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p53 and bcl-2 in Oral Cancer – An Overview

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ABSTRACT

Globally, cancer is one of the leading causes of death with its relative position varying with age, sex and geographic location. In India, oral cancer is considered to be one of the most common causes of cancer related deaths. Oral carcinogenesis is a multi-hit process that involves a number of aberrant genetic events. Many surrogate markers have been used to identify such aberrations; especially biomarkers p53 and bcl-2 have been extensively studied to identify their probable role and prognostic value.

Key Words: oral, cancer, squamous cell carcinoma, p53, bcl-2

Introduction

Cancer is one of the main causes of death all over the world and oral cancer particularly, is the sixth most common cause of cancer related deaths. [1] In India, oral cancer is one of the five leading types of cancer. [2] Over 80% of cancers of the oral cavity are diagnosed as oral squamous cell carcinoma (OSCC) which have poor prognosis. The overall five-year survival rate of patients with OSCC is in the range of 35-50%. [3] The first genetic model for OSCC described that it may follow a progression pattern preceded by lesions exhibiting dysplasia.[4] Oral epithelial dysplasias are considered potentially malignant and the percentage of these lesions that progress to OSCC is accepted to be directly proportional to the severity of the dysplastic changes.[5] Many immunohistochemical markers have been used in the past to identify those dysplastic lesions that can eventually convert to OSCC.[6] The most frequently involved and the best studied marker is p53, a tumor suppressor gene that controls cell proliferation and plays a role in the deletion of cells with DNA damage by induction of apoptosis. Aberrant bcl-2 expression leads to extended cell survival and can facilitate the acquisition of additional mutations and eventual clonal expansion. Much attention has therefore been paid to the simultaneous studies of p53 and bcl-2 abnormalities in order to obtain more accurate information about their potential role in oral carcinogenesis and prognostication.[7]

Literature Review

Sulkowska M et al observed a correlation between p53 and bcl-2 expression and degree of epithelial dysplasia with increased expression in severe dysplasia. [8] Similarly, Yao L et al observed that bcl-2 expression correlated with histologic grade of tonge squamous cell carcinomas and p53 expression was associated with mode of tumor invasion and lymph node status; they concluded that the combined evaluation of p53 and bcl-2 may help in the assessment of tumor aggressiveness. [9] Also, Saranath D et al from their studies affirmed that aberrant p53 and bcl-2 expression may play a difinitive role in the tumorigenesis of OSCC by allowing escape from apoptosis and enabling additional genetic alterations to accumulate. [10,2] Furthermore, Ravi D et al in their studies analysed the expression of apoptosis regulatory proteins in OSCC and their predictive value in relation to prognosis and stated that, increased p53 and bcl-2 expression was associated with poor prognosis. [11,12]

Whereas, Pena JC et al and Piffko J et al correlated immunohistochemical expression of various biomarkers with clinicopathologic parameters in squamous cell carcinomas of the head and neck and concluded that bcl-2 immunoreactive cases may be treated successfully with less toxic therapy and favorable prognosis. [13,14] Hotz MA et al observed an inverse correlation in the expression of apoptosis-regulating proteins p53 and bcl-2 in advanced head neck squamous cell carcinomas. [15]

Alternatively, Schoelch ML et al evaluated the expression of apoptosis-associated proteins in premalignant and malignant oral epithelial lesions and observed that p53 and bcl-2 are altered in variable, non-related patterns. [16] Likewise, Badaracco G et al suggested that p53 and bcl-2 expression are independent events in head and neck cancers and Vora HH et al observed no significant correlation between p53 and bcl-2 positive expression. [17,18]

Discussion

Aberrant p53 expression is considered one of the most common genetic events in OSCC and the protein expression of bcl-2 gene, an anti-apoptotic marker, is found to occur early in oral carcinogenesis. [19] Combined studies on p53 and bcl-2 have provided insights into the apoptotic pathway and the probable role in oral carcinogenesis. These studies point to either of the following facts:

- p53 and bcl-2 expression are correlated and are significant events in the development of oral carcinogenesis. [2,10-12]
- p53 and bcl-2 expression are inversely related i.e. overexpression of p53 and bcl-2 are mutually exclusive of each other and overexpression of any one of these proteins may substitute each other in the induction of oral carcinogenesis. [15,19]
- p53 and bcl-2 expression are not related and oral carcinogenesis may involve different genetic aberrations and may involve multiple genes, acting not necessarily together. [16-18]

Conclusion

Determining aberrant genetic events in oral carcinogenesis can play a crucial role in the early detection of oral cancer and it's treatment. Oral carcinogenesis may involve multiple genes and p53 and bcl-2 expression may be of prognostic significance.

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