FOCAL NODULAR HYPERPLASIA OF THE LIVER: A CASE REPORT AND REVIEW OF THE LITERATURE*

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Abstract **In this case report we discuss a focal nodular hyperplasia diagnosed in a female, six-year old patient, as well as her follow-up from the diagnosis to the present time. Imaging techniques, particularly hepatosplenic scintigraphy and computed tomography, are essential for the diagnosis. Also, a literature review is presented.**
Keywords: Focal nodular hyperplasia; Scintigraphy; Computed tomography; Ultrasonography.

Resumo *Hiperplasia nodular focal do fígado: apresentação de um caso e revisão da literatura.*
Neste trabalho apresentamos um caso de hiperplasia nodular focal que foi diagnosticado aos seis anos de idade e que está sendo acompanhado até o momento presente. Para o diagnóstico foram imprescindíveis as técnicas de imagem, tendo importância de realce a cintilografia hepatoesplênica e a tomografia computadorizada. Apresentamos, também, revisão da literatura sobre o assunto.
Unitermos: Hiperplasia nodular focal; Cintilografia; Tomografia computadorizada; Ultra-sonografia.

INTRODUCTION

Focal nodular hyperplasia (FNH) is the second most frequent benign tumor of the liver, surpassed in prevalence only by hepatic hemangiomas, and corresponding to 8% of all the primary hepatic tumors[(1)]. Most of times, FNH is found as a solitary nodule smaller than 5 cm in diameter, although larger lesions with more than 15 cm in diameter have already been found[(1)]. Usually, the course of the disease is asymptomatic, and, most of times, the lesion is incidentally found either at a clinical examination, as an imaging finding, or during autopsy [(2)]. Macroscopically, FNH presents as a well circumscribed, lobulated and non-encapsulated lesion[(3)]. Typical histological alterations include a dense, central star-like scar with radiating fibrous septa dividing the tumor into several nodules[(3)]. Microscopically, these fibrous septa are composed of biliary structures surrounded by inflammatory cells, Kupffer cells and vascular malformations including arteries and capillaries[(3)].

Developments in imaging studies have made the diagnosis easier without necessity of laparotomy or surgical, besides the differentiation between FNH and other benign diseases of the liver and hepatocellular carcinoma[(2)].

CASE REPORT

The present study reports the case of a black, female, 19-year-old patient who, at six year of age, had presented complaining of mesogastric pain and abdominal distention. Clinically, the patient presented a good general condition, flushed and hydrated. Weight and height were near the 25th percentile, according to her chronological age (weight: 20.4 kg, height: 116 cm). The liver was palpable at 6.5 cm from the right costal border, and at 11.5 cm from the xiphoid appendix, painless, with an irregular surface and hardened consistency. Liver function tests were normal.

Ultrasound evidenced hepatomegaly with lobulated margins (Figure 1). Hepatosplenic scintigraphy was suggestive of FNH, since it has shown the left lobule increased in volume and with increased uptake (Figure 2). Laparotomy has evidenced a large mass measuring 20 cm × 15 cm × 10 cm in the anterior portion of the liver, presenting a nodular aspect, reddish color, solid consistency and central venous irrigation, suggesting a tumor-like process (Figure 3). Open biopsy was performed, confirming the diagnosis suggested by the hepatosplenic scintigraphy (Figure 4). These studies were performed at the time of the diagnosis.

Along these 13 years of follow-up, a conservative approach has been adopted, and the progression has shown hepatic enlargement documented by abdominal ultrasound. Hepatosplenic scintigraphy has evidenced increase of the left lobe with heterogeneously decreased radionuclide uptake. Biliary tract scintigraphy has shown a hyperconcentrating left lobe, with a more heterogeneous aspect. Abdominal helical computed tomography, performed

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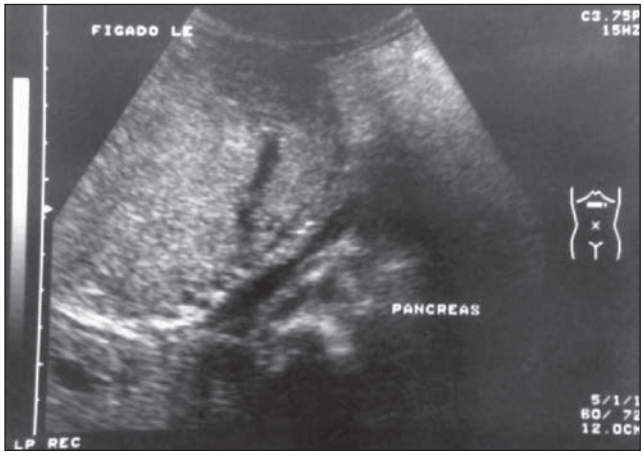


Figure 1. Abdominal ultrasound demonstrating a liver increased in volume because of a lesion in the left lobe, with heterogeneous, nodular images with clearly defined margins.

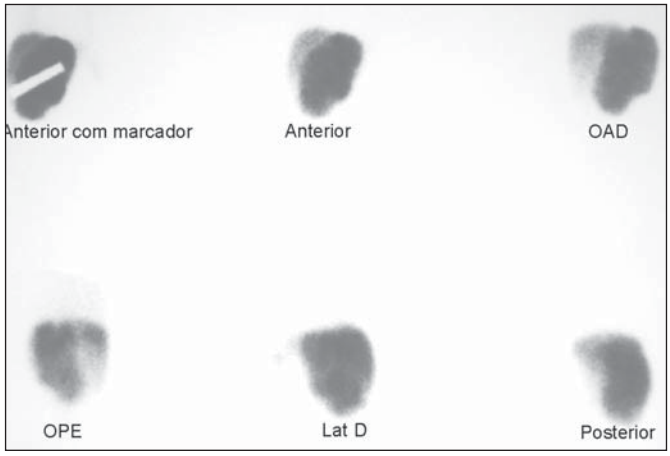


Figure 2. Hepatosplenic scintigraphy with colloidal sulfur (^{99m}Tc). Planar images demonstrating an increased left lobe with increased uptake.

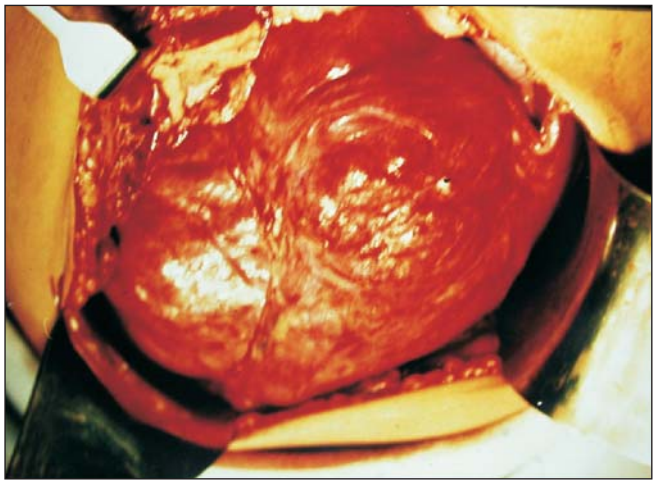


Figure 3. Abdominal laparotomy showing a large mass measuring 20 cm × 15 cm × 10 cm in the anterior portion of the liver, presenting a nodular aspect, reddish color, solid consistency and central venous irrigation.

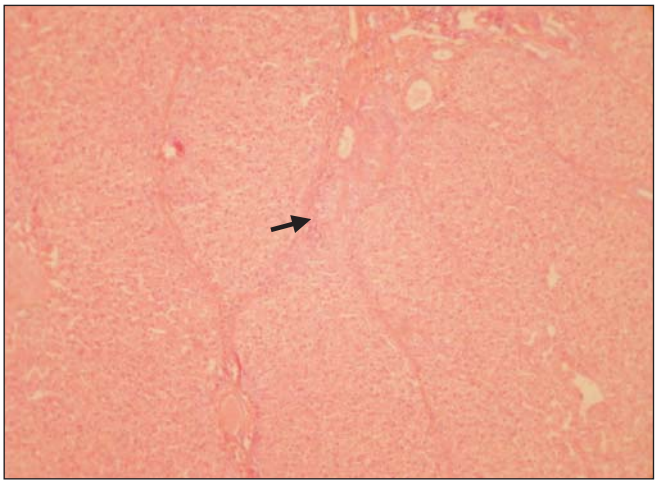


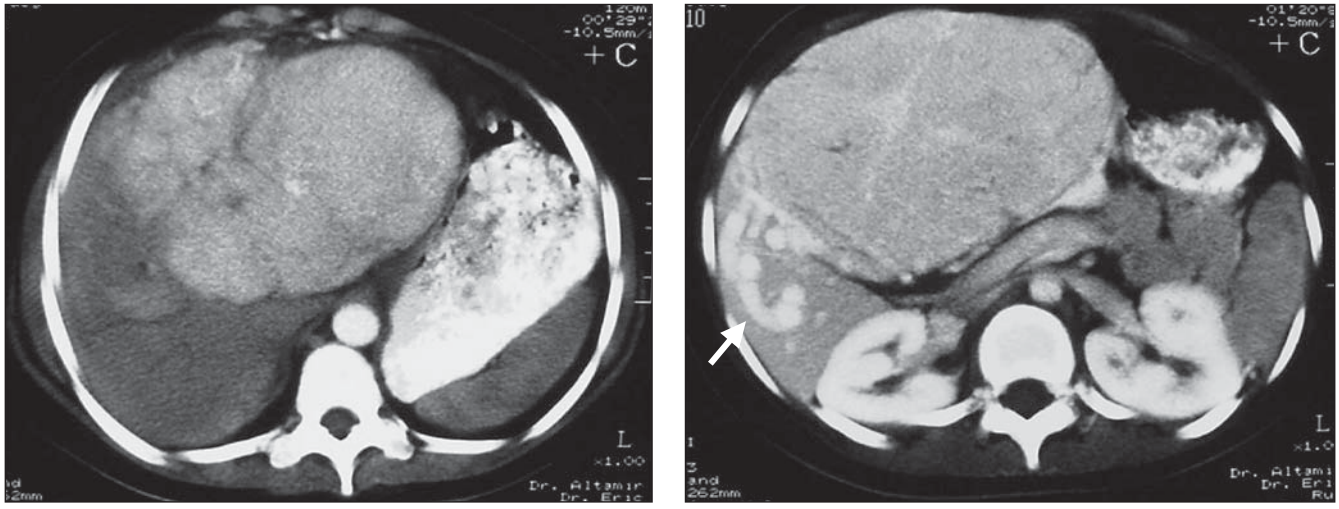
Figure 4. Nodular areas corresponding to focal nodular hyperplasia. Anatomopathological study: Hematoxilin-eosin staining demonstrating fibrosis with formation of incomplete septa (arrow).

at 16 years of age, also demonstrated findings suggestive of FNH (Figure 5).

DISCUSSION

Developments in imaging techniques have contributed to the increase in the number of diagnosis of benign hepatic tumors, the differential diagnosis between FNH and hepatic adenoma being extremely important in the clinical practice, considering the risk of rupture and bleeding of hepatic adenomas[1]. The apparent increase in the incidence of FNH starting in 1960, although coinciding with the time where oral contraceptives were made available in the United States, may be just a result of the development of imaging diagnosis techniques and the improvement in the quality of ultrasound studies[4,5].

The FNH pathogenesis is still to be defined, despite a study reporting a simultaneous occurrence of hemangioma, FNH and hepatic adenoma, suggesting that these three lesions are different manifestations of a same malformation[6]. A pre-existing vascular anomaly could cause a local hyperplastic response of hepatocytes[7]. The possible role of sexual hormones, including oral contraceptives, in the FNH development has been suggested due to the higher prevalence in women (80% to 95% of cases)[8] and potential spontaneous regression of the FNH as a result of an interruption in the use of oral contraceptives[10]. However, the assumption that a FNH may not be associated with the use of oral contraceptives is evidenced by the occurrence of this type of lesion even before the introduction of oral contraceptives, and by the presence of FNH in children, men and women who have never utilized them[5,8]. Actually, the use of oral contraceptives may be associated with the development of FNH, even accelerating its growth, but their possible implication in the occurrence of this lesion has not been demonstrated[3,8]. Nevertheless, new studies are necessary to



A B

Figure 5. Abdominal helical computed tomography. In the center of the lesion there is a hypointense central scar with 1 cm in diameter (**A**), that becomes hyperintense (**B**) on delayed phases. There are tortuous and dilated vessels (**C**) in the preserved right lobe (arteriovenous malformation) "feeding" the hypervascularized hepatic mass.

clarify the role of oral contraceptives in the occurrence of FNH[2].

The definition of the type of lesion is essential, and, among the lesions more easily confused with FNH, hepatic adenoma should be highlighted because of its unequivocal relationship with the use of oral contraceptives, especially in high doses and during long periods of time[2]. In contrast to the usually conservative approach adopted for FNH, in case of hepatic adenoma a surgical excision is performed because of the risk of bleeding and, mainly, malignization[2]. In cases of FNH surgical intervention is reserved for those which present with symptoms, complications, progressive lesions or adjacent organs compression[2,9].

FNH complications such as abdominal discomfort, intratumoral hemorrhage and intraperitoneal rupture are rare, although some cases of intraperitoneal rupture have been described in the literature and, in this circumstance the surgical approach have been necessary[10,11].

Potential malignant transformation of FNH has not been reported, although FNH coexistence with hepatocellular carcinoma has rarely been described[8].

The following non-invasive diagnostic techniques are increasingly utilized[3,8,12]: a) ultrasound; b) computed tomography, allowing high accuracy in the differentiation between the most frequent types of centrally scarred hepatic tumors, including FNH, fibrolamellar hepatocelullar carcinoma and giant cavernous hemangioma; c) hepatosplenic scintigraphy; d) magnetic resonance imaging. An useful finding in the diagnosis of FNH is the evidence of increase in the hepatic uptake at hepatosplenic scintigraphy, allowing the differential diagnosis with other hepatic masses. Ultrasound, computed tomography and magnetic resonance imaging may demonstrate benign hepatic masses, with typical, although not universal, the presence of a central scar. Although less frequently, a characteristic radiating hypervascular malformation may be found[3].

Notwithstanding the great usefulness of imaging techniques for the diagnosis of this tumor, if doubts persists about the diagnosis, a hepatic biopsy becomes mandatory, considering its significance as a highly specific diagnostic method[3].

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