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Are Small Rectal Neuroendocrine Tumors Safe?

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Article: Natural Course of an Untreated Metastatic Perirectal Lymph Node After the Endoscopic Resection of a Rectal Neuroendocrine Tumor **(Intest Res 2015;13:175-179)**

Neuroendocrine tumors (NETs) are slow-growing tumors with different biological and clinical characteristics. The incidence of NETs varies depending on the organ; however, the rectum is the most prevalent tumor site in the gastrointestinal system, accounting for 60–89% of all gastrointestinal NETs.[1] These tumors are often found incidentally during colonoscopy without any symptoms. They are usually detected on endoscopy as small, protruding subepithelial lesions located between 4–20 cm above the dentate line on the anterior or lateral rectal wall. According to the European Neuroendocrine Tumor Society (ENETS) 2012 Consensus Guidelines,[2] well-differentiated rectal NETs <10 mm without muscle invasion or lymph node involvement could be treated by performing local resection. For local resection, various treatment modalities have evolved, including endoscopic polypectomy, endoscopic mucosal resection (EMR), endoscopic submucosal dissection, transanal excision, and transanal endoscopic microsurgery.[3]

To evaluate the risk of metastasis, pathological examination of lymph nodes should be implemented. However, small rectal NETs are known to have little risk of metastasis, making local resection desirable. Radical surgery is reserved for selected cases with risk factors associated with lymph node metastasis. In rectal NETs <10 mm, the risk of lymph node metastasis is low. However, the risk of lymph node metastasis increases remarkably in rectal NETs with larger than 10 mm.[4,5] Although CT scans do not reflect lymph node metastasis as accurately as a pathologic examination, a case may be regarded as negative for lymph node metastasis if no signs of metastasis appear using CT.[6] Therefore, the authors of the current case[7] re-examined a 7-mm perirectal lymph node identified on a CT scan after EMR for a 8-mm rectal NET. The pathological type of tumor also significantly affects the risk of metastasis.[8] According to the WHO 2000 pathological diagnostic criteria for gastrointestinal NETs based on tissue structures, tumors are graded into three levels on the basis of tumor cell proliferation: tumors with a grade of G1 have a mitotic count <2 per 10 high-power fields (HPF) and/or Ki-67 ≤2%; G2, mitotic count 2–20 per 10 HPF and/or Ki-67 3–20%; and G3, mitotic count >20 per 10 HPF and/or Ki-67 >20%. In the current case,[7] it may be reasonable to omit surgical resection for the perirectal lymph nodes after EMR, as histological analysis of the tumor revealed no lymphovascular invasion, no mitosis per 50 HPF, and a Ki-67 labeling index of 0.8%.

In the current case, the authors followed the patient using annual endoscopy and abdominopelvic CT for 7 years after resection. Fortunately, the perirectal lymph node metastasis was completely removed via laparoscopic surgical resection and lymph node dissection, vigorous surveillance in this case. A population-based study[4] in Japan also reported a prevalence of 3.7% for lymph node metastasis in rectal NETs <5 mm and 10% for tumors <10 mm. In a retrospective study by the Colonoscopy Study Group of the Korean Society of Coloproctology,[6] 7 of 359 (1.95%) tumors less than 10 mm had lymph node metastasis. In two other Japanese studies,[9,10] Kasuga et al.[9] reported a prevalence of 4.9% for lymph node metastasis in G1 tumors ≤10 mm, and Konishi et al.[10] reported a higher metastatic rate (as high as 7%) in rectal NET

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≤10 mm, but did not indicate the tumor grades. As the risk of lymph node metastasis in rectal NETs ≤10 mm vary between studies,[4,6,9,10] local resection may be complicated, even in small rectal NETs. Therefore, careful surveillance is essential, especially when lymph node metastasis cannot be predicted accurately, as in the current case. Currently, there is no data recommending regular follow-up after local resection of rectal NETs <10 mm. ENETS guidelines[2] recommend annual follow-up for G3 tumors <10 mm and G1–G3 tumors 10–20 mm. In addition, ENETS guidelines recommend follow-up for G1–G2 tumors >20 mm within the first year, and every 4–6 months in the first year and at least annually thereafter for G3 tumors.

In the current case, the authors followed the patient using annual endoscopy and abdominopelvic CT. Although ENETS guidelines[3] do not recommend routine follow-up with CT or MRI for rectal NETs <10 mm, follow-up modalities may include endoscopy, EUS or MRI. Considering the possibility of lymph node metastasis in the first presentation of the current case, additional investigation with rectal MRI or EUS that can more accurately assess perirectal lymph nodes than conventional CT may be helpful in assessing the nature of perirectal lymph node enlargement.[11] Furthermore, EUS-guided fine needle aspiration or laparoscopic lymph node sampling may be considered if MRI or EUS suggests the possibility of lymph node metastasis. As the natural course of rectal NETs is not fully understood and the risk of lymph node metastasis has varied in previous studies, the metastatic potential of rectal NETs, even in tumors <10 mm, should not be ignored.

The current case report is very informative for clinicians, because the natural course of untreated perirectal lymph node metastasis of G1 rectal NETs <10 mm has never been described previously. Generally, the risk of lymph node metastasis for rectal NETs <10 mm is low; however, NETs are classified as a malignant disease in the recently revised American Joint Committee on Cancer (AJCC) cancer staging guidelines. Therefore, clinicians should remember that the clinical behavior of rectal NETs might sometimes resemble that of malignant tumors, even when tumors are small.

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