Gastrointestinal tract involvement in hepatocellular carcinoma: two cases illustrating duodenal and oesophageal invasion

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Abstract

We present here two hepatocellular carcinoma (HCC) patients with gastrointestinal tract involvement (GITI). Hemorrhage due to duodenal involvement was the inaugural event of the HCC for the first patient. Dysphagia due to HCC recurrence in the oesophagus four years after left hepatectomy was the call symptom for the second. As incidence of HCC increases, and overall survival improves, incidence of GITI in HCC patients is expected to increase. (Acta gastroenterol. belg., **2021,** 84**, 660-662**).

Key words: direct invasion, heart invasion, chemotherapy.

Introduction

In Belgium, 1063 new cases of liver cancer (LC) were diagnosed in 2018. The 5-year survival rate was 21% (1). Hepatocellular carcinoma (HCC) represents the great majority of LC. Major advances have been performed in the understanding of pathophysiological mechanisms and genomic dysregulation of HCC (2-3).

Autopsies series of HCC patients revealed 1- 4% of gastrointestinal tract involvement (GITI). Since the first premortem report in 1987 (4), GITI has been occasionally described in living HCC patients. The duodenum and the stomach are the most commonly sites affected (5,6), the oesophagus is exceptionally affected (7).

Case 1

A 67-year-old man was presenting melena**.** His medical history included tobacco and alcohol consumption, gouty arthropathy and recent anaemia. No chronic liver disease was detected yet. He was taking colchicine, ibuprofen and iron tablets. Blood pressure was 102/60mmHg and pulse 92/min. Body mass index (BMI) was 25. There was no clinical manifestation of liver disease.

Lab results were: haemoglobin 7.8 g/dL, normal leucocyte and platelet counts, normal INR and bilirubine levels, GGT 126 UI/L (N < 60), ASAT 48 UI/L (N < 48), albumin 25.8 g/L (N 32-46), IgA 6.41 g/L (N 0.70-4), CA19.9 17 kU/L (N < 39), alpha fetoprotein (AFP) 269 microgram/L (N < 73). Tests for hepatitis B surface antigen (HBsAg) and antibodies, hepatitis C antibodies (HCVAb), anti-nuclear and anti-smooth muscle antibodies were negative.

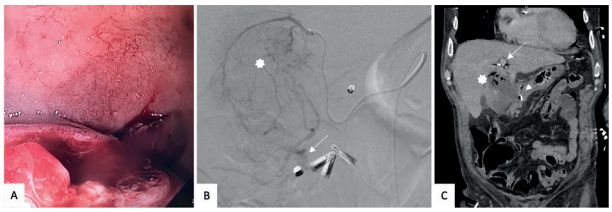

Figure 1. — Images of Case 1. – A. Endoscopic view of a submucosal mass in the duodenal bulb with active oozing (Forrest Ib). B. An arteriographic image demonstrating a liver tumor with vascular atypia's (asterisk) and extravasation of contrast medium in the duodenum (arrow) C. A coronal abdominal CT-scan image showing the hepatic mass invading the duodenum. Note the presence of enteric fistula (asterisk), haemostatic clips (arrow) and microcoils (arrowhead).

Urgent oesophagogastroduodenoscopy revealed an ulcerated submucosal mass into the duodenal bulb with active oozing (Forrest Ib) (fig. 1A). Injection of epinephrine and haemostatic clipping failed to control the bleeding. Percutaneous abdominal arteriography demonstrated a bulky hepatic tumor with vascular atypia's and extravasation of contrast medium just near the clips. Transarterial embolization (TAE) with microcoils stopped the bleeding (fig. 1B).

Computed tomography (CT) scan confirmed a significant tumoral process (70 mm) in segment IV of the liver (Fig. 1C). Magnetic resonance imaging (MRI) detected numerous hepatic metastases. Anatomical examination of transcutaneous tumoral liver biopsy was compatible with a poorly differentiated HCC. Immunohistochemical analysis was positive for hepatocyte-paraffin-1, glypican-3 and arginase-1. Examination of extra-tumoral liver biopsy showed severe liver fibrosis, without steatosis nor inflammatory infiltrates. Prussian Perls staining did not demonstrate iron deposits. There was no evidence of non-alcoholic steatohepatitis or autoimmune liver disease.

Sorafenib treatment and home-based supportive care were initiated. Three months later, the serum level of

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AFP had reached 5243 microg/L. Six months after TAE, the patient died from uncontrollable duodenal rebleeding.

Case 2

In November 2014, following hospitalization for alcoholic hepatitis, HCC was found in a 66-year-old man. An abdominal MRI showed a dysmorphic liver and a large (55 mm) exophytic tumor in segment III. There were no portal vein thrombosis (PVT), no oesogastric varices nor vascular invasion. Chest CT and bone scans were normal. After achieving the alcoholic withdrawal, a left hepatic lobectomy was performed in May 2015. Non-tumor histological examination revealed micronodular cirrhosis. The tumor histological examination was consistent with a well differentiated HCC. The margins of surgical resection were healthy (R0 resection) but the capsule was broken, and multiple vascular emboli in the perihepatic fat were present. Several small infracentimetric tumoral nodules were observed in the liver parenchyma. Based on these pejorative findings, the hepatic transplant was rejected. In October 2015, August 2016 and June 2017, three new small tumors appeared successively in the segments IV and VII at a distance from the section margin and were treated by radiofrequency ablation (RFA).

In April 2019, the patient developed dysphagia. He maintained abstinence from alcohol. On physical examination, he had no jaundice or ascites, blood pressure was 126/86 mmHg and pulse 73/min. BMI was 27.

Laboratory examination showed normal haemogram, INR, albumin, liver enzymes and AFP levels. Decarboxyprothrombin level was elevated (2851 mUA/mL, N < 45). HBsAg and HCVAb tests were negative.

Oesophagogastroduodenoscopy revealed a large tumor in the lower third of the oesophagus, occupying 80% of the lumen but allowing endoscopic passage (Fig. 2A). It evidenced signs of portal hypertensive gastropathy but no oesogastric varices. Biopsy specimens obtained from the oesophageal mass showed a tumor histologically consistent with HCC. The staining was positive for glypican-3, arginase-1 and hepatocyte-paraffin-1 (Fig. 2B).

Chest CT scan showed the oesophageal tumor (53 mm) and a tumor thrombus (40 mm) growing into the right atrium (Fig. 2C-2D). There was no new hepatic nodule, no PVT, no thrombosis of the hepatic veins (THV). On cardiac MRI, the tumor thrombus originated in the distal inferior vena cava (IVC) and extended in the right atrium (figure 2E); in one section, continuity between oesophageal and atrial masses was observed (figure 2F). The nutritional requirements were fulfilled through gastrostomy with a jejunal extension (PEXACT system) because of the presence of gastroparesis. However, sorafenib treatment by this route seemed uncertain. As the patient was not eligible at that time for inclusion in a therapeutic trial, intravenous chemotherapy associating gemcitabine and oxaliplatin was initiated

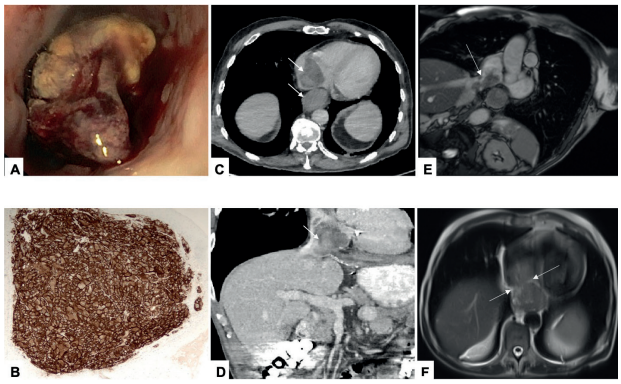

Figure 2. — Images of Case 2. – A. Endoscopic view of a large exophytic oesophageal tumor. B. Immunohistological staining of oesophageal biopsy specimens revealing high positivity for glypican-3. C. An axial CT-scan image showing the oesophageal and atrial masses (arrows). D. A coronal CT-scan image showing normal hepatic parenchyma and an endoluminal mass in the right atrium (arrow). E. A cardiac magnetic resonance image showing the tumor thrombus in the distal inferior vena cava extending in the right atrium (arrow). F. A cardiac magnetic resonance image demonstrating continuity between oesophageal and atrial masses (between arrows).

with antithrombotic treatment. Fiftheen months later, the patient was doing well and fed himself properly per os. He had not developed chemotherapy toxicity nor presented respiratory symptoms. On the chest and abdominal CT scans, the oesophageal tumor had shrunk in size (12 mm), but the atrial tumor remained the same size. No new liver tumor nor pulmonary lesions had appeared. Decarboxyprothrombine level was 8484 mUA/mL.

Discussion

HCC can spread to the digestive tract by direct infiltration; it can disseminate through blood vessels or lymphatics. Predisposing factors for direct invasion include large liver lesions (> 5 cm), subcapsular location, an exophytic growth pattern (5, 6), former regional therapy (transarterial chemoembolization or arterial chemotherapy) and abdominal surgery. Haematogenous intestinal metastasis is usually the result of tumor emboli disseminated by hepatofugal portal blood via the portal venous system. PVT is usually observed in this case.

Direct invasion of the duodenum by the contiguous HCC was the responsible mechanism for the first patient. For the second patient, there was no PVT, THV or esophageal varices. Vascular emboli were present in the perihepatic fatty tissue of the resected lobe, four years earlier. This latter fact could explain a late involvement of the IVC, close to the previous tumor site with the development of tumor thrombus spreading to the right atrium, then perforating the pericardium and invading the esophageal wall. Right atrium invasion is rare (8, 9) and to our knowledge, the occurrence of both heart and oesophageal involvement has not been reported to date.

The most common clinical presentation of GITI by HCC is frank gastrointestinal bleeding followed by occult blood loss (10). Occlusion, perforation, abdominal pain are unusual.

The endoscopic assessment reveals various features ranging from a penetrating ulcer to a tumoral polypoid mass or a submucosal mass with or without extrinsic compression (5,6,7). The haemorrhagic risk must be considered before performing a biopsy.

GITI in HCC is generally occurring late during the tumor disease. Median survival rate ranges between 3 and 9 months. Long term survival had been reported, mostly when surgery with curative intent was possible (6). Therapy is decided on a case-by-case basis.

Our case reports illustrate the broad spectrum of clinical presentations of GITI in HCC. The first case highlights the fact that GITI can be the inaugural event leading to the diagnosis of HCC. The second case is exceptional for two reasons: the occurrence of both atrial and oesophageal involvement and the remarkable response to gemcitabine-oxaliplatin chemotherapy, a well-known but rarely used regimen for advanced HCC (11).

Conflict of interest

The authors declare that there is no conflict of interest.

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