C-31

Goblet Cell Adenocarcinoma (GCA) of the Appendix: Interrogating Proteomics to Identify Potential Actionable Targets

Krutika Patel, MBBS, MD[1], Liping Du, PhD[2], Frank Revetta, PhD[1], Mary Kay Washington, MD, PhD[1], Jordan Berlin, MD[3], and Satya Das, MD, MSCI[3].

[1]Department of Pathology, Immunology and Microbiology, Vanderbilt University Medical Center; [2]Department of Biostatistics, Vanderbilt University Medical Center; [3]Department of Medicine, Vanderbilt University Medical Center.

BACKGROUND

Appendiceal GCA is a tumor which has been misunderstood for decades. GCAs are comprised of goblet-like mucinous cells, with variable numbers of neuroendocrine and Paneth-like cells and lie on the spectrum between appendiceal adenocarcinoma and neuroendocrine tumors. Prognosis depends on the stage and tumor grade; 30% of patients with low-grade and 50-70% of high grade GCAs present with metastatic disease. Currently, there are limited systemic therapy options and definitive therapy such as cytoreductive surgery and hyperthermic intraperitoneal chemotherapy are applicable to only a small number of patients. In this clinicopathologic study, we aimed to interrogate tumor proteomic profiles to identify possible actionable targets for future therapeutic interventions.

METHODS

We identified GCAs of the appendix from our institutional pathology cohort after obtaining IRB approval. Demographic details and survival data were recorded. We performed immunohistochemical staining for claudin-18.2, somatostatin receptor 2 (SSTR2), PD-1, PD-L1, and human epidermal growth factor 2 (HER-2) expression. Chi-squared tests and log-rank tests were used when comparing groups.

RESULTS

We identified 15 patients with appendiceal GCAs (10 female, 5 male) with a median age of 57.5 years at diagnosis. Of 14 patients with T category information available, 13 (92.8%) possessed T3 or T4 primary tumors. Six (42.8%) patients presented with metastatic disease while 3 patients developed metastatic disease. None (0%) of the patients possessed tumors with any degree of SSTR2, PD-1 or PD-L1 expression. Only 2 patients (13.3%) possessed tumors with weak claudin 18.2 expression. Eight (57.1%) patients possessed tumors with HER-2 overexpression by immunohistochemistry (3+ membranous staining, > 10% of tumor cells in 4 patients and 2+ membranous staining, > 10% of tumor cells in 4 patients). Patients with GCAs with HER-2 overexpression had median survival of 46.9 months (95% confidence interval (CI) .5-not reached) compared to a median survival of 26.5 months (95% CI 15.7-not reached) in patients with HER2 unamplified disease (Log-rank test p=.2). There were no statistically significant clinicopathologic differences between patients with HER2 2+/3+ and HER2 1+ tumors though patients with HER2 overamplified disease were more likely to recur compared to patients with HER2 unamplified disease (43% versus 0%, Chi-squared test p= .09).

CONCLUSIONS

For the first time we have demonstrated that HER-2 is overexpressed in a significant proportion of patients with GCAs, suggesting that this can be a potential therapeutic target to explore clinically. Furthermore, the absence of SSTR2 in GCAs suggests that the tumor is much more akin to an adenocarcinoma than low grade NET.

ABSTRACT ID 21374