BJCR
Brazilian Journal of Case Reports

PCAA
Publicações Científicas de Acesso Aberto

Case Report

Gastric Neuroendocrine Tumour and Pernicious Anemia in a Young Male: Case Report

Ana Bento Leite [1,*], Luis Veiga [1], Gonçalo Mesquita [1], Filipa Novo [1], Anita Campos [1]

[1] Póvoa Varzim Local Health Unit, Vila Conde, Portugal.

* Correspondence: anaspooky82@yahoo.com.

Abstract: Gastric neuroendocrine tumours (G-NETs) are rare, but incidence is increasing due to the broader use of endoscopy. Most of them are asymptomatic and incidentally detected on endoscopy. Their prognosis is associated with histological grade. Type 1 G-NETs are the most common subtype and are typically associated with chronic atrophic gastritis (CAG) and pernicious anaemia (PA), conditions that impact cyanocobalamin (vitamin B12) absorption. The authors report a case of a 44-year-old male with paresthesias of upper and lower limbs, cyanocobalamin deficiency, positive parietal cell antibodies and severe sensory motor polyneuropathy. Upper endoscopy revealed CAG and gastric polyp. Histopathology confirmed a well-differentiated type 1 G-NET. He was treated with cyanocobalamin supplementation and mucosectomy. Surveillance endoscopy was recommended. This case highlights the diagnostic complexity of type 1 G-NETs in young patients with PA, demonstrating the connection between these conditions and underscores the importance of multidisciplinary management strategies.

Keywords: Type 1 Gastric Neuroendocrine Tumours; Endoscopy; Pernicious Anaemia; Cyanocobalamin Deficiency; Polyneuropathy.

Citation: Leite AB, Veiga L, Mesquita G, Novo F, Campos A. Gastric Neuroendocrine Tumour and Pernicious Anemia in a Young Male: Case Report. Brazilian Journal of Case Reports. 2025 Jan-Dec;05(1):bjcr107.

https://doi.org/10.52600/2763-583X.bjcr.2025.5.1.bjcr107

Received: 1 July 2025
Accepted: 3 August 2025
Published: 6 August 2025

1. Introduction

Gastric neuroendocrine tumors (G-NETs) are rare and originate from enterochromaffin-like neuroendocrine cells of the gastric mucosa. These enterochromaffin cells are so named due to their affinity for silver salts and play a key role in the regulation of acid secretion. After food intake, G cells in the antrum secrete gastrin, which stimulates enterochromaffin-like cells to produce histamine and parietal cells to secrete hydrochloric acid (HCl). Histamine, in turn, also acts on parietal cells to enhance HCl production. A negative feedback mechanism involves somatostatin, secreted by D cells, which are stimulated by HCl and act on G cells to reduce gastrin secretion. Understanding these mechanisms is essential for classifying G-NETs into four well-defined clinical types, each with distinct prognoses and management approaches. This clinical classification into four types differs from the histological classification into three grades. Clinical types 1, 2, and 4 tend to be more indolent, whereas type 3 is more aggressive. Most G-NETs are asymptomatic [1–5].

We present the case of a 44-year-old man with paresthesia and severe sensorimotor polyneuropathy due to cobalamin deficiency. Endoscopy revealed a gastric polyp that was diagnosed as a well-differentiated type 1, grade I G-NET in the context of chronic atrophic gastritis and positive anti-parietal cell antibodies. Treatment included endoscopic mucosal resection, injectable cobalamin, and a proton pump inhibitor.

2. Case Report

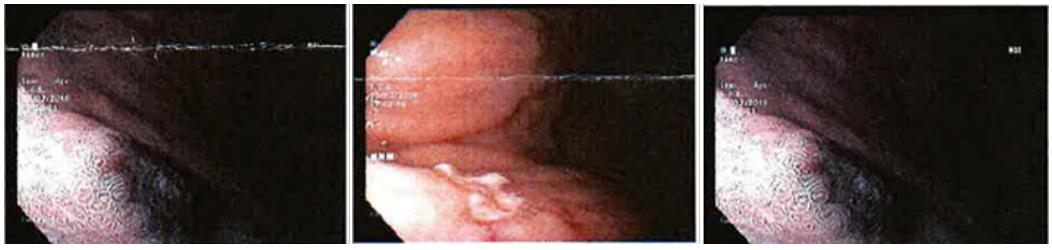
A 44-year-old male patient with a prior diagnosis of systemic arterial hypertension, under regular treatment with amlodipine + valsartan (5 mg + 160 mg) and indapamide 1.5 mg. No family history of neoplasms or autoimmune diseases. He presented for medical evaluation due to paresthesia in both upper and lower limbs, accompanied by weight loss of 4 kg over the past six months. Neurological examination revealed hypoesthesia in upper and lower limbs, with a "glove and stocking" sensory distribution pattern. No lymphadenopathy or organomegaly was observed.

Laboratory tests showed cobalamin deficiency (178 pg/mL; reference range: 187–883 pg/mL) and positive anti-gastric parietal cell antibodies (titer 1/80; reference: positive > 1/40), consistent with a diagnosis of pernicious anemia. The remaining autoimmune panel was negative. HbA1c was 5.3%, TSH, serum immunoglobulins, and serum protein electrophoresis were within normal limits. Serologies for Borrelia, hepatitis B, hepatitis C, and HIV were negative, as were tumor markers. Syphilis tests (TPHA and VDRL) were nonreactive. The patient denied alcohol consumption or adherence to a vegetarian diet.

Cervical spine computed tomography (CT) showed kyphosis, while lumbar and sacrococcygeal spine CT scans revealed no abnormalities. Brain magnetic resonance imaging (MRI) showed no evidence of demyelinating disease. Electroneuromyography (ENMG) of the upper and lower limbs demonstrated generalized slowing of both motor and sensory nerve conduction velocities, with preserved motor amplitudes but very low or unmeasurable sensory potentials. These findings are consistent with an axonal-type sensorimotor polyneuropathy, predominantly affecting sensory fibers.

Neurological assessment concluded that the paresthesia was due to severe sensorimotor polyneuropathy of nutritional etiology, secondary to cobalamin deficiency. Genetic testing for transthyretin (TTR) mutations excluded hereditary amyloidosis. Transthoracic echocardiography with Doppler and abdominal ultrasound were unremarkable. Colonoscopy was normal. Upper gastrointestinal endoscopy showed no abnormalities in the esophagus or duodenum. The gastric mucosa of the antrum and body exhibited diffuse erythema with an atrophic appearance, reduced rugal folds, and an 8 mm sessile, eroded polyp located on the greater curvature (Figure 1).

Figure 1. Upper gastrointestinal endoscopy. Gastric mucosa of the antrum and body showing erythema with an atrophic appearance, reduced rugal fold volume, and an 8 mm sessile, eroded gastric polyp located on the greater curvature.



Biopsies of the gastric body and antrum revealed chronic atrophic gastritis with intestinal metaplasia and were negative for Helicobacter pylori. The polypectomy biopsy confirmed the histological diagnosis of a well-differentiated gastric neuroendocrine tumor (G-NET), classified clinically as type 1 and histologically as grade I, measuring 6 mm. Immunohistochemistry was positive for chromogranin A (CgA) and synaptophysin; mitoses and necrosis were absent, and the Ki-67 proliferation index was below 2%. The resection was superficial but complete. Thoracoabdominopelvic CT scan showed no evidence of metastasis.

Endocrinology evaluation showed hypergastrinemia (264 pg/mL; reference: 13–115 pg/mL) and elevated chromogranin A (175 ng/mL; reference: <102 ng/mL). Treatment included esomeprazole 40 mg daily and injectable cobalamin weekly for four weeks, followed by monthly maintenance doses. After six months of supplementation, there was

progressive improvement in paresthesia and normalization of serum cobalamin levels. A multidisciplinary team, including Internal Medicine, Oncology, Endocrinology, Surgery, and Gastroenterology, was crucial for achieving a favorable outcome. It was determined that the type 1 G-NET did not require surgical intervention. The patient underwent endoscopic mucosal resection without complications.

During follow-up, upper endoscopies were performed every six months. At the four-year mark, endoscopy revealed an erosion on a polypoid fold at the cardia (biopsied), as well as mucosal atrophy in the gastric fundus and body. Biopsy showed chronic gastritis with no intestinal metaplasia, dysplasia, or malignancy, and tested positive for Helicobacter pylori. Eradication therapy was initiated with bismuth, metronidazole, and tetracycline (140 mg + 125 mg + 125 mg), three tablets with meals (breakfast, lunch, dinner, and bedtime), 12 tablets daily, combined with omeprazole 20 mg every 12 hours for 10 days. After five years, the indication for upper endoscopy surveillance followed the general population guidelines. The patient had a favorable clinical course.

3. Discussion

Although a rare neoplasm, the incidence of gastric neuroendocrine tumors (G-NETs) has increased due to early detection facilitated by the widespread use of upper gastrointestinal endoscopy. In Portugal, they represent approximately 10% of all neuroendocrine tumors (NETs) of the gastrointestinal tract. Type 1 G-NET is a challenging diagnosis because it is usually asymptomatic and may be incidentally identified during endoscopy in the differential diagnosis of gastric neoplasms [1–6].

The authors present the case of a 44-year-old man with severe sensorimotor polyneuropathy associated with cobalamin deficiency, whose etiological investigation led to the diagnosis of type 1 G-NET. The patient exhibited paresthesias in the upper and lower limbs, weight loss, and positive anti-parietal cell antibodies. Upper gastrointestinal endoscopy revealed chronic atrophic gastritis and the presence of a gastric polyp. Biopsy after polypectomy showed a well-differentiated G-NET, clinically classified as type 1 and histologically as grade I. Immunohistochemistry confirmed the diagnosis of NET, with positivity for chromogranin A (CgA) and synaptophysin. The patient started treatment with injectable cobalamin and underwent endoscopic mucosectomy, with good clinical evolution. Other possible causes of sensorimotor polyneuropathy were excluded, including diabetes mellitus, alcoholism, paraneoplastic syndromes, monoclonal gammopathies, thyroid dysfunctions, autoimmune diseases, infections (HIV, Borrelia, hepatitis B and C), and demyelinating diseases. Considering the epidemiological context of the patient's residence (Póvoa de Varzim, Portugal), where familial amyloid polyneuropathy (paramyloidosis) is endemic, genetic screening was performed and returned negative.

Pernicious anemia (PA) is an autoimmune gastritis caused by antibodies directed against parietal cells and/or intrinsic factor, leading to malabsorption and cobalamin deficiency. In this case, anti-gastric parietal cell antibodies were identified. Other causes of cobalamin deficiency were excluded: strict vegetarian diet, use of medications (neomycin, biguanides, proton pump inhibitors), history of gastrectomy, bariatric surgery, malabsorption syndromes, ileal resection, inflammatory bowel disease, celiac disease, and pancreatic insufficiency [7–13]. The main risk factors for developing type 1 G-NET include chronic atrophic gastritis, pernicious anemia, advanced age, intestinal metaplasia, and elevated CgA levels. In patients with chronic atrophic gastritis, elevated serum CgA is a strong predictor of type 1 G-NET. This subtype is often associated with other autoimmune diseases such as type 1 diabetes, autoimmune thyroiditis, and primary biliary cirrhosis [7–13].

Most patients with type 1 G-NET have pernicious anemia. These individuals have a two- to threefold increased risk of developing gastric neoplasms due to chronic atrophic gastritis. The risk of G-NET in patients with PA justifies performing upper gastrointestinal endoscopy to screen for preneoplastic lesions, as PA is considered a precursor of G-NET [7–13]. The incidence of type 1 G-NET in patients with chronic atrophic gastritis and PA

is higher in elderly women, especially after the sixth decade of life [7–13]. However, the present case describes the occurrence of this neoplasm in a young 44-year-old man, highlighting the rarity of this presentation. In patients with chronic atrophic gastritis, the estimated annual incidence of type 1 G-NET is approximately 0.4%. In chronic atrophic gastritis, there is loss of glandular cells in the gastric fundus, leading to hypochlorhydria, which stimulates hyperplasia of the antral G cells and results in persistent hypergastrinemia.

Hypergastrinemia causes stimulation of enterochromaffin-like cells, leading to cellular hyperplasia and resulting in CgA-positive G-NETs. In pernicious anemia (PA), gastric pH is elevated due to loss of acid secretion by parietal cells. The autoimmune destruction of gastric parietal cells in PA causes achlorhydria and consequent hypergastrinemia, and is responsible for decreased intrinsic factor, which is essential for cobalamin absorption in the ileum, resulting in deficiency [7–13].

In this case, the coexistence of G-NET and cobalamin deficiency is due to both being consequences of chronic atrophic gastritis and PA. Type 1 G-NET is a consequence of hypergastrinemia resulting from the autoimmune disease PA. The polyneuropathy is not a direct paraneoplastic manifestation of the G-NET, but rather a symptom of the underlying autoimmune disease, PA, which also caused the G-NET. Elevated serum gastrin and CgA support the diagnosis of G-NET. Anti-parietal cell antibodies triggered hypergastrinemia, resulting in type 1 G-NET and cobalamin deficiency [7–13]. The patient was not using proton pump inhibitors, excluding drug-induced hypergastrinemia and supporting chronic atrophic gastritis associated with PA as the underlying cause. Patients with chronic atrophic gastritis can be asymptomatic, and diagnosis is made by gastric biopsy.

Type 1 G-NETs originate from enterochromaffin-like cells, which transform into G-NETs through chronic stimulation by hypergastrinemia in chronic atrophic gastritis. Gastric epithelial cells secrete gastrin, which stimulates enterochromaffin-like cells to produce histamine. Histamine causes positive feedback on gastric parietal cells, which secrete hydrochloric acid (HCl), increasing acid secretion. This process triggers negative feedback on D cells, which secrete somatostatin, reducing gastrin secretion [1–14]. The diagnosis of type 1 G-NET includes endoscopic and histological findings, along with serum markers such as CgA and gastrin. G-NETs are generally diagnosed by endoscopy, as CT and MRI have limited ability to detect small G-NETs [1–14].

On endoscopy, type 1 G-NETs are generally smaller than 1 cm, and may present as multiple polyps with ulceration. Approximately 22% of type 1 G-NETs range from 0.5 mm to 5 mm, making them invisible and undetectable by direct endoscopy; they may be underdiagnosed and only identified by random gastric biopsies through gastric mapping. G-NETs are covered by normal mucosa, so biopsies should be taken from multiple sites including the antrum and gastric fundus [6]. Knowledge of the classifications and clinical presentations of G-NETs is essential for accurate identification of clinical type and histological grade, as different subtypes have distinct treatment and prognosis. G-NETs are diagnosed by endoscopy and biopsy, confirmed by immunohistochemistry (CgA positivity). They are classified into four distinct types based on endoscopic, histological, and biochemical characteristics. Types 1 and 2 are more indolent, whereas types 3 and 4 exhibit more aggressive growth [1–14].

Type 1 G-NET is the most common (70–80%), with a good prognosis, generally associated with chronic atrophic gastritis and PA. They are usually benign, small, multiple, and located in the mucosa/submucosa of the gastric fundus or body. Endoscopic findings include pale, yellowish antral mucosa with transparent blood vessels, contrasting with the smooth, reddish mucosa of normal areas. Histology shows mucosal cell atrophy, absence of parietal cells, and neuroendocrine cell hyperplasia [1–14].

Histological classification of G-NETs is performed through mitotic count in high-power fields and by the percentage of the proliferative index Ki67. The Ki67 protein is a marker of cellular proliferation that determines the growth fraction in a cell. It correlates

with the clinical course of G-NETs and has prognostic value for tumor survival and recurrence. Determination of the Ki67 proliferation index and mitotic count per high-power field are mandatory. G-NETs are divided into 3 grades: Grade I (well-differentiated, better prognosis) with Ki67 < 2% and/or < 2 mitoses; Grade II (well-differentiated) with Ki67 between 2% and 20% and/or 2 to 20 mitoses; Grade III (poorly differentiated, worse prognosis) with Ki67 > 20% and mitoses > 20 [1–14]. Our patient had a well-differentiated G-NET, histological grade I (Ki67 proliferation index < 2%, no mitoses).

The proliferation rate and grade of gastric dysplasia are difficult to assess histologically. Chromogranin A (CgA) is a group of proteins present in neuroendocrine tissues. Synaptophysin is located in the secretory vesicles of neuronal cells. Immunohistochemistry positive for CgA and synaptophysin is essential for diagnostic confirmation, identifying hyperplasia, dysplasia, or malignant transformation of enterochromaffin cells. CgA expression may be weak in poorly differentiated tumors, but synaptophysin expression is generally present even in these tumors [1–14].

CgA is a secretory protein released from chromaffin cytoplasmic granules into the blood, and its serum measurement helps confirm the diagnosis of G-NET. Serum measurement of gastrin, CgA, and 5-hydroxyindoleacetic acid (5-HIAA), the main serotonin metabolite, is not routinely recommended for surveillance to detect recurrence. Proton pump inhibitors can falsely elevate CgA levels. CgA is not recommended for screening but should be used when the pretest probability is high. Some tumors are unlikely to produce serotonin, making 24-hour urinary 5-HIAA measurement unhelpful. Its measurement requires adherence to dietary restrictions before and during urine collection [1–14].

For staging type 1 G-NET, contrast-enhanced abdominal computed tomography (CT) is recommended to exclude lymphadenopathy and liver metastases. Endoscopic ultrasound can help determine the depth of invasion in the gastric wall for tumors larger than 1 cm. For small tumors (<1 cm), upper gastrointestinal endoscopy is the only recommended imaging procedure. When metastasis is suspected, such as in patients with invasive disease on endoscopic ultrasound or with type 3 tumors larger than 1 cm, imaging exams such as CT or magnetic resonance imaging (MRI) are indicated to search for metastases. CT is the best exam for staging, surveillance, and post-treatment monitoring. MRI can be used when CT is inconclusive and may have greater sensitivity, being the best test to detect metastases. Fluorodeoxyglucose positron emission tomography (FDG-PET) is rarely useful as it measures glucose uptake and most NETs have low glucose affinity [1–14]. Treatment varies according to clinical type, disease extent, lesion differentiation grade, and the presence or absence of poor prognostic factors. According to the WHO, G-NETs are classified into 4 histological grades with distinct prognoses. Poor prognostic factors include: lesion ≥ 2 cm, invasion beyond the deep submucosa, Ki-67 ≥ 3%, vascular invasion, low structural differentiation grade, presence of atypia and/or necrosis [1–14].

The therapeutic approach should be individualized. In this case, the type 1 G-NET had an indolent course, with a polyp < 1 cm, low grade, well differentiated, and no metastases. The multidisciplinary team opted for endoscopic mucosectomy, cobalamin supplementation, and proton pump inhibitor therapy. Endoscopic resection of small polyps is associated with a low risk of recurrence. During follow-up after treatment, type 1 G-NETs smaller than 2 cm are generally benign and have a metastasis risk below 10%. The prognosis is favorable, with a 5-year survival rate of 90-95% [1–14]. In this case, surveillance was performed with upper endoscopy every 6 months due to enterochromaffin cell hyperplasia and mucosal changes caused by hypergastrinemia. At 4 years, endoscopy revealed an erosion on a polypoid fold in the cardia, and biopsy showed chronic gastritis and Helicobacter pylori infection. Eradication therapy with bismuth, metronidazole, and tetracycline was performed. After 5 years, the indication for surveillance by upper endoscopy became similar to that of the general population. The patient had a good prognosis.

Helicobacter pylori is a gram-negative bacterium with high worldwide prevalence. Its prevalence is high in developing countries and lower in developed countries. Transmission occurs mainly via oral-oral or fecal-oral routes. Risk factors include lack of sanitation, absence of potable water, poor hygiene, and overcrowding. Once acquired, *Helicobacter pylori* infection persists and may or may not cause gastrointestinal disease. This bacterium has been implicated in the development of gastric and duodenal ulcers, gastric neoplasia, and mucosa-associated lymphoid tissue (MALT) lymphomas. Treatment of the infection is indicated in cases of gastric/duodenal ulcers and in patients at high risk for gastric neoplasia. Patients infected with *Helicobacter pylori* have a higher likelihood of presenting anti-parietal cell and anti-intrinsic factor antibodies. An association exists between Helicobacter pylori infection and cobalamin deficiency [15].

4. Conclusion

This case highlights the importance of investigating the diagnosis of G-NET in patients presenting with chronic atrophic gastritis and pernicious anemia during the workup of cobalamin deficiency-related polyneuropathy. G-NETs encompass different subtypes with distinct management and prognosis. Accurate identification of the clinical type and histological grade allows for individualized treatment. Through this clinical case, we aim to emphasize the crucial role of the laboratory in diagnosing this pathology, particularly in distinguishing its various subtypes, as well as its role in the treatment, follow-up, and prognosis of G-NET. This case underscores that not all G-NETs are aggressive. Understanding the different types of G-NET is essential, as their subtype and size have significant therapeutic and prognostic implications.

Funding: None.

Research Ethics Committee Approval: We declare that the patient approved the study by signing an informed consent form and the study followed the ethical guidelines established by the Declaration of Helsinki.

Acknowledgments: None.

Conflicts of Interest: The authors declare no conflicts of interest.

References

1. Frediano Inzani, Alessandro Vanoli, Guido Rindi. Pathological Classification: Gastroenteropancreatic, Thoracic, and Rare Non-endocrine Sites. Neuroendocrine Neoplasia. 2024 Jun;1-17. doi:10.1007/978-3-030-67823-4-2_1.
2. Panzuto F, Ramage J, et al. European Neuroendocrine Tumor Society (ENETS) 2023 guidance paper for gastroduodenal neuroendocrine tumours (NETs) G1–G3. J Neuroendocrinol. 2023;35:e13306. doi:10.1111/jne.13306.
3. Jacobson BC, Bhatt A, Greer KB, Lee LS, Park WG, Sauer BG, Shami VM. ACG clinical guideline: diagnosis and management of gastrointestinal subepithelial lesions. Am J Gastroenterol. 2023;118:46-58. doi:10.14309/ajg.0000000000002100.
4. Modica R, Liccardi A, Minotta R, Cannavale G, Benevento E, Colao A. Current understanding of pathogenetic mechanisms in neuroendocrine neoplasms. Expert Rev Endocrinol Metab. 2024;19:49-61. doi:10.1080/17446651.2023.2279540.
5. Panzuto F, Ramage J, Pritchard DM, et al. European Neuroendocrine Tumor Society (ENETS) 2023 guidance paper for gastroduodenal neuroendocrine tumours (NETs) G1-G3. J Neuroendocrinol. 2023;35:e13306. doi:10.1111/jne.13306.
6. Gopakumar H, Jahagirdar V, Koyi J, Dahiya DS, Goyal H, Sharma NR, Perisetti A. Role of advanced gastrointestinal endoscopy in the comprehensive management of neuroendocrine neoplasms. Cancers (Basel). 2023;15:4175. doi:10.3390/cancers15164175.
7. Karam K, Saleh S, Chebbo H, Jalloul S, Fiani E. The investigation of B12 deficiency leading to the serendipitous diagnosis of gastric carcinoid tumour. EJCRIM. 2024;11. doi:10.12890/2024_004673.
8. Rudolph JJ, Agyei O, Telvizian T, et al. Gastric Neuroendocrine Tumors and Pernicious Anemia: A Case Report and Literature Review. Cureus. 2024 Nov 12;16(11):e73553. doi:10.7759/cureus.73553.
9. Castellana C, Eusebi LH, Dajti E, et al. Autoimmune atrophic gastritis: A clinical review. Cancers (Basel). 2024;16:1310. doi:10.3390/cancers16071310.
10. Massironi S, Gallo C, Elvevi A, Stegagnini M, Coltro LA, Invernizzi P. Incidence and prevalence of gastric neuroendocrine tumors in patients with chronic atrophic autoimmune gastritis. World J Gastrointest Oncol. 2023;15:1451-60. doi:10.4251/wjgo.v15.i8.1451.
11. Nanda Gopal S, Vakati D, Palanisamy S, et al. A Rare Case of Gastric Neuroendocrine Tumor in a Patient With Vitamin B12 Deficiency. Cureus. 2024 Sep 9;16(9):e68968. doi:10.7759/cureus.68968.

12. Serjilus A, Zimmer SK, Bush AM, et al. Unmasking the Silent Culprit: Gastric Neuroendocrine Tumor in the Setting of Iron Deficiency Anemia. Cureus. 2025 Jun 14;17(6):e86010. doi:10.7759/cureus.86010.
13. Cortés-Marín EE, González-Rodríguez JC, Cristofori M, et al. Gastric Type 1 Neuroendocrine Tumor in an Elderly Patient: A Case Report and Diagnostic Approach Review. Cureus. 2025 Jul 7;17(7):e87429. doi:10.7759/cureus.87429.
14. Sok C, Ajay PS, Tsagkalidis V, Kooby DA, Shah MM. Management of gastric neuroendocrine tumors: a review. Ann Surg Oncol. 2024;31:1509-18. doi:10.1245/s10434-023-14712-9.
15. Jadalah K, Awadi E, Alawneh K, Khassawneh B. Association between vitamin B12 level and anti-parietal cells and anti-intrinsic factor antibodies among adult Jordanian patients with Helicobacter pylori infection. Braz J Infect Dis. 2013;17(6):629–632. doi:10.1016/j.bjid.2013.01.009.