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Case Report

A Case of Colon Cancer with Extramural Tumor Deposits in the Main Lymph Node Area: A Case Report

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Abstract

A 72-year-old man with type 2 sub-circumferential tumors in the descending colon and two nodules around the pedicle of the inferior mesenteric artery (main lymph node area) underwent laparoscopic left hemicolectomy with D3 lymphadenectomy. Two lymph nodes around the inferior mesenteric artery pedicle were completely excised. Pathological examination revealed a moderately differentiated tubular adenocarcinoma. Nodules were only found in the main lymph node area, and no lymph node structures were observed in these nodules. These tumor deposits (TDs) may be extramural TDs without lymph node structure or lymph node skip metastasis. The presence of TDs in colorectal cancer is associated with an adverse prognosis, and the requirement of chemotherapy in such cases should be examined. Therefore, it is important to correctly recognize TDs and categorize the disease into a high- or low-risk group within stage III. We report this case because it is necessary to review the definition of TDs, and the assessment of extramural TDs remains controversial.

Keywords

colorectal cancer, adenocarcinoma, extramural tumor deposits without lymph node structure, lymph node skip metastasis

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Introduction

Extramural tumor deposits (TDs) are defined as all extramural malignant TDs in the lymph node (LN) area without an LN structure, and the presence of the TDs in colorectal cancer (CRC) is associated with an adverse prognosis [1]. And so, even in the absence of metastasis positive regional LN, the cancer should be classified and treated as stage III.

The National Comprehensive Cancer Network (NCCN) guidelines for the diagnosis of colon cancer categorize regional LN metastasis positive (LN+) disease as N1a-b and N 2a-b stages, and extramural TDs metastasis positive (TDs+) disease as N1c stage [1,2].

On the other hand, although Japanese Classification of Colorectal, Appendiceal, and Anal Carcinoma state that TDs without vascular or nerve invasion should be treated as lymph node metastasis, the recognition of this concept is still low. Also in other countries, recent large retrospective studies have shown that patients with TD+LN− cancer are less likely to receive adjuvant chemotherapy than those with LN+ cancer [1,3,4].

We encountered a case of colon cancer with extramural TDs in the area of the main LNs.

We report this information in order to increase awareness of TDs and to link them to appropriate treatment.

In addition, it has been reported that TD+LN- cases are present in about 4% of all colorectal cancers [1], but the location of TDs is not described.

Therefore, there are no existing reports of cases such as the present case, in which TDs are found only in the main

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lymph node region without lymph node metastasis.

Case Report

A 72-year-old man with constipation and abdominal pain during bowel movements was referred to our hospital with a positive result for a fecal occult blood test performed at another hospital. Physical examination did not reveal any evidence of complete intestinal occlusion. The patient had a history of hypertension treated with an oral angiotensin-converting-enzyme inhibitor, calcium channel blocker, and beta-adrenergic blocking agent. There was no relevant family history.

Laboratory examination results were unremarkable. The serum levels of all tumor markers were within the normal ranges (CEA, 5.0 ng/mL; CA19-9, 11.4 U/mL). However, colonoscopy revealed an advanced type 2 subcircumferential tumor in the descending colon (Figure 1), which was recognized as a well-differentiated adenocarcinoma following a histopathological study.

Contrast computed tomography revealed tumors in the descending colon and two nodules around the pedicle of the inferior mesenteric artery (IMA), a main LN area (Figure 2). There was no evidence of metastasis to other organs, such as the liver and lungs, and peritoneal metastasis. The barium enema test showed sub-obstruction of the descending colon; therefore, we performed laparoscopic left hemicolectomy with D3 lymphadenectomy. IMA was detached at the pedicle, LCA also transected.

Two nodules 8 mm in size around the pedicle of the inferior mesenteric artery were completely excised (Figure 3). The tumor was 45 x 40 mm in size and had an annular circumference of 73%. Pathological examination of the tumor revealed moderately differentiated tubular adenocarcinoma. The cancer invaded up to the subserosal layer. Involvement of lymphatic vessels, veins, and nerves were observed, re-

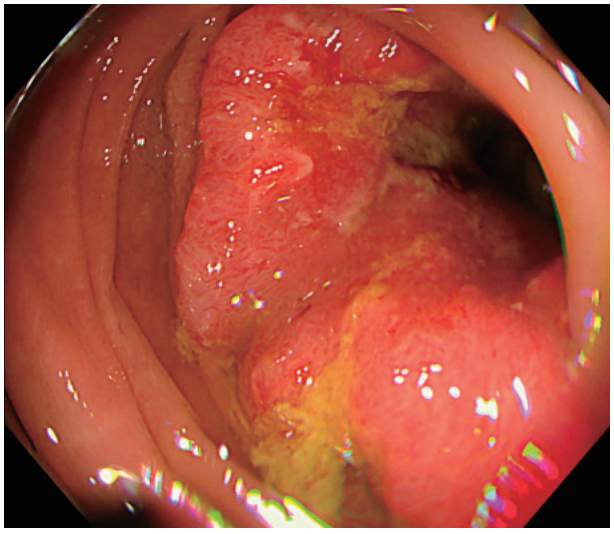


Figure 1. Colonoscopy image showing an advanced type 2 subcircumferential tumor in the descending colon.

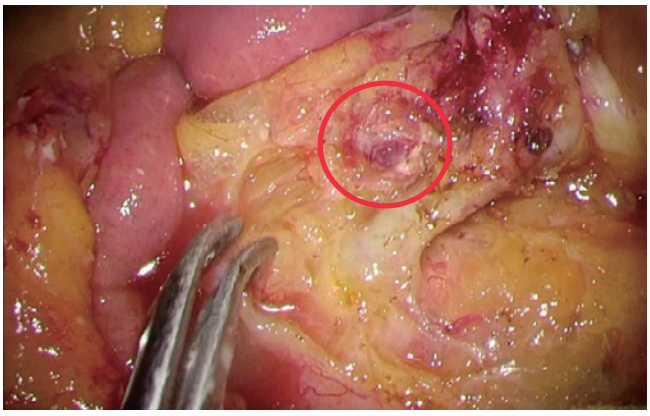
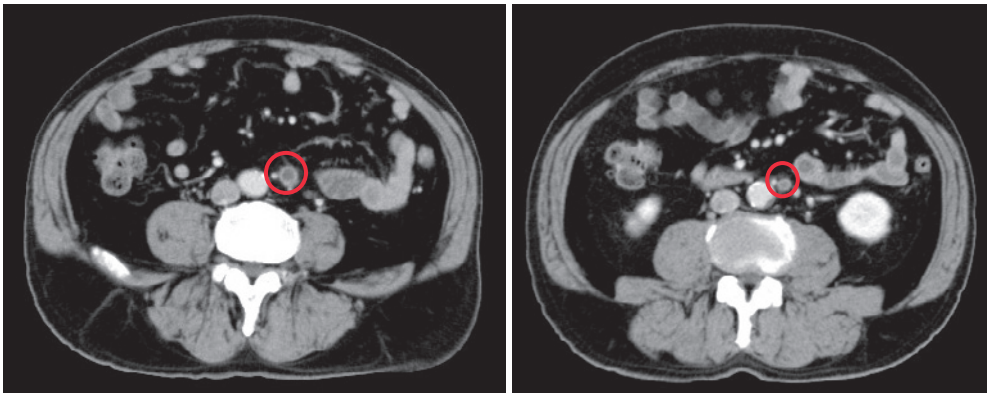


Figure 3. Tumor nodules (red circle) are observed around the pedicle of the inferior mesenteric artery on laparoscopy.



a b

Figure 2. a, b Contrast computed tomography images showing two nodules around the pedicle of the inferior mesenteric artery, a main lymph node area (red circle).

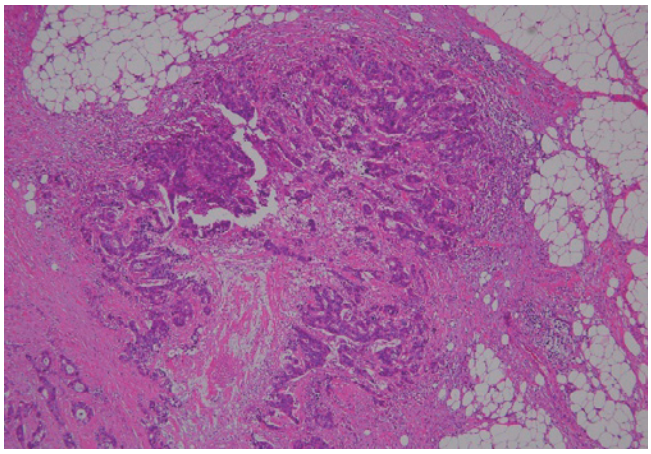


Figure 4. No lymph node structures are observed in the tumor nodules on histopathological examination (HE×40).

spectively. Two nodules were found in the main LN area, and no LN structures were observed in these nodules (Figure 4). The patient was diagnosed with descending colon cancer pT3N3M0, pStageIIIc (JSCCR 9th), and was discharged 8 days after surgery due to good postoperative progress. One month after the surgery, the patient developed stenosis in the third part of the duodenum, which was caused by an ileus operation at two months after surgery. The patient is being followed up at another hospital.

Informed consent was obtained from the patient for the publication of this case report.

Discussion

CRC is one of the most common malignancies in the world. Some patients develop local or distant recurrence within five years of curative resection. Assessment of the risk of recurrence is important for improving CRC prognosis. The risk of recurrence in patients after curative resection is generally based on the tumor stage, which is determined by the depth of the tumor (T factor) and LN metastasis (N factor).

Although the concept of extramural TDs, they are defined as discrete tumor foci in the mesocolic (or perirectal) fat within the lymphatic drainage area of the primary tumor but without an LN structure. In the fifth editions of the American Joint Committee on Cancer staging system (AJCC), a TD of 3 mm or more is considered to be an involved lymph node, in smaller than 3 mm, TDs were classified in the pT category(3 mm rule) [5]. In the 6th edition, tumor nodules that have a round smooth contour were considered to be lymph nodes and designated as N1/2(the contour rule) [5]. However, in the seventh edition, TDs are recognized as a separate entity [5], and the NCCN guidelines for the diagnosis of colon cancer state that TD metastasis positivity represents the N1c stage. This classification was maintained without change in the eighth edition, published in 2018 [1,2]. In the present patient, TDs were found only in the main LN area beside the primary lesion. It is possible that these TDs are extramural TDs without a LN structure.

Wong-Chong et al. showed that approximately 25% of all stage III colon cancers had TDs [4]. Moreover, TDs have been reported to be associated with poor prognosis in patients with CRC. The presence of TDs in patients with stage III colon cancer is associated with a 2.2-fold increased risk of developing disease recurrence [6]. TDs have also been reported as a risk factor for liver metastases [7,8] and pelvic recurrence [8]. Victor et al. showed that patients with LN+ TD+ disease (5-year survival rates is 41.5%) had significantly worse 5-year survival rates than those with LN+TD− (59.8%) and LN−TD+ (58.2%) disease [1]. It is important to incorporate TDs into the TNM classification as a predictor of recurrence. Therefore, accurate recognition of TDs is essential.

The Japanese Society for Cancer of the Colon and Rectum(JSCCR) calls extramural TDs “Ex”. Of these, NDs are defined as those in which vascular and nerve invasion is not the main lesion, and classified in the pN category (ND rule) [9]. Ueno et al. showed that Ex-based categorization had a stronger effect on N staging than on T staging and ND rule could more effectively stratify the survival outcome than the contour rule [10].

Although the JSCCR definition is a useful classification that reflects prognosis, the fact that it is not well known is a problem.

In this case, there was no metastasis in the lymph nodes near the tumor, but TDs were found in the main lymph node area. If lymph node structures are found in the TDs, it is LN skip metastasis (LNSM), and a search on PubMed reveals scattered reports. On the other hand, there are no reports of skip metastasis of extramural TDs without LN structures.

Patients with LNSM tend to have smaller tumor diameters and shallower tumor invasion than patients in the skip-negative group [12]. Previous studies have found that patients with LNSM have a better prognosis than patients without LNSM after radical D3 lymphadenectomy [11,13]. Because the presence of TDs has a poor prognosis, it seems contradictory that TDs can result in skip metastasis.

On the other hand, one possible mechanism for the development of LNSM is that lymphatic vessels near the tumor may be blocked by cancerous tissues, and the drainage bypasses the LNs that are near the tumor and occurs towards distant LNs [12]. This mechanism could also cause skip metastasis of epidural TD without LN structure.

As in the present case, if the tumor nodules are found only in the main LN region, the prognosis varies widely depending on whether the nodules are diagnosed as TDs or LNSM. This may have a significant impact on postoperative

recovery.

Also, it follows that the current patient with TDs should receive adjuvant chemotherapy. If the nodule is identified preoperatively, as in this case, it should be removed. Moreover, we should determine the number of TDs and categorize the disease into a high-risk or low-risk group within stage III, and appropriate chemotherapy selected according to risk. It has been suggested that these patients should be treated with drugs such as oxaliplatin and, by extension, bevacizumab, an antibody against vascular endothelial growth factor [5]. In contrast, as a limitation, postoperative treatment could not be performed in our hospital, even though the patient wanted it.

In this case, the extramural TDs were surgically removed without excess or deficiency, and the pathologist was able to make an appropriate diagnosis. TDs should be noted and considered along with other prognostic factors to inform surgeons and pathologists.

Conflicts of Interest

There are no conflicts of interest.

Author Contributions

All authors agree to be accountable for all aspects of the work. Yukari Ono wrote the manuscript with support from Manabu Shiozawa.

Approval by Institutional Review Board (IRB)

Approval code issued by the institutional review board, and the name of the institution that granted the approval: Kanagawa Cancer Center (2023 疫 6)

Informed Consent

Ethical approval was obtained from the patient for the publication of this case report.

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