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CLINICAL NOTE

Adult hepatoblastoma

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ABSTRACT

Adult hepatoblastoma (AHB) is a very rare tumor, having been described 45 cases up to June 2012. In contrast to HB in infancy (IHB), it has poor prognosis. We present the case of a 37-year-old asymptomatic woman who consulted for a large –12 cm diameter– mass involving segments 5 and 6 of the liver, and alfa-fetoprotein of 1,556,30 UI/mL. A bisegmentectomy was carried out. The microscopic study confirmed the AHB diagnosis, revealing the presence of epithelial cells forming clusters, trabecular patterns and tubules. The patient died on the 10th postoperative month due to progression disease.

The Wnt/β-Catenin signaling pathway mutation has been reported and associated with a poor prognosis in IHB. Due to the AHB poor prognosis, seems reasonable to introduce the therapeutic regimens described in children who have a better outcome.

Key words: Adult hepatoblastoma. Wnt/β-Catenin signaling pathway.

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INTRODUCTION

The adult hepatoblastoma (AHB) is an uncommon tumor. Forty five cases have been described up to may 2012 (1). In contrast to the children hepatoblastoma (HBI) it has a fatal prognosis, with a mean survival time of two months and one-year survival of 24 % (1,2). Several hypothesis have been raised regarding its embryo origin and the role of pluripotent hepatic stem cells as well (3,4). We report herein the third case of HBA in our country, and the 46th in the literature (1,5,6).

CASE REPORT

A healthy 37-year-old woman consulted for the presence of a mass in right hypochondrium since one month, without other symptoms. She referred oral contraceptives since 12 years. No previous blood transfusions. She was diagnosed, seven years before, with hepatitis B virus infection with occasion of pregnancy. Her family history revealed that her mother was diagnosed with hepatic cirrhosis, of unknown etiology.

On examination: hepatomegaly of 5 cm below the costal border, without splenomegaly or ascites. Blood analysis: hemoglobin and liver function test were normal. Alpha-feto-protein (AFP): 1556.30 UI/mL (normal value: 0-10 UI/mL). Hepatitis B serology: HBsAg positive; anti-HBs negative; HBeAg negative; anti-HBe positive; anti-HBc positive.

The abdominal ultrasound (US) and the computed tomography (CT) revealed a heterogeneous mass of 12 cm diameter well defined, localized on segments 5 and 6, displacing the right branch of the portal vein and without vascular invasion signs (Fig. 1). A resection of segments 5 and 6 was carried out with 10 minutes ischemic pre-conditioning under vascular occlusion and under echographic control,

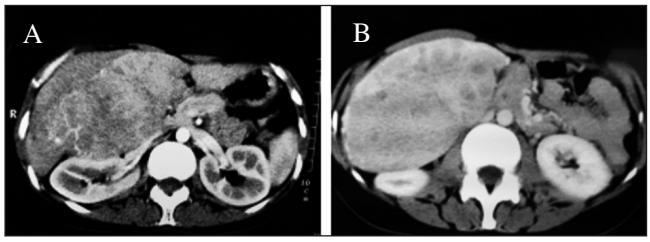

Fig. 1. Abdominal CT scan with contrast, arterial phase (A) and venous phase (B), showing a large hypodense mass 12 cm diameter with peripheral enhancement, localized in segments 5 and 6 and displacing the right kidney and pancreas.

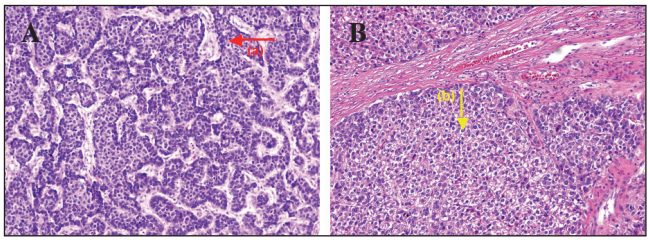

Fig. 2. Microscopic view: Epithelial neoformation developing tubular structures (arrow a) and sheets of immature of hepatocytes (arrow b) scattered in mesenchymal tissue (hematoxylin-eosin).

without complications. The patient died at the 10 month postprocedure, due to tumor progression. Pathology report: lobulated single mass of 11 cm diameter, well defined, which displaced the normal parenchyma. The tumor had a grey aspect, solid, and surrounded by fibrous tracts. Microscopic description: epithelial tumor composed by epithelial cells forming nets and tubular structures, and trabeculae as well, separated by vascularized fibrous tissue and circumscribed from normal parenchyma by a thin capsule (Fig. 2). The cells were of normal size with cytoplasm, nuclei resembling fetal and embryonal pattern, without vascular and capsule invasion. The tumor cells showed intense immunoreactivity to cytokeratins CAM5.2 and locally to cytokeratines AE3/AE1. The rest of markers for chromogranine, sinaptofisine and desmosine were negative.

DISCUSSION

The hepatoblastoma is a rare tumor in the infancy (annual incidence: 0.5-1.5/1,000,000); which generally appears between sixth month and 5 years of age (2,7). The first case of an adult hepatoblastoma was described in 1958 (8,9), having been reported 45 cases up to June 2012 and recently collected by Rougemont (1). Similarly as the pediatric cases, they usually present as a right upper quadrant mass, generally asymptomatic, and without previous history of liver disease, although hepatitis virus infection (HAV, HBV, HCV) has been reported in 25 % of the adult cases, as occurred in our case (1,2).

The abdominal ultrasonography, computerized tomography and magnetic resonance imaging, showed a large nodular mass (range 5-24 cm diameter) circumscribed by a thin fibrous capsule or pseudocapsule. Serum alfa-fetoprotein is elevated in 90 % of the pediatric cases and is a good marker of tumor response to treatment (2,7). The AFT was elevated in 18 out of the 45 adult reported cases. It was normal in 8 cases and unknown in the other 19 cases (1).

The macroscopic appearance usually reveals a well defined tumor, circumscribed by a thin capsule, which separates from the adjacent compressed normal parenchyma and vascular structures. Depending on the mesenchymal composition, areas of hemorrhage and necrosis can be revealed. In the mixed hepatoblastomas (epithelial and mesenchymal) –45 % of AHB–, osteoid and cartilage tissue can be identified showing a teratogenic pattern (1,10). The AHB histology has been compared with the pediatric hepatoblastoma. The epithelial IHB has been broadly subdivided into four histological patterns: the fetal pattern (1/3 of cases), the mixed fetal and embryonic pattern (20 %), the macrotrabecular pattern (3 %) and the small cell undifferentiated type (2-3 %) (2,7,8,10).

Approximately 25 % of the published AHB revealed fibrosis and cirrhosis (1). Different mesenchymal components resembling fibrosarcoma, osteosarcoma, chondrosarcoma, angiosarcoma and rhabdomyosarcoma features have been described (1,10).

The most common cellular components are the hepatoblasts –originated from the endoderm of the floor of the foregut– or diploid progenitor bipotential cells, which can differentiate into hepatocytes or cholangiocytes (1,2,7). In the first type, alfa-fetoprotein, alfa-1-antitripsin and albumin are expressed in immunohistochemistry staining meanwhile cytokeratin 7 and 19 (CK-19) and gammaglutamiltranspeptidase (GGT) phenotypes in the other one. During the fetal and neonatal period, the hepatoblasts are widespread or forming cellular clusters surrounding the terminal biliary canal of Hering. They progressively disappear in the neonatal period, accounting less than 0.01 % of the parenchymal cell population (3).

The hepatoblasts have a large cytoplasm than its precursor cells, the hepatic pluripotent stem cells (CMHp). The CMHp have a diameter of 7-9 m with a very high nucleocytoplasmatic ratio, and represent between 0.5-2 % of the parenchymal cell during the life time. In addition to the previous mentioned phenotypes, they express hematopoietic stem cells markers: THY-1, CD117, CD34, CD45, epithelial adhesion molecules (EpCAM), neuronal (NCAM), CD133 and cytokeratines (CK 8/18/19) (10,11,12).

A mutation in Wnt/β-Catenin signaling pathway has recently been reported in 50-90 % of the IHB cases. A higher presence of β-Catenin in the cellular nuclei has been described in the less differentiated tumors and associated with a poorer outcome (13).

The pleiomorfic features of HB denotes its common origin from pluripotential cells, showing epithelial (hepato-

cytes, cholangiocytes) and also mesenchymal phenotypes (endothelium, sinusoidal) as well (14,15).

The oncologic complete resection (R0) is the gold-standard treatment although, due to the indolent symptoms, more of the AHB are unresectable at the time of diagnosis. The results are very poor, with a 1 year global survival of 24 %. The 1 year survival is 0 % in the non-resectable patients, and 41% in the resected. A better survival has been reported in resected patients younger than 45 years (42 %) in contrast to the older than 45 years (0 %) (1).

In non-resectable tumors, transcatheter arterial chemoembolization (TACE) with cisplatin and systemic pirarubicin has shown good tumors response.

The published outcomes in the pediatric population are much better than in adults. In children, the patients have been staged based into two systems: PRETEX system (pretreatment extent), established by the European group SIOPEL (http//www.siopel.org) (2); which stages the patients according to the tumor extension previous to the neoadjuvant treatment; and the Children's Oncology Group (http//www.childrensoncologygroup.org) (2) which classifies the pathologic findings into four stages. Several chemotherapeutic schemes based on concomitant cisplatin and doxorrubicin (PLADO) as neoadjuvant and vincristine, cisplatin and 5-FU as adjuvant have been reported. With these treatment regimens and curative resections (R0) (hepatectomy or liver transplant), 75 % five-year survival rate and 66 % free of recurrence survival have been described. In children with good prognostic factors, Cisplatin monotherapy neoadjuvant regimen has been shown as effective as poli-chemotherapy, although with less toxicity (2,7). In spite of the scarce experience in adults, it seems reasonable to apply the staging and therapeutic regimens previously described in children, due to the tumor pattern similarities as well as to exploit new molecular targets.

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