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CASE REPORT

Alpha-fetoprotein and focal nodular hyperplasia: An unconventional couple

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Abstract

We report the case of a 36-year-old patient who was initially managed for gynecomastia. The first biological analyses showed a moderately elevated alpha-fetoprotein (AFP) level. After an endocrine etiology was excluded, an abdominal computed tomography scan showed typical focal nodular hyperplasia (FNH) proven by biopsy and showing expression of AFP in FNH cells. After follow-up for 24 months, the serum AFP and liver radiology remained unchanged. The association between an elevated AFP and FNH is rarely described in the medical literature.

Introduction

Focal nodular hyperplasia (FNH) is a frequent liver tumor with no risk of malignant transformation. Alpha-fetoprotein (AFP) is a tumoral marker, classically associated with hepatocellular carcinoma (HCC) and, also, with embryonic tumors like testicular seminoma. The role of AFP in HCC screening is still debated. Furthermore, AFP is classically not elevated in nonmalignant tumors, such as FNH. We report a case of a man initially consulting for a gynecomastia leading to the detection of an elevated serum AFP concentration and asymptomatic liver tumors.

Case Report

A 34-year-old man was managed for a gynecomastia. Initial investigations showed a moderate elevation of serum AFP: 59 ng/mL. He had no personal or familial medical history and apart gynecomastia clinical examination was normal especially testicles and abdominal examination. Liver tests (alanine transaminase [ALT], aspartate transaminase [AST], gamma-glutamyltransferase [GGT], alkaline phosphatase, and total bilirubin) were normal. Because of an association between elevated AFP and gynecomastia, ultrasound and magnetic resonance imaging (MRI) of the testicles were performed, normal. Sex-binding protein, Follicle Stimulating Hormone (FSH), Thyroid Stimulating Hormone (TSH), Hunan Chorionic Gonadotropin (HCG), testosterone, and 17-β-œstradiol were without abnormality. 18-FluoroDeoxyGlucose Positron Emission Tomography scan (18-FDG PET) did not show any suspect fixation.

Liver computed tomography (CT) simultaneously revealed a nodule of 23 mm located in segment IV with benign presentation, arterial enhancement, portal washout and a central scar in favor of FNH. MRI showed a T2 slight hyperintensity, an arterial enhancement, an equilibration with the adjacent liver during the portal phase and confirmed the central scar, in favor of a FNH. A liver biopsy was performed and showed a cellular proliferation with a nodular architecture. Fibrous septa contained a lymphocytic inflammatory infiltrate and large vessels. A ductular proliferation was focally observed at the edge of the septa. On immunohistochemistry, glutamine synthetase staining showed a "map-like" pattern. Rare hepatocytes (less than 1%) that were scattered or grouped in small clusters harbored AFP expression. These morphological data supported the diagnosis of FNH (Fig. 1).

The patient underwent gynecomastia surgery: Histology was banal, just showing normal fat tissue. Relationship between gynecomastia and elevated serum AFP and furthermore FNH, was not established.

A radical treatment of FNH by thermic ablation or surgery was discussed: The benefic-risk ratio was not favorable. After a follow-up of 24 months, the serum AFP concentration (between 45 and 60 UI/mL) and the liver iconography remained unchanged.

Discussion

FNH is a frequent liver benign lesion, associated with a local vascular disorder. Its prevalence is between 0.6 and 3% in the general population.[1] It essentially occurs in women. Surgery is reserved for symptomatic patients, and is of rare indication. The average age at presentation is 35–50 years old. Diagnosis can be obtained reliably by an MRI with a hepatobiliary phase, the

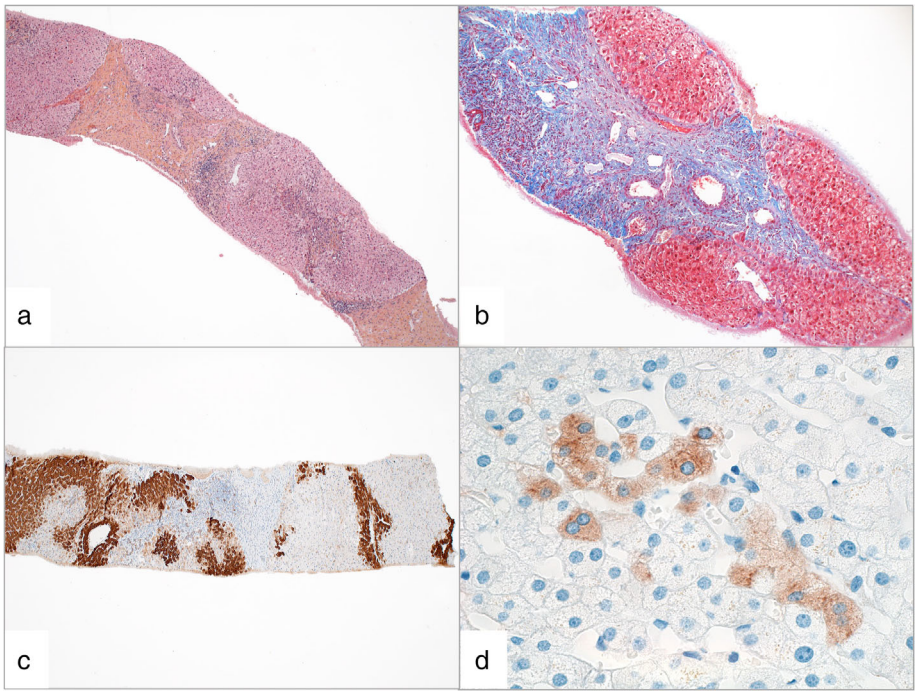

Figure 1 (a) Nodular architecture. Hematein eosin saffron. Original magnification ×40. (b) Large and thick-walled vessels in fibrous septa with inflammatory infiltrate and ductular proliferation. Masson's trichrome. Original magnification ×100. (c) Glutamine synthetase immunostaining with a "map-like" pattern. Original magnification ×40. (d) Immunohistochemistry: Alpha-fetoprotein expression in hepatocytes in a focal nodular hyperplasia (FNH) nodule. Original magnification ×630.

sensitivity varying from 87 to 95%: It usually shows a homogeneous lesion, slightly different from normal liver parenchyma on precontrast images, with a strong enhancement during the arterial phase before the lesion recovers an aspect close to the adjacent parenchyma, and finally a central scar. The macroscopic appearance of FNH explains the radiological data. This lesion is well circumscribed, multinodular, and typically shows a central stellate scar with radiating septa. As previously mentioned, a surgical resection is rarely performed. In atypical cases, as in our observation, a histological confirmation of the diagnosis is required, and a biopsy is carried out. Histologically, main criteria of diagnosis are: A nodular architecture with fibrous septa containing thick-walled vessels and mononuclear inflammatory infiltrate; a ductular reaction seen at the junction between septa and parenchyma; a "map-like" immunostaining pattern of glutamine synthetase.[2] In our case, it is important to underline that rare cells harbored AFP expression. This expression can explain high AFP concentration.

AFP is a tumor marker usually associated with HCC. Its role in 6-months screening of cirrhosis is controversial. On one side, clinical practice guidelines do not recommend its dosage during follow-up as its impact on HCC mortality is discussed in recent studies.[3] On the other side, some studies emphasized the role of AFP in order to increase the sensitivity of HCC screening.[4] Serum AFP elevation is not specific of HCC: it can be increased in 20% of liver cirrhosis without HCC, and may exceed 100 ng/mL in 3% of patients.[5] Other causes are well described: Teratoma, pregnancy, cholangiocarcinoma, nonseminoma testicle cancer; AFP elevation is also reported in rare cases of gastric, pancreas, kidney, and other type of testicle cancer. In our patient, gynecomastia and elevated AFP led to unsuccessful testicle cancer screening.

Association between increased AFP level and FNH is not classical. Descriptions in the literature are very rare.[6,7] French Beaujon's team described a case of FNH associated with high serum AFP. It was hypothesized that, as FNH is associated with some features of progenitor cells, regenerative process can lead to an elevated serum AFP concentration.[8] Furthermore, in a Chinese prospective study, increased serum AFP was described in less than 3.1% of patients with FNH, but the exact levels were not reported.[9] Adenomas are rarely associated with elevated AFP, and to our knowledge, there is no description in case of hemangioma.[10]

To conclude, high serum AFP can have a discriminant role to differentiate HCC from other liver tumors, including FNH.[9] Nevertheless, FNH can be rarely associated with a high serum AFP level: Clinicians must be aware of this possible association.

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