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Massive and life-threatening upper gastrointestinal bleeding due to invasive hepatocellular carcinoma: A case report

Semih Hot (M.D.)[a,*], Metin Yeşiltaş (M.D.)[a], Berk Gökçek (M.D.)[a], Seracettin Eğin (M.D.)[a], Selma Şengiz (M.D.)[b]

[a] General Surgery Dep., Okmeydanı Training Research Hospital, İstanbul, Turkey
[b] Pathology Department, Okmeydanı Training Research Hospital, İstanbul, Turkey

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ABSTRACT

BACKGROUND: The mean survival is less than 6 months in hepatocellular carcinoma (HCC) patients with extrahepatic metastasis. Gastrointestinal(GI) bleeding frequency due to HCC invasion is 0.05% to 2.0%, and may be fatal.
CASE PRESENTATION: We encountered a case of HCC with direct invasion to the gastrium that caused a life-threatening upper GI bleeding. Our patient was a 62 year old male who was a heavy smoker and drinker for almost 30 years. He had several upper GI bleeding episodes during the previous 6 months. Computed tomography (CT) revealed a 13 cm liver tumour directly invading the gastrium. Partial hepatic resection and subtotal gastrectomy were performed. Unfortunately, the patient died at the intensive care unit postoperatively due to hepatic failure.
DISCUSSION: Although the prognosis of HCC that has invaded the gastrium is very poor due to the advanced stage of the disease, surgical resection may be a favourable treatment option for patients with a massive upper GI bleeding.
CONCLUSIONS: The incidence of patients with massive bleeding due to gastric invasion of HCC is low, and only a few cases have been reported in the literature. Our purpose while presenting this rare case is to increase the awareness about the issue.

1. Introduction

Hepatocellular carcinoma (HCC), which constitutes more than 90% of primary liver cancers, is a major global health problem [1]. Globally, HCC is the fifth most common type of cancer and the third leading cause of cancer-related death [2]. Its incidence has an increasing trend in the United States and European countries, but there are some geographical differences as well [3]. Approximately 90% of HCCs are associated with underlying risk factors which are most commonly found as chronic viral hepatitis (types B and C), alcohol intake and aflatoxin exposure. Smoking is known to be a co-factor as heavy smokers have higher risks [4]. In the general population, the incidence of HCC is increased among patients with HIV infection indicating that HIV is also an additive co-factor which exacerbates the risk of HCC in patients with chronic viral hepatitis [5]. Extrahepatic metastasis is found in more than 15% of patients at the time of diagnosis and HCC is commonly metastasised to lungs, lymph nodes, bone and adrenal glands [6]. The mean survival is less than 6 months for patients with extrahepatic metastasis [7]. In patients with HCC, 30% of cancer-related deaths are due to hepatic failure, and 10% are due to gastrointestinal (GI) bleeding. GI metastasis is reported as 0.4%–2.0% [8]. GI bleeding frequency due to HCC direct invasion is 0.05%–2.0%, and may be fatal [9]. In one study, all patients died within 9 months [9]. The median survival was reported as 4 weeks in patients with HCC and GI involvement in another study [10]. The incidence of patients with massive bleeding due to gastric invasion is low, and only a few cases have been reported in the literature. We presented this rare case to increase awareness about the issue.

2. Case

A 62 year old male patient had been smoking 2 packs of cigarettes/day for more than 30 years, and the alcohol consumption of the patient was >80 g/day. The cause of death of the patient's father was lung cancer. The patient had dyspeptic complaints, and he received medical treatment. The patient had received medical treatment for dyspeptic complaints in another health centre initially. The tumour with 15 × 13 cm diameter was

* Corresponding author at: Avrupa Konutları Atakent 1 No:11A/3 Halkalı Küçükçekmece, İstanbul, Turkey.
E-mail addresses: semihhot@hotmail.com (S. Hot), metintesiltas@gmail.com (M. Yeşiltaş), berkgokcek@hotmail.com (B. Gökçek), seracettin.egin@hotmail.com (S. Eğin), selmaserhan@hotmail.com (S. Şengiz).

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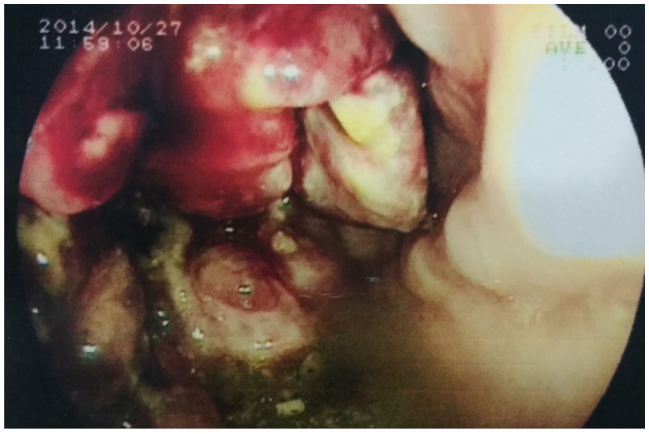

Fig. 1. Endoscopic image of tumor.

first diagnosed in the gastric antrum 6 months previously during fibreoptic endoscopy performed due to upper GI bleeding (Fig. 1). Endoscopic haemostasis was successful to stop bleeding and a biopsy was performed. Gastric metastasis of HCC was reported in the pathological examination. The patient had two upper GI bleeding episodes within a one month interval and the bleeding was controlled by supportive treatment. In oral and IV contrasted CT examination, a mass lesion was observed. This lesion which had 13 × 11 cm diameter with gastric lumen involvement, containing air images in the centrum and compact content; it extended between the hepatic hilus and distal part of the stomach and could not be differentiated from adjacent fatty planes. Multiple lymphadenopathies were detected in the hepatic hilus, para-aortic and hepatogastric regions. Activity distributions were evaluated as normal in whole body bone scintigraphy. In echocardiography, left ventricular hypertrophy, mild mitral and tricuspid insufficiency, dilations of aortic root and left atrium were reported. The laboratory test results were normal for tumour markers (Carcinoembryonic antigen (CEA) = 3.06 ng/ml, carbohydrate antigen (CA 19-9) = 11.19 U/ml, alpha-fetoprotein (AFP) = 2.82 IU/ml), and albumin = 2.2 g/L, total bilirubin = 0.77 mg/dl, AST = 30 IU/L, ALT = 38 IU/L, leukocyte = 10,400/mm^3, haemoglobin = 9 g/dl, haematocrit = 28%, platelets = 390,000/mm^3. The coagulation profile indicated INR of 1.12 and an activated partial thromboplastin time of 26. Serum HIV, hepatitis B and C antigens were all negative. The patient was evaluated as having advanced stage cancer, and cisplatin, docetaxel and capecitabine treatment protocol was given by the oncology clinic. Oral nutrition of the patient was planned according to the oncological treatment regimen. However, the patient refused to follow the course of oncological treatment, so chemotherapy was administered only once. The general status of the patient deteriorated and he had a massive and life-threatening upper GI bleeding while he was having the supportive treatment at the internal medicine clinic. The haemoglobin value was reduced from 9 g/dl to 3 g/dl, and the patient was transfused with 6 units of erythrocyte suspension and resuscitative treatments were administered. However, the haemodynamics of the patient did not improve, so emergency surgery was performed. During the exploration, a perforated and bleeding mass with necrosis and approximately 18 cm in diameter was observed, which originated from the left lobe of the liver invading the gastrium (Fig. 2). Subtotal gastrectomy and partial hepatic resection were performed. Pathological examination of operation material revealed HCC with negative surgical borders (Figs. 3–5). Immunohistochemical findings were Heppar-1 (+), sinusoidal staining (+), CD10 canalicular staining (+), MUCSAC focal (+), P53 (−), AFP (−), CK19 (−), CK20 (−), and CDX2 (−).

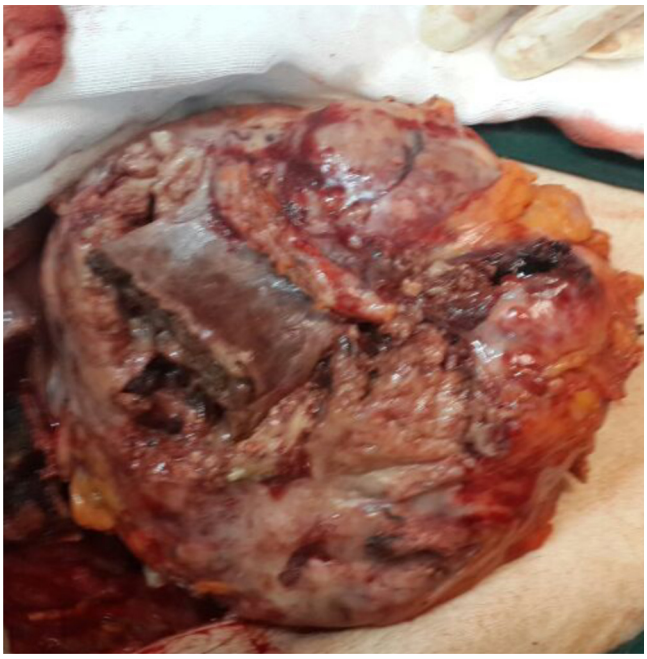

Fig. 2. Macroscopic image of tumor.

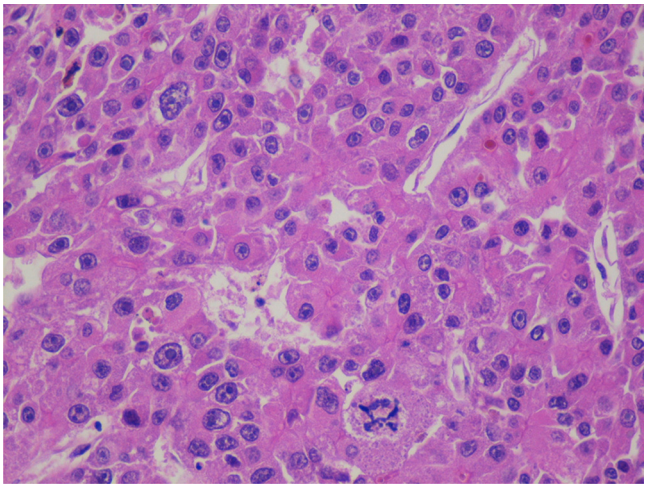

Fig. 3. Atypic mitosis in tumor tissue.

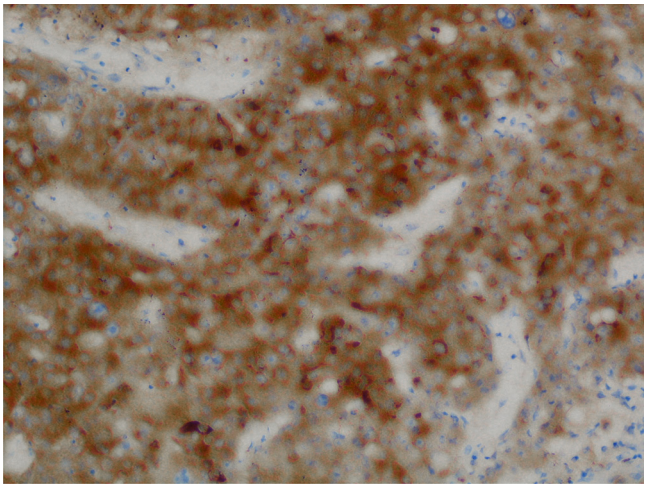

Fig. 4. Heppar-1 immunohistochemical staining.

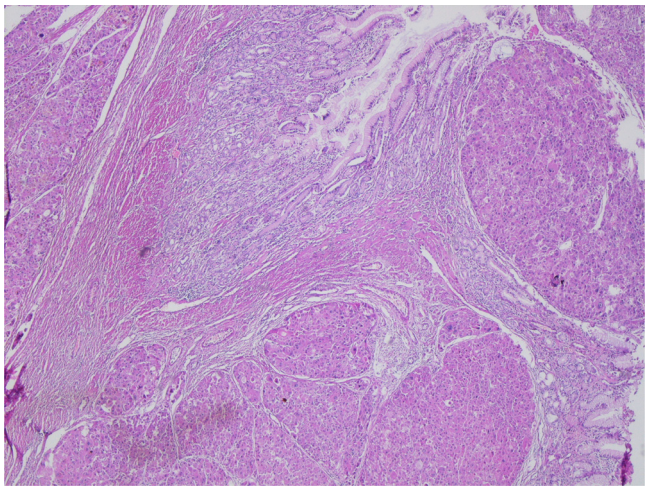

Fig. 5. Tumor islands located in the lamina propria of the stomach tissue ×40.

Morphological signs were evaluated with immunohistochemical signs. Although the tumour was observed diffusely in the gastrium, its lamina propria extensions were observed in two focus with very small sizes. We also observed that there was no paraneoplastic lesion accompanying the tumour in the gastric mucosa, which was ulcerated due to tumour in many areas, and that hepatic tissue showed a nodular structure formed by anastomosed fibrotic bands. Thus, it was decided that the primary focus was the liver, and the tumour was diagnosed as HCC. However, the patient died at the intensive care unit postoperatively due to hepatic failure.

3. Discussion

Generally, oesophageal varices or peptic ulcer disease cause GI bleeding in HCC cases. When there is hematemesis, it is considered that hypervascular HCC directly invades the gastrium. Although it is difficult to implant a clip rapidly via endoscopy, it may be a solution. However, surgery should usually be performed in these patients. GI involvement is rare in HCC, but if present, it directly involves most commonly the gastrium, duodenum, and colon [11–13]. In our case, there was direct gastric invasion, and the massive bleeding was a serious danger to life. Some predisposing factors have been proposed for rarely encountered direct invasion. These propositions were that the GI wall was affected by inflammatory response as the result of regional therapies such as transcatheter arterial embolisation (TAE), and so it adhered to the liver or tumour capsule [11]. Therefore, vital tumour tissue can easily invade the GI system. However, GI involvement has also been reported in HCC patients who did not receive any treatments [12]. Thus, it is assumed that the main factors in direct invasion are growth pattern, size, and location of these masses, rather than previous treatment modalities. The majority of patients with direct invasion have large (>5 cm in size) subcapsular HCC with exophytic growth pattern [12]. Similarly, the tumour in our case was located subcapsularly and very large.

If the patient has sufficient liver reserve, surgical removal of the bleeding tumour should be considered first [10,14]. It was reported in other case series that surgical intervention prolonged survival with the median survival rate of 9.7 months when compared to 3.0 months with nonsurgical therapy [13,15]. However, prognosis is quite bad in HCC patients with GI involvement due to massive bleeding and hepatic failure. Non-surgical methods in sustaining haemostasis are TAE, injection of ethanol or adrenalin or both, and radiotherapy [16,17].

HCC which is metastasised to the gastrium should be differentiated especially from hepatoid adenocarcinoma of the gastrium which is metastasised to the liver. Serious lymphovascular invasions such as venous tumour emboli which may result in early metastasis, especially in liver and other organs, may be observed in these cancer types [18]. Moreover, hepatoid adenocarcinoma of the gastrium is very similar to HCC due to its mutual clinical and pathological structures such as high AFP level, hepatoid morphology and AFP, polyclonal CEA and antitrypsin presence [19].

Although GI bleeding due to HCC involvement is rare, the possibility of direct gastric invasion should be considered in HCC patients who have hematemesis and/or melena in addition to the common bleeding causes such as varices and peptic ulcer. Besides, the repetition of TAE, intra-arterial chemotherapy, radiotherapy, and individualised treatmentplans have recently increased survival in unresectable HCC patients [20], and thus it is expected that GI involvement will be more commonly encountered in HCC patients in the near future.

In conclusion, while the prognosis of gastric invasion of HCC is usually poor because of the advanced stage of the disease, surgery can be suitable treatment choice in patients before the potential complications occurred.

Conflicts of interest

We have no conflicts of interest with any organization or individual.

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Ethical approval

We do not need the ethical approval from the Ethical Committee of our Hospital, for the case reports.

Consent

Written informed consent was obtained from the patient's first degree relatives. A copy of the consent is available for review by the Editor in Chief of your journal on request.

Author contribution

The following is the list of contributing authors;

Dr. Semih Hot: Data analysis, Concept, Writing the paper, Related literature review.

Dr. Metin Yesiltas: Concept, Data analysis, interpretation.

Dr. Berk Gökçek: Design, interpretation.

Dr. Seracettin Eğin: Data collection.

Dr. Selma Şengiz: Data analysis.

Guarantor

Dr. Semih Hot is the guarantor of our study.

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