Editorial

Inherited Oral Cancer: A Rare Reality

Majority of oral cancers (around 90–95%) found today are caused by various environmental factors. These generally include the chemical and physical carcinogens, like tobacco, diet, microorganisms, radiations, etc. The remaining 5% of the cases are caused by inherited mutated genes carrying the defect. Cancer inheritance can be explained by the Knudson's two hit hypothesis which states that the first hit of gene is the inherited mutation while the second hit occurs later in life.[1] The clustering of cancer in families is relatively common and is attributed to the shared environmental carcinogenic and/or inherited genetic factors, including complex interactions between the two. Cancer tends to occur at younger ages and can occur even in the absence of carcinogen exposure.[2] The known hereditary cancer susceptibility genes are rare but they are seen to have a high penetrance. Though these genes account for only a small proportion of cancers, a larger proportion is due to the common variation in one or several low penetrance genes that interact with other genes or environmental carcinogens.[3] Ankathil et al[4] observed familial aggregation was mostly site-specific, with an autosomal dominant mode of inheritance in 0.94% of the total oral cancers. Thus, various inherited cancer syndromes have been identified which are also known as genetic instability syndromes, such as xeroderma pigmentosum, ataxia telangiectasia, Bloom syndrome, Fanconi's anemia and Li-Fraumeni syndrome.

The onset of many of these cancers starts with occurrence of potentially malignant disorders. 'Potentially malignant disorders' are referred as all the clinical presentations that carry the risk of cancer including the above mentioned syndromes associated with a greater than normal risk of malignant transformation by the current working group World health organization (WHO). Sarode et al[5,6] have classified oral potentially malignant disorders (OPMDs) under the group III of inherited disorders that do not necessarily alter the clinical appearance of local tissue but are associated with a greater than normal risk of OPMD or malignant transformation. All these syndromes included either carry some risk and/or predispose the individual to cancer development. In these autosomal recessive genetic diseases, single gene defects lead to genetic instability, increased mutation rates and cancer. Deficiencies in the ability to effectively repair deoxyribonucleic acid (DNA) lesions have been suggested for all of these syndromes.

In cancer-inherited syndromes, morphological alterations may not be present in the oral cavity and mucosa may appear apparently normal. However, individual person is susceptible to the development of oral cancer. Hence, our recently proposed term 'oral squamous cell carcinoma prone disorders/individuals' is more apt for such situations.[7,8]

With advent of knowledge on inherited cancer syndrome and their inclusion in classification of OPMDs, a need for modified definition of OPMD was raised in the literature. With this in mind, we had made an attempt to propose a definition for OPMDs which is as follows:[9]

'It is a group of disorders of varying etiologies, usually tobacco; characterized by mutagen associated, spontaneous or hereditary alterations or mutations in the genetic material of oral epithelial cells with or without clinical and histomorphological alterations that may lead to oral squamous cell carcinoma transformation.'

Prime et al[10] examined the genetic defects associated with inherited cancer syndromes and their relevance to oral cancer. Tumor suppressor genes either control cell growth directly by inhibiting cell proliferation and/or promoting cell death (gatekeepers) or whether they maintain the integrity of the genome by DNA repair mechanisms (caretakers). In xeroderma pigmentosum, ataxia telangiectasia, Bloom syndrome and Fanconi's anemia, there is a defect in caretaker genes. Li-Fraumeni syndrome shows abnormalities of gatekeeper genes. Generally, defective gatekeeper genes do not predispose the individual to oral cancer. But, Li-Fraumeni patients develop second primary malignancies. P16 germline mutations have been seen in individuals from families with oral cancer. Thus, it has been suggested that genetic instability is necessary in the pathogenesis of oral cancer.[11]

The term 'second primary tumor' was proposed to be allocated for the second tumor that develops independently from the first tumor. There is an increased incidence of second primary malignancies, including oral cancer in the inherited cancer syndromes. A component contributing to the poor overall survival in such cases, particularly in patients with early tumors of the larynx, oral cavity and oropharynx, is the 10 to 30% chance of developing a second malignancy or multiple primary tumor of the aerodigestive tract or elsewhere within 5 years.[12]

We believe that knowledge and awareness about cancer-inherited syndromes is the need of the hour for general dental practitioners. Such cases can be followed-up in routine dental practice, which will help in early detection of oral cancer and improving the prognosis.[13]

Although, no permanent cure has been found till date, yet the advancement of the technology has led to a wide center of active research by the experts. As identification and validation of the defective genes is challenging, there is no clinical value at the present. The rate of mortality is high but nevertheless, advances have been made to increase the life span of the individual with inherited cancer syndromes. Thus counseling sessions are must which lead to positivity in the life of such patients.

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