

Hepatocellular Carcinoma in an Infant due to Hepatitis B Virus Vertical Transmission

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ABSTRACT

Hepatocellular carcinoma (HCC) is one of the common tumors in the world. The incidence of HCC generally increases with age in all population but there is a tendency of decreasing incidence in the elderly and it is very rare in children. This is a case report of HCC in a 9-month-old boy, who was admitted to the hospital with palpable abdominal mass in the right upper quadrant. Imaging modality by ultrasonography could not adequately demonstrate definite findings demonstrating that the tumor was derived from liver, and the diagnosis was neuroblastoma. Intra-operatively, the tumor mass appeared to be derived from the surface of the posterior edge of the liver, so it was a pedunculated tumor. The histopathological examination revealed a pedunculated hepatocellular carcinoma grade 3. The Victorian blue staining and immunohistochemical staining were done afterward, which showed HBsAg positive result as found in non-tumor lesion as well as inneoplastic lesion of liver tissue.

Keywords: *hepatocellular carcinoma, pedunculated HCC, infant HCC, occult hepatitis B virus infection*

INTRODUCTION

Hepatocellular Carcinoma (HCC) is a malignant tumor composed of cells that differentiate in some way in the manner of hepatocytes.¹ Most common etiological factors are viral infection (hepatitis B virus, hepatitis C virus), dietary aflatoxin B ingestion and chronic alcohol abuse.² The incidence of HCC generally increases with age in all population but there is a tendency of decreasing incidence in the elderly^{1,3} and it is very rare in children.⁴ Various authors have suggested that the prevalence of primary hepatic neoplasm is 0.5-2.0% of pediatric tumors with primary

accounting for 20% of them.⁴ There is epidemiological and molecularevidence to suggest that Hepatitis B Virus (HBV) is an important factor in the development of HCC. Here we present a case of pedunculated hepatocellular carcinoma in an infant. However this patient is not the youngest patient who has hepatitis B – related HCC.^{5,6}

CASE

A 9-month-old boy was admitted with mild jaundice. Physical examination showed palpable abdominal mass in the right upper quadrant. The laboratory findings of routine blood examination were within normal limit, except increased leukocytes count of 19,600/UL. Imaging modality by USG showed a solid tumor mass in upper right quadrant abdomen, below the liver, above the right kidney. It was measured and the size was 77 x 67 x 73 mm with in-homogenous echoic and well-defined borders.

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The patient was diagnosed as having neuroblastoma. The intra-operative result showed that the tumor mass was derived from the surface of the posterior edge of the liver (pedunculated). The serologic examination post-operatively showed that the serum Alpha-Fetoprotein Level (AFP) was 15.2 ng/mL (references range: 0-15 ng/mL); serologically, HBsAg was negative. Only later, we know that this boy had been vaccinated (B hepatitis) 3 times, i.e. at first, second and seventh month-old.

Histopathological examination was performed and macroscopic finding showed that the specimen from the tumor mass measured as 100 x 80 x 60 mm and firmly encapsulated by fibrous connective tissues. The cut surface of the tumor showed several septa toward the peripheral from the core, brown-whitish mass, inhomogeneous with black spots, and small cysts containing blood (figure 1). The microscopic finding showed encapsulated tumor mass with microtrabecular pattern. It consist of tumor cells that resemble hepatocytes, but conspicuously large, bizarre, and pleomorphic. The tumor cells are polygonal, with vesicular nuclei, pleomorphic and have prominent nucleoli. The cytoplasm is finely granular and eosinophilic. The bizarre giant cells are numerous (figure 2). The histological findings were consistent with hepatocellular carcinoma grade 3. The Victorian Blue staining showed HBsAg positive result in the tumor tissue (figure 3). The immunohistochemical staining showed HBsAg positive result in tumor tissue and non-tumor tissue as well (figure 4). The cut margin in some place still contained tumor cells, so chemotherapy was suggested (for us, indeed it is very hard to decide because then there was non-tumor parenchyma shrinkage).

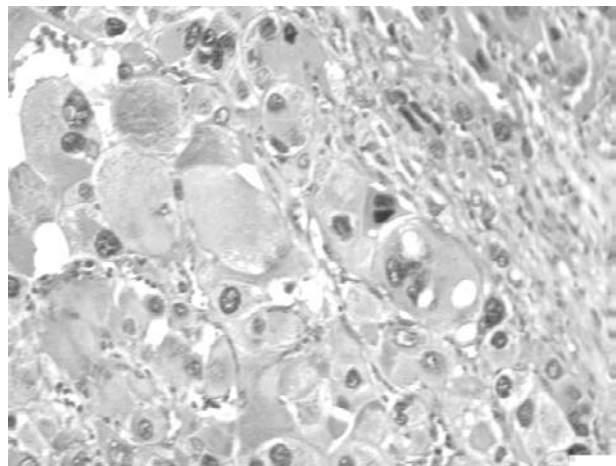


Figure 2. Tumor cells in microtrabecular pattern, large, bizarre polygonal, with vesicular and pleomorphic nuclei, and have prominent nucleoli. The cytoplasm is finely granular and eosinophilic

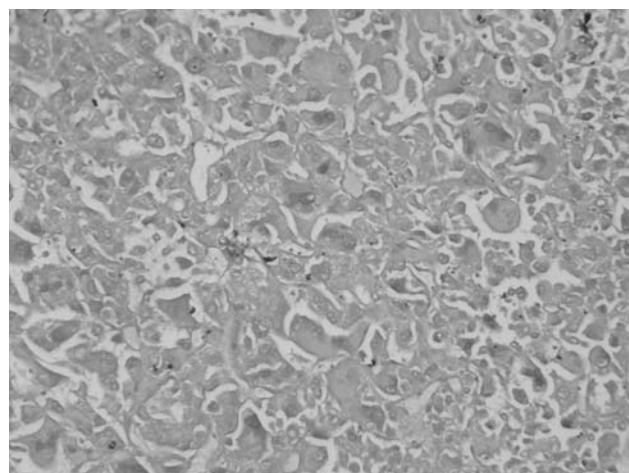


Figure 3. Victorian blue staining shows HBsAg positive result in tumor tissue

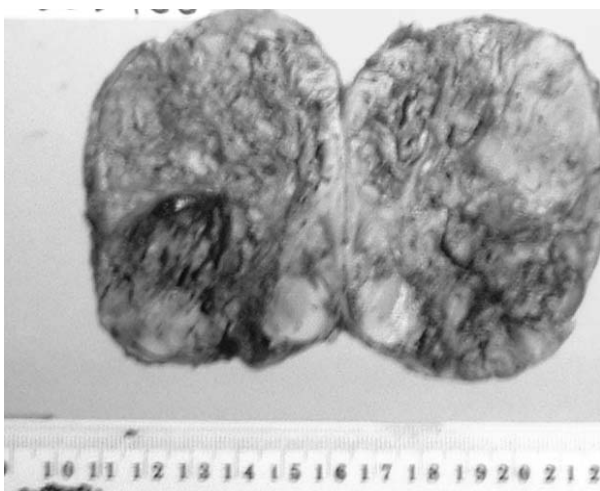


Figure 1. Firmly encapsulated mass by fibrous connective tissues. The cut surface of the tumors shows several septa toward the peripheral from the core, brown- whitish mass, inhomogeneous with black spots, and small cysts containing blood



Figure 4. Immunohistochemical staining shows HbsAg positive result in tumor tissue (thick arrow) and non-tumor tissue as well (thin arrow)

The laboratory examination on 4 months after resection showed that the liver function test was within normal limit. The CEA and AFP serologic results were within normal limit. CT scan performed on 6 months after resection showed that the liver was normal in size and had smooth surface. The parenchyma was homogenous in density and foci of lesion were absent. Blood vessel system was within normal limit. There was no dilatation of intra/extra hepatic biliary duct. Ascites or pleural effusion was absent. CT scan imaging of abdomen and pelvis were within normal limits. There was no other sign on the rest of the neoplasm, so the clinician decided that no further adjuvant treatment was needed. The serologic examination was done later and it showed negative result of HBsAg, positive anti-HBs and negative anti-HBc in double examinations (in duplo).

DISCUSSION

Based on serologic examination, we suggest that the patient had occult HBV infection. Occult HBV infection is defined as the presence of HBV-DNA in the serum or liver without detectable HBsAg with or without anti-HBc or anti-HBs.^{7,8} Diagnosis of occult HBV infection requires sensitive HBV-DNA PCR assay. Several possibilities have been hypothesized as the mechanisms of occult HBV infection. These include mutations of HBV-DNA sequence, integration of HBV-DNA into host's chromosomes, infection of peripheral blood mononuclear cells by HBV, formation of HBV-containing immune complex, altered host immune response, and interference of HBV by other viruses.⁷ The patient had hepatitis B virus from his mother through blood transmission. His mother had positive anti-HBs and anti-HBc as well. The mother had not been vaccinated, so the possibilities that the mother had occult hepatitis could not be excluded. The risk of HBV transmission through blood transmission of HBsAg-negative individuals was recognized. In addition, vertical (i.e. perinatal) transmission of HBV from mother with occult HBV infection to offspring was reported in both human subjects and woodchuck animal models.⁷ To avoid missing diagnosis of occult hepatitis B infection in pregnancy, if one underwent serologic examination, HBsAg should be examined. If HBsAg is positive, HBeAg is then to be examined too. If HBeAg is positive, either HBV-DNA was examined or not, the baby should be injected by HBIG as soon as he was born and be vaccinated. The baby and the mother should be checked for anti-HCV too, since interference with other virus can influence the mechanism of occult hepatitis.⁷

The association between HCC and HBV is stronger in children than in adults.⁹ The youngest HCC patient with HBV reported was an 8-month-old boy.³ A high prevalence of occult HBV has been reported in hepatocellular (HCC) from Asia.¹⁰ The association of overt HBV infection with HCC has been well established. However, it remains controversial whether occult HBV infection may also attribute to the pathogenesis of HCC. The frequency of occult HBV infection varies significantly in patients with HCC.⁸ Considering all available evidences, the role of HBV inducing HCC might occur through integration of DNA viruses into the host genome of the cell, raising the possibility that it may serve as mutagen insertion through activation of oncogen, inactivation of tumor suppressor genes, or mutation in p⁵³ or other tumor suppressor gene that result in oncogen activation.^{1,3}

The laboratory findings are in part determined by the underlying liver disease, which is manifested in elevations of various liver enzymes. Serum AFP has been frequently used to screen for HCC to differentiate it from other abdominal tumors.¹¹

A significant increased level of AFP > 500 ng/mL, or continuous rising values even if it is less than 100 ng/mL, strongly suggest HCC diagnosis. However, not all cases of HCC are associated with AFP elevation, and increased AFP level may also be found in liver disease without HCC. Most of patients with pedunculated HCC show normal or slightly elevated level that remained below 100 ng/mL.¹¹ AFP serologic result of this patient was within normal limit.

Ultrasonography imaging was performed in this patient, but definite finding that the tumor aside from the liver could not be adequately demonstrated by such imaging modality. Surgery on this patient then revealed a pedunculated HCC arising from the surface of the posterior edge of the liver. Edmonson and Steiner,¹² described macroscopically an extrahepatic growth of HCC as pedunculated hepatocellular carcinoma. Pedunculated HCC could arise from an accessory lobe that is often found on the right main lobe, and is frequently attached by pedicles containing blood vessels and bile ducts.

Treatment modalities have included surgical resection, hepatic arterial embolization, injection of alcohol, radiation, systemic and local chemotherapy, and hepatectomy followed by transplantation. Prognosis of this patient is relatively good, due to its surgical resectability, i.e. it was pedunculated, had slow expansive growth, and was encapsulated. But periodic CT scan examination was suggested since the cut margin in some place still contained tumor cells.

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