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REVIEW ARTICLE

VIRAL ONCOGENESIS- A BRIEF REVIEW

Neeraj Grover[1], Adil Rasool Malik[2], Sanjeet Singh[3], Nishant Singh[3]

[1]Professor and Head, [2]PG Student, [3]Reader, Department of Oral and Maxillofacial Pathology, D.J. College of Dental Sciences & Research, Ghaziabad, UP, India.

ABSTRACT:
The infectious nature of oncogenic viruses sets them apart from other carcinogenic agents. The studies of virus-associated head and neck cancers have provided many critical insights into key mechanisms of carcinogenesis. As such, a thorough study of both the pathogenesis of viral infection and the host response is crucial to a full understanding of the resulting cancer. Hence, in the present review, we aim to highlight some of important viruses and their role in carcinogenesis.
Key words: Carcinogenesis, Viruses.

Corresponding author: Dr. Neeraj Grover, Professor and Head, Department of Oral and Maxillofacial Pathology, D.J. College of Dental Sciences & Research, Ghaziabad, UP, India.

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INTRODUCTION

Cancer is a group of diseases characterized by uncontrolled growth and spread of abnormal cells. If the spread is not controlled, it can result in death. According to estimates from the International Agency for Research on Cancer (IARC), there were 12.7 million new cancer cases in 2008 worldwide, of which 5.6 million occurred in economically developed countries and 7.1 million in economically developing countries.[1-3]

In general terms, carcinogenesis represents a complex, multi-step process. During the past 30 years it has become exceedingly apparent that several viruses play significant roles in the multistage development of human neoplasms; in fact, approximately 15% to 20% of cancers are associated with viral infections.Although the traditional risk factors for developing oropharyngeal cancer remain tobacco use and heavy alcohol consumption, other risk factors, such as HPV, may play significant roles in determining whether it develops and how quickly it may progress.[4]

VIRAL CARCINOGENESIS

Even though human oncogenic viruses belong to different virus families and utilize diverse strategies to contribute to cancer development, they share many common features. One key feature is their ability to infect, but not kill, their host cell. In contrast to many other viruses that cause disease, oncogenic viruses have the tendency to establish long-term persistent infections.[5]

HUMAN PAPILLOMAVIRUS (HPV)- INDUCED CARCINOGENESIS

High-risk HPV E6 and E7 oncoproteins expressed in epithelial cells infected with HPV are implicated in the increased proliferation and in the abnormal differentiation of these cells.[6-8] When the E6/E7 proteins are the expression of infection of the cell with low-risk HPV, then these active proteins may induce benign neoplasms. However, when E6/E7 proteins are the expression of high-risk HPV infection, they subserve the role of oncoproteins and they have the capacity to induce dysplastic and malignant epithelial lesions. The association between cancer of the uterine cervix and high-risk HPV infection is well established. It is evident that HPV is an essential agent, but is not by itself sufficient to induce squamous cell carcinoma of the cervix. HPV DNA is found in more than 99% of biopsy specimens of squamous cell carcinoma of the cervix. In more than 70% of these HPV DNA positive biopsy specimens, the DNA is of high-risk HPV-16 and HPV-18 origin.[9-11]

In order to prove a causal relationship between HPV and SCC of the mouth and oropharynx, as has been proven in the case of SCC of the cervix uteri, there should be evidence that in a significant number of cases of apparently normal oral or oropharyngeal epithelium infected with HPV, in time SCC will develop. The demonstration of HPV DNA, even of high-risk HPV oncogenes in squamous cell carcinoma is not in itself sufficient evidence of oncogenesis by the HPV in that

context. HPV may well have been either present but a non-participant during the oncogenesis, or have been superimposed upon the malignancy.[12]

EBV INDUCED CARCINOGENESIS

To be oncogenic, EBV must maintain its viral genome in the cell, avoid killing the cell, and prevent the cell from becoming a target for destruction by the immune system. Finally, the virus must activate cellular growth control pathways.[13]

Detection of the EBERs by in situ hybridization has become the standard method to detect EBV infection in routinely processed tumour tissues. Although the EBERs are thought to be expressed in all forms of latency, two studies have suggested the possibility of EBER-negative forms of latency and that such forms of latency might exist in hitherto unrecognized EBVassociated malignancies. In the first of these, the detection of EBV in a proportion of classical breast tumours was reported by PCR, immunohistochemistry for EBNA1 protein, and Southern blotting.[12]

Clearly, further studies are required to substantiate these findings. In our opinion, definitive designation of a tumour as 'EBV associated' should require unequivocal demonstration of the EBV genome or virus gene products within the tumour cell population. Unfortunately, much of the methodology used to detect EBV in many of these studies (where EBER expression is presumed to be undetectable) has involved either analysis of whole tumour sections or antibody reagents that lack specificity. Future studies using robust methodologies will be required to establish whether any of the common epithelial neoplasms are truly EBV associated.[14]

HERPES SIMPLEX VIRUS (HSV)

Herpes simplex viruses were the first of the human herpesviruses to be discovered and are among the most intensively investigated of all viruses. Induction of cellular proteins has been studied as a possible mechanism for transformation by HSV. It is known that infection by HSV-1 induces the expression of "stress" or "heat shock" proteins. The mechanism of induction is not known, but does depend on the expression of the immediate-early family of HSV proteins. Since HSV might transform cells by stimulating the expression of cellular proteins, some workers have started to study such proteins by isolating cDNA from cells that were trans- formed by HSV-2. Host cell shut off process infected cell ceases to synthesize cellular proteins and cell RNA would be very quickly degraded. A mediating gene was located in the same region of the genome as the mtr-2 region of HSV 2 that mediates cell transformation.[15- 16]

CONCLUSION

Oral cancer ranks from the sixth to eighth most common cancer around the world, with a great variability in incidence among countries. It is a disease with a complex etiology.

The ability to control oral cancer depends on three basic cornerstones: prevention, detection, and early diagnosis. There is evidence for important roles of smoking, drinking, and genetic susceptibility, as well as strong indications that DNA viruses could be involved.

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