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Contents

Thrice Monthly Volume 12 Number 4 February 6, 2024

EDITORIAL

- 671 Tenosynovitis of hand: Causes and complications Muthu S, Annamalai S, Kandasamy V
- 677 Early antiplatelet therapy used for acute ischemic stroke and intracranial hemorrhage Buddhavarapu V, Kashyap R, Surani S

MINIREVIEWS

681 Postoperative accurate pain assessment of children and artificial intelligence: A medical hypothesis and planned study

Yue JM, Wang Q, Liu B, Zhou L

688 Application and mechanisms of Sanhua Decoction in the treatment of cerebral ischemia-reperfusion injury Wang YK, Lin H, Wang SR, Bian RT, Tong Y, Zhang WT, Cui YL

ORIGINAL ARTICLE

Clinical and Translational Research

700 Identification and validation of a new prognostic signature based on cancer-associated fibroblast-driven genes in breast cancer

Wu ZZ, Wei YJ, Li T, Zheng J, Liu YF, Han M

Retrospective Study

- 721 Rehabilitation care for pain in elderly knee replacement patients Liu L, Guan QZ, Wang LF
- 729 Effect of early stepwise cardiopulmonary rehabilitation on function and quality of life in sepsis patients Zheng MH, Liu WJ, Yang J
- Influence of initial check, information exchange, final accuracy check, reaction information nursing on the 737 psychology of elderly with lung cancer

Jiang C, Ma J, He W, Zhang HY

746 Experience of primary intestinal lymphangiectasia in adults: Twelve case series from a tertiary referral hospital

Na JE, Kim JE, Park S, Kim ER, Hong SN, Kim YH, Chang DK

Observational Study

758 Perceived stress among staff in Saudi Arabian dental colleges before and after an accreditation process: A cross-sectional study

Shaiban AS



World Journal of Clinical Cases

Contents

Thrice Monthly Volume 12 Number 4 February 6, 2024

META-ANALYSIS

Comprehensive effects of traditional Chinese medicine treatment on heart failure and changes in B-type 766 natriuretic peptide levels: A meta-analysis

Xia LL, Yang SY, Xu JY, Chen HQ, Fang ZY

CASE REPORT

777 Mechanical upper bowel obstruction caused by a large trichobezoar in a young woman: A very unusual case report

Scherrer M, Kornprat P, Sucher R, Muehlsteiner J, Wagner D

782 Accidental placement of venous return catheter in the superior vena cava during venovenous extracorporeal membrane oxygenation for severe pneumonia: A case report

Song XQ, Jiang YL, Zou XB, Chen SC, Qu AJ, Guo LL

787 Gestational diabetes mellitus combined with fulminant type 1 diabetes mellitus, four cases of double diabetes: A case report

Li H, Chai Y, Guo WH, Huang YM, Zhang XN, Feng WL, He Q, Cui J, Liu M

- 795 Clinical experience sharing on gastric microneuroendocrine tumors: A case report Wang YJ, Fan DM, Xu YS, Zhao Q, Li ZF
- 801 Endoscopic retrograde appendicitis treatment for periappendiceal abscess: A case report Li OM, Ye B, Liu JW, Yang SW
- 806 Hemichorea in patients with temporal lobe infarcts: Two case reports Wang XD, Li X, Pan CL
- 814 Monomorphic epitheliotropic intestinal T-cell lymphoma with bone marrow involved: A case report Zhang FJ, Fang WJ, Zhang CJ
- 820 Inetetamab combined with tegafur as second-line treatment for human epidermal growth factor receptor-2-positive gastric cancer: A case report

Zhou JH, Yi QJ, Li MY, Xu Y, Dong Q, Wang CY, Liu HY

828 Pedicled abdominal flap using deep inferior epigastric artery perforators for forearm reconstruction: A case report

Jeon JH, Kim KW, Jeon HB

835 Individualized anti-thrombotic therapy for acute myocardial infarction complicated with left ventricular thrombus: A case report

Song Y, Li H, Zhang X, Wang L, Xu HY, Lu ZC, Wang XG, Liu B

842 Multiple paradoxical embolisms caused by central venous catheter thrombus passing through a patent foramen ovale: A case report

Li JD, Xu N, Zhao Q, Li B, Li L



Carta	World Journal of Clinical C	
Conter	Thrice Monthly Volume 12 Number 4 February 6, 2024	
847	Rupture of a giant jejunal mesenteric cystic lymphangioma misdiagnosed as ovarian torsion: A case report	
	Xu J, Lv TF	
853	Adenocarcinoma of sigmoid colon with metastasis to an ovarian mature teratoma: A case report	
	Wang W, Lin CC, Liang WY, Chang SC, Jiang JK	
859	Perforated gastric ulcer causing mediastinal emphysema: A case report	
	Dai ZC, Gui XW, Yang FH, Zhang HY, Zhang WF	
865	Appendicitis combined with Meckel's diverticulum obstruction, perforation, and inflammation in children: Three case reports	
	Sun YM, Xin W, Liu YF, Guan ZM, Du HW, Sun NN, Liu YD	



Contents

Thrice Monthly Volume 12 Number 4 February 6, 2024

ABOUT COVER

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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.

WJCC mainly publishes articles reporting research results and findings obtained in the field of clinical medicine and covering a wide range of topics, including case control studies, retrospective cohort studies, retrospective studies, clinical trials studies, observational studies, prospective studies, randomized controlled trials, randomized clinical trials, systematic reviews, meta-analysis, and case reports.

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CASE REPORT

Clinical experience sharing on gastric microneuroendocrine tumors: A case report

You-Jun Wang, Da-Ming Fan, Yu-Shuang Xu, Qi Zhao, Zhen-Fang Li

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Abstract

BACKGROUND

The majority of gastric neuroendocrine tumors (G-NENs) are present in various lesions under endoscopy, and they can be polypoid uplifts, submucosal tumors or papules, erosions, and ulcers. The lesions are mostly confined to the mucosal or submucosal layer, usually less than 2 cm, and exclusively localized to the gastric body or fundus. In type 1 G-NENs, about 22% of cases have no visible lesions under an endoscope, and such lesions can only be detected via biopsies (microcarcinoids).

CASE SUMMARY

A 67-year-old female patient with appetite loss for more than half a year and personal history of hyperthyroidism was admitted to our hospital. After admission, a random multi-point biopsy was performed on the gastric body, fundus, angle, and antrum through gastroscopy. Pathological examination showed chronic severe atrophic gastritis in the fundus and body of the stomach. The small curvature of the gastric body, the anterior wall of the gastric body, and the posterior wall of the gastric body displayed proliferation of intestinal chromaffin cells. The curvature of the gastric body showed neuroendocrine tumor G1 (carcinoid), while the antrum and angle of the stomach showed mild atrophic gastritis with mild intestinal metaplasia. Immunohistochemical examination showed that the greater curvature of the gastric body was Syn (+), CgA (+), and Ki-67 (+, approximately 1%), which is consistent with neuroendocrine tumors (grade 1). Regular gastroscopy and biopsy should be performed every one to two years to monitor G-NENs.



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Wang YJ et al. Clinical experience sharing on gastric microneuroendocrine tumors

CONCLUSION

In the case under study, the patient did not have any visible raised lesions under a gastroscope, and the lesions were found only after a random biopsy. This article combines the endoscopic manifestations and clinical features of the lesions in this case to improve the diagnosis of G-NENs.

Key Words: Neuroendocrine tumor; Micro carcinoids; Endoscopy; Case report

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Core Tip: Gastric neuroendocrine tumor (G-NEN) is a group of rare tumors originating from neuroendocrine cells in the stomach. Especially in type 1 G-NEN, some cases have no visible lesions under endoscopy, and these lesions can only be detected via biopsies (microcarcinoids). Therefore, it is particularly important to correctly identify and diagnose diseases. This article reports a case of a 67-year-old female patient with gastric microneuroendocrine tumors, and reviews relevant literature to better identify and diagnose gastric microneuroendocrine tumors.

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INTRODUCTION

Gastric neuroendocrine tumor (G-NEN) is a group of rare tumors originating from neuroendocrine cells in the stomach. However, with the development of endoscopic technology and the improvement of clinical understanding of diseases, more and more G-NEN has been found, and the incidence rate is increasing year by year. For different types of G-NEN, it is necessary to fully understand and master the endoscopic manifestations based on different background diseases, cell origins, and pathogenesis, in order to diagnose and differentiate.

In the case under study, the patient did not have any visible raised lesions under a gastroscope, and the lesions were found only after a random biopsy. By studying this case and reviewing relevant literature, we believe that endoscopists should improve their understanding of the endoscopic manifestations of G-NENs, especially in the identification of small lesions. Gastroscopic examination should be closely combined with the patient's medical history and clinical characteristics and carefully standardized. For patients at risk of developing G-NENs (such as patients with chronic atrophic gastritis who test negative for Helicobacter pylori (H. pylori) and have a dominant gastric body or patients with autoimmune gastritis and a medical history of more than two years), even though no visible protruding lesions are observed under an endoscope, random multipoint biopsy should be performed (especially on the four walls of the gastric body) to improve the positive rate of G-NEN diagnosis.

CASE PRESENTATION

Chief complaints

A 67-year-old female patient with appetite loss for more than half a year and personal history of hyperthyroidism was admitted to our hospital.

History of present illness

The patient suffered chronic anemia.

History of past illness

The patient has a history of chronic anemia and has not been treated.

Personal and family history

The patient denies any family history of anemia and tumors.

Physical examination

On physical examination, the vital signs were as follows: Body temperature, 36.3 °C; blood pressure, 121/73 mmHg; heart rate, 84 beats per min; respiratory rate, 18 breaths per min. Furthermore, the patient has anemic appearance and pale skin mucosa.



Laboratory examinations

Auxiliary examination after admission revealed the following: Hemoglobin = 69 g/L, mean corpuscular volume = 119 fL, vitamin B12 < 50 pg/mL, folic acid = 32.5 ng/mL, ferritin = 208.9 ng/mL, parietal cell antibody was negative, internal factor antibody was positive, gastrin 17 = 97.1 pmol/L (1.7-7.6 pmol/L), pepsinogen I/pepsinogen II = 2.17, C13 urea breath test was negative, and serum *H. pylori* antibody was negative.

Imaging examinations

Whole-body imaging procedures (computed tomography scan and abdominal ultrasonography) did not reveal metastatic involvement of any other organ.

Further diagnostic work-up

Gastroscopy was performed after admission and showed that the gastric body and fundus mucosa were thinned, red, and white (but mainly white). The submucosal vascular network was transparent, and the gastric antrum mucosa was normal (Figure 1). The diagnosis was chronic atrophic gastritis. In order to clarify the type of atrophic gastritis, random multipoint biopsies were performed on the gastric body, fundus, angle, and antrum. Pathological examination showed that the gastric fundus and gastric body had chronic severe atrophic gastritis. The lesser curvature of the gastric body, the anterior wall of the gastric body, and the posterior wall of the gastric body exhibited hyperplasia of enterochromaffin cells. The greater curvature of the gastric body showed neuroendocrine tumor G1 (carcinoid), and the gastric antrum and gastric angle exhibited mild atrophic gastritis with mild intestinal epithelial metaplasia. Immunohistochemical examination revealed that the greater curvature of the gastric body was Syn (+), CgA (+), and Ki-67 (+, about 1%), which is consistent with neuroendocrine tumors (Grade 1; Figure 2).

FINAL DIAGNOSIS

Based on the patient's medical history, clinical manifestations, laboratory examinations, and gastroscopy pathological results, we ultimately diagnosed the case as type 1 G-NENs grade G1 and autoimmune gastritis.

TREATMENT

Regular gastroscopy and biopsy should be performed every one to two years to monitor G-NENs. The patient also suffers from pernicious anemia. After being diagnosed upon admission, she has been taking oral vitamin B12 and folic acid, and have undergone regular blood routine checkups.

DISCUSSION

G-NENs can be classified into three types on the basis of the 2016 European Neuroendocrine Tumor Society (ENETS) guidelines (Table 1)[1]. Type 1 G-NENs are common in women, usually G1 level, and rarely metastasize[2]. The background mucosa of autoimmune gastritis should be identified first. Under white light endoscopy, it appears as extensive atrophy of the gastric fundus and body, and the gastric antrum has a normal mucosa and can be accompanied with atrophy^[3]. Atrophic mucosa can be seen *via* magnifying narrowband imaging endoscopy (ME-NBI); it has tightly arranged small circular and oval pores surrounded by a network of capillaries[4]. It is considerably different from the granular or papillary atrophy caused by *H. pylori* infection. In this context, multiple different phenotypes of protruding lesions, including residual gastric fundus glands, proliferative polyps, early gastric cancer, and type I g-NET, often occur [3], and endoscopists should learn to recognize and differentiate them. Typical type I g-NET often presents as submucosal protrusion lesions with a yellow or red color under white light endoscopy and sometimes a central depression [5,6]. NBI shows a light-brown area, and ME-NBI shows a cyan, spiral-shaped, abnormally dilated subepithelial blood vessel in the white area, which is dilated like a gyrus[6]. This ME-NBI endoscopic appearance needs to be differentiated from gastric fundus adenocarcinoma, which often occurs in a nonatrophic, H. pylori-negative, gastric mucosa background with a single submucosal protuberant lesion. Endoscopists can easily diagnose G-NENs via biopsy pathology and immunohistochemistry as long as suspected lesions are found through endoscopy. However, for type 1 G-NENs, about 22% of cases have no visible lesions under an endoscope, and only through blind examination of the stomach body and fundus can the lesions be found under a microscope[7]. In the case presented in this study, the patient did not have any obvious gastrointestinal discomfort symptoms, and no visible raised lesions were found under an endoscope. Under ordinary white light gastroscopy, this case was manifested as chronic atrophic gastritis. If the endoscopist had not performed random biopsy at the time, the G-NENs would have been missed in the diagnosis.

Given the inert growth of type 1 G-NENs, the lesions can be followed up for a long time. Researchers recommend the use of biopsy forceps to remove all visible lesions and endoscopic mucosal resection for lesions greater than 5 mm[8]. ENETS guidelines recommend that for tumors \geq 1 cm, endoscopic resection can be considered, and preoperative endoscopic ultrasound examination is required to assess the risk of metastasis. The patient in this case did not have any visible elevated lesions under a gastroscope, so regular follow-up with gastroscopy and biopsy every 1-2 years is

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Table 1 Classification of gastric neuroendocrine neoplasms on the basis of the 2016 European Neuroendocrine Tumor Society auidelines

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	Туре 1	Туре 2	Туре 3
Proportion among G- NENs, %	70-80	5-6	14-25
Tumor characteristics	Often small (< 1-2 cm), multiple in 65% of cases, polypoid in 78% of cases	Often small (< 1-2 cm) and multiple, polypoid	Unique, often large (> 2 cm) polypoid and ulcerated
Associated conditions	Atrophic body, gastritis	Gastrinoma/MEN-1	None
Pathology	NET G1-G2	NET G1-G2	NET G3
Serum gastrin levels	↑	\uparrow	Normal
Gastric pH	↑	Ļ	Normal
Metastases, %	2-5	10-30	50-100
Tumor-related deaths, %	0	< 10	25-30

G-NENs: Gastric neuroendocrine tumors; NET: Neuroendocrine tumor; MEN-1: Multiple endocrine neoplasia type 1.



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Figure 1 Gastroscopy in a patient with gastric microneuroendocrine neoplasms. The gastric body and fundus mucosa were obviously thinned, red and white, mainly white, the submucosal vascular network was transparent, and the gastric antrum mucosa was normal. A: Upper part of the greater curvature of the stomach; B: The lower part of the greater curvature of the stomach; C: The posterior wall of the lesser curvature of the gastric body; D: Gastric angle; E: Gastric fundus; F: Gastric antrum.

recommended.

CONCLUSION

In summary, by studying this case and reviewing relevant literature, we believe that endoscopists should improve their understanding of the endoscopic manifestations of G-NENs, especially in the identification of small lesions. Gastroscopic examination should be closely combined with the patient's medical history and clinical characteristics and carefully standardized. For patients at risk of developing G-NENs (such as patients with chronic atrophic gastritis who test



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Figure 2 Pathological and immunohistochemical examination of the greater curvature of the gastric body. A: Hematoxylin and eosin mucosal tissue atrophy, lamina propria oxyntic glands disappeared, replaced by incomplete intestinal metaplasia glands and pseudopyloric glands, local mucosal lamina propria showed loss of proper glands, replaced by epithelioid/spindle-like cells nest; B: Ki-67 (+, about 1%); C: CgA (+); D: Syn (+).

negative for *H. pylori* and have a dominant gastric body or patients with autoimmune gastritis and a medical history of more than two years), even though no visible protruding lesions are observed under an endoscope, random multipoint biopsy should be performed (especially on the four walls of the gastric body) to improve the positive rate of GNEN diagnosis. For patients with a clear diagnosis of gastric microneuroendocrine tumors, magnifying gastroscopy coupled with NBI and endoscopic staining can be performed during long-term endoscopic follow-up to avoid missing gastric microlesions.

FOOTNOTES

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Wang YJ et al. Clinical experience sharing on gastric microneuroendocrine tumors

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