A challenging alfa-fetoprotein in a cirrhotic patient

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Abstract

A 57-year-old Italian man was admitted to our Hospital for investigation of a progressively raising alfa-fetoprotein (AFP) on the background of chronic hepatitis B infection. At abdominal imaging, liver morphology was suspected for advanced fibrosis but without any focal lesion. Clinical and ultrasonographic examinations were negative for testicular masses. When the patient was screened for gastroesophageal varices, upper intestinal endoscopy did not show signs of portal hypertension, while it revealed a gastric lesion which was histologically characterized as hepatoid adenocarcinoma of the stomach (HAS), with strong immunohistochemical positivity for AFP. The patient underwent subtotal gastrectomy and AFP fell within the normal range. This is a very rare case in which AFP-producing gastric cancer (AFPPGC), in the form of HAS, presented in a patient with chronic liver disease. Physicians should be particularly aware of AFPPGC when following patients with liver disorders due to the common use of AFP in this setting. (Acta gastroenterol. belg., **2014**, 77, **66-67**).

Key words : AFP-producing gastric cancer, hepatoid adenocarcinoma of the stomach.

Introduction

Alfa-fetoprotein (AFP) level is one of the most widely used biochemical blood tests in patients with chronic liver disease, although its use as a screening test for hepatocellular carcinoma (HCC) has been recently discouraged (1). The incidence of AFP-producing gastric cancer (AFPPGC) has been reported to be 1.3-15% of all gastric cancers (2). Here we report a rare case of AFPPGC on the background of chronic hepatitis B virus (HBV) infection.

Case report

On January 2012, a 57-year-old Italian man was admitted to our Hospital for investigation of severely elevated AFP levels.

HBsAg-positivity was known since 1992 but, at that time, he had been regarded as a "healthy carrier" not requiring specific controls. A few months before admission, HBV infection was re-evaluated by his new family physician and a progressive rise of AFP was noticed (until 1156 ng/ml, reference range : 0-10 ng/mL).

On admission, blood exams showed only mild thrombocytopenia (120.000/μL) and a slight elevation of alanine aminotransferase (ALT : 49 U/L ; upper normal limit : 35 U/L), while hepatic function tests (bilirubin, albumin, prothrombin time) were within the normal range. HBV-DNA was 396 IU/mL. At ultrasonography and magnetic resonance, liver morphology was suspected for advanced fibrosis (irregular edges, hyperthrophic caudate lobe), but only a small nodule (7 mm) was detected in the VII segment, slightly hypervascular in the arterial phase and almost isointense in the portal venous and delayed ones. Moreover, the nodule was barely hypointense in the delayed phases of a second magnetic resonance with the hepatospecific contrast medium gadoxetic acid. All together, these dynamic features were compatible with a high-flux hemangioma or with an intrahepatic artero-venous shunt, but limited dimensions of the lesion did not permit a definite characterization. Clinical and ultrasound examination were negative for testicular masses. Meanwhile, the patient was screened for gastroesophageal varices. Upper intestinal endoscopy showed no sign of portal hypertension, while it revealed an ulcerated lesion at the gastric angulus, whose histology was suspected for hepatoid adenocarcinoma of the stomach (HAS), with strong immunohistochemical positivity for AFP. Total-body CT scan was negative for other organ involvement.

The patient underwent subtotal gastrectomy during which a liver biopsy was also performed. Histology confirmed the diagnosis of HAS (Fig. 1), and revealed moderate interface hepatitis but, surprisingly, only slight portal and periportal fibrosis (grading 5 and staging 1 by Knodell's classification). One month after surgery, AFP fell within the normal range. CT scan performed two months after surgery showed abdominal nodal metastases, and chemotherapy was started with 5-fluorouracil, cisplatin and trastuzumab according to the ToGA regimen (3). Entecavir 0.5 mg daily was also started mainly to prevent a possible viral reactivation favoured by chemotherapy-induced immunosuppression. At the moment, chemotherapy is ongoing, with substantial stability in the dimensions of the nodal metastases and without evidence of other secondary lesions in the last CT scan performed eight months after the beginning of therapy. Also the dimensions of the hepatic nodule were stable (7 mm), supporting the impression of a benign lesion.

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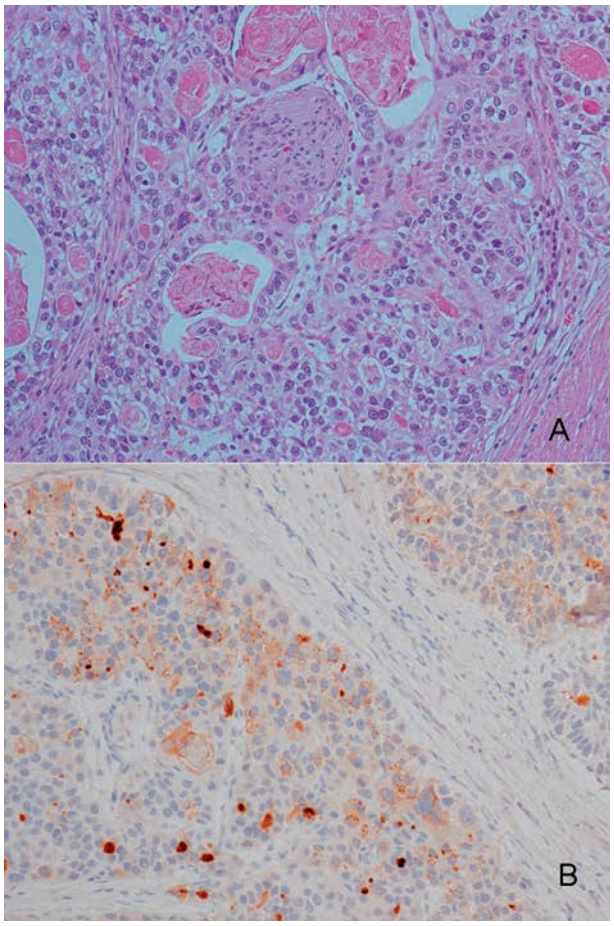

Fig. 1. — Hepatoid adenocarcinoma of the stomach by haematoxylin and eosin staining (Panel A), and immunohistochemistry for alpha-fetoprotein (Panel B) (original magnification 20×).

Discussion

In adults, if one excludes pregnancy and liver regeneration after acute or chronic damage, high blood levels of AFP are generally associated with cancers, the most frequent of which are HCC and germ cell tumors. Since the first case of AFPPGC reported in 1970 (4), a few other cases have been described, showing that AFPPGC is usually diagnosed in advanced stage, with liver metastases and a poor prognosis (4-5). It has been also shown that some AFPPGCs display histological features strongly reminiscent of HCC, and, in these cases, the name HAS has been proposed. Both AFPPGC and HAS carry a poorer prognosis than classical gastric cancer and HAS showed an even more aggressive behaviour than other AFPPGCs (6).

The present case highlights the confounding clinical picture of AFPPGC occurring on the background of chronic liver disease. To the best of our knowledge, AFPPGC has been described in patients with hepatopathy in only three previous cases (7-9), and in one single case AFPPGC was characterized as HAS (8). Therefore, although AFPPGC incidence doesn't seem higher in patients with liver disease, hepatologists should be particularly aware of its existence when following hepatopathic patients due to the common use of AFP in this setting.

In conclusion, we suggest that the stomach should be among the organs to be investigated when facing elevated AFP levels of unknown etiology, even in patients with chronic liver disease. *Vice versa*, the risk is to "stress" the liver while missing the diagnosis.

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