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Association of long-term PPI use with low-risk gastric neuroendocrine tumor

Taymeyah Al-Toubah MPH, Eleonora Pelle MD, Jonathan Strosberg MD.

Department of GI Oncology, H. Lee Moffitt Cancer Center and Research Institute.

BACKGROUND

Gastric neuroendocrine tumors are rare neoplasms, comprising approximately 2% of all gastric tumors, and develop from enterochromaffin-like (ECL) cells in the gastric mucosa. Type I and II develop due to hypergastrinemia and ECL cell hyperplasia; type III typically occur sporadically, tend to be more aggressive, present metastatically in > 50% of cases, have normal fasting gastrin levels, and vary histopathologically from well- to poorly differentiated tumors. While long-term proton pump inhibitor (PPI) use has been known to lead to chronic hypergastrinemia, only a few cases of gastric NETs associated with PPI use are reported, and the classification of these cases remains undefined.

METHODS

Retrospective study of all gastric NETs seen at MCC between 1/2008 and 9/2021. Patients (pts) with clear type I and type II gastric carcinoids, and poorly differentiated NECs were excluded. Data was collected on pts with type 3 gastric NETs, including PPI use, gastrin levels (both on and off PPI), pathologic features, and the presence of metastatic disease.

RESULTS

76 patients met eligibility criteria. 51% had long-term PPI use defined as > 1 year of consecutive treatment. All had well-differentiated tumors; 33 grade 1, 35 grade 2, 4 grade 3 & grade unknown in 4. Median ki67% was 4.5 (range 1 – 40). Of patients on long-term PPI, 21 (54%) had normal gastrin levels off PPI: 7 pts had mildly elevated gastrin, and the remaining patients did not have a gastrin level while off PPI (or had no gastrin level available). Among 37 patients who received long-term PPI, 4 (10%) had metastatic disease, whereas the remaining patients without long-term PPI use, 68% had metastatic disease ($p < 0.0001$).

CONCLUSIONS

Gastric NETs diagnosed in patients with long-term PPI use tend to be less aggressive than those occurring sporadically and may represent a separate subtype of gastric NETs that is biologically more similar to type 1 than type 3.

ABSTRACT ID 23765