Epidemiological, Biochemical and Molecular factors Associated with Clinical outcome of Esophageal Squamous Cell Carcinoma in the North Eastern India

Abstract

Every individual is unique and that implies on cancer too in terms of their genome complexity. The concept of personalized therapy comes from here. It is a well known fact that cancer patients with the same histological grade and clinical stage may respond differently to the common therapeutic regime. Therefore, predicting response to neo adjuvant chemotherapy (NACT) is of immense clinical value in cancer management where we could able to tailor made the treatment modality for better clinical outcome in different cancers including esophageal squamous cell carcinoma (ESCC).

108 ESCC patients who underwent NACT were recruited from a local cancer hospital after the Institutional Review Board approval. Patients clinical, demographic, epidemiological, life style, and pre treated biochemical data was extracted from their respective medical records. Immunohistochemistry of molecular marker aldehyde dehydrogenase 1 (ALDH1), human epidermal growth factor receptor 2 (HER2) and $p16^{INK4A}$ and flow cytometer based cell cycle analysis was performed on their excised tumor tissues to investigate their possible impact on the NACT response assessment in ESCC.

It was found that those who weren't smokers lived longer. This was found true with female patients also who lived longer than their male counterpart. Other habits like use of alcohol, pan, and tobacco chewing except areca nut use couldn't correlate with response to chemotherapy. Follow up duration was found longer in non pan users. In most of the studied patients, we reported normal serum biochemical values,

which indicate good performance status, better capacity to tolerate neo adjuvant chemotherapy and low possibilities of metastases.

ALDH1 over expression was found correlating with poor response to neo adjuvant chemotherapy whereas p16 over expression was found correlating with the better response in the same group of the ESCC patients. HER2 over expression in ESCC didn't show any impact on predicting treatment response but showed significant correlation with ALDH1 positivity. Significant percentage of diploid tumors had high S phase fraction and responded to neo adjuvant chemotherapy.

A model for response assessment of the treatment modality in esophageal squamous cell carcinoma is developed and proposed based on the findings of this study. We propose assessing tumor, node and initial performance status clinically, and testing ALDH1, p16 through immunohistochemistry, and analyzing ploidy status with S phase fraction through flow cytometer upfront in ESCC patient.

In conclusion, ALDH1 can have a role as biomarker in predicting response to neo adjuvant chemotherapy in ESCC patients. p16 could predict responder among those who underwent neo adjuvant chemotherapy. The association between ALDH1 and HER2 and their cumulative impact on the clinical course of ESCC requires further evaluation in larger patient population. More cancer stem cell marker like ALDH1 on larger ESCC patients number need to be investigated in future to propose definite NACT response assessment model. This proposed model for response assessment against neo adjuvatant chemotherapy for esophageal squamous cell carcinoma patients may be validated over a large number of patients of other parts of the country in the future study that would help the findings of current research to move from the realm of the lab to the clinics for the benefit of the patients.