Short Review

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p53 and Oral Cancer: A Short Review

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Abstract

Oral squamous cell carcinoma, commonly referred to as oral cancer, is considered to develop as a result of multi-hit process that involves a number of aberrant genetic events. Determining which event leads to the eventual development of oral cancer can be of a great significance in its prevention and control. p53 a tumor suppressor gene, in its mutated form is believed to exert tumorigenic influences and has been a subject of intensive study over several years in order to understand its role in the process of carcinogenesis.

Keywords: Oral, Cancer, Squamous cell carcinoma, p53.

INTRODUCTION

Cancer is one of the leading causes of death all over the world with its relative position varying in terms of age, sex, and geographic location.[1] Globally, oral cancer is the sixth most common cause of cancer related deaths.[2] In India, oral cancer is one of the five leading types of cancer in either sex and comprises about 40% of all the cancers.[3] Over 80% of cancers of the oral cavity are squamous cell carcinomas of the lining mucosa and it is for this reason the term oral cancer has become synonymous with oral squamous cell carcinoma (OSCC).[1] OSCC has a relatively unfavorable prognosis and the growing increase in its incidence also accentuates the mortality. The overall five year survival rate of OSCC, which has virtually remained unchanged over the past many years, is around 35-50%.[2]

Potentially Malignant Lesions

Oral epithelial dysplasias are considered potentially malignant lesions as they have a high probability of developing into squamous cell carcinomas. Oral epithelial dysplasias are classified as mild, moderate, or severe depending on the extent of dysplastic changes. The percentage of these lesions that progress to OSCC is accepted to be directly proportional to the severity of the dysplastic changes.[4] Although the figures are variable and generally range between 0.3% and 17.5%; a consensus range has been regarded to be 3-6%.[5] Furthermore, transformation into OSCC in moderate or severe dysplasias appears to be at least double than in mild dysplasia or hyperplasia.[6]

Genetic Progression Model of Oral Cancer

The pioneering work by Fearon and Vogelstein characterizing the genetic alterations in colorectal

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cancers has become a paradigm for other neoplasms.[7] OSCC is one of the few cancer types which is easily accessible to obtain biopsies at all stages of cancer progression. Consequently, it is possible to define a genetic progression model of this disease. The frequency of genomic alterations in tumor and histopathologically defined precursor lesions has formed the basis for the description of the first genetic progression model for OSCC by Califano *et al*.[8] This has led to the belief that OSCC may follow a progression pattern preceded by lesions exhibiting dysplasia.[9]

p53

Many surrogate markers have been used in the past to identify those lesions that can eventually convert to OSCC. The most frequently involved and the best studied biomarker p53 is a tumor suppression gene that participates in cell proliferation control and plays a role in deletion of cells with DNA damage by induction of apoptosis.[10] Aberrant p53 expression is considered one of the most common genetic events in OSCC.[11]

The p53 gene plays a tumor suppressor role in its normal state (wild-type), but in its mutated form it is believed to exert tumor initiating and promoting influences, largely through sequence-specific DNA binding and transcriptional regulation.[12] This gene, which mediates its function through its protein product has been the subject of study in several oral sites and a spectrum of oral lesions in order to help understand the process of carcinogenesis, to evaluate potential risk and as a prognostic marker.[6,13] Immunohistochemical studies of p53 rely on the principle that the majority of changes in p53 gene are missense mutations, which result in confirmational change and stabilization of the transformed protein.[14] The stabilized protein can then be detected by immunohistochemistry in tissue sections, in contrast to the wild-type which has a short half-life and cannot be readily detected.[14,15] The advantage of immunohistochemical staining is the direct demonstration of the spatial relationship of cells that have altered protein expression, which is of particular importance in the study of clonal expansion of altered cell populations during multi-step carcinogenesis.[15]

CONCLUSION

Development of oral cancer, considered a multi-hit process, involves a number of aberrant genetic events. A minimum of five events in humans are required to transform a normal cell into a cancer cell.[11] Determining which event leads to malignant transformation can be of particular significance in the prevention of oral cancer.

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