doi: 10.1038/s41572-024-00515-z; Article citation ID: (2024) 10:26 For the Primer, visit doi: 10.1038/s41572-024-00508-y

PrimeView
Gastric neuroendocrine neoplasms

Gastric neuroendocrine neoplasms (gNENs) are rare cancers of the neuroendocrine cells of the stomach and comprise well-differentiated gastric neuroendocrine tumours (gNETs) or poorly differentiated neuroendocrine carcinomas (NECs).

Epidemiology

Studies have demonstrated an increase in the incidence and prevalence of gNETs, likely owing to increased use of oesophagogastroduodenoscopy and improved understanding and awareness of NENs. Overall, gNETs have an incidence of ~0.4 per 100,000 individuals and account for ~6% of all gastric malignancies. However, data show a higher incidence of NENs in Asian countries, such as Japan and Korea, than the rest of the world. gNETs are classified into three types based on their aetiology. Type 1 gNETs (70–80%) and type II gNETs (~5%) are gastrin dependent and develop on a background of chronic atrophic gastritis or as part of Zollinger–Ellison syndrome within a multiple endocrine neoplasia type 1 (MEN1) syndrome, respectively. Type III or sporadic gNETs develop in a near-normal-to-inflamed mucosa and in the absence of hypergastrinaemia. Analysis of survival data from referral centres based on gNET type showed better prognosis for type 1 gNETs than type III gNETs; the prognosis of type II gNETs depends on the underlying MEN1 syndrome.

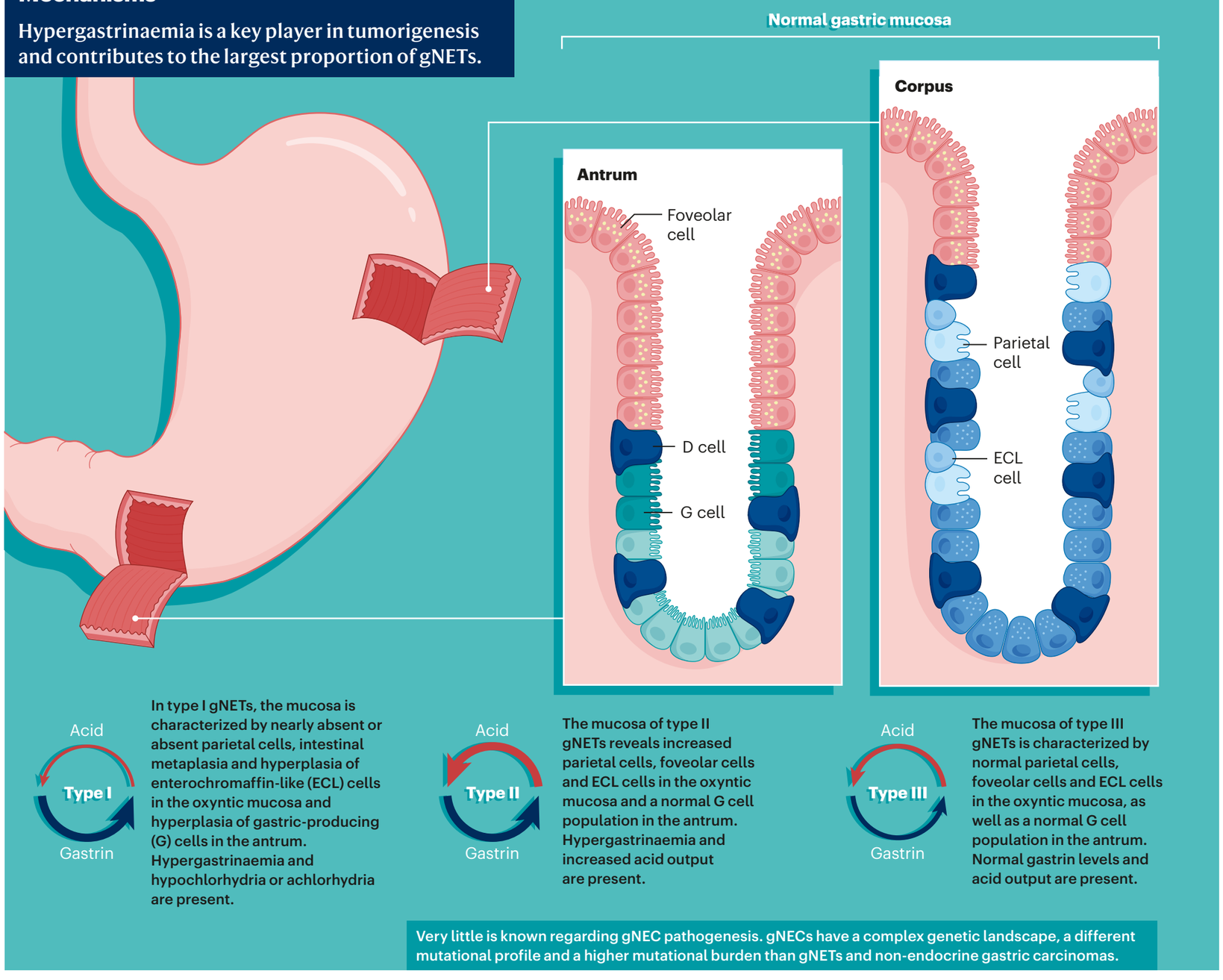
- Studies specifically evaluating the effect of diagnosis, resection and/or endoscopic surveillance on the quality of lives of patients with type I gNETs are lacking. However, patients with metastatic gNENs often present with aggressive disease and experience substantial burden, such as extensive liver metastases and peritoneal carcinomatosis.

Outlook

An improved understanding of the genetic landscape of the different types of gNETs is required. In addition, clinical trials that guide treatment for metastatic gNETs, especially type I and type II, are needed.

Mechanisms

Hypergastrinaemia is a key player in tumorigenesis and contributes to the largest proportion of gNETs.



Very little is known regarding gNEC pathogenesis. gNECs have a complex genetic landscape, a different mutational profile and a higher mutational burden than gNETs and non-endocrine gastric carcinomas.

Diagnosis

Patients with gNETs are generally asymptomatic and are frequently discovered incidentally during endoscopy performed for other reasons, such as anaemia or autoimmune thyroid disease. During endoscopy, anatomical localization within the gastric cavity, tumour appearance (shape, size and number of lesions) and any background abnormality in the gastric mucosa, such as atrophy or hypertrophy, should be accurately annotated. Following initial assessment, biopsies are performed to check for background chronic atrophic gastritis as endoscopic and/or histological confirmation of atrophic gastritis is crucial to establish the diagnosis of type I gNETs. Tumours of type I and type II gNETs are often observed as multiple clumps or lesions, often small (<1 cm). Solitary tumours, particularly those >1 cm in a normal gastric mucosa, are usually characteristic of type III gNETs or gNECs and require further characterization using endoscopic ultrasonography to guide management. In addition to endoscopy, functional imaging, such as PET–CT using radiopharmaceuticals is used for the assessment of NENs.

Management

The management of localized type I gNETs is based on tumour size and grading and involves endoscopic mucosal resection, modified endoscopic mucosal resection, submucosal dissection or full-thickness endoscopic resection. As type II gNETs are a part of the MEN1 syndrome, management depends on the associated gastrinoma; surgical resection is the first-line treatment. Total or subtotal gastrectomy with loco-regional lymphadenectomy is the treatment of choice for all patients with localized type III gNETs or locally advanced (non-metastatic) type III gNETs. Metastatic tumours require systemic treatment, which differs between gNETs and gNECs.

Written by Deepitha Maennich; designed by Laura Marshall; based on Lamberti et al. (2024)