Case Report Intramucosal colorectal carcinoma with lymphatic metastasis: a case report and review of literature

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Abstract: Intramucosal colorectal carcinoma refers to the invasive colorectal carcinoma with invasion confined to the lamina propria. For it lacks access to lymphatics and has no potential for metastases, local intervention is recommended. However, we report a case which is pathologically diagnosed as intramucosal colorectal carcinoma with lymphatic metastasis. And the patient undertook radical resection for colorectal carcinoma (Dixon operation) and preventive terminal ileum colostomy in laparoscope. The review discusses the recent researches on intramucosal carcinoma with metastasis and the choice of clinical decisions.

Keywords: Intramucosal colorectal carcinoma, lymphatic metastasis, laparoscopic-assisted colorectal surgery

Introduction

In the United States, colorectal cancer (CRC) is the third most common cancer diagnosed in men and women and the third leading cause of death from cancer [1]. While in China, it ranks fifth and has a trend of increasing [2]. When the cancer is limited to the lamina propria (LP), it is often called intramucosal carcinoma (IMC), and is classified as Tis in the TNM system. In theory, for colonic lamina propria lacks lymphatics, it has no potential path for metastatic spread [3]. However, recent reports showed that a proportion of Tis colon cancers had lymph node metastasis with a very low incidence [4], and had come up with the proposal of an alternative pathway of de novo colon carcinogenesis, which involves a quick infiltration of neighbouring tissue and lymph nodes [5-7]. Interestingly, we could find that intramucosal cancer has lymph nodes metastasis in gastric cancer [8]. But in colorectal cancer, data are still lacking regarding lymph node metastasis in intramucosal tumors [9]. Herein, we report a rare case of a middle-aged female of intramocusal colorectal carcinoma with lymphatic metastasis, and present a review on current research of intramocusal colorectal carcinoma.

Case report

In November 2015, a 48-year-old female came to our hospital for medical treatment with a four-month history of difficulty in defecation and hematochezia. Physical examination indicated no tenderness or rebound tenderness in abdomen, and the shifting dullness was negative. Digital rectal examination found a 1 cm × 0.5 cm mass about 5 cm away from anus. The mass was soft and without tenderness, meanwhile there was no blood on finger cot after retreating. Further abdominal and pelvic CT scan revealed the local thickening of distal rectum with a size of 1.2 cm × 1.0 cm, and the front wall was more obvious. The fat clearance of the Dow cavity was unclear. Enhanced CT scan showed that the lesion was apparently strengthened, and lymphadenopathy could be seen in the abdominal pelvic cavity and retroperitoneum (Figure 1). Previous biopsy result elucidated that the nature of the lesion was villioustublar adenoma with high-grade intraepithelial neoplasia.

According to these results of preoperative evaluation, the patient underwent radical resection for colorectal carcinoma (Dixon operation) and



Figure 1. Computed tomography shows the mass and suspected lymphadenopathy.



Figure 2. The upper circle area indicates intramucosal carcinoma, while the nether one shows the intermediate grade intraepithelial neoplasia (H&E staining, magnification × 400).

preventive terminal ileum colostomy in laparoscope. During the surgery, we found the rectal neoplasm below the peritoneal reflection, and no transfer lesion could be seen in abdominal cavity. After exploration, we did total mesorectum excision of the rectum until muscular pelvic floor plane. Then we cut the rectum slightly above the dentate line, and the margin was 3 cm away from rectal neoplasm. When rectal resection was done, we undertook sigmoiddentate line anastomosis and preventive terminal ileum colostomy.

Postoperative pathological examination identified a 1.2 cm \times 1 cm cauliflower-like polyp (1 cm away from one side of the resection margin) as villioustublar adenoma with high-grade intraepithelial neoplasia-intramucosal carcinoma (**Figure 2**). And metastasis was found in surrounding lymph nude (1/9) (**Figure 3**), while the surgical margins were clean. Additionally,



Figure 3. Intestinal epithelium in this lymph node which is identified in the circle (H&E staining, magnification \times 100).

immunohistochemistry (IHC) studies showed that the specimen was positive for CDX2, an intestine-specific transcription factor, and cyto-keratin 20 (CK20) (**Figure 4**), a cytoskeletal protein usually found in the colonic epithelium.

The patient began to drink water three days later and resumed oral intake in six days. No severe complications like obstruction after diverting colostomy, narrow fistula or incisional hernia were found during the hospital stay after the surgery. For the patient got lymphatic metastasis, we suggested the patient to receive further chemotherapy.

Discussion

It's recommended that high-grade lesions invading the submucosa should be treated with a more definitive resection. However, it has not been well documented whether IMCs with poor differentiation limited to the lamia propria behave more aggressively or moderately differentiated counterparts according to the polypectomy specimens [10]. It is deemed to have little possibility of lymph node metastasis in the patients with intramucosal colorectal cancer, and the size and location of the tumor make en bloc resection possible. Therefore the endoscopic treatment is recommended in this situation. Although it's believed that the lymph node dissection is unnecessary for Tis cancer, D1 dissection can be performed because of the accuracy of the preoperative diagnosis may be insufficient [11]. We have also summarized the articles which mentioned about intramucosal or submucosal colorectal carcinoma with



Figure 4. IHC staining of the intramucosal carcinoma including CD20 (magnification \times 40) and CDX2 (magnification \times 40).

 Table 1. Similar cases of Intramucosal or submucosal colorectal carcinoma with lymphatic metastasis

Authors	Year	Deep	Cases	Node positive N (%)
Al Natour RH	2012	Intramucosal	43	6 (14)
		Submucosal	40	10 (25)
Mi Na Kim	2011	Intramucosal	64	0 (0)
		Submucosal	65	7 (11)
Gunderson	2010	Intramucosal	5935	114 (2)
		Submucosal	20574	1072 (5)

lymphatic metastasis in **Table 1**, while the results were varied and under discussion.

In this patient specifically, the preoperative biopsy result indicated the nature of the lesion was villioustublar adenoma with high-grade intraepithelial neoplasia, and the CT scan also pointed out the possibility of metastasis. These evaluations made polypectomy alone had a high risk of recurrence. And in our experience, the lesions with high-grade intraepithelial neoplasia usually undergo the radical resection, and it could bring more benefits to our patients. After further discussion, we developed a treatment plan of radical resection for colorectal carcinoma (Dixon operation) and preventive terminal ileum colostomy in laparoscope. For radical surgery of rectal cancer, the principle is total mesorectal excision or tumor-specific mesorectal excision [12, 13]. And there is no doubt that en bloc excision of the lymphatic drainage of the tumor, including the lymph nodes located therein, has been shown to have fundamentally influence the long-term prognosis after the surgery of CRC [14, 15]. It's also reported that aggressive surgical strategies with the aim of complete malignancy elimination are associated with improved disease-free as well as overall survival in most cases of primary and secondary CRC [16, 17].

The choice between endoscopic submucosal dissection (ESD) and laparoscopic-assisted colorectal surgery (LAC) for early-stage colorectal cancer is equivocal and under discussion. Although ESD becomes a minimally invasive treatment for superficial colorectal cancers, the patients who underwent ESD would have faced similar risks of morbidity to the patients who were treated with surgery, and the noncurative resection rate in a previous prospective, multicenter study of colorectal ESD was 9% [18, 19]. In addition, the existence of different indications for both ESD and LAC procedures worldwide and different costs associated with the different

procedures also let the clinical decisions more difficult to make. In general, the choice of treatment is a combination of clinical indications, technical skills, and patients' will, which aimed at bringing the biggest benefit to the patients.

The mechanism of metastasis of the intramucosal colorectal carcinoma is still requiring further study. As we have known, the most common pathway of colorectal cancer development is thought to be the adenoma-carcinoma sequence, in which carcinoma develops from an adenomatous polyp [20]. Alternately, several Japanese researchers suggest that colorectal cancer can also develop from normal mucosa, in a de novo process involving morphological changes from a small superficial-type carcinoma to depressed-type carcinoma. In addition, the poor differentiated type or signet-ring cell carcinoma attributes to quick metastasis [5].

In conclusion, this is a rare case of intramucosal colorectal carcinoma with lymphatic metastasis. Although the mechanism is still unknown, it strongly recommends us to reconsider the preoperative evaluations of metastasis. The MRI or enhanced CT scan is suggested to identify the lymphatic metastasis before making the clinical decisions. And it has been reported that the short diameter size criterion of ≥ 4.1 mm for metastatic lymph nodes was optimal for nodal staging in early colorectal cancer [21]. Narrow band imaging colonoscopy also brings us a new method to evaluate colorectal mucosal lesions [22]. For it's able to represent more clearly boundary between different types of tissue, which is necessary in diagnosing a tumor in its early stage, and achieved better visualization of the mucosal vascular network and of the hue of lesions [23]. These advantages could help us with diagnosing more accurately. As we have discussed above, for the lesions which are confined and without metastasis we still recommend en bloc resection in endoscope. As for the patients who has diagnosed with metastasis, radical resection would bring more benefits.

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Disclosure of conflict of interest

None.

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References

- [1] Siegel RL, Miller KD and Jemal A. Cancer statistics, 2016. CA Cancer J Clin 2016; 66: 7-30.
- [2] Chen W, Zheng R, Baade PD, Zhang S, Zeng H, Bray F, Jemal A, Yu XQ and He J. Cancer statistics in China, 2015. CA Cancer J Clin 2016; 66: 115-132.
- [3] Fenoglio CM, Kaye GI and Lane N. Distribution of human colonic lymphatics in normal, hyperplastic, and adenomatous tissue. Its relationship to metastasis from small carcinomas in pedunculated adenomas, with two case reports. Gastroenterology 1973; 64: 51-66.
- [4] Gunderson LL, Jessup JM, Sargent DJ, Greene FL and Stewart AK. Revised TN categorization

for colon cancer based on national survival outcomes data. J Clin Oncol 2010; 28: 264-271.

- [5] Matsumoto M, Nakajima T, Kato K, Kouno T, Sakamoto T, Matsuda T, Kushima R and Saito Y. Small invasive colon cancer with systemic metastasis: a case report. BMC Gastroenterol 2011; 11: 59.
- [6] Nakajima T, Saito Y, Matsuda T, Hoshino T, Yamamoto S, Tamura T, Moriya Y and Saito D. Minute depressed-type submucosal invasive cancer-5 mm in diameter with intermediate lymph-node metastasis: report of a case. Dis Colon Rectum 2007; 50: 677-681.
- [7] Shimoda T, Ikegami M, Fujisaki J, Matsui T, Aizawa S and Ishikawa E. Early colorectal carcinoma with special reference to its development de novo. Cancer 1989; 64: 1138-1146.
- [8] Gotoda T, Yanagisawa A, Sasako M, Ono H, Nakanishi Y, Shimoda T and Kato Y. Incidence of lymph node metastasis from early gastric cancer: estimation with a large number of cases at two large centers. Gastric Cancer 2000; 3: 219-225.
- [9] Lan YT, Yang SH, Li AF and Lin JK. Conflicting finding on intramucosal colon cancers based on national survival outcomes data. J Clin Oncol 2010; 28: e469; author reply e470.
- [10] Lewin MR, Fenton H, Burkart AL, Sheridan T, Abu-Alfa AK and Montgomery EA. Poorly differentiated colorectal carcinoma with invasion restricted to lamina propria (intramucosal carcinoma): a follow-up study of 15 cases. Am J Surg Pathol 2007; 31: 1882-1886.
- [11] Watanabe T, Itabashi M, Shimada Y, Tanaka S, Ito Y, Ajioka Y, Hamaguchi T, Hyodo I, Igarashi M, Ishida H, Ishihara S, Ishiguro M, Kanemitsu Y, Kokudo N, Muro K, Ochiai A, Oguchi M, Ohkura Y, Saito Y, Sakai Y, Ueno H, Yoshino T, Boku N, Fujimori T, Koinuma N, Morita T, Nishimura G, Sakata Y, Takahashi K, Tsuruta O, Yamaguchi T, Yoshida M, Yamaguchi N, Kotake K and Sugihara K. Japanese society for cancer of the colon and rectum (JSCCR) guidelines 2014 for treatment of colorectal cancer. Int J Clin Oncol 2015; 20: 207-239.
- [12] MacFarlane JK, Ryall RD and Heald RJ. Mesorectal excision for rectal cancer. Lancet 1993; 341: 457-460.
- [13] Enker WE, Thaler HT, Cranor ML and Polyak T. Total mesorectal excision in the operative treatment of carcinoma of the rectum. J Am Coll Surg 1995; 181: 335-346.
- [14] Le Voyer TE, Sigurdson ER, Hanlon AL, Mayer RJ, Macdonald JS, Catalano PJ and Haller DG. Colon cancer survival is associated with increasing number of lymph nodes analyzed: a secondary survey of intergroup trial INT-0089. J Clin Oncol 2003; 21: 2912-2919.

- [15] Lykke J, Jess P and Roikjaer O. Increased lymph node yield is associated with improved survival in rectal cancer irrespective of neoadjuvant treatment: results from a national cohort study. Dis Colon Rectum 2015; 58: 823-830.
- [16] West NP, Hohenberger W, Weber K, Perrakis A, Finan PJ and Quirke P. Complete mesocolic excision with central vascular ligation produces an oncologically superior specimen compared with standard surgery for carcinoma of the colon. J Clin Oncol 2010; 28: 272-278.
- [17] Rentsch M, Schiergens T, Khandoga A and Werner J. Surgery for colorectal cancer trends, developments, and future perspectives. Visc Med 2016; 32: 184-191.
- [18] Saito Y, Uraoka T, Yamaguchi Y, Hotta K, Sakamoto N, Ikematsu H, Fukuzawa M, Kobayashi N, Nasu J, Michida T, Yoshida S, Ikehara H, Otake Y, Nakajima T, Matsuda T and Saito D. A prospective, multicenter study of 1111 colorectal endoscopic submucosal dissections (with video). Gastrointest Endosc 2010; 72: 1217-1225.
- [19] Kiriyama S, Saito Y, Yamamoto S, Soetikno R, Matsuda T, Nakajima T and Kuwano H. Comparison of endoscopic submucosal dissection with laparoscopic-assisted colorectal surgery for early-stage colorectal cancer: a retrospective analysis. Endoscopy 2012; 44: 1024-1030.

- [20] Vogelstein B, Fearon ER, Hamilton SR, Kern SE, Preisinger AC, Leppert M, Nakamura Y, White R, Smits AM and Bos JL. Genetic alterations during colorectal-tumor development. N Engl J Med 1988; 319: 525-532.
- [21] Choi J, Oh SN, Yeo DM, Kang WK, Jung CK, Kim SW and Park MY. Computed tomography and magnetic resonance imaging evaluation of lymph node metastasis in early colorectal cancer. World J Gastroenterol 2015; 21: 556-562.
- [22] Machida H, Sano Y, Hamamoto Y, Muto M, Kozu T, Tajiri H and Yoshida S. Narrow-band imaging in the diagnosis of colorectal mucosal lesions: a pilot study. Endoscopy 2004; 36: 1094-1098.
- [23] Gono K, Obi T, Yamaguchi M, Ohyama N, Machida H, Sano Y, Yoshida S, Hamamoto Y and Endo T. Appearance of enhanced tissue features in narrow-band endoscopic imaging. J Biomed Opt 2004; 9: 568-577.