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Genetics of Head and Neck Cancers

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The knowledge of genetics of head and neck cancers can prove to be a game-changer for treatment decisions.



Head and Neck Cancers refer to a group of cancers inside the mouth, nose and throat. The cancer types included in head and neck cancers are lip and oral cavity (upper palate, lower palate, and gums area behind the wisdom teeth), pharynx (nasopharynx, oropharynx and hypopharynx), Larynx, Paranasal sinuses and nasal cavity and salivary gland cancers.

According to GLOBOCAN 2018 data, the incidence of only lip and oral cavity cancers account for 11.4% of all cancer cases with 1.2 lakhs new cases registered in 2018, which is only second to breast cancer in India. If we look at head and neck cancers as a whole, the incidence in India surpasses that of breast cancer, making head and neck cancers highest occurring cancer in India. With such a high incidence, accurate testing that provides insights to make informed treatment decisions can be pivotal.

The causes of head and neck cancer can be broadly classified in two different categories- genetic predisposition and carcinogen exposure. The carcinogen factor is tobacco, either in terms of smoking or chewing tobacco containing products. Alcohol is another substance which is one of the leading causes of this form of cancer. Additionally, several studies have reported the role of human papilloma virus (HPV) in head and neck cancer. Frequent genetic alterations in several genes (*TP53, PIK3CA, CDKN2A, NOTCH1* and *MET*). CDKN2A and TP53 along with some other markers are associated with poor prognosis in head and neck canncer, meaning the disease is likely to follow an aggressive path, thus guiding physicians in the personalized management of the disease, based on the genomic profiling.

Like in the case of 57-year old Nishitha (name changed) who was diagnosed of cancer of the tissue behind left wisdom tooth, where the tumor has progressed to nearby lymph nodes, but not metastasized yet.

A missense variation was identified in the *CDKN2A* gene of the patient which is a loss of function mutation. Genomic alterations in *CDKN2A* gene correlate with poor overall survival in head and neck cancer patients. Additionally, a nonsense variation was detected in the *TP53* gene. Presence of pathogenic *TP53* mutation is associated with cisplatin resistance is most of the head and neck cancer patients. In a study of 141 head and neck cancer (98 oral cavity), they demonstrated: similar truncating mutations in *TP53* gene were associated with poor prognosis. Hence, both the mutations suggesting poor prognosis, gave the treating clinician an insight based on which he can take the treatment decision toward aggressive management of the disease. Today, we have abemaciclib and palbociclib as targeted treatment options in patients with *CDKN2A* loss of function mutations approved for other cancers. In head and neck cancers, Abemaciclib, is currently under clinical trials for advanced head and neck cancers with CDKN2A loss of function, CDKN2A mutations/deletions.

When it comes to therapy, several studies have shown the impact of combining chemotherapy with radiotherapy which proven to be most effective in managing this cancer. Lately, the concept of immunotherapy has come into application with US-FDA approving pembrolizumab for the first-line treatment of patients with metastatic or unresectable recurrent head and neck cancer. So far, Tumor mutation burden stands out to be one of the potential biomarker that could have a predictive role for immunotherapy response in Head and Neck Cancer.

The knowledge of genetics of head and neck cancers can prove to be a game-changer for treatment decisions. The concept of diagnostics and targeted treatment based on genetic alterations is picking pace in India, not just for Head and Neck cancers, but for various other types as well.

Currently, the need of the hour is awareness specially for this cancer type which not many know about. Educational events on oral hygiene, rehabilitation programs related to harmful effects of chewing tobacco, smoking and alcohol consumption helps in reducing the incidence of head and neck cancers in India.

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