Fibrolamellar Hepatocellular Carcinoma- Report of A Case

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Fibrolamellar hepatocellular carcinoma (FLH) is a variant of hepatocellular carcinoma (HCC) with distinct clinical, histologic and prognostic features different from conventional HCC. Herein, we present a 14-year-old girl with a palpable mass over the right upper -quadrant of the abdomen. A well-defined mass in the left liver with heterogeneous density and a central linear band was demonstrated by ultrasound and computed tomogram. FLH was proved by the histopathology study of a liver specimen taken from an echo-guided liver core needle biopsy before surgery and from a left hepatectomy. No tumor recurrence was detected by ultrasound in the 2-year follow-up. *(Chang Gung Med J 2009;32:336-9)*

Key words: fibrolamellar hepatocellular carcinoma

Fibrolamellar hepatocellular carcinoma (FLH) is a unique subtype with different clinical and histological characteristics from conventional hepatocellular carcinoma (HCC).[1-3] FLH represents less than 3% of HCC, with no cirrhosis in most patients, and a good prognosis if resectable (average survival of 32 months from diagnosis).[1-3] FLH characteristically manifests as a large hepatic mass in adolescents or young adults.[1,4] Cirrhosis, an elevated alpha-fetoprotein (AFP) level and other risk factors for HCC, such as hepatitis, alcohol abuse, and metabolic diseases, are typically absent in FLH.[3] Clinical recognition of this variant of HCC is important because of the excellent results of complete surgical resection.[1,3]

CASE REPORT

A fourteen-year-old girl had abdominal pain over the right upper quadrant of the abdomen for one month, with subsequent development of a protruding mass. There was no body weight loss, fever, nausea, vomiting, tea-colored urine, clayed-colored stools, or jaundice. She denied a history of blood transfusion, foreign travel, and liver disease. Physical examination on admission revealed a solid 7 x 7 cm bulging mass palpable over the right upper quadrant of the abdomen.

Laboratory investigations revealed the following: hemoglobin 13 g/dL; white blood cell count 10,700/mL, platelet count 536,000/mL, prothrombin time 12.8 sec. (INR 1.08); activated partial thromboplastin time 46.7 sec (normal control 34.1 sec); aspartate aminotransferase 58 U/L; alanine aminotransferase 72 U/L; alkaline phosphatase 160 U/L; γ-glutamyl transferase 37 U/L; albumin 4.0 g/dL; and total protein 8.2 g/dL. The serum level of AFP was 25 ng/mL (normal < 20 ng/mL) and beta-human chorionic gonadotropin was less than 3 mIU/mL (normal < 3 mIU/mL). Tests for hepatitis B surface antigen and anti-HCV antibodies were negative.

An abdominal ultrasonogram revealed a heterogeneously hyperechogenic mass, about 10 cm in diameter, with a central linear echogenic band over the left lobe of the liver. A computed tomogram (CT) showed a well-defined lobulated mass over the left lobe of liver with a central low-density area and calcification (Fig. 1). Celiac-hepatic-superior mesenteric artery angiography demonstrated it was hyper-

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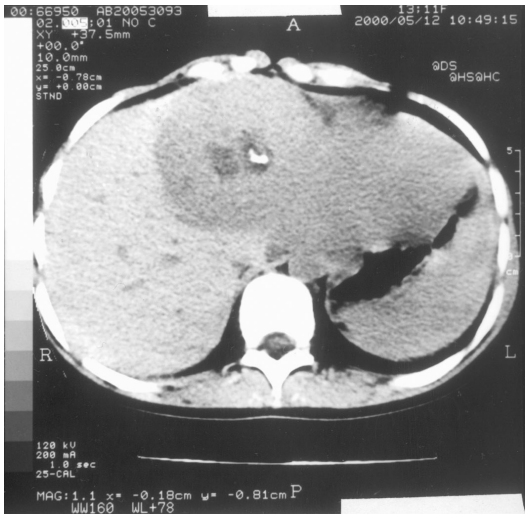

Fig. 1 Abdominal computed tomography shows a well-defined lobulated mass with a central low-density area and calcification.

vascular, and mainly supplied by the left hepatic artery, left gastric artery, and branches of the right hepatic artery. A bone scan did not reveal any evidence of metastasis. Histopathological study of the liver specimen taken from an echo-guided core needle biopsy showed a FLH. She received a left hepatectomy, which disclosed a 13.2 x 14 x 7.5 cm multinodular encapsulated mass. A central fibrotic scar was shown on the cutting. She has had no recurrence in the 2-year follow-up.

DISCUSSION

FLH is a distinctive subtype of HCC. Conventional HCC usually occurs after the fifth decade with a male predominance,[1] and it is also the most common primary malignant tumor of the liver in older children.[5] Most children with conventional HCC have liver cirrhosis or chronic liver disease, such as hepatitis B, glycogen storage disease, tyrosinemia, or alpha-1 antitrypsin deficiency. In Taiwan, the annual incidence of conventional HCC in children 6 to 14 years of age declined from 0.70 per 100,000 children between 1981 and 1986 to 0.36 between 1990 and 1994 after initiation of the universal hepatitis B vaccination program.[6] However, FLH often occurs in younger adults and adolescents, and no sex predilection is noted.[1] FLH patients usually have no history of chronic liver disease or cirrhosis. Abdominal pain, usually present in 70% of cases, and malaise are the most common complaints in FLH.[1] Hepatomegaly or an abdominal mass is noted sometimes, and jaundice is found occasionally.[1]

Liver function tests and viral hepatitis markers in patients with FLH are usually normal.[1,7] As in our patient, slightly elevated serum levels of aminotransaminase and AFP were noted initially, but they fell to normal soon after surgery. Some immunohistochemical abnormalities are helpful in distinguishing FLH from conventional HCC, such as a low AFP, high serum unsaturated vitamin B12 binding capacity, and elevated serum neurotensin.[3,7] However, these laboratory studies cannot serve as definite and reliable tools to distinguish FLH from other HCC.

Diagnostic images appear to be useful in the diagnosis of FLH. On plain radiographs in FLH patients, hepatomegaly is the most common finding and calcification of tumor can sometimes be demonstrated. Ultrasonography (US) remains the primary and the most important tool for evaluating FLH. On US, FLH usually appears as a solitary, well-defined lobulated mass with a variable echo-texture predominantly containing hyperechoic or isoechoic components.[3,8] The central scar, which presents in 33%-60% of patients, may be visualized as a central area of hyperechogenicity.[9] The CT presentation is usually a solitary, hypo-attenuating mass with a well-defined lobulated surface.[3,4] The central scar is non-enhanced, which could be used to distinguish FLH from other lesions with delayed enhancement, such as focal nodular hyperplasia (FNH).[10] Calcification within the central scars can be seen in 33%-58% of FLH cases.

The most distinctive and characteristic histologic feature of FLH is polygonal neoplastic cells with eosinophilic cytoplasm clustered in small groups separated by fibrous bands.[1] Tumor necrosis or hemorrhage is rare. Copper deposits,[11,12] fibrin[12] and fibronogen[12] are abundant in the tumor cells noted on immunohistochemical studies.

In addition to conventional HCC, the differential diagnosis of FLH includes FNH, adenomas, cavernous hemangioma, and hepatoblastoma.[4] FNH and adenomas are homogeneous and hypervascular on enhanced CT scans.[4] Calcification is noted in about 70% of cases of FLH, but is rare in FNH or adenoma.[4] Sometimes a central scar is demonstrated in

FNH.[4] Spontaneous hemorrhage and focal fat content, which are rare in FLH, often can be noted in adenomas.[4] In addition, FNH and adenomas primarily consist of well-differentiated hepatocytes arranged in cords or plates without a normal lobular pattern. Cavernous hemangioma, the primary benign liver tumor in adults, is rare in children. It often has central scarring or necrosis without central calcification.[4] On CT scans, the non-necrotic areas of hemangiomas are isoattenuating to blood vessels, and progressive nodular or cloud-like enhancement can be obtained during all phases of enhancement.[4] Hepatoblastoma is the most common primary liver tumor in infants and young children under 2 years of age, accounting for just over 1% of pediatric cancers.[13] Hepatoblastoma usually appears as a focal or multifocal solid tumor. The serum AFP level is almost always elevated. Stippled or chunky calcifications can be detected in 40-50% of patients.[13]

The management of choice of FLH is complete tumor resection if possible. However, late metastasis[14] and local recurrence[15,16] after tumor resection have been reported. Traditionally, it was thought that FLH patients had a favorable prognosis in comparison with patients with conventional HCC, although several reports found FLH patients did not fare better.[15-17] Katzenstein et al analyzed published reports and found that only 36% of pediatric patients with FLH have survived disease free, and in their experience, 6 of 10 pediatric cases with FLH died.[16] Houben et al reported the 5-year survival rate was greater in patients who underwent liver transplantation for FLH than in transplant patients with other HCC.[18]

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纖維板層肝細胞癌

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纖維板層肝細胞癌是肝細胞癌的一種變種，具有與一般肝細胞癌不同之臨床及病理學上的表現。在本文中我們報告一例十四歲女童右上腹的腫瘤。腹部超音波顯示此約十公分大的腫瘤，具有不均勻的高超音波回音及不規則的邊緣，並在腫瘤中央有一個帶狀物。在電腦斷層則發現此瘤中央有低密度部位、鈣化點及血管。利用超音波定位穿刺取得的肝組織及左肝切除手術取得的肝組織病理切片，均證實腫瘤爲纖維板層肝細胞癌，並在腫瘤中心發現纖維化疤痕。在兩年的追蹤期間，我們利用超音波證實沒有腫瘤復發的情形。(長庚醫誌 2009;32:336-9)

關鍵詞：纖維板層肝細胞癌

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