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Contents

Thrice Monthly Volume 12 Number 7 March 6, 2024

EDITORIAL

- 1196 Relevance of sleep for wellness: New trends in using artificial intelligence and machine learning
Nag DS, Swain A, Sahu S, Chatterjee A, Swain BP

MINIREVIEWS

- 1200 Expect the unexpected: Brown tumor of the mandible as the first manifestation of primary hyperparathyroidism
Majic Teng A, Cigrovski Berkovic M, Zajc I, Salaric I, Müller D, Markota I
- 1205 Research progress in spasmodic torticollis rehabilitation treatment
Zhang S, Zeng N, Wu S, Wu HH, Kong MW

ORIGINAL ARTICLE

Clinical and Translational Research

- 1215 Investigating the causal associations between five anthropometric indicators and nonalcoholic fatty liver disease: Mendelian randomization study
Xiao XP, Dai YJ, Zhang Y, Yang M, Xie J, Chen G, Yang ZJ
- 1227 Causal role of immune cells in obstructive sleep apnea hypopnea syndrome: Mendelian randomization study
Zhao HH, Ma Z, Guan DS

Case Control Study

- 1235 Significant risk factors for intensive care unit-acquired weakness: A processing strategy based on repeated machine learning
Wang L, Long DY

Retrospective Cohort Study

- 1243 Perioperative and long-term results of ultrasonography-guided single- and multiple-tract percutaneous nephrolithotomy for staghorn calculi
Cheng RX, Dai N, Wang YM, Qi P, Chen F

Retrospective Study

- 1251 Clinical characteristics of testicular torsion and factors influencing testicular salvage in children: A 12-year study in tertiary center
Gang XH, Duan YY, Zhang B, Jiang ZG, Zhang R, Chen J, Teng XY, Zhang DB

META-ANALYSIS

- 1260 Effectiveness of sensory integration therapy in children, focusing on Korean children: A systematic review and meta-analysis
Oh S, Jang JS, Jeon AR, Kim G, Kwon M, Cho B, Lee N
- 1272 Safety and efficacy comparison of remimazolam and propofol for intravenous anesthesia during gastroenteroscopic surgery of older patients: A meta-analysis
Li FZ, Zhao C, Tang YX, Liu JT

CASE REPORT

- 1284 Sporadic gastrinoma with refractory benign esophageal stricture: A case report
Chen QN, Bai BQ, Xu Y, Mei Q, Liu XC
- 1290 Efficacy of borneol-gypsum in skin regeneration and pain control in toxic epidermal necrolysis: A case report
Yang LW, Zhang LJ, Zhou BB, Lin XY, Chen YT, Qin XY, Tian HY, Ma LL, Sun Y, Jiang LD
- 1296 Extended survival with metastatic pancreatic cancer under fruquintinib treatment after failed chemotherapy: Two case reports
Wu D, Wang Q, Yan S, Sun X, Qin Y, Yuan M, Wang NY, Huang XT
- 1305 Reconstruction of cervical necrotizing fasciitis defect with the modified keystone flap technique: Two case reports
Cho W, Jang EA, Kim KN
- 1313 Reversal of complete atrioventricular block in dialysis patients following parathyroidectomy: A case report
Xu SS, Hao LH, Guan YM
- 1320 Treatment of bilateral developmental dysplasia of the hip joint with an improved technique: A case report
Yu XX, Chen JY, Zhan HS, Liu MD, Li YF, Jia YY
- 1326 Misdiagnosis of synovial sarcoma - cellular myofibroma with *SRF-RELA* gene fusion: A case report
Zhou Y, Sun YW, Liu XY, Shen DH
- 1333 Heterochronous multiple primary prostate cancer and lymphoma: A case report
Liang JL, Bu YQ, Peng LL, Zhang HZ
- 1339 Cardiac remodeling in patients with atrial fibrillation reversing bradycardia-induced cardiomyopathy: A case report
Gao DK, Ye XL, Duan Z, Zhang HY, Xiong T, Li ZH, Pei HF
- 1346 Microsurgical management of radicular cyst using guided tissue regeneration technique: A case report
Gómez Mireles JC, Martínez Carrillo EK, Alcalá Barbosa K, Gutiérrez Cortés E, González Ramos J, González Gómez LA, Bayardo González RA, Lomeli Martínez SM
- 1356 Delayed neurological dysfunction following posterior laminectomy with lateral mass screw fixation: A case report and review of literature
Yan RZ, Chen C, Lin CR, Wei YH, Guo ZJ, Li YK, Zhang Q, Shen HY, Sun HL

- 1365** Translocation of a fish spike from the pharynx to the thyroid gland: A case report

Li D, Zeng WT, Jiang JG, Chen JC

- 1371** Double plasma molecular adsorption system for Stevens–Johnson syndrome/toxic epidermal necrolysis: A case report

Tan YW, Liu LP, Zhang K

LETTER TO THE EDITOR

- 1378** Enhancing competency of clinical research nurses: A comprehensive training and evaluation framework

Liu YX, Xu Y

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The primary aim of *World Journal of Clinical Cases* (WJCC, *World J Clin Cases*) is to provide scholars and readers from various fields of clinical medicine with a platform to publish high-quality clinical research articles and communicate their research findings online.

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Sporadic gastrinoma with refractory benign esophageal stricture: A case report

Qian-Nan Chen, Bing-Qing Bai, Yan Xu, Qiao Mei, Xiao-Chang Liu

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Abstract

BACKGROUND

Gastrinoma is characterized by an excessive release of gastrin, leading to hypersecretion of gastric acid, subsequently resulting in recurrent peptic ulcers, chronic diarrhea, and even esophageal strictures. This case report aims to improve awareness and facilitate early diagnosis and treatment of gastrinoma by presenting a rare case of gastrinoma with refractory benign esophageal stricture (RBES). Additionally, it highlights the persistent challenges that gastroenterologists encounter in managing RBES.

CASE SUMMARY

This case demonstrates a patient with gastrinoma who developed RBES and complete esophageal obstruction despite management with maximal acid suppressive therapy, multiple endoscopic bougie dilations and endoscopic incisional therapy (EIT).

CONCLUSION

It is essential to diagnose gastrinoma as early as possible, as inadequately controlled acid secretion over an extended period increases the risk of developing severe esophageal strictures. In patients with esophageal strictures causing complete luminal obstruction, blind reopening EIT presents challenges and carries a high risk of perforation.

Key Words: Gastrinoma; Zollinger-Ellison syndrome; Neuroendocrine neoplasm; Chronic diarrhea; Refractory benign esophageal stricture; Case report

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Core Tip: We report a rare case of sporadic gastrinoma in a young woman who presented with chronic diarrhea, multiple peptic ulcers, and a refractory benign esophageal stricture. The case indicates that inadequately controlled acid secretion over an extended period increases the risk of developing severe esophageal strictures. It also highlights that in patients with complete esophageal strictures, blind reopening endoscopic incisional therapy presents challenges and carries a high risk of perforation.

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INTRODUCTION

Gastrinoma, also known as Zollinger-Ellison syndrome (ZES), is a rare pancreatic neuroendocrine neoplasm characterized by excessive gastrin release leading to hypersecretion of gastric acid and subsequent manifestations of recurrent peptic ulcers, vomiting, abdominal pain, and chronic diarrhea[1]. Many of these symptoms can be significantly alleviated through treatment with acid inhibitors, particularly proton pump inhibitors.

The diagnosis of ZES is challenging, as its symptoms are nonspecific and often overlap with those of other gastrointestinal disorders, leading to an initial correct diagnosis by the referring physician in only 3% of patients. Moreover, its rarity, with an incidence of 0.5 to 15 cases per million population, makes it extremely difficult to diagnose accurately in an acute setting[2]. Consequently, patients are typically diagnosed only after years of presenting symptoms.

In this report, we present a rare case of sporadic ZES in a young woman who presented with chronic diarrhea, abdominal pain, and vomiting and later developed dysphagia because of severe reflux esophagitis with esophageal stricture. We will discuss in detail the diagnostic process and the treatments administered for her refractory benign esophageal stricture (RBES). This case report aims to improve awareness and facilitate early diagnosis and treatment of gastrinoma by presenting a rare case of gastrinoma with RBES. Additionally, it highlights that blind reopening endoscopic incisional therapy (EIT) presents challenges and carries a high risk of perforation.

CASE PRESENTATION

Chief complaints

A 33-year-old female patient was admitted with intermittent chronic watery diarrhea, abdominal pain, vomiting, and progressive dysphagia.

History of the present illness

Over the past 2 years, the patient sought medical attention at a local hospital and was initially diagnosed with chronic idiopathic diarrhea. Laboratory and radiological investigations including stool for culture, parasites, fat analysis, a computed tomography (CT) scan of the abdomen, colonoscopy, and enteroscopy showed no abnormal findings. However, her condition worsened, with more frequent watery diarrhea combined with abdominal pain, vomiting, progressive dysphagia, and weight loss (10 kg over 3 months).

History of past illness

The patient also had a history of multiple peptic ulcers and had undergone an exploratory laparotomy with gastric perforation repair 3 months ago.

Personal and family history

The patient denied a family history of hereditary diseases or cancer.

Physical examination

Upon physical examination, mild tenderness in the epigastrium was noted.

Laboratory examinations

General and antidiarrheal treatments had shown no effect, but somatostatin analog infusion with a dose of 3 mg was effective in alleviating her symptoms. Consequently, fasting serum gastrin and chromogranin A levels were measured, showing elevated values of fasting serum gastrin (845.00 pg/mL, normal range: 30-100 pg/mL) and chromogranin A (500 ng/mL, normal range: 10-110 ng/mL). These findings immediately raised suspicion of a neuroendocrine neoplasm in the form of gastrinoma. The gastrinoma was considered sporadic owing to the absence of a pituitary tumor, normal serum calcium, and parathyroid hormone levels.

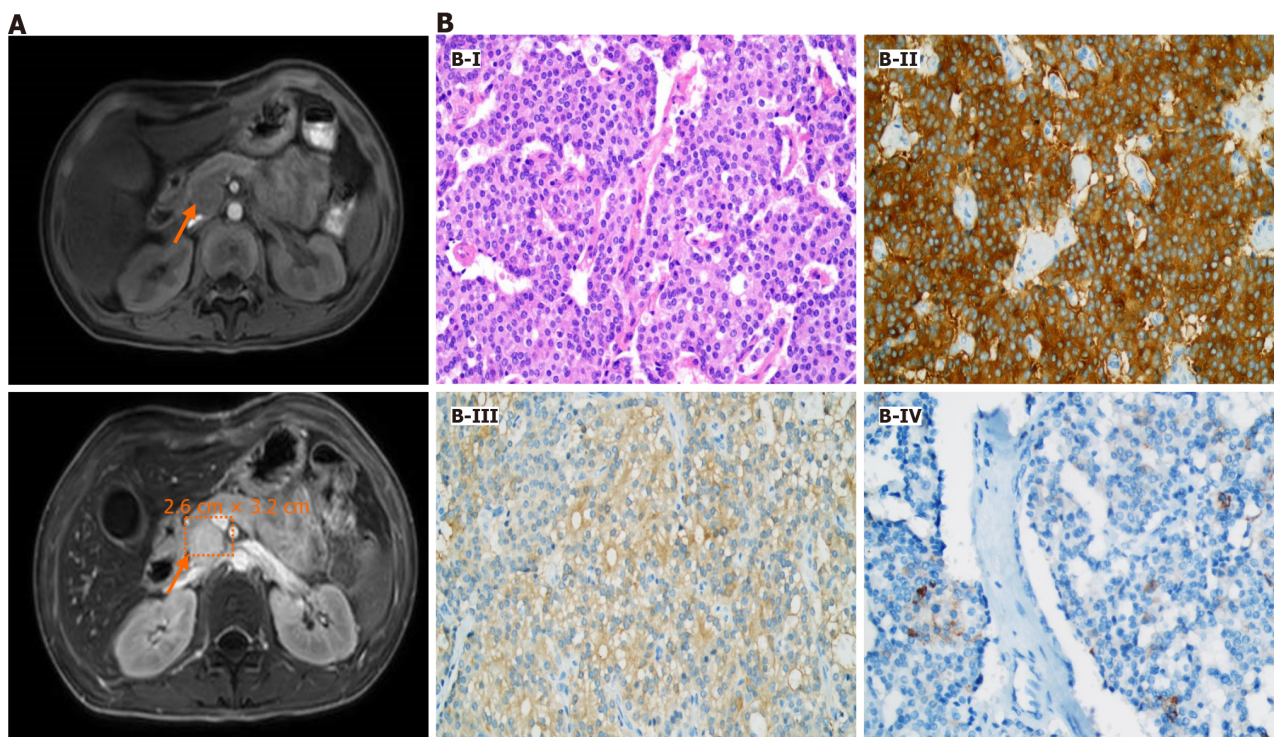


Figure 1 Diagnosis of gastrinoma. A: Plain and enhanced magnetic resonance imaging scans of the pancreas showed a mass approximately 2.6 cm × 3.2 cm in size located at the head of the pancreas (indicated by orange arrows); B: Hematoxylin-eosin staining (× 400) and immunohistochemical stains (× 400) of the mass: The tumor cells, arranged into solid nests, exhibited abundant cytoplasm, fine and granulated chromatin, and inconspicuous nucleoli (B-I); Tumor cells were positive for synaptophysin (B-II), neuron-specific enolase (B-III), and gastrin (B-IV).

Imaging examinations

Upon admission to our unit, the esophagus-gastro-duodenoscopy revealed severe reflux esophagitis (grade D), esophageal ulcers, and strictures. Due to the negative findings obtained from the previous CT scan, we opted for abdominal contrast-enhanced magnetic resonance imaging (MRI) as the preferred diagnostic modality. This approach unveiled a mass of approximately 2.6 cm × 3.2 cm at the head of the pancreas without liver metastasis (Figure 1A).

PATHOLOGY AND IMMUNOHISTOCHEMISTRY

The patient successfully underwent the operation, and the diagnosis of gastrinoma was confirmed through postoperative pathology and immunohistochemistry (Figure 1B). The tumor cells, arranged into solid nests, exhibited abundant cytoplasm, fine and granulated chromatin, and inconspicuous nucleoli. Tumor cells showed positivity for synaptophysin, neuron-specific enolase, and gastrin.

FINAL DIAGNOSIS

Sporadic gastrinoma; RBES.

TREATMENT

According to the consensus of Chinese experts in pancreatic neuroendocrine tumors, radical pancreatic resection surgery should be performed for pancreatic neuroendocrine tumors with a diameter greater than 2 cm, regardless of their functionality. For neuroendocrine tumors in the head of the pancreas, it is recommended to undergo pancreaticoduodenectomy[3]. Therefore, our team opted for pancreaticoduodenectomy. Although the patient's watery diarrhea resolved after surgery, she continued to experience severe dysphagia due to an esophageal stricture during the follow-up period. Comprehensive evaluations of the esophageal stricture by esophagus-gastro-duodenoscopy, endoscopic ultrasonography, and esophagography showed severe esophageal stricture (Figure 2A). Her esophageal stricture led to the decision to improve her symptoms through periodic wire-guided endoscopic bougie dilations (EBD). However, despite five sessions of EBD (Figure 2B), it was not possible to maintain a satisfactory luminal diameter, indicating the presence of RBES. According to the guidelines, we performed ultrasonography-guided and wire-guided EIT combined with

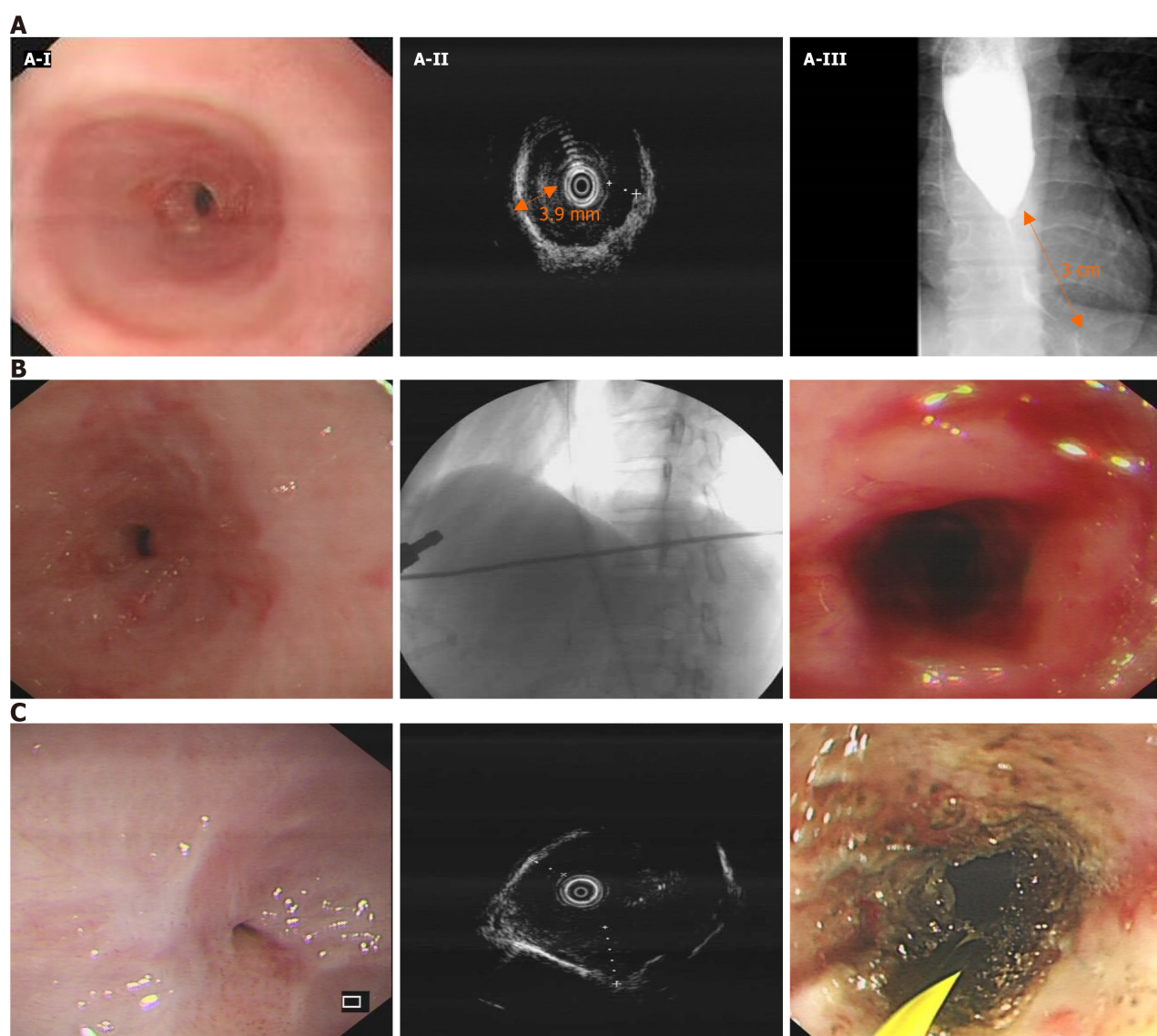


Figure 2 Treatment of esophageal stricture. A: Assessment of esophageal stricture. The esophagus-gastro-duodenoscopy shows severe esophageal stricture with endoscopy unable to pass through (A-I); Endoscopic ultrasonography shows prominent thickening of the esophageal muscular layer, with the thickest part measuring approximately 3.9 mm (A-II); Esophagography shows severe lower esophageal stricture with a luminal diameter of 1.8 mm, involving a 3 cm length of the esophagus (A-III); B: A representative wire-guided endoscopic bougie dilations. The bougie is used to expand along with the wire; C: A representative ultrasonography-guided and wire-guided endoscopic incisional therapy. The needle knife is used to cut through the muscle layer along with the wire.

triamcinolone acetonide injection (Figure 2C).

OUTCOME AND FOLLOW-UP

During the 2-year follow-up, the patient recovered from watery diarrhea after surgery. Unfortunately, during the patient's fourth EIT session, when the esophageal lumen was completely obstructed, she unexpectedly developed esophageal perforation. She was managed with conservative treatment because she declined further surgery. As a result, she could only receive long-term enteral nutrition through a nasogastric tube, significantly reducing her quality of life.

DISCUSSION

The reported case exhibits several distinctive features that warrant discussion. Firstly, the patient presented with chronic diarrhea and multiple peptic ulcers, which were initially misdiagnosed as chronic idiopathic diarrhea and sporadic peptic ulcers. However, it is important to note that ZES-related ulcers are usually multiple, located at unusual sites, and usually complicated by bleeding, perforation, or esophageal strictures, in contrast to sporadic peptic ulcers. Moreover, approximately 75% of patients with gastrinoma presenting with watery diarrhea, which can easily be misdiagnosed as chronic

idiopathic diarrhea, as in this case[4].

Interestingly, the case presented with an uncommon symptom of refractory esophageal stricture. ZES is typically associated with minimal esophageal morbidity because of advancements in antisecretory medications. A prospective study investigating esophageal involvement and its complications in ZES found that sporadic ZES rarely presents with a benign esophageal stricture, with a frequency as low as 0.4%[5]. After excluding esophageal cancer and drug or chemical-induced esophageal stricture, we considered that the prolonged acid reflux, attributed to gastrinoma, led to the formation of esophageal ulcers and scars, consequently resulting in refractory esophageal stricture. It is also noteworthy that the abdominal CT of the patient did not reveal any abnormalities, while the contrast-enhanced MRI showed a mass in the head of the pancreas. A study from Peking Union Medical College Hospital indicates that, compared with conventional contrast-enhanced CT, MRI has higher sensitivity and specificity in diagnosing pancreatic gastrinoma[6]. Additionally, MRI aids in determining the proximity of the tumor to the pancreatic duct.

The patient experienced a severe esophageal stricture and proton pump inhibitor therapy was not effective. Therefore, endoscopic treatment was considered to improve esophageal stricture. Fugazza *et al*[7] reported that endoscopic dilation employing bougies or a balloon was proven successful in the majority of cases. However, it was difficult to maintain a satisfactory luminal diameter despite five sessions of EBD in our case, indicating the presence of RBES. RBES is not only difficult to dilate but also tends to recur within weeks. In such instances, alternative endoscopic treatments like stent placement or EIT combined with steroid injections should be considered. Manfredi *et al*[8] conducted a study to evaluate the safety and efficacy of EIT in a pediatric population with refractory esophageal strictures and showed that in the refractory group, 61% of the patients met the criteria for treatment success and 2.3% with adverse events. The patient in our case underwent ultrasonography-guided and wire-guided EIT combined with triamcinolone acetonide injection and showed great improvements initially. Unfortunately, the patient experienced esophageal perforation following the fourth session of EIT. Therefore, even though EIT shows promise as an adjunct treatment option for RBES and may be considered before surgical resection even in severe cases, the complication rate, albeit low, is significant. Consequently, EIT should only be considered by experienced endoscopists in close consultation with surgeons. Further prospective longitudinal studies are needed to validate this.

CONCLUSION

In conclusion, it is essential to diagnose gastrinoma as early as possible, as inadequately controlled acid secretion over an extended period increases the risk of developing severe esophageal strictures. In patients with esophageal strictures causing complete luminal obstruction, the blind reopening EIT presents challenges and carries a high risk of perforation. Additionally, it highlights the persistent challenges that gastroenterologists encounter in managing RBES despite the availability of various treatment options.

FOOTNOTES

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