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CASE REPORT

A case of rectal multiple neuroendocrine tumors by endoscopic treatment

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Abstract

Rectal multiple neuroendocrine tumors (M-NETs) are rare, with few reports on the characteristics and treatment. This report describes a case of a 35-year-old man who developed rectal M-NETs, with 5 tumors, measuring 1-6 mm. All the 5 tumors were removed by endoscopic submucosal dissection (ESD), with a sufficient pathologically normal margin. This case of rectal M-NETs, which was treated successfully by endoscopy, therefore contributes to providing new insights into the diagnosis and treatment of rectal M-NETs. This article discussed the presentation, diagnosis, and management of rectal M-NETs to help gastroenterologists provide diagnosis and treatment for patients with rectal M-NETs.

Introduction

Neuroendocrine tumors (NETs) are a group of tumors originating from neuroendocrine cells. Typically, NETs present as a single lesion, mainly in the in gastrointestinal tract and pancreas (Kawasaki, 2023). It is reported that the incidence of rectal NETs is 0.17% (Maione, 2021). Multiple neuroendocrine tumors (M-NETs) are particularly rare in the rectum (Park, 2018). Common symptoms of rectal M-NETs include abdominal pain, changes in bowel habits, and hematochezia, which are similar to the common rectal diseases, thus complicating the accuracy of disease diagnosis (Xie, 2018). These tumors often metastasize to the liver, and the treatment requires a multi-disciplinary approach (Harrelson, 2023). However, due to the rarity of rectal M-NETs, there is no guideline or consensus on clinical characteristics and treatment, so it is urgent to accumulate similar cases. This study will report a case of rectal M-NETs, aiming to discuss its clinical, endoscopic and pathological feature.

Case Report

The patient was a 35-year-old man with a history of hematochezia for 1 week and no signs of diarrhea, hematochezia, abdominal pain, and carcinoid syndrome. He underwent colonoscopy, which showed five yellowish subepithelial nodules in the

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rectum. Based on endoscopic findings, those lesions were strongly suspected as rectal M-NETs. Therefore, he was transferred to our institute for treatment of rectal M-NETs. Apart from gout and smoking, he has no other specific illnesses, alcohol consumption, or a family history of cancer. There were no abnormalities in hemoglobin, white blood cells, platelets and tumor markers.

Colonoscopy revealed five yellow subepithelial lesions in the rectum, 1-6 mm in diameter (Figure 1). To detect separation of a submucosal tumor from muscularis propria and determine treatment options, the patient then underwent ultrasonography colonoscopy. 20 MHz ultrasound probe showed that the tumors originate from the submucosal, and the internal echo is uniform (Figure 2). Lesions were removed by endoscopic submucosal dissection (ESD) (Figure 3). Chromogranin A (CgA) and synaptophysin (SYN) immunohistochemical staining were positive, which were neuroendocrine tumor markers (Figure 4). All five epithelial lesions were limited to the submucosal, and confirmed by pathologists as WHO grades NET G1 (Rindi, 2022). 1%–2% of the cells were Ki67-positive, while mitosis was observed to be less than 2/10 high power fields (Figure 4). P53 staining positive cells were rarely observed in tumors (Figure 4). Also, postoperative pathology were negative for all surgical margins, vascular and lymphatic invasion.

Computed tomography (CT) of the pelvic revealed a slight local thickening of the rectal wall (Figure 5A). While CT of the abdominal showed no evidence of liver, lymph nodes, and other distant metastasis (Figure 5B).

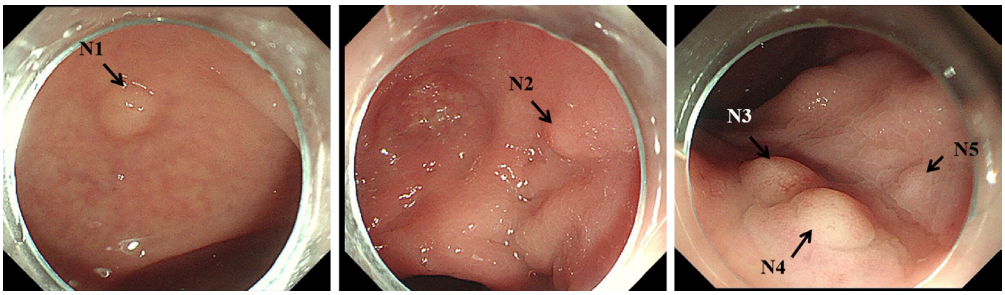

Figure 1. Endoscopic views of the patient

Notes: Five yellowish sub-epithelial lesions at the rectum were observed, measuring 6 × 5 mm, 4 × 3 mm, 5 × 5 mm, 6 × 5 mm and 1 × 1 mm, respectively.

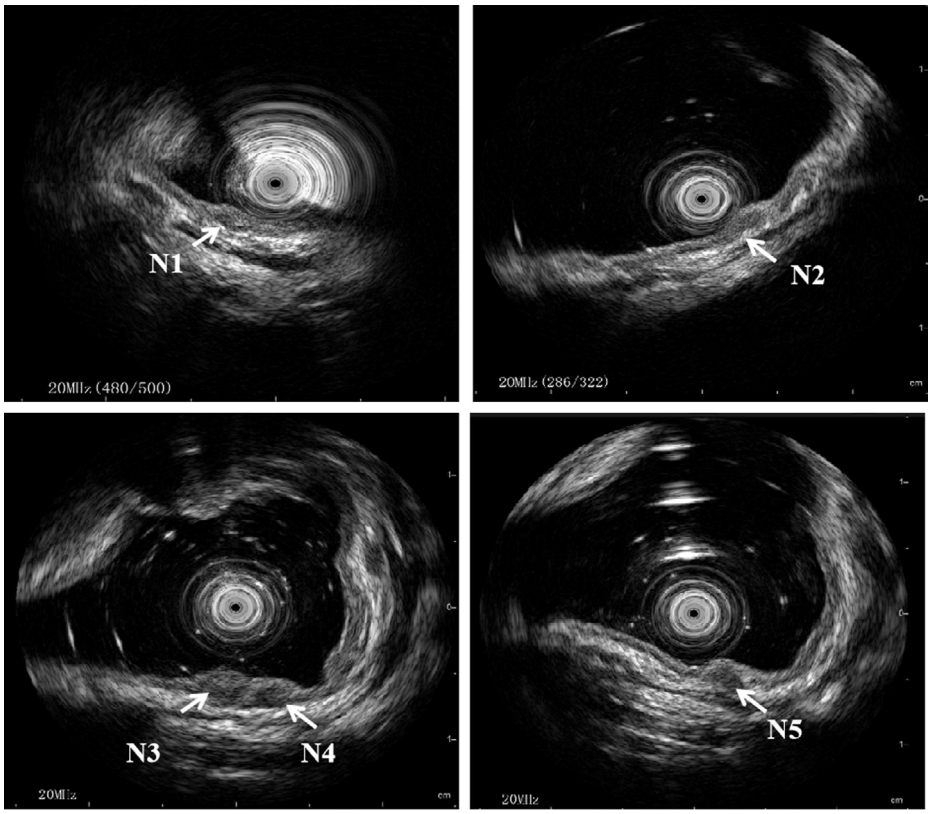

Figure 2. Ultrasonography colonoscopy of the patient

Notes: The lesions originated from the submucosal layer, and the internal echo was homogeneous, with low echo and clear boundaries.

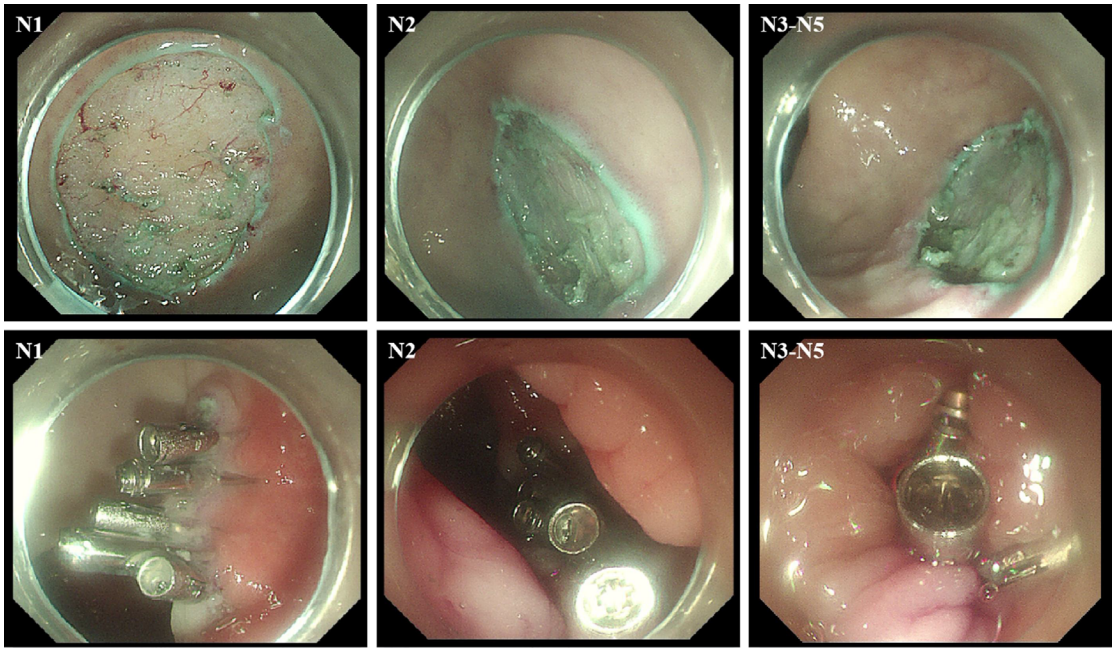

Figure 3. Lesions were removed by ESD

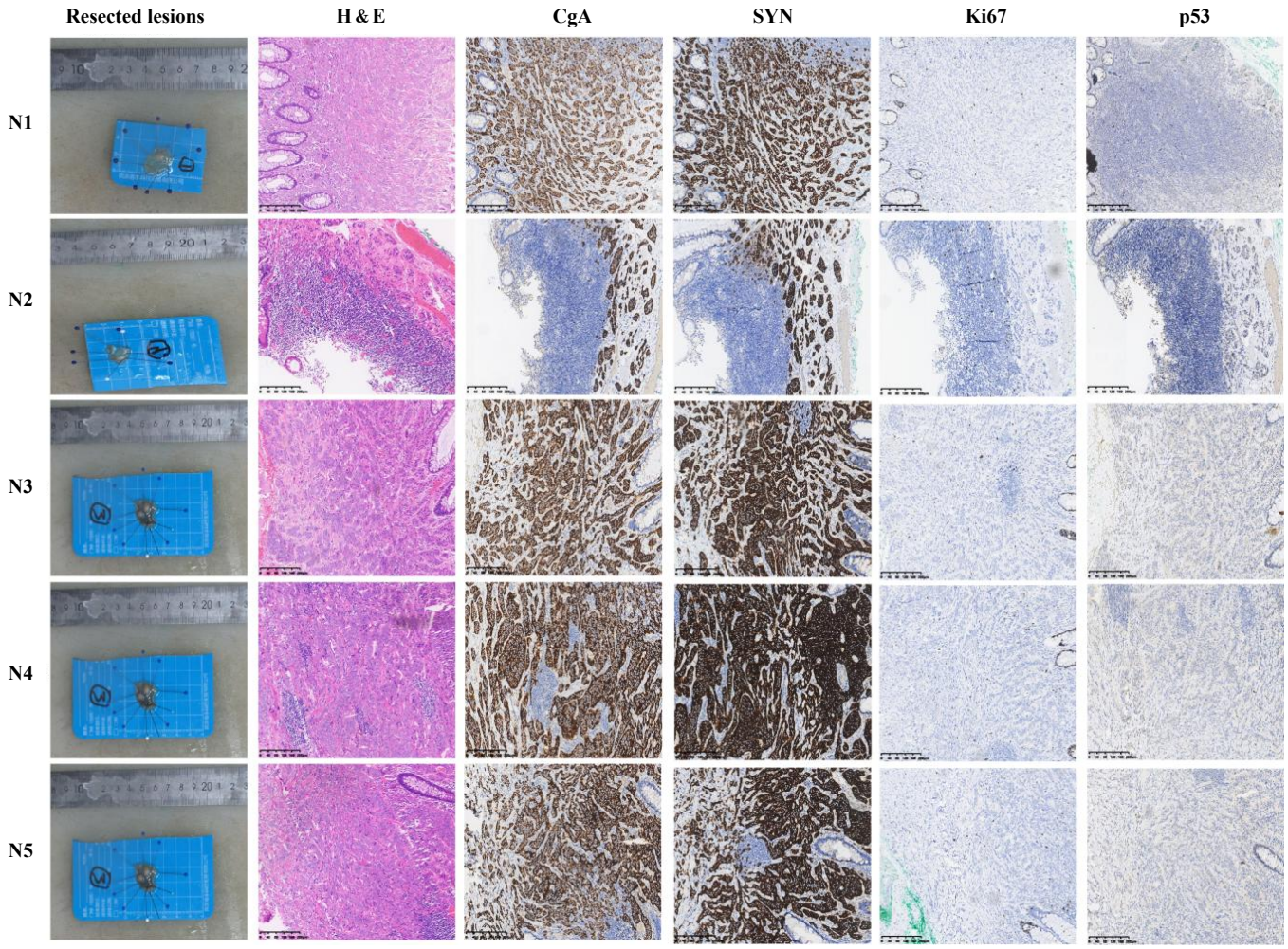

Figure 4. Pathologic findings

Notes: Resected lesions were stained with Hematoxylin-eosin (H & E). And immunohistochemistry for CgA, SYN, Ki-67 and p53 were shown.

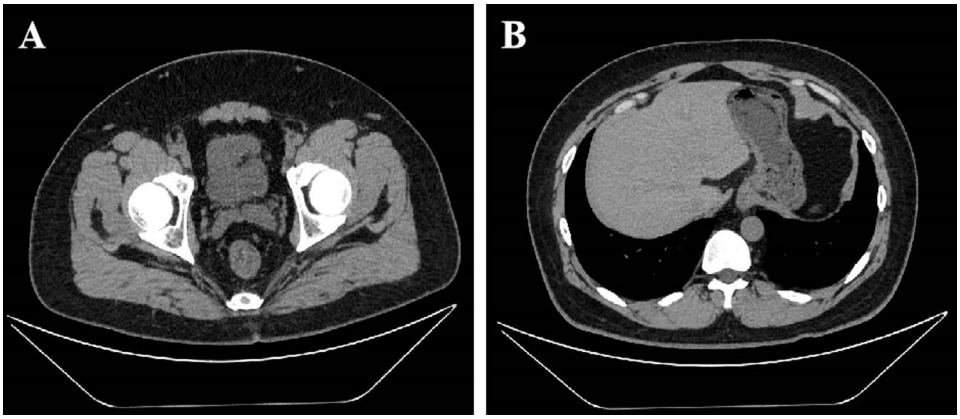

Figure 5. CT scan of the patient

Notes: CT of (A) pelvic and (B) abdominal.

Discussion

In recent years, the incidence of gastroenteropancreatic neuroendocrine tumors (GEP-NETs) is increasing (Rinke, 2023). R-NETs represent 12%–27% of all GEP-NETs, and 1%–2% of all rectal tumors are neuroendocrine (Pang, 2022). The reported r-NETs are rare, with an incidence of 0.17% (Maione, 2021). Rectal M-NETs are even rarer and are rarely reported globally. Therefore, many aspects of the disease remain unclear, in part due to its rarity.

Patients with rectal M-NETs may present with non-specific symptoms, such as abdominal pain, diarrhea, changes in stool habits or traits. They may also have no symptoms. Only 18% of neuroendocrine lesions are suspected to be neuroendocrine in nature (Rinke, 2023), presenting with paroxysmal skin flushing, palpitations, and watery diarrhea, usually suggesting advanced tumor and liver metastasis. In this article, symptoms of this patient were changes in stool traits. Digital rectal examination is mostly manifested as submucosal protrusion to the intestinal lumen, broad-based or sub-pedicled protrusion, with hard texture. B-ultrasound, CT and MRI have no specific diagnostic value for the primary focus, but they can be used to evaluate the progression of the disease.

The endoscopic appearance of rectal M-NETs is unique, with a yellowish-white bulge and smooth surface mucosa (Pang, 2022). The lesions under endoscopic ultrasound originated in the mucosal layer or submucosal layer, and the internal echo was uniform, with low or medium-low echo and clear boundaries (Pang, 2022).

The patient underwent a comprehensive metastatic risk assessment. Firstly, risk factors for metastasis need to be considered. It is generally agreed that tumor size ≥ 10 mm is the main parameter to determine the risk of rectal NET (rNET) metastatic disease (Gallo, 2022). The incidence of lymph node metastasis in tumors ≤ 10 mm was 1.1% (Zhao, 2021). Our patient's tumors were 1-6 mm in diameter, and were considered low-risk M-NETs. In addition, lymphovascular invasion is valuable in metastasis prediction. Postoperative pathology of this patient was negative for all surgical margins, vascular and lymphatic invasion. The reported incidence of distant metastases in tumors ≥ 11.5 mm was 13.8% (Concors, 2018), with liver being the most common metastasis site, followed by bone, mesentery, and lymph nodes. In our reported patients, abdominopelvic CT showed no evidence of liver, lymph nodes, and other distant metastasis. Finally, the relationship between tumor markers and M-NETs remains to be supported by more data (Pang, 2022). In this patient, serum tumor markers, including alpha-fetoprotein (AFP), carcinoembryonic antigen (CEA), cancer antigen 19-9 (CA19-9), cancer antigen 72-4 (CA72-4), cytokeratin 19 fragment 21-1 (Cyfra21-1), vascular endothelial growth factor (VEGF), and free prostate-specific antigen (FPSA)/total prostate-specific antigen (TPSA), were not increased.

According to the European Society of Neuroendocrine Tumors (ENETS) 2023 guidelines, for single rectal NET of 10mm or less, endoscopic resection (ESD, etc.) is recommended, and recurrence rates are low (Rinke, 2023). However, treatment for rectal M-NETs is still not clear. The five lesions of this patient were removed by three ESD. All lesions were small (≤ 10 mm), without muscularis propria invasion and no metastases found by abdominopelvic CT, complete resection with negative margins.

Posttreatment surveillance is not recommended for patients with a single rectal NET, small (≤ 10 mm) and confined to the submucosal (Rinke, 2023). Since the number of tumors may be associated with a high risk of lymph node metastases (Zheng, 2023), follow-up is necessary for rectal M-NETs patient in this case. The patient will have surveillance after 6 months, with symptoms, digital rectal examination, tumor markers, imaging, and colonic endoscopy.

In recent years, with the popularity of endoscopy, the incidence of rectal M-NETs has been on the rise. However,

hitherto, there is no guideline or consensus for the diagnosis, treatment and prognosis of rectal M-NETs. We report a case of rectal M-NETs that was successfully treated. It is hoped that by discussing the accumulated cases of rectal M-NETs, the treatment strategy, long-term prognosis and follow-up methods will be formulated in the future.

Authors contributions

J Zhao was involved in patient's care. CR Wang, XL Li were involved in data collection and analysis. ESD surgery was done by BB Yan. JJ Shou completed the pathology. J Zhao, XL Li drafted the manuscript. All authors read and approved the final manuscript.

Potential conflicts of interest

The authors declare no conflict of interest.

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