CLINICAL CASE

Liver cell adenomas and portosystemic shunt
Adénomes hépatocellulaires et shunt portosystémique

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Summary We report the case of a young man who developed multiple liver cell adenomas 13 years after a mesentericocaval shunt. Radiological findings did not provide diagnosis. Histological findings of two biopsied nodules were compatible with liver cell adenoma. Our patient had no known risk factors for liver cell adenomas. We discuss the hypothesis that disturbed hepatic vascularisation could promote the development of liver cell adenomas.

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Résumé Nous rapportons le cas d’un jeune homme qui a développé de multiples adénomes hépatocellulaires 13 ans après la réalisation d’une anastomose mésentéricocave. Les données de l’imagerie n’ont pas permis de faire le diagnostic des lésions. L’histologie de deux nodules hépatiques biopsiés a conclu à un adénome hépatocellulaire. Le patient n’avait aucun facteur de risque associé aux adénomes hépatocellulaires. Nous suggérons que les lésions observées chez ce patient pourraient s’être développées secondairement aux perturbations de la vascularisation hépatique induite par l’intervention.

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Introduction

Hepatocellular adenomas are benign tumours mainly observed in young women [1,2]. Patients who develop liver cell adenomas often have no known risk factors, except oral estroprogestative use. Sometimes, an underlayed metabolic disease such as a glycogen storage disease, galactosemia or HNF1-α type diabetes is identified. Some patients who have taken androgenic steroids may develop hepatocellular carcinoma or liver cell adenomas [3,4].

Portosystemic shunts were frequently performed in the 1970s and 1980s in young patients with gastrointestinal hemorrhage from portal hypertension [5].
Liver cell adenomas and portosystemic shunt

To our knowledge, there is little information concerning the development of liver nodules, particularly liver cell adenomas and focal nodular hyperplasia after portosystemic shunts [6,7]. We report the case of a young man who developed multiple hepatocellular adenomas 13 years after a mesentericocaval shunt and discuss the pathogenesis of these lesions.

Case report

A four-year old boy was referred to Bicêtre University Hospital for gastrointestinal bleeding from esophageal varices. Congenital hepatic fibrosis and Caroli’s disease were diagnosed and a mesentericocaval anastomosis was successfully performed for recurrent varical bleeding. Every one or two years, an ultrasound was performed and the follow-up was uneventful until the patient was 17. There was no hormone therapy. The patient had three episodes of cholangitis between the age of 17 and 21, which were successfully treated with antibiotics. Liver tests were normal except for the episodes of cholangitis. At the age of 18, renal dysfunction confirmed the autosomal recessive polycystic renal disease that had been identified during kidney ultrasound examinations since the age of four. Creatinine clearance was 77 ml/min and there was no arterial hypertension. At the age of 19, liver ultrasound showed three hypoechogenic liver nodules of 42, 30 and 20 mm in diameter located in segments V and VI, respectively, associated with the multiple cysts of Caroli’s disease. One year later, liver ultrasound showed two additional 50 and 17 mm sized nodules, located in segments VII and VI, respectively. The three other previously recorded nodules measured 56, 23 and 22 mm in diameter, respectively. Magnetic resonance imaging showed the five nodular lesions, which appeared hyperintense on T1, weighted magnetic resonance imaging and iso- or hyperintense on T2 weighted magnetic resonance imaging. Lesions were not enhanced in the arterial phase and became homogeneous in the later phase of dynamic gadolinium-enhanced imaging. There was no central scar even for nodules more than 40 mm in diameter. There was no arterial enhancement of the whole liver. Doppler did not show any arterial enhancement of these lesions. Serum α-fetoprotein concentration was normal. Because the radiological features did not provide a clear diagnosis and the lesions were increasing over time, an ultrasound-guided core needle liver biopsy, using a 18 G needle, was performed on two out of five liver nodules, which measured 23 and 22 mm. Length of biopsy was 15 and 12 mm, respectively. Histological examination showed a benign hepatocellular proliferation of enlarged liver trabeculae lined by non dilated CD34 negative sinusoids, devoid of portal tract and ductular proliferation and vascularized by small isolated arteries without stromal or inflammatory reaction (Fig. 1). Some rosette formations were present, with cytokeratin 7. There was no dysplasia, steatosis cholestasis or inflammatory proliferation. The histological diagnosis was liver cell adenoma. There was no suggestion of focal nodular hyperplasia or nodular regenerative hyperplasia. Typical features of congenital hepatic fibrosis were also observed on the liver tissue taken from a non tumoral area. Sequencing analysis of HNF1-α gene did not identify germ-line mutations. Hepatic lesions remained stable in the last ultrasound.

Discussion

Benign hepatocellular lesions are diagnostic dilemmas, both clinically and radiologically. However, certain clues can help to provide a differential diagnosis. In our patient, the extensive radiological explorations did not provide a clear diagnosis of the liver tumour. There were several arguments against focal nodular hyperplasia, including kinetic enhancement, presence of a hypointense peripheral ring and no central scar even in the largest lesions. All these elements suggest liver cell adenoma or nodular regenerative nodules. The nodules were not fatty even on magnetic resonance imaging, which does not support liver cell adenoma. All the nodules had the same radiological characteristics. Histological diagnosis of two of the five sampled nodules using core needle biopsy was consistent with liver cell adenoma. The main histological differential diagnoses include focal nodular hyperplasia and large regenerative nodules between distorted liver architecture related to congenital hepatic fibrosis. The main criteria found against focal nodular hyperplasia were the absence of septal fibrosis or ductular proliferation and the presence of hepatocellular proliferation with regular thickened sheets of nearly normal hepatocytes. The absence of cytokeratin 7 and 19 cholangiocytes in the immunohistochemical study supports a diagnosis of liver cell adenoma rather than focal nodular hyperplasia [8,9]. In contrast, the possibility of large regenerative hepatocellular nodules needs to be discussed. These lesions could be difficult to discriminate from adenomas. Core biopsy is recommended because many benign entities have overlapping histologic features, and if fine needle aspiration is performed, a definitive diagnosis may be difficult. A definitive pathological diagnosis still can-
not be made in some cases. Therefore, surgical resection or wedge resection may be necessary if the exact process cannot be definitely ruled out. In fact, the extranodular liver of this patient was probably damaged by the repeated acute attacks of cholangitis. The most likely diagnosis is liver cell adenoma but hepatocellular adenoma-like hyperplastic nodules related to abnormal hepatic circulation cannot be completely excluded without surgical examination.

Since the five lesions had the same radiological features, it is our opinion that the patient developed five adenomas, outside the context of liver cell adenomatosis that usually requires the presence of more than 10 nodules [1,2,10]. The occurrence of this rare lesion 13 years after the mesentericocaval shunt suggests a possible link between the two events. To our knowledge, there is no established link between congenital hepatic fibrosis and liver cell adenomas. Liver cell adenomas are rare in young male patients, unless they have glycogen storage disease or have taken androgenic steroids [3,4]. Our patient was not exposed to these risk factors and did not have the HNF1-α mutation described in association with liver cell adenomatosis [2,10]. In the 1970s and 1980s portosystemic shunts were frequently performed in young patients with the complications of portal hypertension [5]. Portal diversion induces intrahepatic hemodynamic changes that could promote the development of liver tumours [11,12]. In particular, there is an absolute increase in hepatic arterial blood flow to replace the portal flow, which is absent. Pre-existing vascular abnormalities are believed to represent a predisposing factor for focal nodular hyperplasia, and were reported as a predisposition to liver cell adenoma [13—16]. However, portal diversion is known to induce other modifications. For instance, in animal models, portacaval shunting induces significant hyperestrogenemia and estrogen exposure is a known risk factor for developing liver cell adenomas [11,17]. Moreover, it has been also suggested that the shunt-induced arterial blood flow could bring high levels of trophic factors to the liver and promote the development of liver tumours [11]. Few cases of adenomas associated with spontaneous portosushepatic or portacaval shunts, or surgical shunts, have been described in young patients [6,7]. In some cases, liver cell adenomas were reported in association with focal nodular hyperplasia suggesting a common vascular pathogenesis for these two entities [6,16,18].

We conclude, that liver cell adenomas may appear after portosystemic diversion and hypothesize that the mesentericocaval shunt favoured the development of multiple liver cell adenomas in this young male patient through vascular or hormonal mechanisms. A long-term follow-up study in patients who received portosystemic shunts in early childhood for portal hypertension is warranted.

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References