Bramilla C. Immunohistochemical detection of p53 protein in preneoplastic lesions and squamous cell carcinoma of the head and neck. Acta Otholaryngol 1995; 115: 334-339.
11. Nakanishi Y, Noguchi M, Matsuno Y. P53 expression in multicentric squamous cell carcinoma and surrounding squamous epithelium of the upper aerodigestive tract. Cancer 1995; 75: 1657-1662.