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Case Report

Distal colon metastasis of hepatocellular carcinoma

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ABSTRACT

Hematogenous metastasis of hepatocellular carcinoma (HCC), particularly to colon is extremely rare. We presented two cases of colonic metastasis of HCC to the sigmoid colon and rectum. We followed the first patient for six years with chemotherapy, transcatheter arterial radioembolization (four times), and surgical treatment. Liver transplantation was planned because of the patient's infiltrative HCC in the liver, with no extrahepatic metastasis. Unfortunately, the patient died after the five-year follow-up. The second patient, who was followed for nine years with surgical treatment and chemotherapy, presented with hepatic mass caused by hepatitis B infection. The patient is still in follow-up with multiple peritoneal implants.

Keywords: Colon, hepatocellular carcinoma, metastasis, portal hypertension, transcatheter arterial radioembolization.

Hepatocellular carcinoma (HCC) is one of the most common malignant tumors in the world. Hepatocellular carcinoma accounts for 5.6% of all human cancers and has a poor prognosis. It is mostly diagnosed at intermediate or advanced stages, and only 30% of patients benefit from curative therapies such as resection, liver transplantation, or percutaneous ablation.[1]

Hepatocellular carcinoma shows multiple intrahepatic occurrence and intrahepatic metastasis. Extrahepatic metastasis was present in 30 to 70% of cases, and the major organs involved were the lung, lymph nodes, bone, and adrenal gland.[2] Involvement of the gastrointestinal (GI) tract with HCC mainly occurs through direct invasion. Hepatocellular carcinoma with hematogenous metastasis to the GI tract is very rare.

Here we report two HCC patients with GI tract metastasis presenting in two different scenarios but with similar outcomes.

CASE REPORT

Case 1- A 73-year-old male with a history of fatty liver disease for 25 years, ultrasonographic (US) examination performed in 2013 revealed a mass in the liver. The patient was admitted to our hospital for further evaluation, and a dynamic computed tomography (CT) scan was performed in July 2013. Cirrhotic changes and a 10 cm mass in the right lobe of the liver were revealed. The mass showed enhancement in the arterial phase and washout in the portal venous phase consistent with HCC (Figure 1a, b). Sorafenib treatment and follow-up were planned by a multidisciplinary approach. In the control examination performed after three months under treatment; the mass showed progression in size (Figure 1c). Therefore, Transarterial radioembolization (TARE) treatment was planned and performed. There were no complications. In the six-month follow-up examination, parameters of the patient, including alpha-fetoprotein (AFP) (1.67 ng/mL), were

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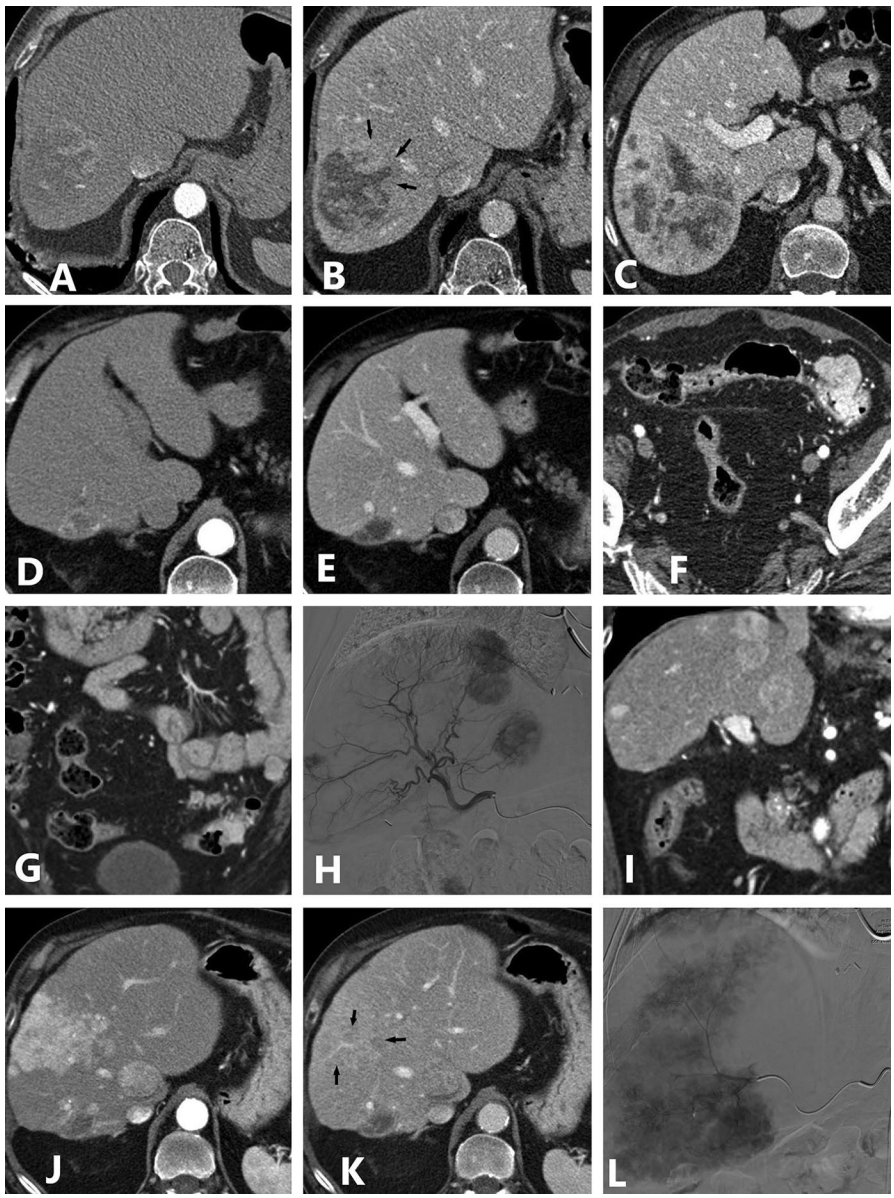

Figure 1. Imaging history of case 1. **(a)** The arterial phase CT image shows a necrotic mass including hypervascular areas in the liver. **(b)** Portal venous phase CT image shows washout in the mass (arrows). **(c)** Follow-up CT image shows progression in size of the mass. **(d)** Arterial phase follow-up image shows marked regression in the size of the mass after TARE treatment. **(e)** Venous phase image shows washout in the peripheric zone of the mass (The image was obtained from the same examination as image d). **(f)** Axial CT image shows a non-obstructed mass lesion in the descending colon that completely involves the colonic wall and extends into the surrounding fatty planes and colonic lumen. **(g)** Coronal section image shows the mass in the descending colon, which narrows the lumen partially but does not cause obstruction. **(h)** Coronal section CT image shows multiple hypervascular liver masses both in the right and left lobe. **(i)** Angiographic image obtained with hepatic arterial catheterization shows multiple hypervascular liver masses (one in the right and three in the left lobe) during TARE therapy. **(j)** Arterial phase axial section CT image shows marked enhancement in an infiltrative mass in the right lobe of the liver. **(k)** Portal venous phase axial section CT image shows washout in the infiltrative liver mass (arrows). **(l)** Image of an infiltrative liver mass that was superselectively catheterized during TARE therapy.

CT: Computed tomography; TARE: Transcatheter arterial radioembolization.

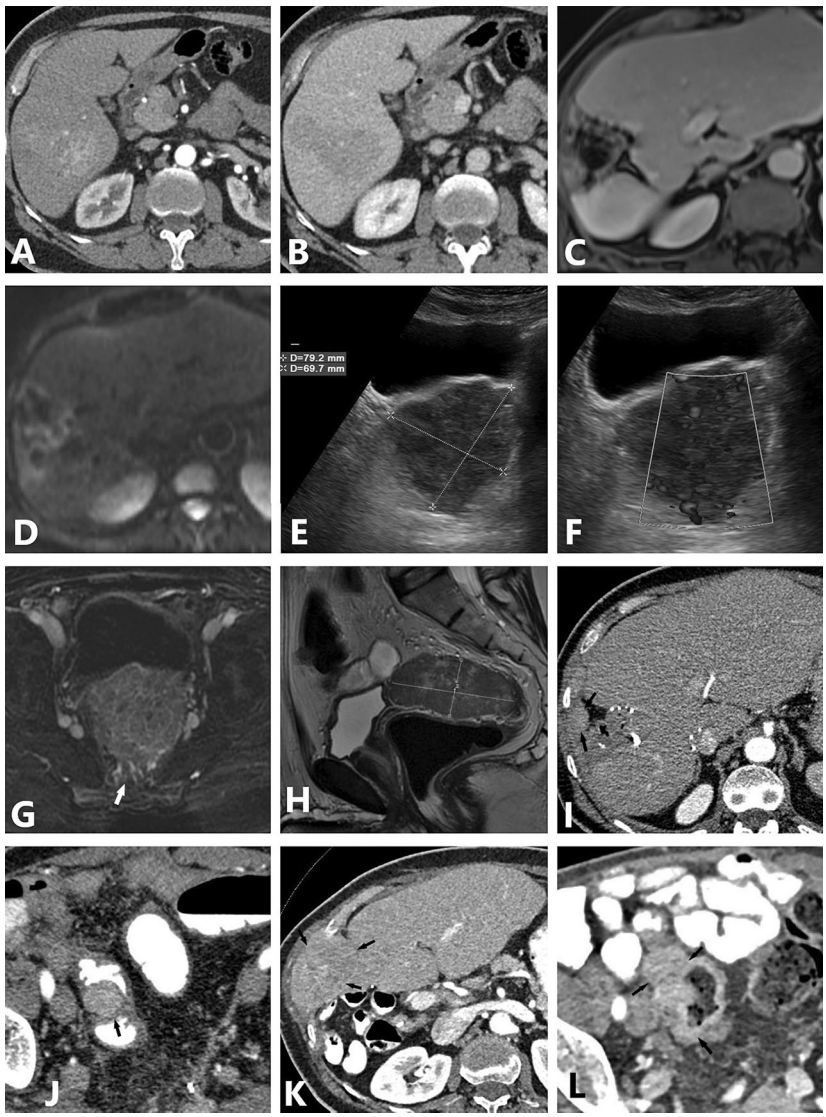

Figure 2. Imaging history of case 2. **(a)** Arterial phase axial section CT image shows enhancement in the mass located in the right lobe of the liver. **(b)** Portal venous phase CT image shows washout in the same mass. **(c)** Portal venous phase dynamic magnetic resonance image shows parenchymal changes in the right lobe of the liver due to mass resection. No contrast enhancement is seen. **(d)** Diffusion-weighted imaging shows no diffusion restriction in the operation zone consistent with residual tumor. **(e)** A pelvic mass is observed in the grey-scale ultrasonographic image. **(f)** Color Doppler ultrasonographic image shows vascularization in the mass. **(g)** Contrast enhanced magnetic resonance image with feature extraction algorithm shows enhancement in the pelvic mass. In addition, rectal mucosa is observed (arrow). **(h)** Sagittal section T2-weighted magnetic resonance image shows that the pelvis mass located in the rectum wall is extending to the bladder along the presacral space. **(i)** Late arterial phase axial section CT image shows relapsed nodular tumor tissue (arrow) in the operation zone. **(j)** Oral and intravenous contrast abdomen CT image shows a non-obstructive mass located in the sigmoid colon wall, extending into the lumen (arrow). **(k)** Axial section CT image shows marked progression in size of the relapsed tumor (arrows). **(l)** Oral and intravenous contrast abdomen CT image shows marked progression in size of the mass located in the sigmoid colon wall (arrows). The mass still does not cause intestinal obstruction.

CT: Computed tomography.

normal, the size of the mass was regressed to 2 cm, and necrotic changes were revealed (Figure 1d, e). After several follow-up examinations with stable findings, a routine follow-up in November 2016 was planned. In this examination, 2 cm and 1 cm diameter nodules compatible with HCC in segments 2 and 1, respectively, and a 5 cm diameter non-obstructed mass lesion in the descending colon were detected (Figure 1f, g). Segmental colon resection and liver nodule resection for curative therapy were planned by a multidisciplinary approach. Surgical findings and postoperative pathology results were consistent with Grade 2 HCC in liver nodules and colonic mass. According to the pathologic evaluation, colonic mass was located in the entire wall of the colonic segment, and serosal invasion was detected. In addition, there was tumoral spread to 5 of 12 lymph nodes that were resected around the mass. In the immunohistochemical evaluation of the colonic mass, arginase, hepatocyte-specific antigen (HSA), MLH1, MSH2, MSH6, PMS2 were positive. After seven months from the surgery, the patient was admitted with weakness and nausea. Computed tomography examination was performed and an infiltrative HCC mass and multiple satellite nodules in the liver were detected (Figure 1i-k). Transarterial radioembolization treatment was applied an additional three times in different control periods (Figure 1h, l). After the five-year follow-up, the patient was admitted to our hospital with altered mental status, and the AFP level was elevated to 257 ng/mL. Liver transplantation was decided by a multidisciplinary approach, but unfortunately, the patient died because of hepatic failure in June 2018.

Case 2- Sixty-seven-year-old male with a history of chronic hepatitis B followed for 26 years. The routine US examination in 2010 revealed cirrhotic morphological changes in the liver and an 8 cm diameter mass in the right lobe. Dynamic contrast abdominal CT was performed and the mass showed enhancement in the arterial phase and early washout in the portal venous phase consistent with HCC (Figure 2a, b). Mass resection was performed for curative therapy. No operative complications occurred. In the routine follow-up period, the patient presented with a complaint of tenesmus in January 2018. Abdominal US examination revealed pelvic mass (Figure 2e, f), and therefore abdominal CT and pelvic magnetic resonance imaging (Figure 2g, h) were performed as further investigations. A subcentimetric nodular implant near the operation zone and a hypervascular colonic mass 8 cm in diameter on the rectosigmoid junction were revealed. The AFP level was 26.37 ng/mL and other parameters were normal. Segmental colon resection and recurrent nodule resection were planned and performed in August 2018. No operative complications occurred. According to the pathologic evaluation, this colonic mass was also located in the entire wall of the colonic segment and serosal invasion was detected, as in the first patient. There was tumoral spread to 2 of 10 lymph nodes that were resected around the mass. It was revealed as a Grade 2 tumor histologically. Immunohistochemical features were positive for arginase and HSA. Three months later, the patient came for a routine control examination with no significant postoperative complaints. Multiple metastatic nodularities in the sigmoid colon and mesenteric surfaces were seen in dynamic abdomen CT examination (Figure 2i, j). Sorafenib treatment and palliative care were planned for the patient with a multidisciplinary approach. In the last follow-up examination performed in October 2019, there was a significant increase in implant sizes (Figure 2k, l). We still follow-up with this patient with multiple metastatic implants on peritoneal surfaces.

DISCUSSION

Hepatocellular carcinoma is known for its tendency to directly invade the portal and hepatic veins, but a significant number of patients develop extrahepatic vascular invasion and other distant metastases. Hepatocellular carcinoma can metastasize to the intestines by direct invasion, but hematogenous metastasis to the colon is very rare. However, it is hypothesized that HCC may hematogenously disseminate to distant GI tracts.

Clinical manifestations of the GI tract metastasis is variable. The patient may be asymptomatic or present with abdominal pain, constipation, diarrhea, change in stool color, nausea, vomiting, jaundice, heartburn, and tenesmus. It depends on where the tumor has spread. Our first patient did not have any

complaints of a GI tract mass since the masses were detected in follow-up images after TARE therapy, and the lack of complaints may be due to lesions not growing enough to show symptoms. Whereas the second patient was suffering from tenesmus because the patient had not come to follow-up examinations regularly, and the mass was about 8 cm in diameter when detected.

Colonoscopic-endoscopic findings of the gastrointestinal system (GIS) metastasis of HCC were varied, mimicking polypoid tumor or submucosal tumor. Although some immunohistochemical findings are important to differentiate HCC from adenocarcinoma in the diagnosis of the GIS metastasis, histopathological evaluation is essential. Both of our patients had undergone surgical resection for their GI tract metastasis and pathological reports showed they metastasized from HCC.

Gastrointestinal system metastases of HCC have been reported in some case reports however most reports contain all types of metastasis including direct invasion.[3] A limited number of reports were published on hematogenous metastasis of HCC to the colon, and to our knowledge, this is the first report on left-sided colonic metastasis of HCC, including two cases treated with surgical resection.[3-5] Gastrointestinal metastasis occurs mostly in patients with advanced-stage HCC. The prognosis of GI involvement with HCC is known to be poor with a median survival time of 4.9-8.1 months.[6-8] The major cause of mortality may be related to the progression of the intrahepatic lesion and not associated with the metastasis itself. Thus, in a functional hepatic reserve, symptomatic or life-threatening metastasis should be treated.[6,7] Surgical resection is the best choice for curative treatment. Both of our cases underwent surgery for their metastasis. In the first case, the result was curative for extrahepatic metastasis. However, in the second patient, the behavior of malignancy was aggressive, and recurrent metastatic colonic metastasis occurred after resection. Nevertheless, we think that we positively influenced the prognosis and symptoms of the second patient.

High-pressure values in the portal venous system may be essential to the hematogenous spread to the GI tract.[9,10] The main causes of this situation are portal hypertension secondary to cirrhosis and portal vein thrombosis.[9] Previous studies reported that transarterial embolization (TAE) therapy may be responsible for hematogenous spread due to the elevation of the pressure in the portal venous system.[4,5,11-13] Yoo et al.[13] reported a case with sigmoid colon metastasis of HCC after transarterial chemoembolization (TACE). In addition, we believe that transcatheter embolization therapies such as TAE, TACE, and TARE may elevate the pressure of the portal venous system, which causes a backward flow of tumor cells. In the first case, the patient was treated with TAE a few times during follow-up.

In conclusion, colonic metastasis of HCC should be considered in patients with portal hypertension.

Declaration of conflicting interests

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REFERENCES

1. Llovet JM, Burroughs A, Bruix J. Hepatocellular carcinoma. Lancet 2003;362:1907-17.
2. Nakashima T, Okuda K, Kojiro M, Jimi A, Yamaguchi R, Sakamoto K, et al. Pathology of hepatocellular carcinoma in Japan. 232 Consecutive cases autopsied in ten years. Cancer 1983;51:863-77.
3. Ou TM, Tsai WC, Hsieh TY, Shih YL. Hepatocellular carcinoma with colonic metastasis. Singapore Med J 2014;55:e93-5.
4. Tapuria N, Sinha CK, Michael NG, Fisher PW. Haematogenous metastasis to ascending colon in a patient with hepatocellular carcinoma and autoimmune hepatitis. Eur J Gastroenterol Hepatol 2007;19:607-9.
5. Ng DSC, Chok KSH, Law WL, Collins RJ, Fan ST. Long-term survival after resection of extrahepatic recurrence of hepatocellular carcinoma at the right colon. Int J Colorectal Dis 2007;22:1411-2.
6. Uka K, Aikata H, Takaki S, Shirakawa H, Jeong SC, Yamashina K, et al. Clinical features and prognosis of patients with extrahepatic metastases from hepatocellular carcinoma. World J Gastroenterol 2007;13:414-20.

7. Uchino K, Tateishi R, Shiina S, Kanda M, Masuzaki R, Kondo Y, et al. Hepatocellular carcinoma with extrahepatic metastasis: Clinical features and prognostic factors. Cancer 2011;117:4475-83.
8. Natsuizaka M, Omura T, Akaike T, Kuwata Y, Yamazaki K, Sato T, et al. Clinical features of hepatocellular carcinoma with extrahepatic metastases. J Gastroenterol Hepatol 2005;20:1781-7.
9. Lin CP, Cheng JS, Lai KH, Lo GH, Hsu PI, Chan HH, et al. Gastrointestinal metastasis in hepatocellular carcinoma: Radiological and endoscopic studies of 11 cases. J Gastroenterol Hepatol 2000;15:536-41.
10. Hu ML, Tai WC, Chuah SK, Chiu YC, Wu KL, Chou YP, et al. Gastric metastasis of hepatocellular carcinoma via a possible existing retrograde hematogenous pathway. J Gastroenterol Hepatol 2010;25:408-12.
11. Ou TM, Tsai WC, Hsieh TY, Shih YL. Hepatocellular carcinoma with colonic metastasis. Singapore Med J 2014;55:e93-5.
12. Cosenza CA, Sher LS, Poletti BJ, Tschirhart D, Noguchi H, Hoffman AL, et al. Metastasis of hepatocellular carcinoma to the right colon manifested by gastrointestinal bleeding. Am Surg 1999;65:218-21.
13. Yoo DJ, Chung YH, Lee YS, Kim SE, Jin YJ, Lee YM, et al. Sigmoid colon metastasis from hepatocellular carcinoma. Korean J Hepatol 2010;16:397-400.