Characteristics of the portal vein thrombosis recurrence pattern without liver parenchymal invasion from colorectal cancer: a case report

Tetsuya Mochizuki, Tomoyuki Abe*, Hironobu Amano, Kenji Nishida, Takuya Yano, Hiroshi Okuda, Tsuyoshi Kobayashi, Hideki Ohdan, Shuji Yonehara, Toshio Noriyuki and Masahiro Nakahara

Abstract

Background: Portal vein tumor thrombosis from colorectal cancer is rare, and this recurrence pattern was mainly reported in patients with renal cell carcinoma and hepatocellular carcinoma. Furthermore, the recurrence pattern of portal vein tumor thrombosis without liver parenchymal invasion from colorectal carcinoma has not been previously reported. Herein, we present a patient with progressive portal vein tumor thrombosis without liver parenchymal invasion following curative resection.

Case presentation: A 61-year-old man with a chief complaint of constipation with abdominal pain associated with rectal carcinoma was admitted to our hospital. Computed tomography (CT) showed that the rectosigmoid colon wall was thickened, regional lymph nodes were swollen, and the light space-occupying lesion (SOL) was detected at segment 8 (S8). Neoadjuvant chemotherapy was performed, which was followed by laparoscopic anterior resection. The final diagnosis was stage IIIb (SS, N2, M0). After operation, systemic adjuvant chemotherapy was introduced. At first, tumor marker levels were within the normal range and there were no accumulations on positron emission tomography (PET). Tumor marker levels were elevated, and contrast-enhanced CT demonstrated that the portal vein SOL slowly extended from S8 to S5. Additionally, PET showed that the standardized uptake value was abnormally high at 5.8. Based on the diagnosis of portal vein tumor thrombosis, right hepatectomy was performed. On pathological analysis, tumor thrombosis was associated with rectal carcinoma, and there was no invasion toward the liver parenchyma. Additionally, the surgical cut end was tumor free. Six months after the hepatectomy, the paraaortic lymph nodes showed swelling. The patient is currently undergoing systemic chemotherapy.

Conclusion: Aggressive surgical resection should be considered in cases of portal vein tumor thrombosis. A good long-term prognosis could be obtained by a combination of curative resection and systemic chemotherapy.

Keywords: Rectal cancer, Tumor thrombosis, Surgical resection

* Correspondence: tabe.hiroshima@gmail.com
1Department of Surgery, Onomichi General Hospital, Onomichi, Hiroshima, Japan
Full list of author information is available at the end of the article

© The Author(s). 2018 Open Access This article is distributed under the terms of the Creative Commons Attribution 4.0 International License (http://creativecommons.org/licenses/by/4.0/), which permits unrestricted use, distribution, and reproduction in any medium, provided you give appropriate credit to the original author(s) and the source, provide a link to the Creative Commons license, and indicate if changes were made.
Background
Hepatectomy for resectable liver metastasis from colorectal cancer is the gold standard treatment approach [1–3]. The risk factors for poor prognosis after hepatectomy include a short interval between primary surgery and recurrence, elevated tumor marker levels, multiple tumors, presence of lymph node metastasis, and a large tumor size [3, 4]. However, the efficacy of perioperative systemic chemotherapy has not been established. Regardless of curative surgery, the 5-year recurrence rate after hepatectomy has been reported to be 36–58% [5–7].

Considering the hypothesis that colorectal cancer tumor metastasis progresses from liver parenchyma through the portal vein wall, circulating tumor cells (CTCs) are believed to play an important role [8, 9]. To our knowledge, the recurrence pattern of portal vein tumor thrombosis (PVTT) without liver parenchymal invasion from colorectal carcinoma has not been previously reported. Herein, we present a patient with progressive PVTT without liver parenchymal invasion following curative resection.

Case presentation
We explained the case report and publication process to the patient and obtained his permission to publish this report.

A 61-year-old man was examined by a local physician for a chief complaint of constipation with abdominal pain. Computed tomography (CT) showed that the rectosigmoid colon wall was thickened, regional lymph nodes were swollen, and the obscure space-occupying lesion (SOL) was detected at S8, especially localized into the portal vein. He was admitted to our hospital for further treatment. Colonography revealed a type 3 tumor in the rectosigmoid colon. Laboratory data demonstrated elevated tumor marker levels (carcinoembryonic antigen, 74.4 ng/mL; cancer antigen 19-9, 53.5 U/mL). Because of obstructive colitis that was associated with his massive cancer, emergency colonostomy was performed. Prior treatment with systemic chemotherapy was performed for curative surgery with suspicion of PVTT: 6 courses of mFOLFOX6 + panitumumab chemotherapy (panitumumab was administered as a 60-min intravenous infusion before oxaliplatin at a dose of 6 mg/kg, leucovorin at 200 mg/m², oxaliplatin at 85 mg/m², and bolus fluorouracil at 400 mg/m², all on day 1, followed by 2400 mg/m²/46 h, each 14-day cycle) were administered as adjuvant chemotherapy, during which tumor marker levels were elevated. On positron emission tomography (PET), abnormal accumulation (maximum standardized uptake value [SUVmax], 5.8) at P8 was detected (Fig. 1). CT showed low intensity in the portal vein (Fig. 2a, b). Magnetic resonance imaging (MRI) with gadolinium ethoxybenzyl diethylenetriamine-pentaacetic acid revealed that the nodule in the portal vein extended from segment 8 (S8) to S5 and had a ring-like high contrast (Fig. 3a, b). Therefore, right hemihepatectomy was performed (operation time, 364 min; bleeding volume, 300 mL). On histopathological analysis, the PVTT was from colon cancer, which had not invaded the hepatic parenchyma. The cut surface was free from tumor invasion (Fig. 4). The patient had no specific postoperative complications, and he was discharged 13 days after the operation. Four months after hepatectomy, paraaortic lymph node recurrence occurred. The patient is currently undergoing systemic chemotherapy.

Discussion
Venous tumor thrombosis occasionally occurs in patients with renal cell carcinoma, pancreatic carcinoma, gastric carcinoma, hepatocellular carcinoma (HCC), adrenal cortical carcinoma, and testicular carcinoma [10–14]. To the best of our knowledge, it is rare for a case to exhibit portal vein tumor recurrence without liver parenchymal invasion following surgical resection. In general, the recurrence sites of colorectal cancer are the lungs and liver, and in the absence of several risk factors for recurrence, curative resection could provide a good long-term prognosis [15]. Otani et al. reported 43
cases of colorectal cancer with adjacent drainage vein tumor thrombosis, and aggressive surgical resection was considered to improve long-term prognosis [11]. In our case, the primary rectal carcinoma itself did not show massive venous (v1) and lymphatic (ly1) invasion; therefore, even after systemic chemotherapy, PVTT could have occurred through this vascular invasion, or CTCs may have been implanted into the portal vein wall.

In the case of HCC, tumor thrombosis is often detected via pathological assessment after surgery, and the presence of portal vein invasion has been reported as a risk factor for recurrence [16, 17]. Surgical removal of the tumor thrombosis was the most effective curative treatment for HCC [18]. However, transcatheter arterial chemoembolization can be considered in patients with severe liver failure or a highly advanced tumor stage [12, 19]. The mechanism of PVTT is different between HCC and colorectal liver metastasis (CRLM). PVTT from HCC is derived from direct invasion, whereas CRLM is considered based on whether direct tumor invasion is through the blood stream or indirect tumor invasion through CTC implantation. The prognosis of patients with venous tumor thrombosis of colorectal cancer is unclear; however, evidence of hepatectomy for CRLM is well established [20]. In HCC, obstructive tumor thrombosis of the bile duct and portal vein thrombosis have been reported, and the dismal prognosis of these conditions could be beneficially changed with curative surgery [21]. Given that metastatic PVTT could be curatively resected, aggressive surgery could potentially be an efficient treatment.

In patients without other distant metastases and with good performance status, aggressive surgical resection should be considered. In our case, early recurrence was noted at the paraaortic lymph nodes, and systemic second-line treatment is currently being administered. Cohen et al. reported that during treatment for metastatic colorectal cancer, the number of CTCs is an independent risk factor for poor overall survival (OS) and progression-free survival. In patients with colorectal metastasis, those with unfavorable CTCs had a dismal prognosis of 3.7 months of OS compared to those with a low number of CTCs with 11.0 months of OS [9]. Even after curative surgery, intrahepatic recurrence occurred approximately 60% [5]. Until now, the relationship between CTC and CRLM remains unclear. Some studies have
demonstrated that CTC is associated with long-term survival in various cancer types [22–24]. Given that most metastatic forms of colorectal cancer are liver metastasis, CTCs could be implanted into the portal vein, consequently resulting in PVTT. Early detection of recurrent disease when traditional clinical indicators, such as radiological findings are negative, is important to improve patient survival. Therefore, CTC investigation would be a breakthrough in cancer metastatic mechanism. In our case, the relatively better survival of 15 months following the first surgery could be achieved because of repeat surgical resection combined with systemic chemotherapy.

Radiological findings of tumor thrombosis are quite similar to those of venous thrombosis, but the precise diagnosis is quite difficult with dynamic-enhanced CT alone. Recently, PET yielded good efficacy for detecting venous tumor thrombosis when using intense radiotracer accumulation [25, 26]. Additionally, MRI plays an essential role in differentiating thrombosis and tumor thrombosis, and T2- and diffusion-weighted imaging were shown to be particularly accurate for diagnosis [27]. PET-CT has an important role in diagnosing cancer recurrence and characterizing a thrombus using abnormal accumulation (SUVmax) over time. The mean SUVmax values for bland thrombosis and tumor thrombosis have been shown to be significantly different. For differentiating tumor thrombosis from bland thrombosis, the measurement of SUVmax (cutoff value of 2.25) on PET is useful [26]. In the present case, tumor marker levels remained elevated during systemic chemotherapy. The diagnosis of tumor thrombosis was made based on a SUVmax value of 5.8 on PET-CT. PET-CT enabled the detection of tumor thrombosis recurrence by revealing an elevated SUVmax.

Conclusions
The recurrence pattern of only portal vein thrombosis from colorectal cancer is extremely rare; however, attention should be paid to tumor thrombosis as a recurrence pattern of colorectal carcinoma. Moreover, the radiological findings of portal vein thrombosis are quite similar to those of PVTT. The present findings reveal that PET plays an important role in distinguishing PVTT and portal vein thrombosis by evaluating SUV. Furthermore, PET can help guide selection of additional treatment, such as surgical resection with systemic chemotherapy.

Abbreviations
CRLM: Colorectal liver metastasis; CT: Computed tomography; CTCs: Circulating tumor cells; HCC: Hepatocellular carcinoma; IV: Intravenous infusion; MRI: Magnetic resonance imaging; OS: Overall survival; PET: Positron emission tomography; PVTT: Portal vein tumor thrombosis; SOL: Space-occupying lesion; SUVmax: Maximum standardized uptake value

Funding
The authors declare that this work was not supported by any grants or funding support.

Availability of data and materials
The data for this case report will not be shared to ensure patient confidentiality.
Authors’ contributions
TM and TA wrote the manuscript. The remaining authors contributed to the collection, analysis, and interpretation of data. TM, TA, HA, TY, HO, and MN performed the surgery. KN and SY performed the pathological diagnosis of the disease. All authors conceived the study, participated in its design and coordination, and helped to draft the manuscript. All authors have read and approved the final manuscript.

Ethics approval and consent to participate
The publication of this case report was approved by the institutional ethics committee.

Consent for publication
Written informed consent was obtained from the patient for publication of this case report and any accompanying images.

Competing interests
The authors declare that they have no competing interests.

Publisher’s Note
Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.

Author details
1 Department of Surgery, Onomichi General Hospital, Onomichi, Hiroshima, Japan. 2 Department of Pathology, Onomichi General Hospital, Onomichi, Hiroshima, Japan. 3 Department of Gastroenterological and Transplant Surgery, Graduate School of Biomedical and Health Sciences, Hiroshima University, Hiroshima, Japan. 4 Department of Pathology, Okayama University Graduate School of Medicine, Dentistry and Pharmaceutical Sciences, Okayama, Japan.

Received: 30 May 2018 Accepted: 28 August 2018
Published online: 04 September 2018

References
1. Minagawa M, Makuchi M, Torzilli G, Takayama T, Kawasaki S, Kosuge T, et al. Extension of the frontiers of surgical indications in the treatment of liver metastases from colorectal cancer: long-term results. Ann Surg. 2000;231:487–99.
2. Choti MA, Sitzmann JV, Tiburi MF, Sunetchotimetha W, Rangsin R, Schullik RD, et al. Trends in long-term survival following liver resection for hepatic colorectal metastases. Ann Surg. 2002;235:759–66.
3. Fong Y, Fortner J, Sun RL, Brennan MF, Blumgart LH. Clinical score for predicting recurrence after hepatic resection for metastatic colorectal cancer: analysis of 1001 consecutive cases. Ann Surg. 1999;230:309–18. Discussion 19-21.
4. Beppu T, Sakamoto Y, Hasegawa K, Honda G, Tanaka K, Koteru Y, et al. A nomogram predicting disease-free survival in patients with colorectal liver metastases treated with hepatic resection: multicenter data collection as a project study for hepatic surgery of the Japanese Society of Hepato-Biliary-Pancreatic Surgery. J Hepatobiliary Pancreat Sci. 2012;19:72–84.
5. Rees M, Tiekis PP, Welsh FK, O’Rourke T, John TG. Evaluation of long-term survival after hepatic resection for metastatic colorectal cancer: a multifactorial model of 929 patients. Ann Surg. 2008;247:125–35.
6. Pawlik TM, Scoggins CR, Zorzi D, Abdalla EK, Andres A, Eng C, et al. Effect of surgical margin status on survival and site of recurrence after hepatic resection for colorectal metastases. Ann Surg. 2005;241:715–22. discussion 22-4.
7. Figueras J, Torres J, Valls C, Liado L, Ramos E, Mari-Ragaz J, et al. Surgical resection of colorectal liver metastases in patients with expanded indications: a single-center experience with 501 patients. Dis Colon Rectum. 2007;50:478–88.
8. Pilati P, Mocellin S, Bertazzza L, Galli F, Birarava M, Mammnno E, et al. Prognostic value of putative circulating cancer stem cells in patients undergoing hepatic resection for colorectal liver metastasis. Ann Surg Oncol. 2012;19:402–8.
9. Cohen SJ, Punt CJ, Iannotti N, Saidman BH, Sabbath KD, Gabrail NY, et al. Relationship of circulating tumor cells to tumor response, progression-free survival, and overall survival in patients with metastatic colorectal cancer. J Clin Oncol. 2008;26:3213–21.
10. Singh O, George AJP, Singh JC, Devasia A. Transitional cell carcinoma of the renal pelvis with venous tumor thrombus. Rev Urol. 2017;19:145–8.
11. Otani K, Ishihara S, Hata K, Murono K, Sasai K, Yasuda K, et al. Colorectal cancer with venous tumor thrombosis. Asian J Surg. 2016; https://doi.org/10.1016/j.asjsur.2016.07.013.
12. Kamiyama T, Kikisaka T, Orito T, Wakayama K. Hepatectomy for hepatocellular carcinoma with portal vein tumor thrombus. World J Hepatol. 2017;9:1296–304.
13. Donohue JP, Thornhill JA, Foster RS, Rowland RG, Bhirke R. Resection of the inferior vena cava or intrauralial vena caval tumor thrombectomy during retroperitoneal lymph node dissection for metastatic germ cell cancer: indications and results. J Urol. 1991;146:346–9.
14. Nguyen BD. Pancreatic neuroendocrine tumor with portal vein tumor thrombus: PET demonstration. Clin Nucl Med. 2005;30:28–9.
15. Tanaka A, Takeda R, Mukihaia S, Hayakawa K, Takaoka K, Tetajima H, et al. Tumor thrombi in the portal vein system originating from gastrointestinal tract cancer. J Gastroenterol. 2002;37:220–8.
16. Ari S, Tanaka J, Yamazoe Y, Minematsu S, Morino T, Fujita K, et al. Predictive factors for intrahepatic recurrence of hepatocellular carcinoma after partial hepatectomy. Cancer. 1992;69:913–9.
17. Iki I, Ari S, Kojio M, Ichida T, Makuchi M, Matsuyama Y, et al. Reevaluation of prognostic factors for survival after liver resection in patients with hepatocellular carcinoma in a Japanese nationwide survey. Cancer. 2004;101:796–802.
18. Minagawa M, Makuchi M, Takayama T, Ohtomo K. Selection criteria for hepatectomy in patients with hepatocellular carcinoma and portal vein tumor thrombus. Ann Surg. 2001;233:739–44.
19. Ando E, Tanaka M, Yamashita F, Kurokota T, Utani S, Fukumori K, et al. Hepatic arterial infusion chemotherapy for advanced hepatocellular carcinoma with portal vein tumor thrombosis. Cancer. 2002;95:588–95.
20. Matsumoto J, Kojima T, Hiraguchi E, Abe M. Portal vein tumor thrombus from colorectal cancer with no definite metastatic nodules in liver parenchyma. J Hepato-Biliary-Pancreat Surg. 2009;16:688–91.
21. Abe T, Kajiyama K, Harimoto N, Shirabe K, Nagai T. Intrahepatic bile duct recurrence of hepatocellular carcinoma without a detectable liver tumor. Int J Surg Case Rep. 2012;3:275–8.