

Macroscopic portal vein tumor thrombi of liver metastasis from colorectal cancer

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Abstract We present a case of multiple colorectal liver metastases with macroscopic portal vein thrombi. A 55-year-old woman presented to us with rectosigmoid cancer and presented with two liver metastases. The tumor in the posterior sector was associated with invasion of first order branches of the portal vein. We performed low anterior resection, hepatic posterior sectorectomy and partial left anterior sectorectomy. Both the colorectal cancer and liver tumors exhibited histological characteristics of moderately differentiated adenocarcinoma with a substantial amount of mucin production. The liver metastases were associated with prominent tumor thrombi in many branches of the portal vein. Stronger staining for endoglin (CD 105) than for Fas ligand (Fas L) and matrix metalloproteinase (MMP-2) was observed in both the colorectal cancer and metastatic liver tumor cells. Expression of the vascular endothelial growth factor within the tumor cells was seen in both the colorectal cancer as well as the metastatic liver tumor cells. Six months after the operation, she was diagnosed to have multiple, more than about 20 liver metastases, and in 9 months after the operation, the patient died. The colorectal cancer with liver metastases associated with portal vein tumor

thrombosis was poor prognosis, found neoplastic microvessel formation.

Keywords Colorectal cancer · Liver metastasis · Tumor thrombi in the portal vein · Endoglin · Neoplastic microvessels

Introduction

Portal vein tumor thrombus is a common finding and a significant negative prognostic indicator in hepatocellular carcinoma [1]. In patients with colorectal liver metastasis, macroscopic portal vein thrombus is rare and has been reported to occur in 2.8% of cases [2]. Microscopic invasion of the portal vein are reportedly present at rates of 22.5% [3]. There are many risk factors for liver metastasis in colorectal cancer with venous invasion [4–8]. However, which factor is most important remains controversial.

In this paper, we report a surgical case of liver metastasis from colorectal cancer with prominent portal vein infiltration.

Case report

A 55-year-old woman was referred to us with the complaint of constipation. Her serum CEA level was elevated 1,077 ng/ml (normal range, ≤ 2.5 ng/ml) and serum CA 19–9 level to 2,838 U/ml (normal range, ≤ 37 ng/ml). Barium enema and colonoscopic examination revealed an ulcerative infiltrating type (type 3) of rectosigmoid cancer. Abdominal computed tomography (CT) showed two liver metastases, one located in the posterior sector with tumor thrombi in the portal vein and biliary invasion (Fig. 1), and

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Fig. 1 Enhanced CT shows a low density mass located in the posterior sector and a low-density area along the posterior portal tract. Arrows indicate liver metastasis involved portal vein in direct

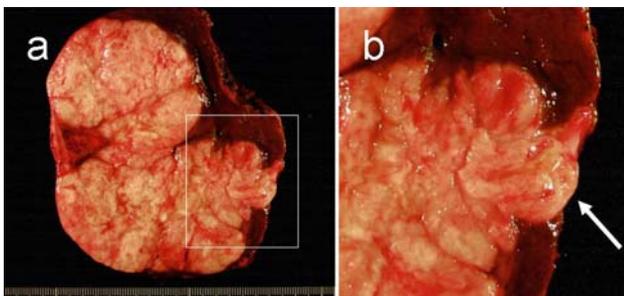


Fig. 2 Liver [S6/7] resected specimen (a). Macroscopic findings of the resected posterior sectorectomy showing tumor thrombi in the portal vein (b). Arrow indicates liver metastasis involved portal vein in direct. The tumors measuring 10 × 8 cm

the other in left lateral sector. Low anterior resection with D3 lymphadenectomy and posterior sectorectomy and partial left anterior sectorectomy were performed.

Macroscopic examination of the resected rectosigmoid colon cancer revealed a type 3 tumor with severe venous involvement. Histopathological examination revealed findings consistent with mucinous moderately differentiated adenocarcinoma, reaching the subserosal layer (a2), with lymphatic duct involvement (ly2), severe venous involvement (v3), and the presence of lymph node metastasis (n1). The cut surface of the resected specimen of the liver demonstrated a solid tumor in the posterior sector, which was whitish in color and measured 10 × 8 cm in size with PV tumor thrombi (Fig. 2), and another tumor in the left anterior sector measuring 3 × 2.5 cm in size, also associated with portal vein tumor thrombi. The extirpated portal vein

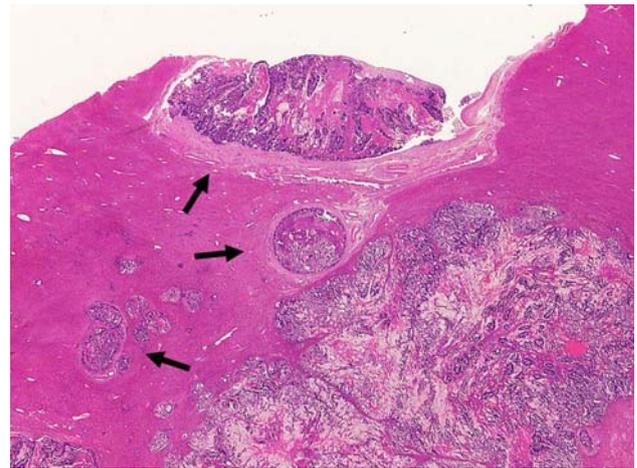


Fig. 3 Histological examination of the liver metastasis (H&E stain). Microscopic findings in the resected posterior sector liver metastasis showing tumor thrombi in many branches of the portal vein. Arrows indicate liver metastasis involved portal vein in direct. [S6/7 (magnification ×4)]

thrombi consisted mainly of fibrous tissue, and proliferative mucinous differentiated adenocarcinoma cells (Fig. 3). Both the colorectal cancer and liver tumors showed positive immunostaining for endoglin (CD 105), Fas ligand (Fas L) and matrix metalloproteinase (MMP-2). Positive staining for CD 105 was observed in the newly formed tumor microvessels, with the staining for CD 105 being stronger and more extensive than that for Fas L or MMP-2 (Fig. 4).

The postoperative course of the patient was uneventful, and she was discharged from our hospital on day 15 after the operation. We did not perform adjuvant chemotherapy, because patient refused it. Six months after the operation, she was diagnosed to have multiple, more than about 20 liver metastases, and in 9 months after the operation, the patient died.

Discussion

We present a rare case of colorectal cancer with liver metastases in which gross tumor thrombi were found in the portal vein, indicative of a poor prognosis. Macroscopic portal vein involvement is considered to be an indicator of poor prognosis in patients with hepatic metastasis.

In this case, we thought that the mechanism of portal tumor thrombus regard to influence angiogenesis, intravasation of tumor cells, transportation by the circulation and adhesive interaction with endothelial cells or extravasation [5, 9].

In this study, to study the influence of tumor angiogenesis on the portal vein infiltration in cases of liver metastasis, we conducted immunostaining for CD 105, Fas L and MMP-2 in both specimens of the colorectal cancer

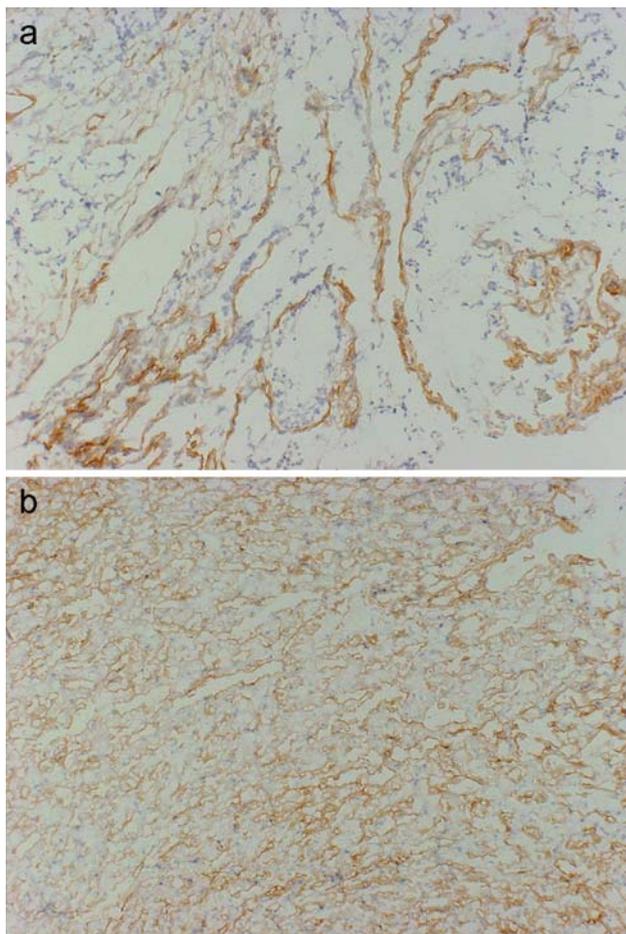


Fig. 4 Endoglin staining is strongest in intensity, with staining of most of the microvessels in both the colorectal cancer (a) and the liver tumors (b) (magnification $\times 100$)

and of the liver tumors showing invasion of the portal vein [4–6]. CD 105 has been shown to be a more useful marker to identify proliferating endothelium involved in tumor angiogenesis. CD 105 staining has been shown to have prognostic significance, showing a positive correlation with angiolymphatic invasion and metastasis to the lymph nodes and liver [4]. Both the colorectal cancer and liver tumors associated with invasion of the portal vein showed strong staining intensity for CD 105. There was a correlation between the staining intensity for CD 105 and the presence of a portal vein tumor thrombus. Liver metastasis from colorectal cancer may show marked angiogenesis. In hepatocellular carcinoma, the tumor microvessel density by CD 105 immunostaining was significantly lower in larger tumors, more aggressive tumors, as indicated by venous infiltration, and tumors with advanced TNM stage [10].

Despite the recent advances in chemotherapy and other treatment modalities, surgical resection is still gold standard for the treatment of liver metastases from colorectal

cancer [11, 12]. Tada et al., observed that precise diagnosis of the tumor thrombus followed by anatomic major hepatic resection is the key to curative treatment [2]. Macroscopic portal vein thrombus is not a contraindication for surgical treatment if removed completely. Patients with synchronous liver metastases from colorectal cancer should undergo radical resection of the primary lesion and simultaneous hepatectomy with an adequate tumor-free margin as a standard surgical course. However, in patients with four or more colorectal lymph node metastases, biological selection by neoadjuvant chemotherapy may be more suitable [13].

In conclusion, although the principle of surgical resection for colorectal liver metastases is complete removal of the tumor, indications for surgical resection remain controversial. This case was poor prognosis with positive correlation with proliferating neoplastic microvessels in colorectal cancer and liver metastases.

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