Neuroendocrine Tumors of the Stomach

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KEYWORDS

• Gastric neuroendocrine tumor • Gastric carcinoid • Chronic atrophic gastritis
• Zollinger-Ellison syndrome • Sporadic carcinoid

KEY POINTS

- Gastric neuroendocrine tumors are increasing in incidence, possibly because of increased detection and better surveillance.
- Management strategies are based on the type of gastric neuroendocrine tumor.
- Type I gastric neuroendocrine tumors are associated with chronic atrophic gastritis and have a good prognosis. Endoscopic resection or surveillance is recommended.
- Type II gastric neuroendocrine tumors are associated with Zollinger-Ellison syndrome and multiple endocrine neoplasia type 1. Gastrinoma and neuroendocrine tumor resection is recommended.
- Type III gastric neuroendocrine tumors are sporadic, and have the worst prognosis, often presenting with metastatic disease. An oncologic resection is recommended if possible.

INTRODUCTION: GASTRIC NEUROENDOCRINE TUMORS

Gastric neuroendocrine tumors (NETs), commonly called carcinoids, are tumors that arise from neuroendocrine cells within the stomach. NETs can be located throughout the body, from solid endocrine organs to endocrine cells within other organs, such as the respiratory tract. This article focuses on a rare location, the stomach, which represents about 7% to 8% of all NETs.[1,2] However, the incidence of gastric NETs is increasing, possibly because of better surveillance or because of the widespread use of proton pump inhibitors.[2,3]

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The understanding of the behavior and pathophysiology of gastric NETs has developed and evolved since the 1970s, when it was noticed that patients with Zollinger-Ellison syndrome (ZES) had a proliferation of enterochromaffin-like (ECL) cells.[4] Clinicians now understand that gastric NETs develop from the histamine-secreting ECL cells of the stomach, although some NETs have been found to arise from serotonin-secreting enterochromaffin cells or ghrelin cells.[5] By the early 1990s, enough evidence was collected about gastric NETs to classify lesions into 3 distinct types (Table 1).[4,6]

TYPE I GASTRIC NEUROENDOCRINE TUMORS

Type I gastric NETs are the most common of the 3 types, comprising approximately 70% to 80% of cases of gastric NETs. They are associated with autoimmune atrophic gastritis, which causes achlorhydria and intrinsic factor deficiency.[4,7] As a result of the chronic achlorhydria, G-cell hyperplasia occurs, causing increased gastrin secretion, with subsequent hypergastrinemia.[7] Chronic proton pump inhibitors are thought to cause the development of gastric NETs in a similar fashion, although this has not been definitively established.[3,8] These tumors are more prevalent in women, and are usually small and multicentric. They tend to be confined to the mucosa or submucosa, and generally behave in a more benign fashion (Fig. 1).[8]

TYPE II GASTRIC NEUROENDOCRINE TUMORS

Type II gastric NETs are also associated with hypergastrinemia, in the setting of gastrinomas and ZES. Sporadic ZES rarely causes type II gastric NETs but they are common in the setting of multiple endocrine neoplasia type 1 (MEN-1).[7,9] They are the least frequently occurring, accounting for approximately 5% to 8%.[1,7,9] Although very similar to type I lesions, they tend to behave more aggressively, with an increased metastatic potential.[8] They occur equally in men and women (Fig. 2).[8,9]

Table 1
Characteristics of gastric neuroendocrine tumors

	Type 1	Type 2	Type 3
Percentage of Tumors	70–80	5–10	10–15
Associated Disease	Chronic atrophic gastritis, pernicious anemia	Multiple endocrine neoplasia type 1, ZES	None
Number of Tumors	>1	>1	1
Tumor Size (cm)	<1	<1	>1
Tumor Location	Fundus and body	Fundus, body, and occasionally antrum	Antrum or fundus
Gastric Acid Level	Low	High	Normal
Plasma Gastrin Level	High	High	Normal
Prognosis	Good	Moderately good	Poor

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