

World Journal of *Clinical Cases*

World J Clin Cases 2023 February 6; 11(4): 719-978



Contents

Thrice Monthly Volume 11 Number 4 February 6, 2023

MINIREVIEWS

- 719 Development and refinement of diagnostic and therapeutic strategies for managing patients with cardiogenic stroke: An arduous journey
Fan ZX, Liu RX, Liu GZ
- 725 Portal vein aneurysm-etiology, multimodal imaging and current management
Kurtcehajic A, Zerem E, Alibegovic E, Kunosic S, Hujdurovic A, Fejzic JA

ORIGINAL ARTICLE

Clinical and Translational Research

- 738 CD93 serves as a potential biomarker of gastric cancer and correlates with the tumor microenvironment
Li Z, Zhang XJ, Sun CY, Fei H, Li ZF, Zhao DB

Retrospective Study

- 756 Chest computed tomography findings of the Omicron variants of SARS-CoV-2 with different cycle threshold values
Ying WF, Chen Q, Jiang ZK, Hao DG, Zhang Y, Han Q
- 764 Major depressive disorders in patients with inflammatory bowel disease and rheumatoid arthritis
Haider MB, Basida B, Kaur J
- 780 Selective laser trabeculoplasty as adjunctive treatment for open-angle glaucoma *vs* following incisional glaucoma surgery in Chinese eyes
Zhu J, Guo J
- 788 Efficacy of transvaginal ultrasound-guided local injections of absolute ethanol for ectopic pregnancies with intrauterine implantation sites
Kakinuma T, Kakinuma K, Matsuda Y, Yanagida K, Ohwada M, Kaijima H

Clinical Trials Study

- 797 Efficacy of incremental loads of cow's milk as a treatment for lactose malabsorption in Japan
Hasegawa M, Okada K, Nagata S, Sugihara S

Observational Study

- 809 Transdiagnostic considerations of mental health for the post-COVID era: Lessons from the first surge of the pandemic
Goldstein Ferber S, Shoval G, Rossi R, Trezza V, Di Lorenzo G, Zalsman G, Weller A, Mann JJ
- 821 Effect of patient COVID-19 vaccine hesitancy on hospital care team perceptions
Caspi I, Freund O, Pines O, Elkana O, Ablin JN, Bornstein G

Randomized Clinical Trial

- 830 Improvement of inflammatory response and gastrointestinal function in perioperative of cholelithiasis by Modified Xiao-Cheng-Qi decoction
Sun BF, Zhang F, Chen QP, Wei Q, Zhu WT, Ji HB, Zhang XY

CASE REPORT

- 844 Metagenomic next-generation sequencing for pleural effusions induced by viral pleurisy: A case report
Liu XP, Mao CX, Wang GS, Zhang MZ
- 852 *Clostridium perfringens* gas gangrene caused by closed abdominal injury: A case report and review of the literature
Li HY, Wang ZX, Wang JC, Zhang XD
- 859 Is lymphatic invasion of microrectal neuroendocrine tumors an incidental event?: A case report
Ran JX, Xu LB, Chen WW, Yang HY, Weng Y, Peng YM
- 866 *Pneumocystis jirovecii* diagnosed by next-generation sequencing of bronchoscopic alveolar lavage fluid: A case report and review of literature
Cheng QW, Shen HL, Dong ZH, Zhang QQ, Wang YF, Yan J, Wang YS, Zhang NG
- 874 Identification of 1q21.1 microduplication in a family: A case report
Huang TT, Xu HF, Wang SY, Lin WX, Tung YH, Khan KU, Zhang HH, Guo H, Zheng G, Zhang G
- 883 Double pigtail catheter reduction for seriously displaced intravenous infusion port catheter: A case report
Liu Y, Du DM
- 888 Thyroid storm in a pregnant woman with COVID-19 infection: A case report and review of literatures
Kim HE, Yang J, Park JE, Baek JC, Jo HC
- 896 Computed tomography diagnosed left ovarian venous thrombophlebitis after vaginal delivery: A case report
Wang JJ, Hui CC, Ji YD, Xu W
- 903 Preoperative 3D reconstruction and fluorescent indocyanine green for laparoscopic duodenum preserving pancreatic head resection: A case report
Li XL, Gong LS
- 909 Unusual presentation of systemic lupus erythematosus as hemophagocytic lymphohistiocytosis in a female patient: A case report
Peng LY, Liu JB, Zuo HJ, Shen GF
- 918 Polyarteritis nodosa presenting as leg pain with resolution of positron emission tomography-images: A case report
Kang JH, Kim J
- 922 Easily misdiagnosed complex Klippel-Trenaunay syndrome: A case report
Li LL, Xie R, Li FQ, Huang C, Tuo BG, Wu HC

- 931 Benign lymphoepithelial cyst of parotid gland without human immunodeficiency virus infection: A case report
Liao Y, Li YJ, Hu XW, Wen R, Wang P
- 938 Epithelioid trophoblastic tumor of the lower uterine segment and cervical canal: A case report
Yuan LQ, Hao T, Pan GY, Guo H, Li DP, Liu NF
- 945 Treatment of portosystemic shunt-borne hepatic encephalopathy in a 97-year-old woman using balloon-occluded retrograde transvenous obliteration: A case report
Nishi A, Kenzaka T, Sogi M, Nakaminato S, Suzuki T
- 952 Development of Henoch-Schoenlein purpura in a child with idiopathic hypereosinophilia syndrome with multiple thrombotic onset: A case report
Xu YY, Huang XB, Wang YG, Zheng LY, Li M, Dai Y, Zhao S
- 962 Three cases of jejunal tumors detected by standard upper gastrointestinal endoscopy: A case series
Lee J, Kim S, Kim D, Lee S, Ryu K
- 972 Omental infarction diagnosed by computed tomography, missed with ultrasonography: A case report
Hwang JK, Cho YJ, Kang BS, Min KW, Cho YS, Kim YJ, Lee KS

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.

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The WJCC is now abstracted and indexed in Science Citation Index Expanded (SCIE, also known as SciSearch®), Journal Citation Reports/Science Edition, Current Contents®/Clinical Medicine, PubMed, PubMed Central, Scopus, Reference Citation Analysis, China National Knowledge Infrastructure, China Science and Technology Journal Database, and Superstar Journals Database. The 2022 Edition of Journal Citation Reports® cites the 2021 impact factor (IF) for WJCC as 1.534; IF without journal self cites: 1.491; 5-year IF: 1.599; Journal Citation Indicator: 0.28; Ranking: 135 among 172 journals in medicine, general and internal; and Quartile category: Q4. The WJCC's CiteScore for 2021 is 1.2 and Scopus CiteScore rank 2021: General Medicine is 443/826.

RESPONSIBLE EDITORS FOR THIS ISSUE

Production Editor: Si Zhao; Production Department Director: Xu Guo; Editorial Office Director: Jin-Lei Wang.

NAME OF JOURNAL

World Journal of Clinical Cases

ISSN

ISSN 2307-8960 (online)

LAUNCH DATE

April 16, 2013

FREQUENCY

Thrice Monthly

EDITORS-IN-CHIEF

Bao-Gan Peng, Jerzy Tadeusz Chudek, George Kontogeorgos, Maurizio Serati, Ja Hyeon Ku

EDITORIAL BOARD MEMBERS

<https://www.wjgnet.com/2307-8960/editorialboard.htm>

PUBLICATION DATE

February 6, 2023

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INSTRUCTIONS TO AUTHORS

<https://www.wjgnet.com/bpg/gerinfo/204>

GUIDELINES FOR ETHICS DOCUMENTS

<https://www.wjgnet.com/bpg/GerInfo/287>

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<https://www.wjgnet.com/bpg/gerinfo/240>

PUBLICATION ETHICS

<https://www.wjgnet.com/bpg/GerInfo/288>

PUBLICATION MISCONDUCT

<https://www.wjgnet.com/bpg/gerinfo/208>

ARTICLE PROCESSING CHARGE

<https://www.wjgnet.com/bpg/gerinfo/242>

STEPS FOR SUBMITTING MANUSCRIPTS

<https://www.wjgnet.com/bpg/GerInfo/239>

ONLINE SUBMISSION

<https://www.f6publishing.com>



Is lymphatic invasion of microrectal neuroendocrine tumors an incidental event?: A case report

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Specialty type: Gastroenterology and hepatology

Provenance and peer review: Unsolicited article; Externally peer reviewed.

Peer-review model: Single blind

Peer-review report's scientific quality classification

Grade A (Excellent): A

Grade B (Very good): 0

Grade C (Good): 0

Grade D (Fair): D

Grade E (Poor): 0

P-Reviewer: Cerwenka H, Austria; Haddadi S, Algeria

Received: August 30, 2022

Peer-review started: August 30, 2022

First decision: December 9, 2022

Revised: January 2, 2023

Accepted: January 16, 2023

Article in press: January 16, 2023

Published online: February 6, 2023



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Abstract

BACKGROUND

A rectal neuroendocrine tumor (rNET) is a malignant tumor originating from neuroendocrine cells. Currently, tumor size is the primary basis for assessing tumor risk.

CASE SUMMARY

This article reports the case of a 46-year-old male patient who underwent a colonoscopy that found a 3 mm rectal polypoid bulge. The pathological examination of a sample collected with biopsy forceps revealed a neuroendocrine tumor. Further endoscopic submucosal dissection rescue therapy was used. The presence of lymphatic vessels indicated that the tumor had infiltrated the negative resection margin. The lesion was located in the distal rectum near the anal canal. Therefore, to ensure the patient's quality of life, follow-up observation was conducted after full communication with the patient. No tumor recurrence or distant metastasis has been found during the 13-mo follow-up after surgery.

CONCLUSION

Despite the presence of lymphatic invasion and extremely small diameter rNETs in our case, this phenomenon may not imply a higher risk of distant lymph node and organ metastasis.

Key Words: Rectal neuroendocrine tumor; Tumor size; Lymphatic invasion; Case report

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Core Tip: Due to the heterogeneity and atypical symptoms of rectal neuroendocrine tumors, in the process of clinical diagnosis and treatment, it is not sufficient to judge the risk of tumor metastasis based only on tumor size and lymphovascular invasion. Therefore, during treatment, it is necessary to formulate an individualized plan, undertake close follow-up observation, and try to improve the quality of life and disease prognosis of patients while reducing the burden of treatment.

Citation: Ran JX, Xu LB, Chen WW, Yang HY, Weng Y, Peng YM. Is lymphatic invasion of microrectal neuroendocrine tumors an incidental event?: A case report. *World J Clin Cases* 2023; 11(4): 859-865

URL: <https://www.wjgnet.com/2307-8960/full/v11/i4/859.htm>

DOI: <https://dx.doi.org/10.12998/wjcc.v11.i4.859>

INTRODUCTION

A rectal neuroendocrine tumor (rNET) is a rectal malignancy that originates from neuroendocrine cells with an insidious onset and a lack of specific first symptoms[1]. In recent years, with the extensive development of colon cancer screening programs and the improvement of endoscopic diagnosis and treatment techniques, the incidence of rNET has increased annually[2]. The incidence of rNET has increased nearly 10 times in the past 30 years, indicating that this type of tumor may not be uncommon [3]. Clinically, rNETs are usually found during endoscopy, the vast majority are 10 mm or less in diameter[4]. According to the European Neuroendocrine Tumor Society guidelines, tumor size greater than 20 mm is a risk factor for tumor invasion and metastasis, but vascular invasion, lymph node metastasis, and distant metastasis may also occur in the case of smaller tumors[5,6]. Currently, for rNETs with a tumor size of 10 mm or less, existing treatment guidelines recommend radical surgery and, in the presence of definite vascular invasion, additional lymph node dissection[7,8]. Here, we report a case of a 3 mm rNET located in the distal rectum with lymphatic invasion after endoscopic resection.

CASE PRESENTATION

Chief complaints

Polypoid bulge found on colonoscopy.

History of present illness

A 46-year-old male patient underwent colonoscopy and was found to have a 3-mm-sized polypoid bulge with a smooth surface in the rectum 3 cm from the anus. After sample collection with biopsy forceps, the pathological diagnosis was neuroendocrine tumor (NET) (Figure 1).

History of past illness

No special history of past illness.

Personal and family history

The patient's father had a history of colon cancer. His Personal history has nothing notable.

Physical examination

No special.

Laboratory examinations

No special.

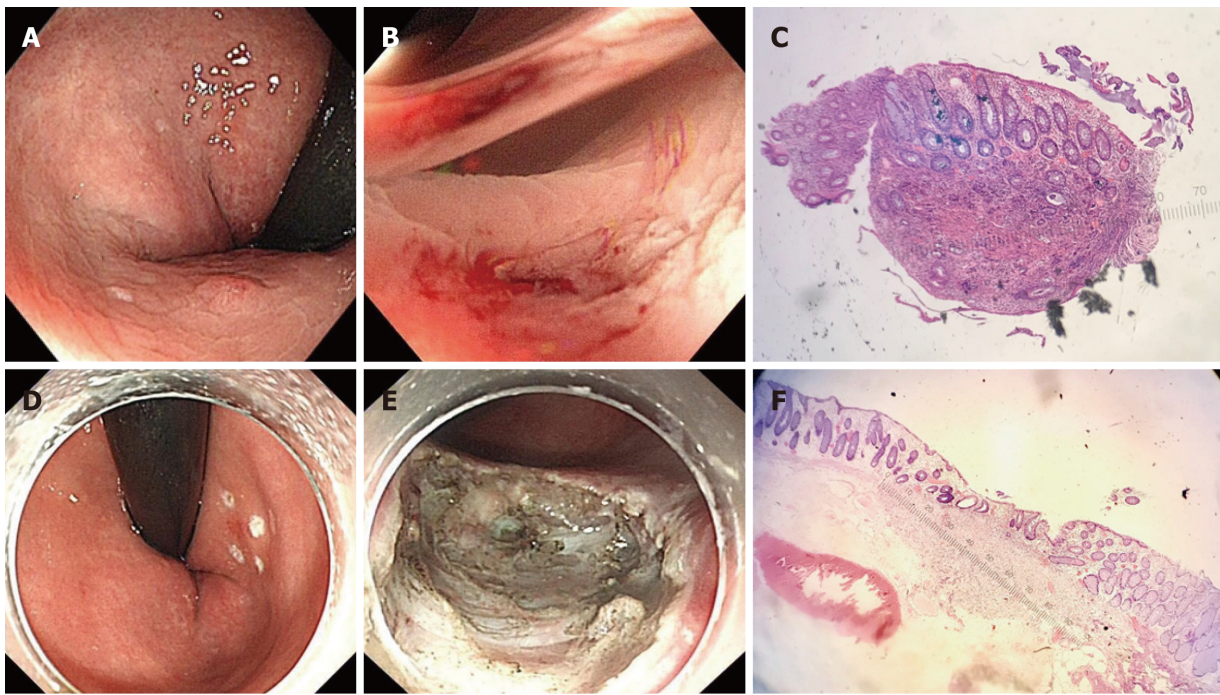
Imaging examinations

Before endoscopic submucosal dissection (ESD), computed tomography (CT) showed no abnormalities in the enhancement of the chest and abdomen.

To clarify whether additional surgery was required, further assessment by ⁶⁸Gallium labeled somatostatin analogues-positron emission tomography (⁶⁸Ga-SSA-PET)/CT was used, but the results showed no abnormalities.

Pathological examinations

The pathological diagnosis of the specimen after ESD rescue therapy was rNET G1. The lesion



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Figure 1 The endoscopic manifestation of the rectal neuroendocrine tumor. A-C: Rectal neuroendocrine tumor (rNET): under a white light endoscope, the surface is smooth, sessile, and the same color as the surrounding mucosa (A); after biopsy forceps (B); the first hematoxylin and eosin (H&E) stained pathological smear after the tumor was removed by biopsy forceps (C, $\times 40$). Endoscopic submucosal dissection (ESD) remedial treatment; D-F: Under white light endoscope, before ESD (D); after additional ESD (E); HE stained pathological smears of specimens after ESD (F, $\times 40$).

infiltrated into the submucosa. The depth of submucosal infiltration was 1000 μm . The distance between the deepest infiltration of the lesion and the basal incision margin was 500 μm . The lesion size was 2550 μm . The horizontal and vertical resection margins were negative (Figure 1). Immunohistochemical (IHC) results were as follows: CK (weak +), Vim (-), Syn (+), CD56 (strong +), CgA (strong +), CK7 (-), CK20 (weak +), Villin (+), CEA (focal+), and Ki-67 (2%; Figure 2). The lymphatic invasion was confirmed by D2-40 and CD31 staining (Figure 3).

MULTIDISCIPLINARY EXPERT CONSULTATION

After the pathological examination of the biopsy clamped specimen suggested neuroendocrine tumor, the patient underwent multidisciplinary consultation with oncology, surgery and nuclear medicine, and finally decided to complete ^{68}Ga -SSA-PET/CT, and no distant metastasis was found. Therefore, we decided to perform ESD after consulting the patient's consent and followed up regularly after the operation.

FINAL DIAGNOSIS

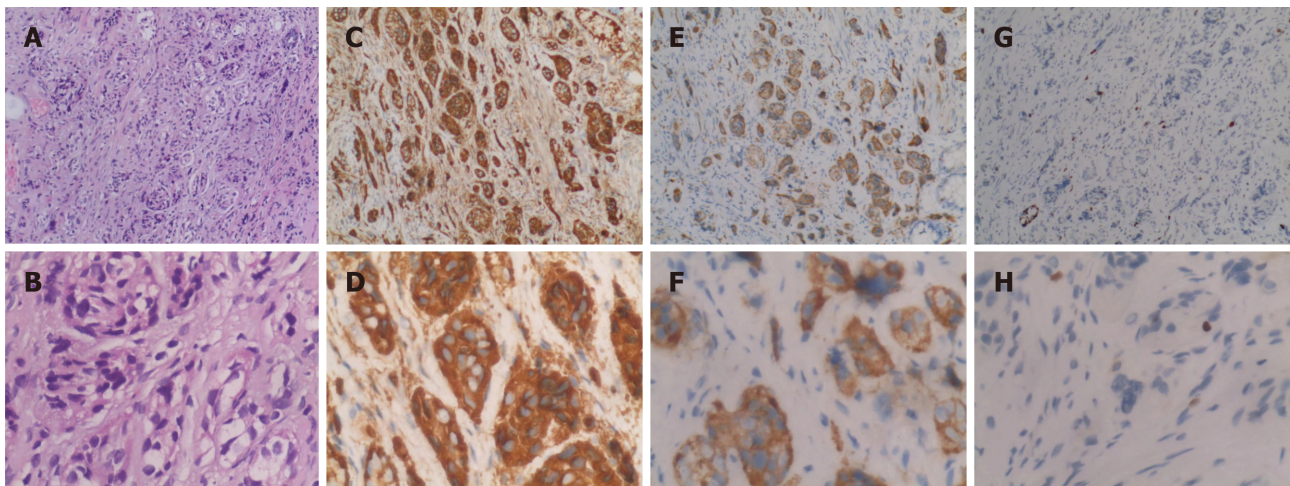
The pathological diagnosis of the specimen after ESD rescue therapy was rNET G1.

TREATMENT

ESD salvage therapy was applied.

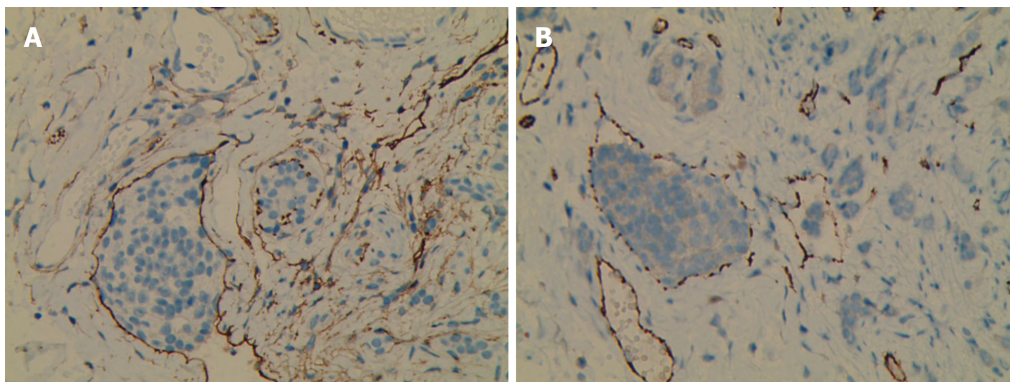
OUTCOME AND FOLLOW-UP

No tumor recurrence or distant metastasis was detected at 13 mo postoperative follow-up using endoscopy and CT-enhanced scans of the whole abdomen (including the pelvis).



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Figure 2 Pathological smears of tumor tissue after various immunohistochemical staining. A-H: HE (A, $\times 100$; B, $\times 400$); CgA (C, $\times 100$; D, $\times 400$); Syn (E, $\times 100$; F, $\times 400$); and ki67 (G, $\times 100$; H, $\times 400$).



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Figure 3 The tumor was found to have lymphatic invasion after staining with CD31 (A) and D2-40 (B). A and B: $\times 200$.

DISCUSSION

Gastroenteropancreatic neuroendocrine tumors (GEP-NETs) are the most common type of NETs[9]. The rectum is the most common site for GEP-NETs in Asian populations[10]. In recent years, with the extensive development of colorectal cancer screening programs and the improvement of endoscopic diagnosis and treatment techniques, the incidence of rNET has continued to rise.

Lymphovascular invasion (LVI) refers to the presence of tumor cells in blood vessels and lymphatic channels. LVI is closely related to tumor metastasis in distant organs and lymph nodes. A meta-analysis found that LVI was associated with an increased risk of distant lymph node metastasis (LNM) after local resection of rNETs[11]. Therefore, LVI is a risk factor for LNM. Another meta-analysis found that, for small rNETs with a tumor size of 10 mm or less, even in the presence of LVI, the prognosis was good after endoscopic resection, with a 5-year follow-up recurrence rate of only 0.3%. In addition, tiny rNETs smaller than 5 mm had a lower incidence of LVI than rNETs with a tumor size of 5-10 mm[12].

In recent years, the detection rate of LVI in rNETs has increased significantly due to immunohistochemical detection methods[12-14]. This increasing trend is proportional to tumor size, even in the fraction of rNETs less than or equal to 5 mm, the detection rate is still about 50%[13]. One study reported that the detection rate of LVI by IHC staining (56.9%) was 6 times higher than that of hematoxylin and eosin (HE) staining alone (8.8%)[15]. This result suggests that the possibility of LVI in small rNETs was underestimated prior to using IHC staining. Both vascular and lymphatic invasion are included in LVI and usually need to be distinguished by IHC detection. Vascular invasion and lymphatic invasion have different effects on LNM. In small rNETs, vascular invasion may have a greater impact on LNM than lymphatic invasion[11].

In this rNET patient, the endoscopic tumor size was 3 mm with lymphatic invasion, the smallest rNET with LVI reporting in all existing research. At the same time, no instances of LNM or distant metastasis were found after the enhanced chest and total abdominal CT and 68G-SSA-PET/CT. During

the 13-mo follow-up after ESD, we did not find tumor recurrence or distant metastasis using endoscopy at the 6-mo and 1-year postoperative follow-up. Whole abdominal CT-enhanced scans did not show tumor recurrence or distant metastasis. These findings suggest that, in small (< 10 mm) or even tiny (< 5 mm) rNETs, although there is lymphatic invasion, lymphatic invasion may not be a determinant of LNM.

A cohort study found that after 6 years of follow-up in patients with rNETs who underwent endoscopic resection, about 1% of the patients developed LNM or distant metastasis, and the tumor grades were G2. In contrast, patients with grade G1 rNETs whose tumor size was less than 20 mm and who underwent endoscopic resection did not develop lymph node or distant metastasis[16]. Therefore, the risk factors for lymph node and distant metastasis of rNETs with a tumor size less than 20 mm need further study.

Although this patient had lymphatic invasion, no lymph node or distant metastasis was found. Therefore, in the absence of a well-established correlation between LVI and LNM of rNETs with a tumor size less than 20 mm, additional surgery may not benefit all patients with LVI. The tumor grade, tumor size, LVI, and depth of invasion may still need to be comprehensively considered to determine whether to perform additional surgery. In addition, imaging studies and radionuclide scintigraphy can be considered when it is unclear whether additional surgery is required[15].

In this patient, the tumor surface was smooth, and endoscopy showed that the tumor size was small. The tumor was misdiagnosed as a hyperplastic polyp and was subjected to examination with biopsy forceps. The size of the lesion was 1500 μ m. Residual lesions were found after ESD salvage surgery, in which the tumor size was found to be 1050 μ m. These results indicated that simple biopsy forceps were insufficient for such rNETs, and ESD salvage was a suitable option. For hyperplastic polyps of the left colon and rectum with a tumor size of 5 mm or less, both the Japanese Society of Gastroenterology and the European Society for Gastrointestinal Endoscopy recommend endoscopic follow-up only[17,18]. The rectum is a high-incidence site of NETs. Therefore, we suggest that, if the lesions are smooth and bulging, especially when the margins of the lesions are not clear, the possibility of NETs should be considered. The possibility of NETs should be excluded by forceps and biopsy.

For this patient, to ensure his quality of life, we did not choose to conduct surgical intervention, but rather continued with follow-up observation. According to previous literature reports, the metastasis of rNETs can occur after more than 10 years[19,20]. Although no LNM and distant metastasis were found in the short-term follow-up of this patient, long-term follow-up is extremely important, especially for lymph node and liver metastasis. Therefore, this patient's end point of follow-up should be at least 10 years. In the subsequent follow-up schedule, we will perform endoscopy and CT-enhanced scans of the whole abdomen (including the pelvis) once a year, with an additional 68Ga-SSA-PET/CT if abnormalities are detected during the follow-up.

CONCLUSION

rNETs have heterogeneity and atypical symptoms. Therefore, it is not sufficient to judge the risk of tumor metastasis during clinical diagnosis and treatment based only on tumor size and LVI. Instead, during treatment, it is necessary to formulate an individualized plan, undertake close follow-up observation, and try to improve the quality of life and disease prognosis of patients while reducing the burden of treatment.

FOOTNOTES

Author contributions: Ran JX was responsible for writing the paper; Xu LB was responsible for patient treatment and study design; Chen WW and Yang HY were responsible for collecting and analyzing data; Weng Y and Peng YM were responsible for patient follow-up.

Supported by Guizhou Science and Technology Plan Project, No. ZK2022-General-443; and Science and Technology Fund of Guizhou Provincial Health and Health Commission, No. gzwkj2023-135.

Informed consent statement: Written informed consent was obtained from the patient for publication of this report and all accompanying images.

Conflict-of-interest statement: The authors have no conflicts of interest to declare.

CARE Checklist (2016) statement: The authors have read the CARE Checklist (2016), and the manuscript was prepared and revised according to the CARE Checklist (2016).

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S-Editor: Gong ZM

L-Editor: A

P-Editor: Gong ZM

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