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Multiple Rectal Neuroendocrine Tumors Treated by Endoscopic Resection: A Case Report

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ABSTRACT

Rectal neuroendocrine tumors (NETs) are typically solitary, and the occurrence of multiple lesions is uncommon. We present a case of multiple rectal NETs in a 41-year-old man. Colonoscopy performed at another hospital revealed three lesions (4 mm in the sigmoid colon and 5 and 10 mm in the rectum), all of which were diagnosed as NET, grade 1 (G1), following endoscopic resection; one lesion had a positive vertical margin. Upon referral to our institution, repeat colonoscopy demonstrated multiple yellowish, slightly elevated lesions throughout the rectum, all of which were histologically confirmed as NETs. Imaging studies showed no evidence of lymph node or distant metastasis. Although additional surgical resection was considered because of the multiplicity of lesions and positive margin, the patient strongly preferred endoscopic therapy. Eight lesions were successfully resected using endoscopic mucosal resection with a cap or endoscopic submucosal dissection. Histopathological examination revealed seven NET, G1 lesions and one NET, G2 lesion. Additional surgery was recommended but was declined by the patient, and no local recurrence or distant metastasis has been observed during 18 months of follow-up. This rare case highlights the potential role and the limitations of endoscopic treatment in patients with multiple rectal NETs.

1 | Introduction

Neuroendocrine tumors (NETs) are low- to intermediate-grade neoplasms arising from neuroendocrine cells [1]. The incidence of NETs has been increasing worldwide [2], partly due to advances in endoscopic techniques and the widespread implementation of colorectal cancer screening programs. Rectal NETs account for 12%–27% of gastrointestinal NETs and 1%–2% of all rectal tumors [3]. Most rectal NETs are solitary, whereas multiple lesions are uncommon [3, 4]. Herein, we report a case of multiple rectal NETs successfully managed by endoscopic resection, along with a brief review of the literature.

2 | Case Report

A 41-year-old man with no significant medical or family history underwent colonoscopy at another hospital. Three lesions (4 mm in the sigmoid colon and 5 and 10 mm in the rectum) were detected, and all were resected endoscopically under suspicion of adenomas. All lesions were histopathologically diagnosed as NET, G1, with one lesion exhibiting a positive vertical margin (Figure 1A,B).

He was referred to our hospital for further evaluation and management. Approximately 6 weeks after the initial endoscopic treatment at the referring hospital, repeat colonoscopy revealed

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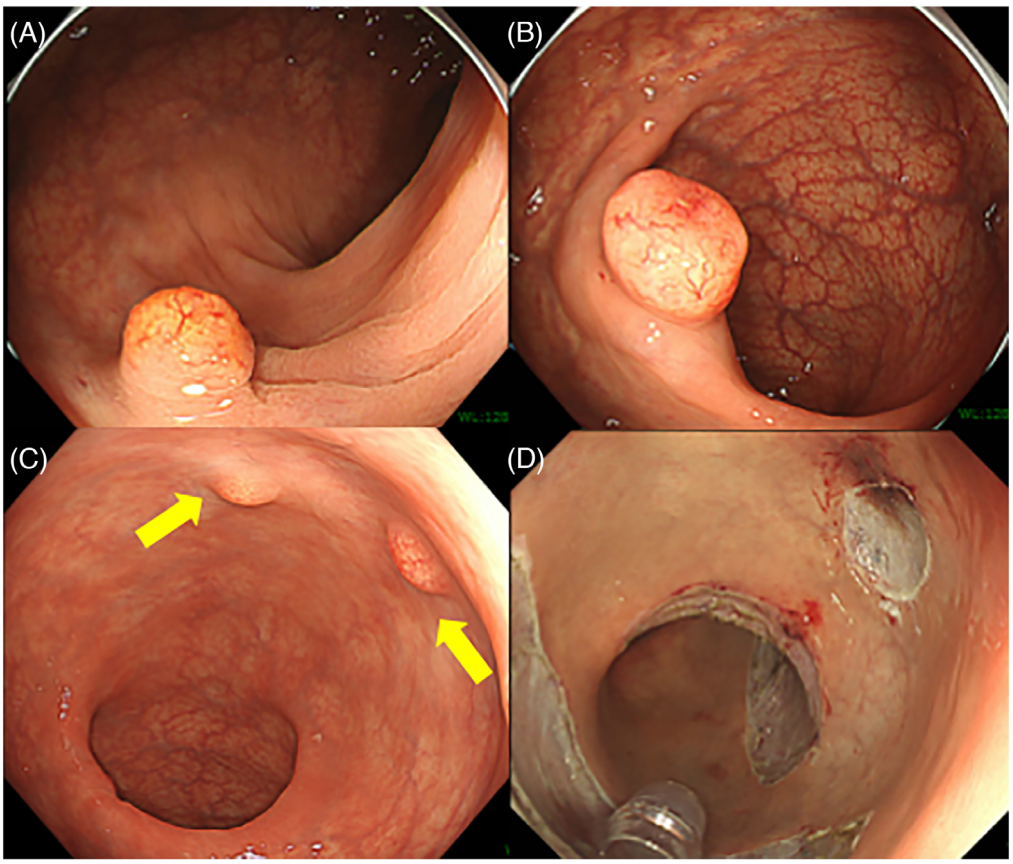


FIGURE 1 | (A, B) Colonoscopy at the referring hospital. Yellowish elevated lesions are seen. (C) Colonoscopy at our hospital showing multiple rectal neuroendocrine tumors (NETs). (D) Colonoscopy image obtained after endoscopic treatment showing post-resection scars.

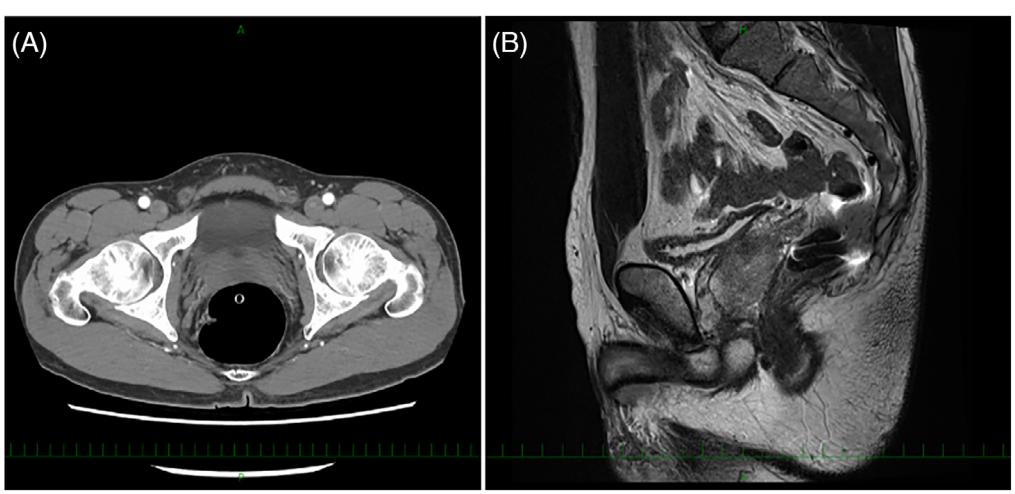


FIGURE 2 | (A) Abdominal computed tomography (CT) showing no evidence of lymph node metastasis. (B) Pelvic magnetic resonance imaging (MRI) showing no evidence of lymph node metastasis.

multiple yellowish, elevated lesions in addition to the previous resection scars (yellow arrow) (Figure 1C). Biopsy confirmed these lesions as NET. Contrast-enhanced computed tomography and pelvic magnetic resonance imaging revealed no lymph node or distant metastasis (Figure 2A,B). Capsule endoscopy showed no lesions in the small intestine.

Although surgical resection was proposed, the patient strongly declined surgery because he was unwilling to accept even a small possibility of stoma formation or postoperative sexual dysfunction. As a result, endoscopic resection was performed. Two lesions were resected by endoscopic mucosal resection with a cap (EMR-C), and the remaining three lesions in the lower

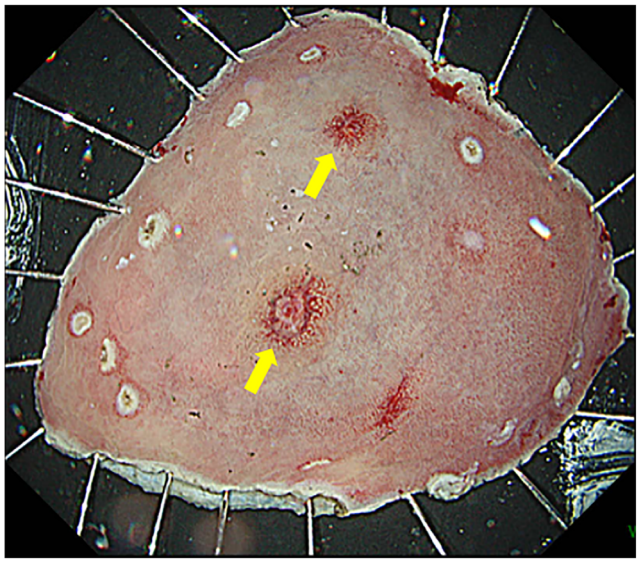


FIGURE 3 | Resected specimens by endoscopic submucosal dissection (ESD), including three neuroendocrine tumor (NET) lesions (yellow arrow).

rectum (Rb) were resected en bloc by endoscopic submucosal dissection (ESD) at two sites without complications (Figures 1D and 3). At one site, two adjacent lesions were resected en bloc. At the other site, a previous resection scar and an adjacent new lesion were removed together by ESD. ESD was selected for lesions involving previous treatment scars and when multiple adjacent lesions were intended to be resected en bloc, whereas EMR-C was selected for isolated single lesions.

The postoperative course was uneventful, and the patient was discharged on postoperative day 3. Histopathological examination revealed that all eight lesions were NETs, pT1a (UICC ninth edition), with no evidence of lymphovascular invasion and clear endoscopic resection margins (Figure 4A,B). Seven lesions were classified as NET G1. One lesion lacked mitotic figures on hematoxylin and eosin staining but had a Ki-67 labeling index of 3.2% (26/806 tumor cells), leading to a diagnosis of NET G2 (Figure 4C). The NET G1 lesions measured 2.5–7 mm in diameter, whereas the NET G2 lesion measured 1.1 mm.

Additional surgery was recommended but was declined by the patient after thorough discussion. Surveillance with imaging examinations every 3–6 months and colonoscopy approximately every 6 months was therefore continued. No local recurrence or distant metastasis has been observed during 18 months of follow-up after endoscopic treatment.

3 | Discussion

Rectal NETs are relatively uncommon. In a large-scale Japanese cohort study, the detection rate among patients undergoing colonoscopies was 0.087%, with most lesions being small and only a few exceeding 10 mm in diameter [5]. The mean age at diagnosis has been reported as 58 years, with a slight male predominance [3].

Most rectal NETs are solitary; multiple lesions are considered rare, with a reported prevalence of 2–4.5% in Western series. Although the pathogenesis of multiple lesions remains unclear, genetic syndromes such as neurofibromatosis type 1 and chronic inflammatory conditions including ulcerative colitis have been implicated [3]. Our patient had no such background.

Treatment strategies are based on tumor size, depth of invasion, histologic grade, and the presence of metastasis [1, 6, 7]. Lesions smaller than 10 mm without muscularis propria invasion or evidence of metastasis are generally considered suitable for endoscopic treatment, whereas tumors larger than 10 mm, G2 lesions, those with muscularis propria invasion, or those with suspected lymph node metastasis warrant consideration of surgical resection [1]. Extraglandular endocrine cell proliferation has also

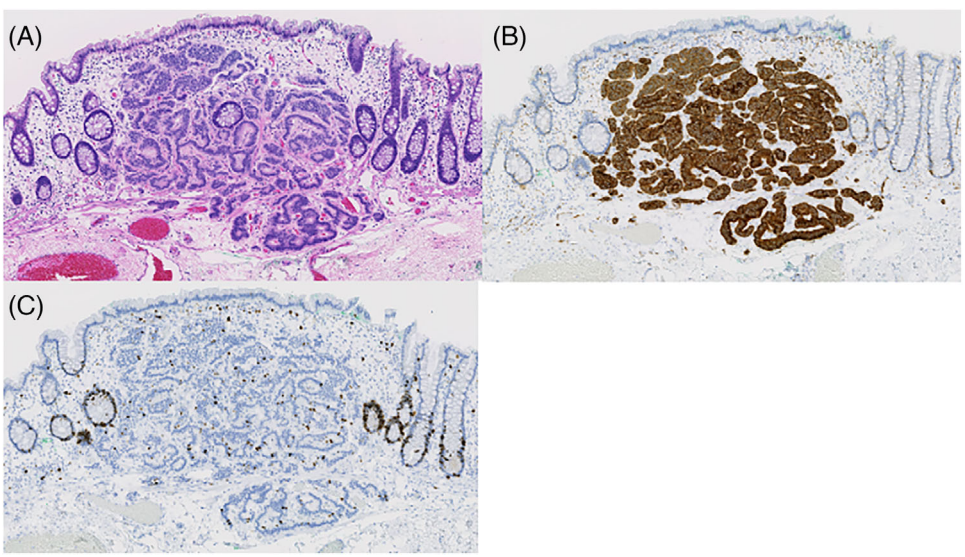


FIGURE 4 | (A–C) One of eight neuroendocrine tumor (NET) lesions. The tumor demonstrates cord-like, ribbon-like, and small nested architectural patterns, extending from the lamina propria into the submucosa. Although mitotic figures are infrequent, the Ki-67 labeling index is slightly above 3%.

been proposed as a possible mechanism for the development of multiple rectal NETs [8].

In cases of multiple rectal NETs, previous studies have suggested that the number of tumors may be associated with an increased risk of lymph node metastasis. Pang et al. reported seven patients with lymph node metastasis, all of whom had multiple small lesions confined to the submucosa, with the number of NETs ranging from 6 to 69 per patient [3]. Nishikawa et al. reported that cases with eight or more lesions accounted for only 0.8% of all rectal NET cases in the single-center series. They categorized patients into groups with fewer than eight tumors and those with eight or more. Patients with fewer than eight lesions exhibited pathological features similar to those of solitary NETs, whereas those with eight or more showed a higher incidence of lymphovascular invasion and nodal metastasis, even when the lesions were small [4]. Furthermore, multiple rectal NETs containing a G2 lesion appear to be uncommon. In a literature review of 47 patients with multiple rectal neuroendocrine neoplasms, G2 tumors were reported in only three patients (6.4%) [9]. In our case, eight lesions were identified, including one G2 lesion.

Although additional surgery was strongly recommended, the patient opted for endoscopic treatment followed by close surveillance. No recurrence has been observed during the follow-up period. This case highlights the importance of considering both tumor number and histologic grade when determining the optimal treatment strategy for multiple rectal NETs.

We report a rare case of multiple rectal NETs managed by endoscopic resection. Although surgery is generally recommended for cases with multiple lesions or G2 histology, endoscopic therapy with careful follow-up may be an option for selected patients who decline surgical intervention. However, the long-term oncological safety and outcomes of this approach remain uncertain, and longer follow-up and further investigation are required. In addition, when a NET is identified, a careful endoscopic examination of the entire colorectum may be useful for detecting additional lesions. Nevertheless, the clinical implications of this approach for treatment selection remain uncertain, and further studies are needed to validate its usefulness.

Author Contributions

Hitomi Matsuki and **Ryoji Ichijima** drafted the manuscript. **Masau Sekiguchi**, **Naoya Toyoshima**, **Reona Kawamura**, **Yasuhiko Mizuguchi**, **Hiroyuki Takamaru**, **Masayoshi Yamada**, **Toshihiro Haga**, and **Yutaka Saito** contributed to the clinical management, data interpretation, and critical revision of the manuscript. All authors read and approved the final manuscript.

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Ethics Statement

This case report was conducted in accordance with the ethical standards of the institution and the principles of the Declaration of Helsinki. Institutional review board approval was not required for this case report according to the institutional policy.

Consent

Written informed consent was obtained from the patient for publication of this case report and the accompanying images.

Conflicts of Interest

The authors declare no conflicts of interest.

Data Availability Statement

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

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