Multiple rectal neuroendocrine tumors

A 32-year-old male visited to our hospital for treatment of rectal neuroendocrine tumors after health screening at a local medical center. He had no specific past medical history, or familial history. He also had no specific symptoms or signs. Peripheral blood test showed as follows: hemoglobin 16.7 mg/dL, white blood cell count 5,650/mm³, and platelet 246,000/mm³ and other laboratory tests, including tumor markers, showed no abnormalities. Colonoscopic finding showed three yellowish subepithelial lesions at rectum; lesions were measured 5 mm, 5 mm, and 7 mm in diameter, respectively (Fig. 1 A, B). These lesions were removed by endoscopic submucosal resection using a ligation device (ESMR-L) (Fig. 1 C). Although bleeding occurred during procedure, it was treated successfully with endoscopic hemoclipping (Fig. 1 D, E). The triple lesions were confirmed as WHO grade 1 neuroendocrine tumors (NETs) (Fig. 2). Abdominal CT and PET scan showed no evidence of distant metastasis. Follow-up colonoscopy after 6, 12, 18 months did not show remnant tumor or local recurrence.

Figure 1 Colonoscopic findings. (A) Yellowish triple subepithelial lesions at the rectum are noted. (B) Lifting of lesions by hypertonic saline injection and band ligation is performed. (C) Submucosal resection using a ligation device (ESMR-L) is done. Triple rectal carcinoids are removed by ESMR-L. (D) Bleeding related to the endoscopic submucosal resection using a ligation device is noted. (E) Bleeding is controlled by endoscopic hemoclipping.
Carcinoid tumors were first named as "karzinoide" by Oberndorfer in 1907. The appropriate term for carcinoid is neuroendocrine neoplasm. Recently, the concept of carcinoid can be divided into NETs and neuroendocrine carcinoma (NEC).1

Annual incidence of NETs has generally been reported as 1 to 2/100,000/year.2 Sixty-four percent of NETs arise in the gastrointestinal tract, especially rectum and stomach in Korea.2,3 Based on the past studies, 80-90% of rectal NETs are diagnosed incidentally by sigmoidoscopy for examination of anal diseases or for health screening.4 Incidence rate of rectal NETs found by sigmoidoscopy is 1/2,500 people.4 However, frequency of rectal NETs has increased by 800-1,000% compared with the past 35 years in USA.5 This rise is probably related to the increase of colonoscopic screening, which has also resulted in incidentally detected NETs. Similar to USA, in the era of screening colonoscopy, rectal NETs are becoming more common in Korea.

However, multicentric rectal NETs are rare, and have been reported as 2 to 4%.6 Saha et al.7 reported that up to 10% of rectal NETs show multicentricity and three to 10 lesions can occur in the same area. Several cases of multiple NETs in patients with neurofibromatosis or ganglioneuromatosis have also been reported.8 Two cases of double rectal NET have been reported in the Korean literature.9,10 Multicentricity is a poor prognostic factor in small intestinal carcinoids, however, its prognostic effect in rectal NET is not known.11

In the case of a single rectal NET, metastasis is found in 0-3% when the size of the rectal NET is less than 10 mm, 10% when 10-19 mm, and 80-100% when greater than 20 mm.12 If size is less than 20 mm, invasion to muscularis propria occurs in 20%. If greater than 20 mm, it occurs in 94%. As size of NET increases, the possibility of malignancy and distant metastasis is also increased. Therefore, the method of endoscopic resection differs according to size and depth of invasion. Typically, if the tumor size is less than 10 mm and if it does not invade to muscularis propria, endoscopic resection is recommended at first. Even small rectal NETs can primarily invade the submucosa, therefore, a special technique for reliable resection of deep regions of the submucosal layer is needed, and ESMR-L is a good method for complete resection of rectal NET. This procedure is known to be technically simple, minimally invasive, and relatively safe. In addition, the treatment efficacy of ESMR-L was far better in the aspect of margin negativity and local recurrence than that of conventional polypectomy.13,14 In contrast
with consensual treatment options for single rectal NET, there are no standard guidelines for treatment of multiple rectal NETs. In addition, the long-term prognosis of endoscopic resection for multiple rectal NETs is still uncertain. In our case, multiple NETs were removed successfully by endoscopic resection and the short-term prognosis was good, without local recurrence.

The rectal NETs in our case were confined to the mucosa and submucosa layer and were less than 10 mm in size, with no vascular or neural invasion and we can get clear resection margins: mitotic count was under 2 and Ki-67 count was below 2% at 10 high power field (HPF), indicating a grade 1 NET. There are no established principles concerning follow-up periods and modalities for multiple NETs. Merely, in the case of multiple NETs, relatively short term follow-up endoscopy might be needed in order not to miss other residual NET lesions.

Rectal EUS can determine size, depth of invasion, metastasis status to adjacent lymph node, and can detect separation of a submucosal tumor from muscularis propria. It is essential for decision of a treatment plan or evaluation of the stability of endoscopic resection.\textsuperscript{13,14} However, as distant lymph node or liver metastasis is not identifiable by EUS, abdominal CT or PET should be performed in order to confirm distant metastasis.

In recent years, the incidence of rectal NET in Korea has increased beyond our expectation. In addition, as in our case, the endoscopist might encounter multiple rectal NETs. Thus, when incidental rectal NET is found, the possibility of multicentricity should be considered. According to our results, in cases of multiple rectal NETs, tumors that are 10 mm or less, which do not infiltrate the muscularis propria, can also be successfully treated endoscopically. The treatment policy, long-term prognosis, and methods of follow-up for multiple rectal NETs should also be discussed in the future by accumulating cases like these described in our report.

REFERENCES