Abstract

Introduction

Gastric cancer is the third most common cause of cancer related deaths in the world and is the fifth most common cancer worldwide.

Though it is not a leading cancer type, a rise in the Gastric cancer incidence is present in Sri Lanka. However in the absence of screening tests, a late presentation with advanced disease associated with poor prognosis prevails. Most stomach cancers are Gastric carcinomas. The overall prognosis of advanced Gastric carcinomas is poor with a 5-year survival rate of 20%. Human epidermal growth factor receptor 2 (HER2 or Her2/neu) over expression and/or HER2 gene amplification was found to be present in 10–20% of Gastric carcinomas. This molecular aberrancy is linked to the dismal outcome of the disease. Immunohistochemistry (IHC) and fluorescence in situ hybridization (FISH) are the key tests to identify patients who may benefit from targeted therapy with trastuzumab for Her2 over expression. The identified draw backs of both methods require exploration of novel tests to detect HER2 status of Gastric carcinoma.

Objectives

The aim of the study was to determine whether quantitative real time Polymerase Chain Reaction (qPCR) could serve as a supplementary method to evaluate HER2 status of Gastric carcinoma in a cohort of Sri Lankan patients and investigate the correlation between the HER2 status assessed by different methods and the demographic, clinicopathological features of HER2 positive Gastric carcinoma.

Method

A cohort of 20 Sri Lankan primary Gastric carcinoma patients in whom clinicopathological data and HER2 status by IHC were already available was used from a repository at Department of Pathology, Faculty of Medicine, University of Colombo.

Quantitative real-time PCR was performed for the target gene HER2 and a reference gene APP (Ameloid precursor protein) in Formalin fixed paraffin embedded (FFPE) Gastric carcinoma tissue samples from the 20 patients. The threshold values (Ct) of both genes were analyzed using Pfaffl method in relative quantification to detect HER2 gene amplification.

Results

The positive expression of HER2 detected by IHC and q PCR were 20% and 35% respectively .The sensitivity and specificity of q PCR was 67% and 76% respectively, relative to IHC. Q PCR results were reproducible. Positive expression of HER2 protein was significantly correlated with the TNM stage and Lauren's tissue type ($P<0.05$). Positive expression of HER2 gene was significantly correlated with depth of invasion, Lymph node involvement and degree of differentiation ($P<0.05$). No significant correlation was identified between positive expression of HER2 protein/gene and tumor location, age and gender ($P>0.05$). The diagnostic consistency between the two methods, IHC and q PCR ($\kappa=0.146$) was slightly agreeable ($0.01<k<0.20$) having a 65% concordance.

Conclusion

Quantitative real time PCR can be used as a supplementary method, for the detection of HER2 status in Gastric carcinoma.