Colorectal cancer with venous tumor thrombosis


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Summary Colorectal cancer is seldom accompanied by venous tumor thrombosis, and little is known about the features of venous tumor thrombosis in colorectal cancer. However, some reports show that colorectal cancer patients can develop venous tumor thrombosis and warn clinicians not to overlook this complication. In this report, we perform a review of 43 previously reported cases and investigate the characteristics of colorectal cancer accompanied by venous tumor thrombosis. The histological type of more than half of the cases was moderately differentiated adenocarcinoma, which is known to be aggressive. Among 41 cases with available data on liver metastasis, eight patients had synchronous liver metastasis, and liver metastatic recurrence after surgical resection was indicated in 10 patients. This liver metastatic rate was high compared to general colorectal cancer. However, 11 of 43 patients with venous tumor thrombosis could survive for more than 2 years after the diagnosis, although five of the 11 patients had liver metastasis. A long survival can be anticipated for patients following complete tumor resection and adjuvant chemotherapy. A greater accumulation of cases will help elucidate the characteristics of colorectal cancer with venous tumor thrombosis and improve the treatment strategy.

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1. Introduction

Venous tumor thrombosis occasionally accompanies renal cell carcinoma, adrenal cortical carcinoma, hepatoma, pancreatic carcinoma, gastric carcinoma, Wilms’ tumor, and testicular carcinoma; however, colorectal cancer with tumor thrombosis in the portal or superior, inferior mesenteric vein is quite rare. Sato et al. reported that venous tumor thrombosis was detected in three cases (1.7%) out of 176 patients with advanced colorectal cancer. Regarding renal cell carcinoma, it has a high propensity to invade adjacent renal veins and the inferior vena cava. Renal cell carcinoma is an aggressive neoplasm that causes dissemination to the renal veins and inferior vena cava in 24% and 12% of all cases, respectively, and this venous involvement implies a poor prognosis. Regarding hepatic cell cancers, portal vein tumor thrombosis is a risk factor of a poor prognosis.

As diagnostic methods, contrast-enhanced computed tomography (CT), magnetic resonance, and ultrasound (US) are useful to detect venous tumor thrombosis. Venous tumor thrombosis may be noted on CT as a low-attenuation area; however, blood clot thrombosis remains to be diagnosed. Recently, the usefulness of positron emission tomography (PET) in detecting venous tumor thrombosis has been shown by intense radiotracer accumulation, which distinguishes thrombosis from blood clots.

A few reports have shown that colorectal cancer can develop venous tumor thrombosis and warn not to overlook this complication. Little is known about the causes of venous tumor thrombosis and the characteristics or prognosis of colorectal cancer with venous tumor thrombosis. In this report, we perform a literature review and investigate the characteristics of colorectal cancer accompanied by venous tumor thrombosis.

2. Analysis of the cases

Only 43 cases of venous tumor thrombosis in colorectal cancer patients were found in a search of the pertinent literature, most of which were reported in Japanese literature. According to the 1997 Annual of Pathological Autopsy Cases in Japan, the incidence of portal vein metastasis in colorectal cancer was reported to be 0.6% (9/1604). The report also revealed that the incidence of liver metastasis from colorectal cancer was 38.1% (611/1604) and showed the rate of portal vein thrombosis to be fairly low. In 2010, Sato et al. showed in their Japanese report that three cases (1.7%) of 176 patients with advanced colorectal carcinoma were found to have venous tumor thrombosis.

2.1. Clinical data

We identified 43 cases of colorectal cancer with venous tumor thrombosis from international and domestic reports (written in Japanese) from 1992 to 2014. Although colorectal cancer with venous tumor thrombosis remains rare, the number of reports of these cases is increasing because of the development of diagnostic imaging technology. Among 43 patients, there was a slight female predominance [n = 24 (female) vs. n = 19 (male)]. Most patients were in their 60s (n = 16) or 70s (n = 15) (Figure 1), and the median age was 67 years (range, 47–84 years). Regarding the location of the tumor, the ascending colon (n = 12) and rectum (n = 11) were the most frequent sites, followed by the sigmoid colon (n = 8), transverse colon (n = 6), and descending colon (n = 5) (Figure 2). No cases of cecum cancer with venous tumor thrombosis were reported. The invaded vein was dependent on the tumor site—that is, ascending and transverse colon cancer invaded the superior mesenteric vein (n = 17; including the ileocolic vein and right colic vein), whereas descending, sigmoid colon, and rectal cancer invaded the inferior mesenteric vein (n = 24). One case with diffuse colon cancer, which spread over the transverse, descending, sigmoid colon, developed tumor thrombosis in the portal vein, and one case of rectal cancer that invaded the internal iliac vein was observed. Regarding the frequency of cancer in each part of the colorectum (right hemicolon: 29.5% vs. left hemicolon: 70.5%), the superior mesenteric vein was thus considered to more likely be invaded by tumor thrombosis.

2.2. Pathological type

Interestingly enough, the histological type of more than half of the cases was moderately differentiated adenocarcinoma (Figure 3). In epidemiological studies, the histological types of colorectal cancer are commonly divided into two types: well differentiated (including well and moderately differentiated type) versus poorly differentiated (including poorly differentiated, signet ring cell, and mucinous carcinoma). Previous reports about clinico-pathological studies of colorectal cancer revealed that patients with well differentiated tumors have a better prognosis compared to those with poorly differentiated tumors. Poorly differentiated adenocarcinomas of the rectum are considered to behave more aggressively than well or moderately differentiated adenocarcinomas. However, compared to well differentiated adenocarcinoma, moderately differentiated adenocarcinoma...
was shown to have a higher malignant potential.\textsuperscript{60–62} Moreover, moderately differentiated tumors were associated with higher serum carcinoembryonic antigen levels than both well and poorly differentiated tumors.\textsuperscript{63,64} Some studies reported that the circulating carcinoembryonic antigen level is associated with the ability of colorectal cancer to metastasize to the liver.\textsuperscript{65,66} These previous results support our finding that the predominant histological type of developing venous tumor thrombosis from colorectal cancer is the moderately differentiated type. Thus, venous tumor thrombosis may indicate the aggressiveness of moderately differentiated adenocarcinoma.\textsuperscript{62} Iida\textsuperscript{62} studied 408 colorectal cancer patients and reported the occurrence ratio of each histopathological type; well differentiated cancer comprised 70.3% of the cases, moderately differentiated cancer 16.9%, poorly differentiated cancer 3.4%, and mucinous adenocarcinoma 6.6%. Considering these frequencies, poorly differentiated adenocarcinoma also has an aggressive potential of developing venous tumor thrombosis.

2.3. Liver metastasis

All colorectal cancer cases with venous tumor thrombosis carry advanced cancer and show microscopic invasion to the vein around the tumor (with the exception of one case\textsuperscript{27}). We speculated that venous tumor thrombosis may be a strong risk factor for liver metastasis; however, the incidence of synchronous liver metastasis was only 19.5% of the cases (8 out of 41 cases; the data for 2 cases were unclear). Because the incidence liver metastasis for all colorectal cancer (including in the early stage) was only 10.9%,\textsuperscript{55} this result does not indicate a high frequency for colorectal cancer with venous tumor thrombosis consisting of only advanced cancers. We compared the incidence of liver metastasis (including synchronous and metachronous) and found no apparent difference between each pathological type of cancer under the condition of bearing venous tumor thrombosis (Table 1).

After complete surgical resection of the tumor, 10 cases (24.4%) had liver metastatic recurrence. Regarding this recurrence rate, cancer with venous tumor thrombosis leads to a high risk for liver metastasis compared to general colorectal cancer (liver metastatic recurrence rate = 7.1\%\textsuperscript{66}). Among these cases, seven cases underwent adjuvant chemotherapy after surgical resection. However, 14 cases had no recurrence after surgical resection followed by adjuvant chemotherapy. However, owing to the absence of detailed data of the treatment in 14 cases, these data do not indicate that one-third of the patients had liver metastatic recurrence even after complete surgical resection and adjuvant chemotherapy.

Figure 2 Location of the cancer. A = ascending colon; D = descending colon; R = rectum; S = sigmoid colon; T = transverse colon. One case had diffuse colon cancer according to a histopathological evaluation of the colonoscopic biopsy specimens. Its histological type was well differentiated adenocarcinoma.\textsuperscript{28}

Figure 3 Histological type of the cancer. endocrine = endocrine cell carcinoma; mod = moderately differentiated; muc = mucinous adenocarcinoma; por = poorly differentiated; wel = well differentiated. Data were not available for eight cases. Among these histological types in 35 patients, moderately differentiated adenocarcinoma comprised the majority.

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2.4. Treatment

In treatment, it is first important to recognize the existence of tumor thrombosis in the drainage vein from the cancer by CT, PET, or US imaging prior to the operation. Not to leave the tumor thrombosis, both a careful pre-evaluation of the extension level of the thrombosis and an examination of the venous lumen of the resected specimen are necessary. To avoid the movement of cancer fragments during surgical resection, initial tying of the vein with tumor thrombus may be ideal. Among the 43 patients analyzed in this review, complete tumor resection was performed in 32 patients (74.4%). In two patients, the primary tumor with venous thrombosis was resected, leaving liver metastasis. Surgical resection was not performed in four patients, and the treatment was unclear in five patients. The use of laparoscopy-assisted colectomy is increasing. It is difficult to recognize the region of tumor thrombus by touching with laparoscopic forceps. Moreover, the manipulation of pulling out the tumor from a small incision in the abdominal wall squeezes the tumor, which could easily result in the movement of cancer fragments. Therefore, a prudent strategy for resection with no residual cancer is needed.

For patients with venous tumor thrombosis, adjuvant chemotherapy even after complete resection should be considered because of the aggressive character of cancer with tumor thrombosis, which may be a high risk factor of metastasis and recurrence. In this series, adjuvant chemotherapy was performed in 21 of 32 cases that underwent complete tumor resection (65.6%); four cases did not receive adjuvant chemotherapy; and detailed information regarding chemotherapy was unavailable for seven cases.

2.5. Prognosis

The prognosis of patients with venous tumor thrombosis of colorectal cancer is unclear. When considering that venous tumor thrombosis may indicate aggressive cancer, the prognosis of the patients may be poor. However, following surgical complete resection with adjuvant chemotherapy, some patients achieved a long survival. It is difficult to confirm the relationship between the survival time and the existence of liver metastasis or the treatment procedure because of the small number of cases and a short observation time. However, in reports with this information available, 11 patients among 43 patients with venous tumor thrombosis could survive for more than 2 years after the diagnosis, although five patients had liver metastasis (Figure 4). The mean survival time of those who had liver metastasis was 22.5 months. This survival time is not poor for patients with Stage IV colorectal cancer. Recently, especially after 2009, the number of patients treated with adjuvant chemotherapy appears to be increasing. An improvement in the survival of patients with colorectal cancer accompanied by venous tumor thrombosis is anticipated. A greater accumulation of evidence regarding the treatment procedure, incidence of recurrence or metastasis, and survival time will help us determine the appropriate strategy for colorectal cancer with venous tumor thrombosis.

The prognosis of patients with colorectal cancer accompanied by venous tumor thrombosis is not always poor. A long survival can be anticipated for patients...
following complete tumor resection and adjuvant chemotherapy. Surgeons should continue their efforts to remove the tumor by resection and chemical offense.

3. Conclusion

Colorectal cancer with venous tumor thrombosis is rare, and little is known about its features. In this review, we found that moderately differentiated adenocarcinoma has the potential to develop venous tumor thrombosis. Although liver metastasis often accompanies venous tumor thrombosis, complete tumor resection and adjuvant chemotherapy can improve the prognosis. A greater accumulation of cases will help elucidate the characteristics of cancer with venous tumor thrombosis and improve the treatment strategy.

References


