A case of rectal carcinoid, 7 mm in diameter, with skip metastasis to the lateral lymph node

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Abstract. The present case study presented a 59-year-old man with a 7 mm submucosal tumor in the lower rectum and swelling in a 7 mm lateral lymph node (the obturator lymph node). No swelling of the lymph nodes within the mesorectum was observed. The patient underwent laparoscopic intersphincteric resection with left side lateral lymphadenectomy. At the pathological examination, the patient was diagnosed with a rectal neuroendocrine tumor (Grade 1; carcinoid), which had invaded the perirectal tissues and exhibited lateral lymph node metastasis; however, mesorectal lymph node metastasis was not observed, therefore, the definitive diagnosis was rectal carcinoid with skip metastasis to the lateral lymph node. No sign of recurrence was observed at the 3 year follow-up. The treatment algorithm of rectal carcinoid was decided by the risk of lymph node metastasis. The present study confirmed skip metastasis to the lateral lymph node from the rectal carcinoid, which is typically very slow growing and has a low grade malignant potential.

Case report

A 59-year-old man was referred to Meiwa Hospital (Hyogo, Japan) for a routine health examination and underwent a colonoscopy, which revealed a hemispheric submucosal tumor (7 mm in diameter) in the lower rectum, which was located 3 cm from the anal verge at the left side of the rectal wall (Fig. 1A). The lesion revealed no central depression or ulceration. The pathological diagnosis of the biopsy specimen was neuroendocrine tumor (NET). Additionally, signs and symptoms of carcinoid syndrome, including skin flushing, facial skin lesions and diarrhea were not observed. Abdominal computed tomography (CT) detected no liver or lung metastasis. The patient

was further assessed by pelvic magnetic resonance imaging, which revealed swelling in a lateral lymph node located on the left side obturator lymph node (size, 7 mm) and the shape of the node had a clear border and uniform detection (Fig. 1B-D). The other lymph nodes, including the mesorectum lymph node, were not swollen. Laboratory data revealed no abnormal findings and serum tumor markers, including carbohydrate antigen 19.9, carcinoembryonic antigen, neuron-specific enolase and urine 5-hydroxyindole acetic acid, were all negative. Based on these findings, the patient was diagnosed with lateral lymph node metastasis.

A laparoscopic intersphincteric resection (ISR) with left side lateral lymphadenectomy was performed, followed by J-pouch reconstruction without diverting stoma. Specifically, the central lymph node was dissected around the inferior mesenteric artery (IMA) while preserving the IMA and left colic artery. In the pelvic space, a total mesorectal excision was performed up to the anal canal. A left side lateral lymphadenectomy was subsequently performed as follows: The ureter and hypogastric nerve were picked up with forceps, and the lymph nodes and fatty tissue were dissected from the bifurcation of the aorta extending to the common iliac area. The internal iliac vessels were subsequently cleared from the lymphatic tissue at a safe distance from the lateral side of the pelvic plexus. During the dissection, the obturator nerve and vessels were identified medial to the external iliac vein and lateral to the superior vesical artery. Following completion of the pelvic lymph node dissection, only the external vessels, internal iliac vessels and their branches, the obturator nerve, and the pelvic plexus remained. At the anal side approach, the distal resection line was placed on the dentate line and partial-ISR was performed to divide the intersphincteric space though the intra-abdominal space. Finally, the surgical specimen was removed from the anal side and was reconstructed with a colonic J-pouch. This technique has been described previously (1).

The macroscopic findings of the resected specimen indicated that the primary tumor was 7 mm in diameter and the surface was covered with a normal mucous membrane without central depression or ulceration (Fig. 2A). On the microscopic findings, a carcinoid pattern tumor was observed, which had invaded into the perirectal tissues with a multi-growing pattern, including ribbons, festoons and rosette-like glands (Fig. 2B).

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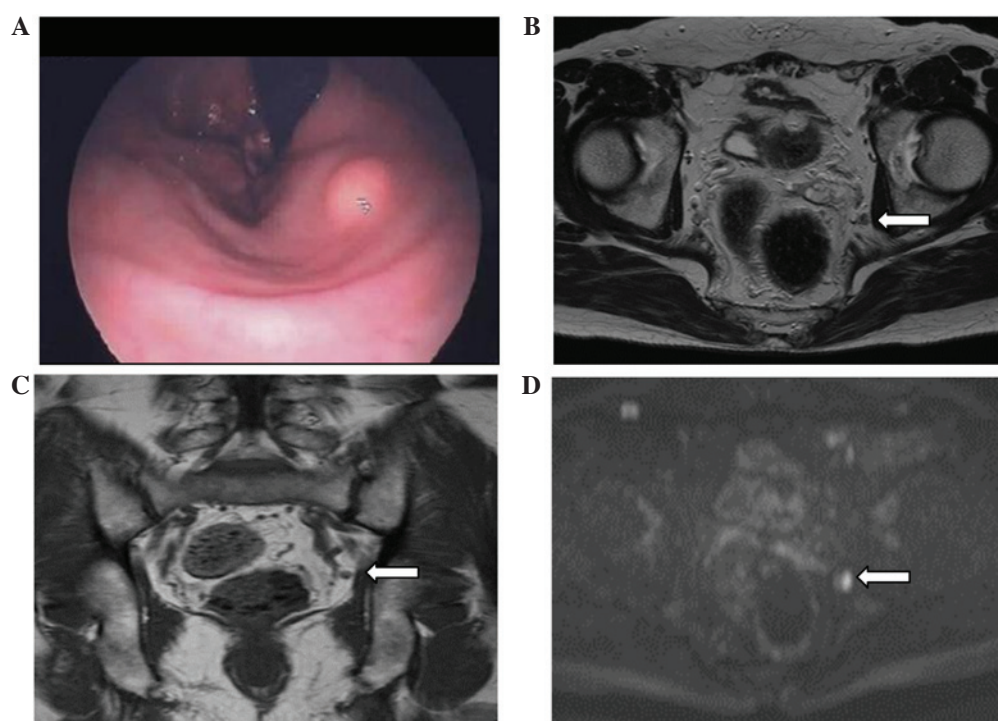E-mail: n_beppu@yahoo.co.jp

Figure 1. (A) Colonoscopy revealed a hemispheric submucosal tumor, 7 mm in diameter, at the low rectum without central depression and ulceration. The (B) T2-eighted axial magnetic resonance image, (C) coronal image and (D) diffusion weighted image revealed lymph node swelling at the left side obturator external iliac space (arrow). The maximum size was 7 mm.
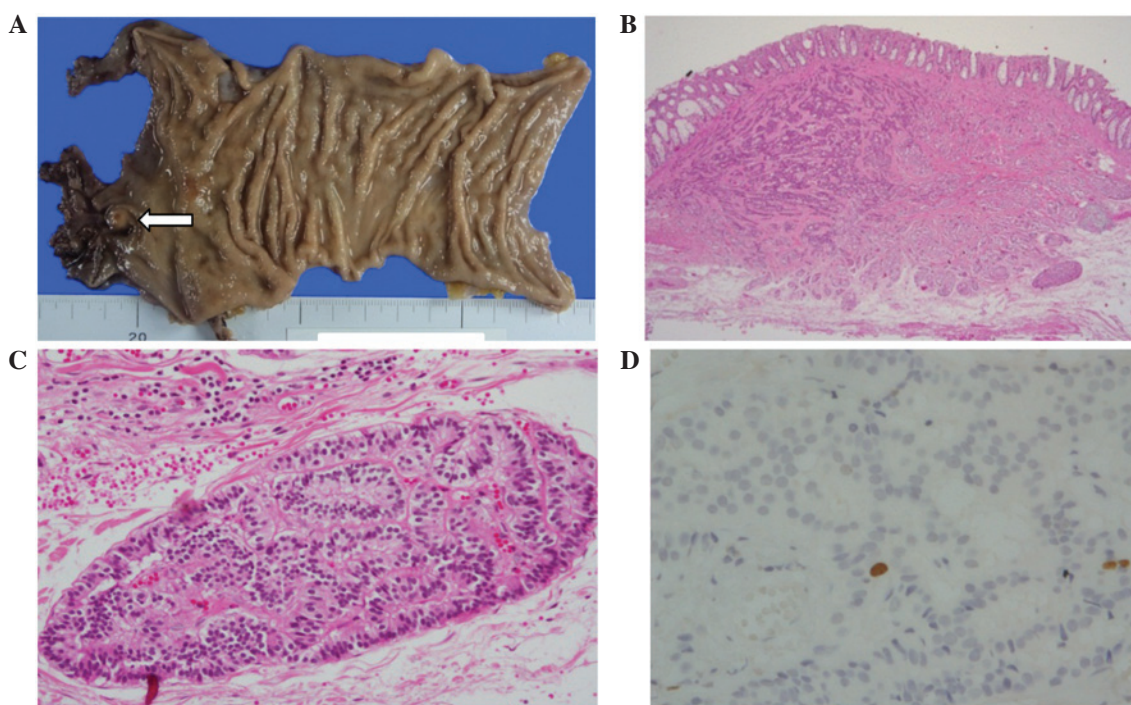

Figure 2. (A) Macroscopic findings of the resected specimen (arrow). (B) A carcinoid pattern tumor invading the perirectal tissues was visible from the microscopic findings (Loupe image of x4 magnification). (C) The lymphatic permeation was confirmed (magnification, x20). (D) The Ki-67 index was 1.1% (magnification, x40).

Furthermore, lymphatic permeation was confirmed (Fig. 2C). The present study diagnosed the tumor as NET with Grade 1 (carcinoid) and from these findings determined that the Ki-67 index was 1.1% (Fig. 2D) without atypia or necrosis (0/10 on High Power Field). The lymph nodes at the meso-rectal fascia, including 14 lymph nodes, were all negative; however, one of seven left side lateral lymph nodes was metastatic (Fig. 3). Immunohistochemistry confirmed that both the primary tumor and the metastatic lymph node were positive for chromogranin and synaptophysin.
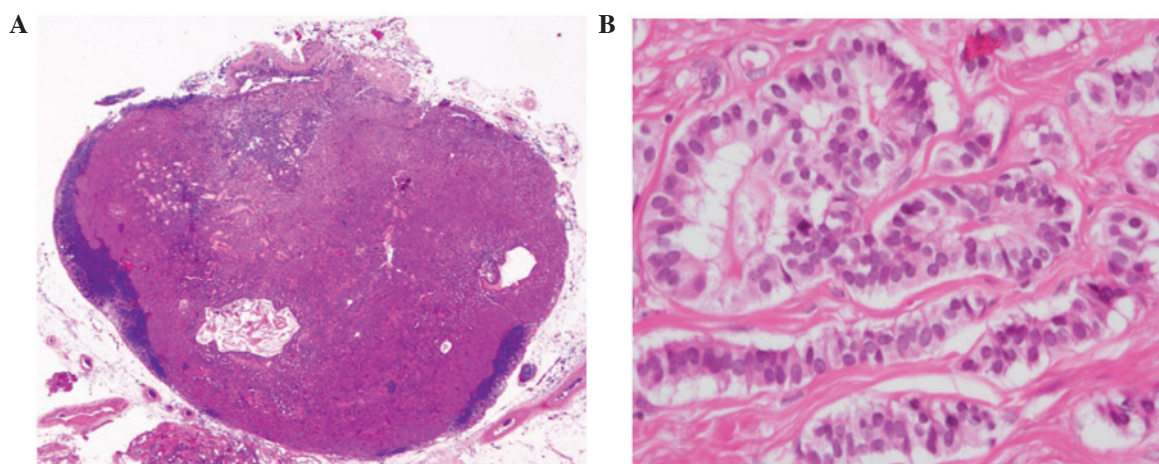
Figure 3. Lymph node metastasis was visible at the obturator external iliac lymph node (A) Loupe image at a magnification of x4 and (B) x40.

The patient was discharged from our hospital 8 days following surgery, and adjuvant therapy was not performed. The patient was followed up with chest-abdominal CT every 6 months and colonoscopy annually. At the 3 year follow-up, recurrence was not observed and the Wexner Fecal Incontinence Score was 3.

Discussion

Skip metastasis is diagnosed if distant nodes are positive and regional nodes are negative. The pattern of lymph node metastasis was decided by the lymphatic tract, which exists along the artery. Also, the distance from the tumor, which follows through the epicolic, paracolic, intermediate and principal lymph nodes, respectively, although different lymphatic pathways may exist suggesting the presence of important variables, including tumor invasion of lymphatic channels, changes in the lymphatic drainage pattern, or direct pressure of tumor bulk leading to drainage by alternative lymphatic channels effecting the transport of a single tumor cell via lymphatics (2). Our previous study detected non-continuous nodal metastasis toward the drainage of the lymphatic tract, which was hypothesized to be skip metastasis of colorectal cancer and the frequency of skip metastasis is ~6.5-10.5% (3,4). In the present case study, skip metastasis was confirmed even with the carcinoid, which is typically very slow growing and exhibits a low grade malignant potential.

In colorectal cancer, tumors develop from the mucosal epithelium and growth expansively. On the other hand, in rectal carcinoids, tumors develop from the Kultschitzky cells, which are normally located in the deep mucosa. Therefore, these tumors invade the submucosa from an early stage. As a result, the genesis of metastasis is hypothesized to be different between colorectal cancer and rectal carcinoids. At rectal carcinoid, the incidence of lymph node metastasis, according to the tumor size, was 5.5% (1-10 mm), 30% (10-20 mm) and 70% (21-30 mm). Based on the depth of tumor invasion, the incidence was 12% in the submucosa and 57% in the muscularis propria. Furthermore, the incidence of central depression and ulceration was revealed to increase in tumors 10 mm in size (5). A meta-analysis of factors associated with lymph node metastasis in rectal carcinoid indicated tumor size >10 mm, an increase in the depth of invasion, venous invasion and central depression (6). Based on those findings, minimum-invasive surgeries were decided by the following factors: Tumor size <10 mm and the lack of central depression, ulceration or muscularis propria invasion. Therefore, a tumor size >10 mm requires surgical resection with lymphadenectomy (6). In the present case, the tumor size was 7 mm without central depression and ulceration; however, the tumors had invaded the perirectal tissues. Additionally, the lymphadenectomy cut-off size for rectal cancer in our institution was 7 mm. Therefore, following this criteria, the present study performed lateral lymphadenectomy. Even with the tumor size <10 mm, it was a rare case. However, the lymph node was involved; therefore, the initial radiological finding of lymph node metastasis was critical.

Considering previous reports, tumor size >10 mm, invasion of muscularis propria, venous invasion and central depression may be risk factors for lymph node invasion, which is an indication for surgical resection with lymphadenectomy. However, the recommended procedure for small rectal carcinoids, which are ≤10 mm in size, with lymph node metastasis is not well described. In general, central depression, ulceration, anisonucleosis, polymorphism, mitosis, lymph-vascular invasion, or biological malignancies are signs of malignant potential. However, small rectal carcinoid with lymph node metastasis are typically low grade biological malignancies, as assessed by Ki-67 or mitosis; therefore, previous reports have suggested that biological malignancies, including carcinoids, are not as easily assessed (7). The present case was also difficult to assess since the primary tumor was a rectal neuroendocrine tumor (Grade 1) and the size was 7 mm; however, the tumor metastasized to the lateral lymph node and permeated the lymphatic tract. Pathologically, the present study confirmed lateral lymph node metastasis; however, carcinoids are typically slow growing tumors. As a result, it may be unclear if the pathological confirmation of lymph node metastasis had certain benefits on the patient outcomes. Long-term outcomes were required to confirm the usefulness of aggressive lymphadenectomy.

In conclusion, the present case study presented a case of rectal carcinoid, 7 mm in size, with skip metastasis to the lateral lymph node. Carcinoids are typically markedly slow

growing and exhibit low grade malignant potential, therefore, minimally invasive therapy may be selected for non-lymph node metastatic cases. However, the present case exhibited small carcinoids (<10 mm) with well-defined differentiation and lymph node metastasis, including the lateral lymph node.

Acknowledgements

References

1. Beppu N, Matsubara N, Noda M, Kimura F, Yamanaka N, Yanagi H and Tomita N: Laparoscopic intersphincteric resection and J-pouch reconstruction without laparotomy. Surg Today 45: 659-662, 2015.

2. Yagci G, Unlu A, Kurt B, Can MF, Kaymakcioglu N, Cetiner S, Tufan T and Sen D: Detection of micrometastases and skip metastases with ex vivo sentinel node mapping in carcinoma of the colon and rectum. Int J Colorectal Dis 22: 167-173, 2007.

3. Hawes D, Neville AM and Cote RJ: Occult metastasis. Biomed Pharmacother 55: 229-242, 2001.

4. Merrie AE, Phillips LV, Yun K and McCall JL: Skip metastases in colon cancer: Assessment by lymph node mapping using molecular detection. Surgery 129: 684-691, 2001.

5. Soga J: Carcinoids of the rectum: An evaluation of 1271 reported cases. Surg Today 27: 112-119, 1997.

6. Zhou X, Xie H, Xie L, Li J and Fu W: Factors associated with lymph node metastasis in radically resected rectal carcinoids: A systematic review and meta-analysis. J Gastrointest Surg 17: 1689-1697, 2013.

7. Takaku H, Suda T, Iiai T, *et al*: Primary neuroendocrine cells of the rectum-carcinoid tumor and endocrine cell carcinoma. Niigata-igaku 125: 611-619, 2011 (In Japanese).