Case Report

Hepatocellular Adenoma: A Case Report

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A case of hepatocellular adenoma (HCA) was described in a 26-year-old woman, who was a potential kidney donor for her father and denied taking the oral contraceptive pill. A hypervascular mass of 4.1 cm in largest dimension was detected in the liver segment V by computerized tomography and magnetic resonance imaging (MRI). The normal levels of liver enzymes, negative serum markers for hepatitis viruses, and non-elevated alpha- fetoprotein level were detected. The wedge resection of segment V was done with an uneventful clinical course. In Western countries, HCAs are known to occur in women in their reproductive periods. It may not be associated with oral contraceptive. Molecular biological studies disclosed three variants of HCAs, i.e., I) with mutation of HNF 1-alpha gene, II) with mutation of beta-catenin gene, and III) no mutation of the two genes. Histological correlations with the three variants as recommended by the Bordeaux group in 2007 could not be accomplished in the present study due to overlapping histological features between the variants I and III. The etiological factors of HCA are known to relate to the contraceptive pill usage in female and the anabolic-androgenic-steroid administration in male. In Thailand, the occurrence of HCA is expected to be only 0.3% of cases with hepatocellular carcinoma.

Keywords: *Liver cell adenoma, Contraceptive pill, Hepatocellular carcinoma*

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Hepatocellular adenoma (HCA) or liver cell adenoma is a rare benign tumor[1]. It can be solitary or multiple, and quite often, there are more than 10 adenomas known as liver adenomatosis[1-4]. HCA nearly always occur in women and during the reproductive period, age 15-45 years, or associated with contraceptive steroid usage[1]. Sporadic cases of the tumor in both sexes were mentioned in relation to the administration of anabolic androgenic steroids, Type Ia and Type III glycogenoses, familial diabetes mellitus, and beta-thalassemia secondary to iron overload[1-6].

In Thailand, four cases of HCA have previously been reported. Two were in beta-thalassemic young females, one was in an old man and the other one was in a woman taking oral contraceptive pills for six years[7-9]. In this report, HCA occurred in a 26-year-old female denying the contraceptive steroid usage.

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Case Report

A 26-year-old Thai woman was a potential kidney donor for her father with chronic renal failure. She had no underlying disease and denied smoking, drinking, or taking the oral contraceptive pill. The physical examination revealed no abnormality. The biochemical studies yielded normal levels of liver enzymes, alpha-fetoprotein level of 3.16 ng/ml (normal adult level less than 25 ng/ml) and negative serum markers for hepatitis viruses. The computerized tomography (24 October 2007) disclosed a hypervascular mass in the hepatic segment V measuring 4.1 x 3.4 x 2.7 cm (Fig. 1). The magnetic resonance imaging (4 December 2007) showed arterial enhancing image. The initial clinical diagnosis was hepatocellular carcinoma with the differential diagnoses of HCA and the tumor-like lesions. She was admitted for the mass

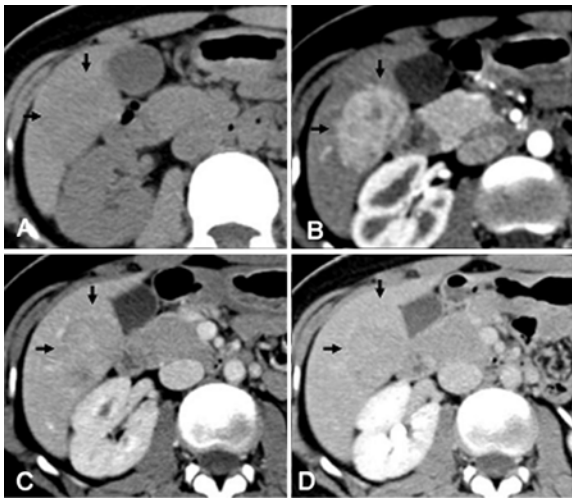

Fig. 1 Axial CT scan of the abdomen: non-contrast (A), arterial phase (B), portovenous phase (C) and delay venous phase (D). The mass shows mark enhancement in the arterial phase (arrows) in B and becoming to isodense mass (arrows) in portovenous and delayed venous phases in C and D

resection. The operative finding was a subcapsular solid mass measuring 4 cm in the greatest dimension. The liver parenchyma was within normal limit. The wedge resection of segment V and cholecystectomy were performed.

The resection specimen of the liver measured 6.5 x 6 x 5 cm. The cut surfaces revealed a well-demarcated tan-gray mass measuring 4 x 3 x 2.5 cm with some hemorrhagic foci (Fig. 2). The gallbladder was within normal limit.

Microscopically, the surrounding liver was not remarkable. The mass was unencapsulated. Some thick- walled and thin-walled large arteries unrelated to the portal tracts were seen adjacent to the mass (Fig. 3). The tumor was composed of polyhedral liver cells of normal size (32-36 m in diameter) and sinusoidal channels. The liver cells were arranged in trabecular pattern with each trabecula being two to three cells in thickness. The cells mainly contained clear cytoplasm rich in glycogen (Fig. 4). Several areas revealed globular fatty change of the liver cells (Fig. 5). Sinusoidal dilatation and peliosis could be seen in association with hemorrhage (Fig. 6). No duct cell was seen in the tumor by the immunostain for cytokeratin 7.

After the operation, the patient was doing well and preparing herself to be the kidney donor for her father as permitted by the transplantation team.

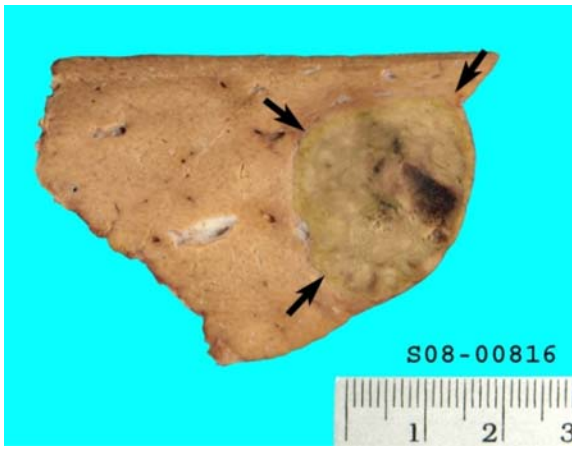

Fig. 2 An unencapsulated mass (arrows) with foci of hemorrhage in the resection specimen

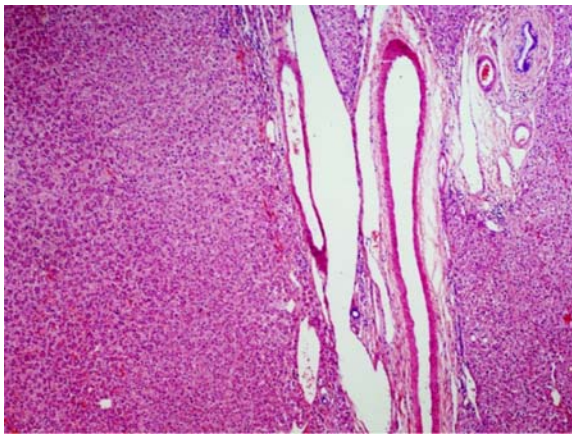

Fig. 3 The unencapsulated mass (left side) composed of liver cells in the trabecular pattern and two supporting thin-walled arteries adjacent to the mass (Hematoxylin and eosin, x40)

Discussion

HCA is known to be very rare in occurrence and needed to be differentiated from commonly occurring hepatocellular carcinoma (HCC), less commonly arising focal nodular hyperplasia (FNH), and nodular regenerative hyperplasia[10]. The Bordeaux group in 2007 defined HCA as "soft well-demarcated tumor with little or no fibrous capsule composed of liver cell plates that are only mildly thickened or irregular. The tumor parenchyma is supported by thin-walled arteries[2]". Some authors described large thick-walled arteries adjacent to the HCA[1].

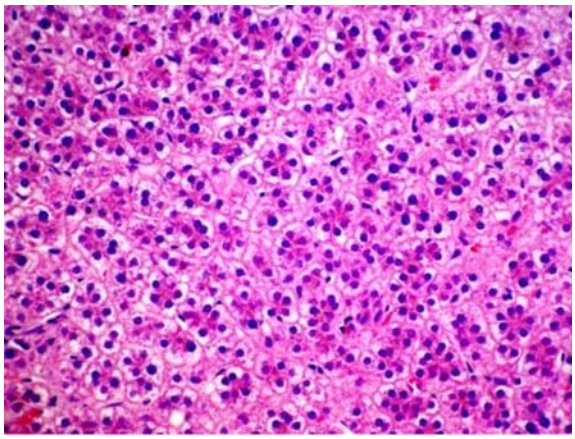

Fig. 4 The liver cells with abundant pale cytoplasm rich in glycogen (Hematoxylin and eosin, x400)

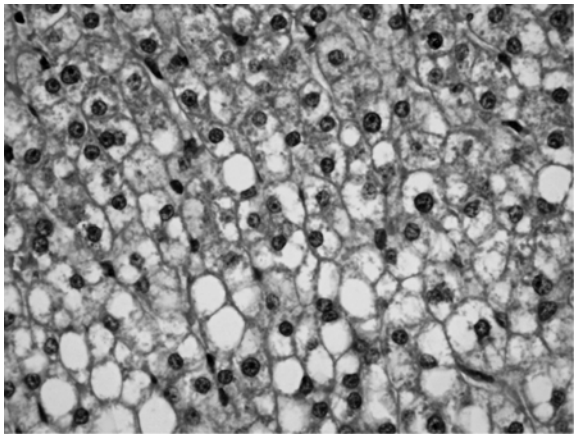

Fig. 5 Globular fatty change of the liver cells (Hematoxylin and eosin, x400)

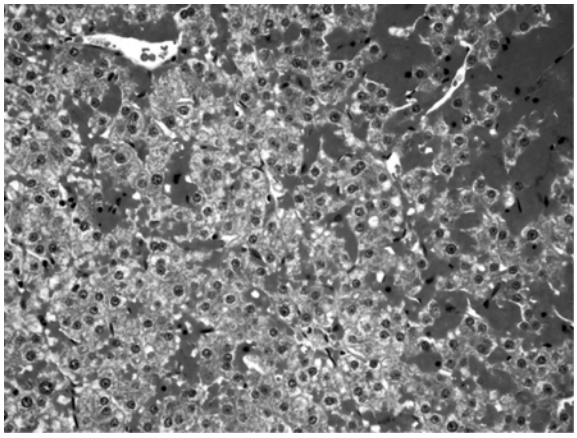

Fig. 6 Sinusoidal dilatation can be seen in the main area and peliosis in the right upper corner (Hematoxylin and eosin, x200)

HCA cannot be identified conclusively by any currently available imaging technique due to the composites of HCA such as globular fatty change and hemorrhage[2,11]. The preoperative needle biopsy may be inconclusive for HCA, HCC, FNH, or nodular regenerative hyperplasia[2,10]. The Bordeaux group considered an adequate liver biopsy or resection specimen as the gold standard to establish the diagnosis of HCA[2]. It was the surgeons' decision of doing the resection without the preoperative biopsy to obtain the definite diagnosis of the mass in the present patient.

In accordance to a review of some new advances in molecular biology by the Bordeaux group, HCAs were classified into three variants[2]. Variant I-HCAs with mutation of HNF1-alpha gene were commonly observed in 50% of HCAs. Correlations with pathological data showed that HCAs in this variant were mainly observed in a histologically homogeneous group of tumors characterized by marked steatosis or fatty change. Variant II-HCAs with mutation of beta-catenin gene were observed in less than 10% of HCAs. Variant II-HCAs occurred more frequently in males and were usually characterized by the occurrence of cytological abnormalities and acinar pattern. It was less frequently associated with steatosis. Variant II-HCA was more frequently interpreted as borderline lesion between HCA and HCC and were more frequently associated with the development of unequivocal HCC. Variant III-HCAs without mutation of HNF 1-alpha or beta-catenin gene occurred in approximately 40% of HCAs. This variant was designated as inflammatory adenoma or telangiectatic adenoma depending on the importance of inflammatory infiltrates or sinusoidal dilatation.

In the absence of data in molecular biology, the present HCA with prominent fatty change, sinusoidal dilatation with peliosis or telangiectasia, but without inflammatory infiltrate could not be histologically classified definitely into the variant I or variant III. The accumulation of glycogen was not mentioned by the Bordeaux group and is very similar to HCA in a Chinese woman not taking the contraceptive pill[4].

Regarding the previously reported cases of HCA in Thailand, classical HCAs lacking fibrous capsule, as in the present case, was reported in a 25-year-old women taking the pills for six years[1,2,8]. The fibrous capsule around HCAs described in two beta-thalassemic young females in Thailand and in a 17-year-old beta-thalassemic woman reported from the

United States may be the exception in the pathological diagnosis of HCA mentioned above[7,9,12]. The reported HCA in a 71-year-old male seems unlikely to be the variant II-HCA due to the presence of definite fibrous capsule presently considered as HCC[7,13].

In spite of the popular usages of various oral contraceptives in Thailand during the past decades, only one contraceptive-pill-related HCA was reported in this country in 1983[8]. The usage of oral contraceptive steroids seems less capable in inducing HCA in Thai females than in women of Western countries. The present HCA case is the first case in Ramathibodi Hospital from an estimate of 380 cases of resected HCC since 1969[14]. The occurrence of HCA is expected to be only 0.3% (1:380) of HCCs in this geographic area. In addition, the cellular abnormality or acinar pattern of the tumor cells were not observed in the present HCA. It is conclusive that female-preponderant HCAs would not transform to male-preponderant HCCs secondary to the assisting roles of chronic viral hepatitis B or C, aflatoxin B_1 and nitrosamines in Thailand[15]. HCA resection is necessary in cases of large or symptomatic mass (es) due to a high risk of bleeding[2,8].

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เฮปปาโตเซลลูลาร์ อะดิโนมา: รายงานผู้ป่วยหนึ่งราย

พัฒนา ศรมยุรา, สุวิภาภรณ์ ศิริพรพิทักษ์, สุรศักดิ์ ลีลาอุดมลิปี, สุขุม บุณยะรัตเวช

คณะผู้นิพนธ์ได้รายงานถึงเฮปปาโตเซลลูลาร์ อะดิโนมาที่เกิดในหญิงอายุ 26 ปี ผู้ซึ่งเตรียมบริจาคไตให้กับบิดาและปฏิเสธการใช้ยาเม็ดคุมกำเนิด ก้อนที่มีเลือดมาเลี้ยงมากขนาด 4.1 ซม. โดยเส้นผ่าศูนย์กลางยาวสุดถูกตรวจพบได้ในกลีบตับที่ V โดยเอกซเรย์คอมพิวเตอร์ และแมกเนติกรีโซแนนซ์ การตรวจค่าเอนไซม์จากตับไวรัสตับอักเสบ และระดับแอลฟาฟีโตโปรทีนไม่พบความผิดปกติ ก้อนถูกผ่าตัดออก และผู้ป่วยไม่มีอาการผิดปกติใด ๆ ในประเทศซีกโลกตะวันตกอะดิโนมาชนิดนี้พบได้ในผู้หญิงวัยเจริญพันธุ์ โดยอาจร่วมกับการใช้หรือไม่ใช้ยาคุมกำเนิด การศึกษาในระดับโมเลกุลทางชีววิทยาแยกได้เป็นสามประเภท คือ I) มีการเปลี่ยนแปลงทางพันธุกรรมของ HNF 1-alpha gene, II) มีการเปลี่ยนแปลงทางพันธุกรรมของ beta-catenin gene, III) ไม่มีการ เปลี่ยนแปลงทางพันธุกรรมการเทียบเคียงทางฮีสโตโลยีกับประเภททั้งสามตามที่เสนอโดยกลุ่มบอร์โดในปี พ.ศ. 2550 ไม่สามารถเทียบเคียงได้อย่างตรงตัวในการศึกษาอะดิโนมานี้เนื่องจากมีการทับซ้อนกันและกันระหว่างลักษณะทางฮิสโตโลยีในประเภทที่ I และ III องค์ประกอบของสาเหตุเท่าที่ทราบเพียงบางส่วนคือ การใช้ยาเม็ดคุมกำเนิดในเพศหญิงและการใช้ anabolic androgenic steroids ในเพศชาย ในประเทศไทยอะดิโนมาชนิดนี้พบได้ราว 0.3% ของผู้ป่วยที่เป็นมะเร็งเซลล์ตับ