



Diagnosis of small-bowel metastasis of hepatocellular carcinoma by double-balloon enteroscopy

Masaki Kunizaki^{a,*}, Shigekazu Hidaka^a, Hajime Isomoto^b, Hiroaki Takeshita^a, Atsushi Nanashima^a, Terumitsu Sawai^a, Toru Yasutake^a, Takeshi Nagayasu^a

^a Division of Surgical Oncology, Department of Translational Medical Sciences, Nagasaki University Graduate School of Biomedical Sciences, 1-7-1 Sakamoto, Nagasaki 852-8501, Japan

^b Division of Gastroenterology and Hepatology, Department of Translational Medical Sciences, Nagasaki University Graduate School of Biomedical Sciences, 1-7-1 Sakamoto, Nagasaki 852-8501, Japan

ARTICLE INFO

Article history:

Received 20 February 2012

Accepted 10 March 2012

Available online 28 March 2012

Keywords:

Hepatocellular carcinoma

Small bowel metastasis

Double-balloon enteroscopy

ABSTRACT

INTRODUCTION: Hepatocellular carcinoma (HCC) is a major cause of cancer-related deaths around the world. Nearly half of patients with HCC display metastatic disease at the time of initial diagnosis, frequently involving the liver, bone, brain, lungs, and adrenal glands, but gastrointestinal involvement is rare. Melena occurring secondary to a metastatic tumor from HCC is particularly rare. Herein, we present a case of melena secondary to metastatic HCC after chemoradiation to lung and brain metastases from HCC, diagnosed preoperatively by double-balloon enteroscopy. To the best of our knowledge, this represents the first such case to be reported.

PRESENTATION OF CASE: 60-Year-old man had been diagnosed with hepatitis B virus-associated hepatocellular carcinoma (HCC). He was readmitted for investigation of general fatigue and iron-deficiency anemia. Esophagogastroduodenoscopy, total colonoscopy, and CT failed to identify any cause for gastrointestinal bleeding. Double-balloon enteroscopy, however, revealed small bowel metastasis from HCC preoperatively. After 5 days of conservative management, segmental small bowel resection and end-to-end anastomosis were performed. The histological appearances were considered typical for moderately differentiated HCC.

DISCUSSION: Endoscopic findings of gastrointestinal metastasis from HCC vary, such as raised and centrally ulcerated lesions, polypoid tumors, or submucosal tumors. Immunohistochemical findings are thus key to differentiating HCC from adenocarcinoma in the diagnosis of GIT metastasis. Some patients with gastrointestinal bleeding remain undiagnosed even after upper endoscopy and total colonoscopy, and most such patients will display bleeding sites in the small bowel. Video capsule endoscopy and DBE have been introduced recently for the evaluation of the small bowel. DBE, which was developed by Yamamoto et al.,⁵ allowed us to obtain biopsy specimens, circumventing one limitation of capsule endoscopy. In this case, DBE contributed significantly to diagnosis and treatment.

CONCLUSION: DBE thus seems to represent a valuable method, particularly in the preoperative setting, due to the possibility of precisely identifying the tumor site and achieving preoperative diagnosis.

© 2012 Surgical Associates Ltd. Published by Elsevier Ltd. All rights reserved.

1. Introduction

Hepatocellular carcinoma (HCC) is a so highly invasive tumor that metastasizes hematogenously and lymphogenously to distant site. Frequent sites are lungs, regional lymphnode, brain, and adrenal glands. But metastasis to the gastrointestinal involvement is rare. Melena occurring secondary to a metastatic tumor from HCC is particularly rare. Small bowel mass lesions are a relatively cause of obscure gastrointestinal bleeding. Their detection has

been limited by the inability to endoscopically examine the entire small intestine. This has changed with the introduction of capsule endoscopy and double balloon enteroscopy (DBE) into clinical practice. Herein, we present a case of melena secondary to metastatic HCC after chemoradiation to lung and brain metastases from HCC, diagnosed preoperatively by DBE.

2. Case report

A 60-year-old man had been diagnosed with hepatitis B virus-associated hepatocellular carcinoma (HCC) (T4N M stage IVB) 3 years earlier. Eleven months before presentation, HCC with lung metastasis and brain metastasis was diagnosed on computed tomography (CT) with elevated levels of serum alpha-fetoprotein (1345 ng/ml) and vitamin K antagonist II (329 mAU/ml).

* Corresponding author. Tel.: +81 095 819 7304; fax: +81 095 819 7306.

E-mail addresses: makuni49@nagasaki-u.ac.jp, kunisakimasaki2002@yahoo.co.jp (M. Kunizaki).

URL: <http://www.med.nagasaki-u.ac.jp/surgery1/> (M. Kunizaki).

Chemoradiation with cisplatin and vinorelbine ditartrate was performed for lung and brain metastases. He had subsequently experienced multiple intrahepatic recurrences and underwent transcatheter arterial chemo-embolization (TACE) and radiofrequency ablation (RFA) on each occasion. Although follow-up was performed with CT and laboratory investigations, he was readmitted for investigation of general fatigue and iron-deficiency anemia. Esophagogastroduodenoscopy, total colonoscopy, and CT failed to identify any cause for gastrointestinal bleeding. DBE, however, revealed protrusions covered with normal mucosa showing central ulceration and mild bleeding (Fig. 1). Examination of biopsy specimens showed these protrusions contained tumor cells, consistent with HCC. Immunohistochemical examination revealed tumor cells positive for polyclonal carcinoembryonic antigen and hepatocyte antigen, and the protrusions were diagnosed as metastatic HCC of the small bowel. After 5 days of conservative management, segmental small bowel resection and end-to-end anastomosis were performed. Macroscopic examination of the surgical specimen showed multiple luminal protruding submucosal masses

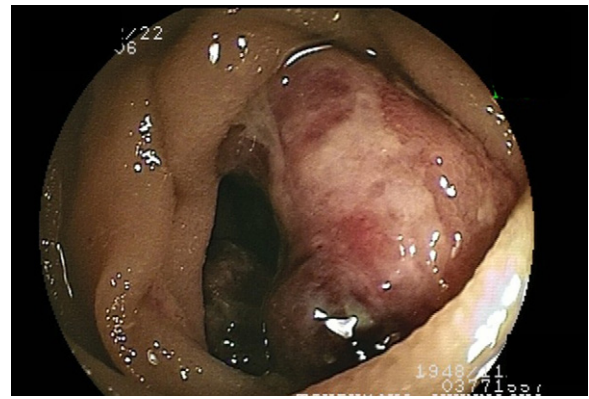


Fig. 1. A protruding lesion measuring 20–30 mm is clearly seen on double-balloon enteroscopy. This protrusion is covered with normal mucosa, with central ulceration and evidence of mild bleeding.

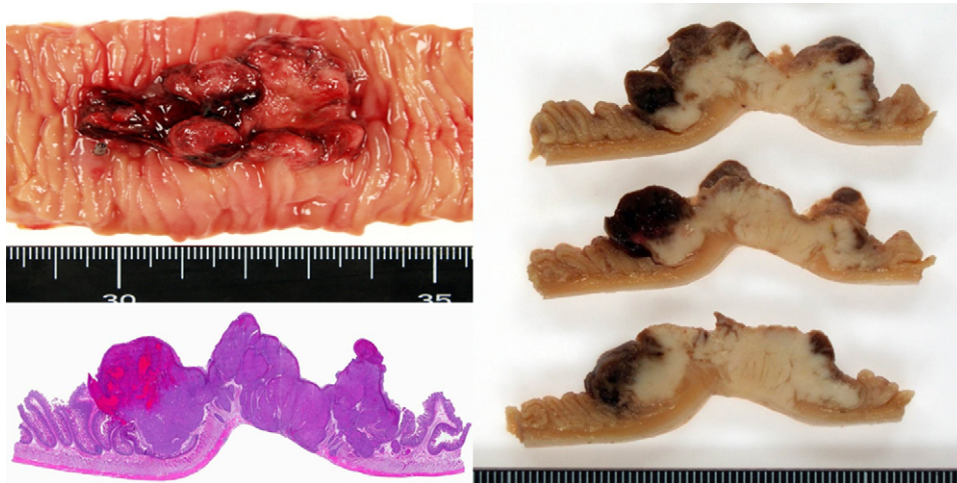


Fig. 2. Surgical specimen showed that the mass arising from the submucosa has grown into the lumen and has a dimpling portion and bleeding portion on the top of the tumor.

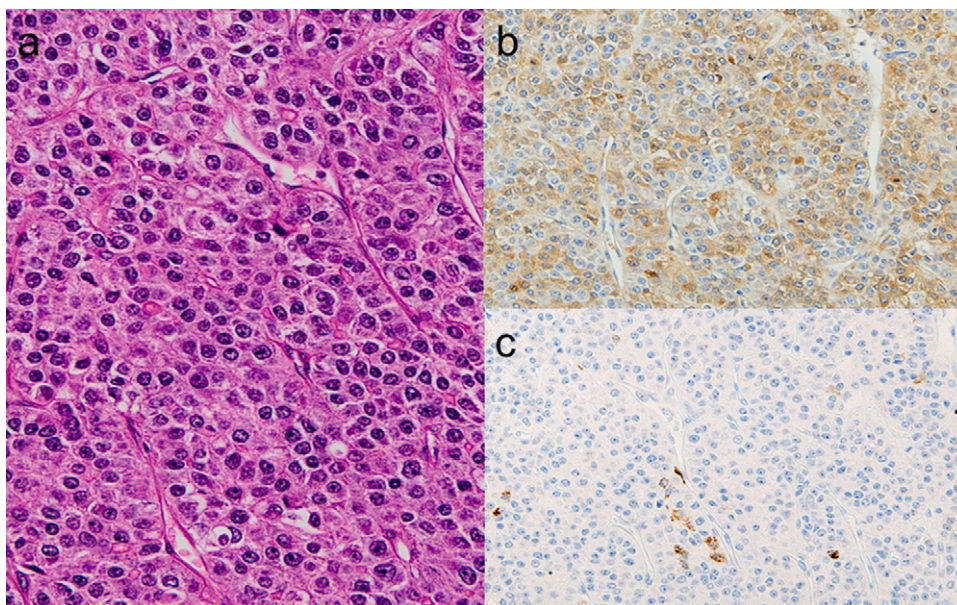


Fig. 3. (a) Tumor cells show eosinophilic granular cytoplasm and large nuclei containing prominent nucleoli, resembling HCC (HE, 400×). (b) Tumor cells are positive for alpha-fetoprotein. (c) Positive results for hepatocytes.

with extension to the subserosa (Fig. 2). The histological appearances were considered typical for moderately differentiated HCC (Fig. 3). These findings supported HCC metastasis to the small bowel.

3. Discussion

HCC is so highly invasive that extrahepatic metastases are frequently observed.^{1,2} The most common site of metastasis is the lung, followed by regional lymph nodes, adrenal glands and bone. HCC metastasis to the gastrointestinal tract is rare, found in only 4–12% of cases from an autopsy series.³ These metastatic lesions are usually asymptomatic, and most are discovered on post-mortem examination. As the survival period of patients with HCC can be relatively long, some unusual metastatic sites originating from HCC have been identified. However, very few reports have described pre-mortem diagnosis of gastrointestinal tract involvement by HCC. In particular, small bowel metastasis from HCC diagnosed by DBE has not previously been reported. HCC metastasis is known to occur hematogenously, by lymphatic spread and by local infiltration.⁴ The presumed mode of metastasis of HCC to the gastrointestinal tract is mostly by direct invasion to the adjacent tract via adhesion to the serosal side of a bulky mass. HCC has a high incidence of venous invasion and thrombosis formation. Hematogenous spread of HCC to the gastrointestinal tract may thus result from tumor thrombi via the portal system, then dissemination by hepatofugal portal spread to the gastrointestinal tract. Endoscopic findings of gastrointestinal metastasis from HCC vary, such as raised and centrally ulcerated lesions, polypoid tumors, or submucosal tumors. Immunohistochemical findings are thus key to differentiating HCC from adenocarcinoma in the diagnosis of GIT metastasis. Some patients with gastrointestinal bleeding remain undiagnosed even after upper endoscopy and total colonoscopy, and most such patients will display bleeding sites in the small bowel. Video capsule endoscopy and DBE have been introduced recently for the evaluation of the small bowel. DBE, which was developed by Yamamoto et al.,⁵ allowed us to obtain biopsy specimens, circumventing one limitation of capsule endoscopy. In this case, DBE contributed significantly to diagnosis and treatment. Nonetheless, we can conclude that gastrointestinal tract metastases should be considered in patients with HCC presenting with abdominal symptoms, and aggressive abdominal surgery for these patients is worthwhile in a selected group of patients despite the poor prognosis of GIT metastasis from HCC, as this intervention provides the potential for good palliation and reasonable survival.

The surgical procedure should be tailored according to the extent of disease and should provide adequate palliation of the presenting symptoms. DBE thus seems to represent a valuable method, particularly in the preoperative setting, due to the possibility of precisely identifying the tumor site and achieving preoperative diagnosis.

4. Conclusion

We reported an extremely rare case of metastatic HCC to small intestine, which diagnosed preoperatively by DBE. Up to our knowledge, this is the first such case to be reported

Conflict of interest statement

No conflict of interest.

Funding

No sources of funding.

Ethical approval

Written informed consent was obtained from the patient for the information to be included in our manuscript. His information has been de-identified to the best of our ability to protect his privacy.

Author contributions

Each author participated in writing the manuscript and all agreed to accept equal responsibility for the accuracy of the content of the paper.

References

1. Kay CJ. Primary hepatic cancer: review of 96 case. *Arch Intern Med* 1964;**113**:120–31.
2. Yeo W, Sung JY, Ward SC, Chung SC, Lee WY, Li AK, et al. A prospective study of upper gastrointestinal hemorrhage in patients with hepatocellular carcinoma. *Dig Dis Sci* 1995;**40**:2516–21.
3. 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.
4. Chen LT, Chen CY, Jan CM, Wang WM, Lan TS, Hsieh MY, et al. Gastrointestinal tract involvement in hepatocellular carcinoma: clinical, radiological and endoscopic studies. *Endoscopy* 1990;**22**:118–23.
5. Yamamoto H, Sekine Y, Sato Y, Higashizawa T, Miyata T, Iino S, et al. Total enteroscopy with a nonsurgical steerable double-balloon method. *Gastrointest Endosc* 2001;**53**:216–20.

Open Access

This article is published Open Access at scimedirect.com. It is distributed under the IJSCR Supplemental terms and conditions, which permits unrestricted non commercial use, distribution, and reproduction in any medium, provided the original authors and source are credited.