Multiple Rectal Neuroendocrine Tumor

So Jung Han¹, Jun Yong Kim², Jae Jun Park¹

¹Division of Gastroenterology, Department of Internal Medicine, Severance Hospital, Yonsei University College of Medicine,

²Department of Pathology, Severance Hospital, Yonsei University College of Medicine, Seoul, Korea

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Corresponding author: Jae Jun Park, E-mail: maranatta@gmail.com, <https://orcid.org/0000-0001-9974-1658>

CASE SUMMARY

A 61-year-old male was transferred to our hospital for treatment of multiple rectal neuroendocrine tumors. The patient had a history of hypertension, dyslipidemia, and segmentectomy of the left upper lobe due to pulmonary tuberculosis ten years ago. The patient was an ex-smoker of 40 pack-years and a non-drinker. He had no complaints of symptoms, such as abdominal pain or changes in bowel habits. The patient was told that he had a rectal neuroendocrine tumor ten years ago and was recommended for surgery, but he refused surgical treatment and did not receive any treatment.

The initial vital sign was within normal range. The results of complete blood count showed mild anemia and thrombocytopenia (white blood count [WBC] 4,270/mm³, hemoglobin 12.0 g/dl, platelets 121,000/mm³). Serological test for liver function was normal (aspartate aminotransferase 24 U/L, alanine aminotransferase 24 U/L, alkaline phosphatase 71 U/L, total bilirubin 1.0 mg/dl). Tumor markers were within normal limits.

Computed tomography (CT) of the chest, abdomen, and pelvis did not show any distant metastasis or enlarged lymph nodes (Fig. 1). Colonoscopy showed multiple less than 10 mm sized hard, round, and yellow submucosal lesions at rectum involving around 80% circumference (Fig. 2A, 2B). Endoscopic treatment of the entire lesion was planned with several rounds of endoscopic resection in piecemeal man-

ner. Accordingly, endoscopic resection using endoscopic submucosal dissection was performed for one part of multiple rectal neuroendocrine tumors (Fig. 2B-2D). The part where endoscopic resection was planned on the first session was completely resected en-bloc manner without complication. The size of the resected specimen was 60 mm in longest diameter. In the pathological report, there were twelve tumors and all of them were confirmed as well differentiated neuroendocrine tumors (NETs) (grade 1), and size of the largest tumor was 6 mm in greatest diameter. The mitotic number of the specimen was less than 1 in 10 high-power fields. Immunohistochemical stain showed Ki-67 index was 0.8% (8/1,000 tumor cells) and revealed chromogranin A and synaptophysin positivity in most of the cells (Fig. 3). Collectively, these data led to a diagnosis of a grade 1 rectal neuroendocrine tumor. Tumor invades the submucosal layer, and perineural invasion was present, but the lymphovascular invasion was not identified. It showed focal tumor abutting at the basal margin, but the lateral margin was free from tumor. Based on histological findings with positive perineural invasion, additional surgery was recommended rather than further staged endoscopic resection. However, the patient wants follow-up without additional surgery. After a full explanation for the risk of tumor recurrence and metastasis, close monitoring using CT scan and further staged endoscopic resection was planned after four months.

Neuroendocrine tumors of the rectum are traditionally referred to as carcinoid tumors which are a group of

Fig. 1. Computed tomography. (A, C) Cross section view. (B, D) Coronal view.

Fig. 2. (A, B) Yellowish multiple subepithelial lesions at the rectum were noted. (C, D) Multiple rectal carcinoids were removed by endoscopic submucosal resection.

Fig. 3. Pathologic findings of colonic NETs removed by ESD. (A) Multiple tumors are seen (H&E, scan view). (B) Tumor invades mucosa and upper submucosa (H&E, $\times 40$). (C) Monotonous and regular tumor cells are arranged in trabecular and nesting pattern (H&E, $\times 100$). (D) Tumor cells show strong and diffuse positivity for synaptophysin (immunohistochemical staining, $\times 100$). NETs, neuroendocrine tumors; ESD, endoscopic submucosal dissection.

well-differentiated NETs of neuroendocrine neoplasms, as described by the World Health Organization (WHO) classification. In a recent study, the rectum represents 17.7% of neoplasms of all NETs [1]. According to the WHO classification, the grade is determined based on the mitotic index and Ki-67 index. Ki-67 is a single factor predicting prognosis among immunochemical staining related to neuroendocrine tumors. The most widely used and reliable neuroendocrine markers are chromogranin A and synaptophysin. Synaptophysin is often regarded as the most sensitive marker in the diagnosis of well-differentiated NETs. The level of chromogranin A expression may vary according to the degree of tumor differentiation.

The principle of treatment for rectal neuroendocrine tumors is complete resection of the tumor. The size of the tumor is a very important factor in predicting the prognosis and deciding whether or not to undergo local treatment or surgical treatment, including lymph node dissection. Other predictive factors include depth of invasion, lymphatic invasion, perineural invasion, and resection margin [2]. The size of NETs in the rectum are generally less than 10 mm, and most have a benign natural course. However, if the size of the tumor exceeds 2 cm, surgical treatment is generally recommended. Small NETs rarely have local recurrence (< 2%), nodal involvement (2.4%) or distant metastatic disease (0.2%) after endoscopic resection [3].

Rectal NETs as multicentricity occur in 2% to 4% of all cases. However, due to the low incidence of multicentricity, no therapeutic consensus for multiple rectal NETs has been established [4]. One recent article showed multiple NET of more than eight lesions to be small; however the incidence of lymphatic invasion was high, suggesting potential aggressive behavior [5].

CONFLICTS OF INTEREST

No potential conflict of interest relevant to this article was reported.

AUTHOR'S CONTRIBUTIONS

Conceptualization: Jae Jun Park. Data acquisition: So Jung Han, Jun Yong Kim. Supervision: Jae Jun Park. Writing - original draft: So Jung Han. Writing - editing: So Jung Han, Jae Jun Park. Writing - review: So Jung Han, Jun Yong Kim, Jae Jun Park.

ORCID

So Jung Han, <https://orcid.org/0000-0002-1906-5723>
Jun Yong Kim, <https://orcid.org/0000-0002-4313-9032>
Jae Jun Park, <https://orcid.org/0000-0001-9974-1658>

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