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Liver Cell Adenoma in a Neonate

—Report of an Autopsy Case—

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A case of liver cell adenoma that was incidentally found at postmortem examination of a neonate who died of E. coli sepsis is described. The adenoma was a sharply demarcated, not encapsulated mass located subcapsularly in the right lobe, and was pale tan to light yellowish round nodule of 0.9cm in diameter. Microscopically, the tumor was composed of sheets and cords of uniform and slightly enlarged hepatocytes separated by dilated sinusoids. There were no portal zones or central veins to suggest the normal lobular architecture. The nuclei were bland and the cytoplasm varied from clear to acidophilic, containing lipid vacuoles. Ultrastructural examination showed that the hepatocytes of the tumor had highly differentiated organelles, reminiscent of normal hepatocytes.

Key Words: *Liver cell adenoma, benign tumor, liver, neonate.*

INTRODUCTION

Liver cell adenoma is benign hepatocellular proliferation mostly found in adults, only occurring in childhood. This tumor constitutes only 2 percent of all types of hepatic tumors (Weinberg et al, 1983). Liver cell adenoma in neonatal period is extremely unusual, the youngest being a 3 weeks old male, who had a small liver cell adenoma associated with many congenital anomalies (Gold et al, 1978). Recently we had a chance to examine a liver cell adenoma in a newborn infant who died of sepsis. Rarity of this neoplasm, particularly in a very young individual prompted this report.

CASE REPORT

This one month old female was admitted to Seoul Red Cross Hospital because of respiratory distress and seizure. It started as mild coughing and loose stool few days ago. She was managed conservatively under the impression of pneumonia until the day of admission, when she developed high fever (42°C) with eyeball deviation and cyanosis. She also showed a moderate respiratory difficulty. Physical examination on admission revealed moist rales on both lung fields. The liver and spleen were not palpated. The hemoglobulin was 9.9gm%, WBC 19,400/mm^3 with a differential count of 10% band, 25% seg, 61% lymphocyte and 4% mono, and platelet 1,310,000/mm^3. Blood sugar level fluctuated from 0 to 156mg/dl. Blood ammonia was 171ug/dl, and SGOT and SGPT 340 and 121IU/l, respectively. After admission the body temperature became subnormal and soon afterwards she lapsed into coma and died on the same day. Clinically she was suspected to have Reye syndrome.

Postmortem examination done 2 hours after death revealed a pale female neonate with generalized skin petechias and hemorrhages of viscera including the lungs, the adrenals and the serosa of bowel. The liver was generally enlarged with pale yellow to grey

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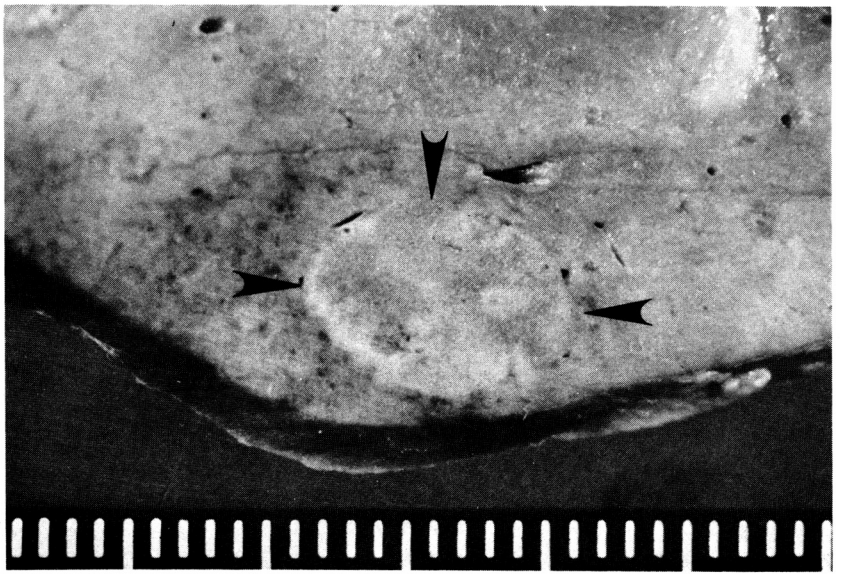

Fig. 1. Cut surface of the liver showing a grayish yellow round nodule (arrowhead) of 0.9cm in diameter, in the subcapsular portion, which is well defined but not encapsulated.

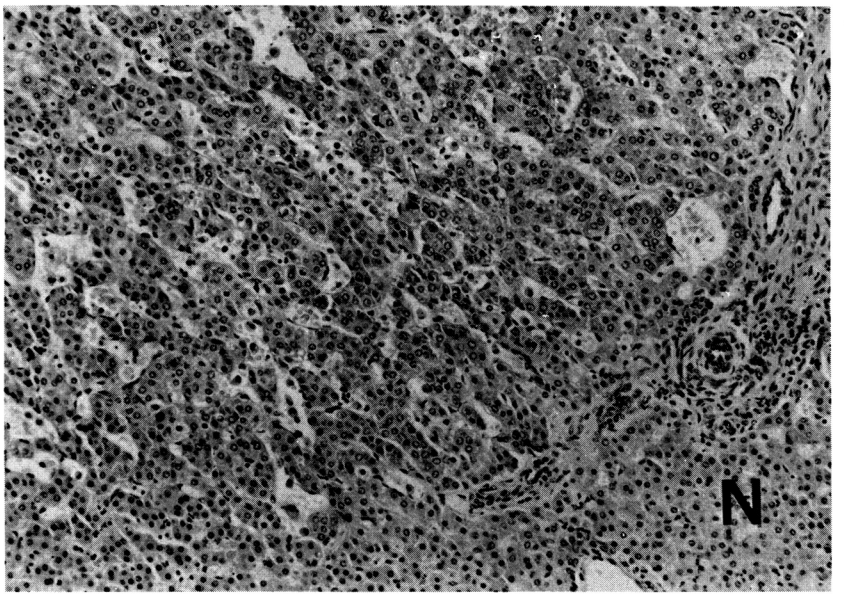

Fig. 2. Microscopically, the tumor consists of sheets and cords of uniform cells which are larger than the surrounding normal hepatocytes (N) (H & E, x100)

Fig. 3. There is no portal zones or central vein to suggest the normal lobular architecture in the nodule. Note the area of markedly dilated sinusoids (arrowhead) (H & E ×100).

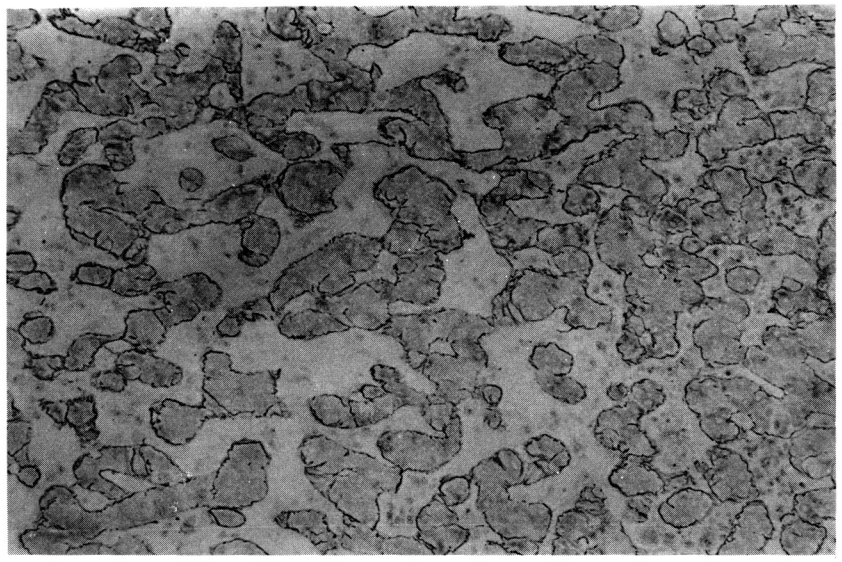

Fig. 4. Reticulum stain emphasizing less the uniformely organized structure of the tumor cells (H&E, X200).

yellow color, and showed a smooth surface. Cut sections of the liver at fresh state showed a gray yellow round nodule in the subcapsular portion of the right lobe, which was well defined but not encapsulated (Fig. 1). It measured 0.9cm in maximum cross. The nodule was somewhat lighter in color than the surrounding liver.

Microscopically, the nodule was composed of generally uniform, but slightly enlarged hepatocytes arranged in cords of two-to three-cell-thick separated by markedly dilated sinusoids (Fig. 2). The nodule contains neither portal structures such as bile ducts and large vessels nor stellate scar (Fig. 3). Most of the hepatocytes within the nodule had bland nuclei and abundant clear to acidophilic, somewhat fine granular cytoplasm. There were no mitosis or pleomorphism. The hepatocytes had large amounts of fat vacuoles of various size, which were equally dispersed in both the nodule and the surrounding liver tissue. Reticulum stain revealed that the hepatocytes of nodule were less uniformely organized than those of the adjacent normal liver (Fig. 4). Periodic acid-Schiff's stain showed that glycogen was extremely poor in the hepatocytes of nodule as well as the remaining liver.

Electron microscopically, the hepatocytes of the mass showed highly differentiated structures simulating normal hepatocyte (Fig. 5). Fat droplets were numerous in most neoplastic liver cells. Glycogen deposits were evident and were more abundant than in the surrounding normal hepatocytes. The rough endoplasmic reticulum was comprised entirely of dilated cisternae which were located predominantly

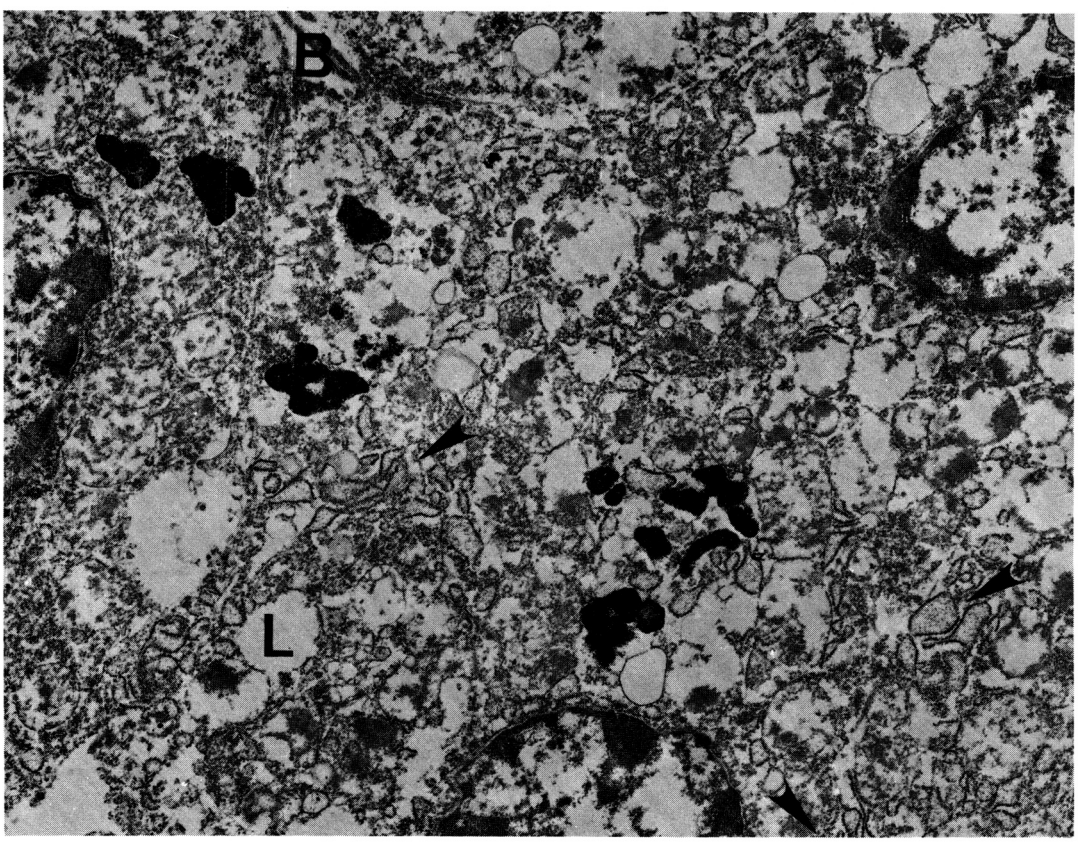

Fig. 5. Electron micrograph of tumor cells showing a bile canaliculus (B) and attachment zone, greatly dilated cisternae of rough endoplasmic reticulum (arrowhead), lipid droplets (L) and glycogen particles (Lead citrate-uranyl acetate, x10,000).

in the cell periphery. Mitochondria were variable in shape and size, and contained crystalloids. Golgi and smooth endoplasmic reticulum were not frequently noted. Lysosomal bodies were of normal structure and were numerous. Bile canaliculi as well as junctional complex were reduced in number compared to normal liver and were usually seen at the junction of three hepatocytes. Most bile canaliculi were very small with small irregular microvilli. Microscopic examination of other organs showed diffuse interstitial pneumonitis with mononuclear cell infiltration. Extensive intraalveolar hemorrhage, hemorrhage in the fetal zone of adrenals and focal hemorrhage of intestinal mucosa were seen. Many glomeruli with epithelial crescents and periglomerular fibrosis were encountered in the both kidneys. Postmortem lung culture grew E. coli.

DISCUSSION

The liver cell adenoma has given a great deal of attention in the recent literature, because it has strikingly increased in incidence paralleling some degree to the popularity of contraceptive steroids (Silverberg, 1983). Most of the patients are woman of the reproductive age and there is uaually, but not always a history of oral contraceptive use. But this tumor is still relatively uncommon and extremely rare in infants and children. There have been cases reported in association with glycogenosis, type 1, androgen treated Fanconi's anemia, familial diabetes mellitus and galactosemia (Chandra, 1984; Howell, 1976; Shapiro, 1977; Edmonds 1952). Gold et al. reported 12 cases of hepatic cell adenoma in which the patient's age ranged from 3 weeks to 74 years with an average of 30 years. Five of 12 cases of liver cell adenoma were discovered incidentally at autopsy. The incidental liver cell adenoma were smaller in size than surgical series, which ranged in size from 0.5cm to 1.5cm with a mean of 1.0cm. The majority of this tumor is solitary (71%) and is located either deep within the lobe or subcapsular and rarely pedunculated. Although liver cell adenoma is well circumscribed, true capsulation is unusual. The liver cell adenoma in children dost not differ from adult counterpart except that in childhood cases the controversy over the etiologic role of contraceptives is not relevant. Dehner et al. (1987) advocated that maternal hormone has not been implicated in their development. Microscopically the hepatic cell adenoma must be differentiated from the hepatocellular carcinoma and focal nodular hyperplasia. Cellular atypia, mitotic activity, and vascular invasion are some of the more important histologic features that are absent in the adenoma but present in the hepatocellular carcinoma. Phillips et al. (1973) described the ultrastructural findings served to differentiate these two types of liver cell tumor. Numerous subcellular structural changes were described in liver cell adenoma and included paucity of the smooth endoplasmic reticulum, inconspicuous Golgi, absence of lipofuscin bodies, greatly distended cisternae of rough endoplasmic reticulum, some bile canaliculi and attachment zone. The overall structure of these neoplasm is greatly simplified compared to that of normal liver cells. The cells of liver cell carcinoma have more free ribosomes, and smaller mitochondria, and are more variable in structure from one cell to another (Toker, 1966; Lee, 1986). Focal nodular hyperplasia is distinguished from adenoma by the presence of fibrous septa that contain bile ducts and large arteries and veins (Foster, 1977). The tumor cells are generally uniform and bland except for a slight enlargement of cells. Because of this similiarity to normal hepatocytes and the lack of encapsulation in the present case, it was difficult on microscopic examination to detect a discrete junction with the adjacent normal parenchyma. The abnormal architectural configuration, two or more cell thickness of hepatocytes separated by sinusoids, was helpful to diagnosis. The reticulin stain emphasized this features. In the present case, diffuse sinusoidal dilatation was seen only within the tumor portion and not in the adjacent normal liver. In focal areas sinusoidal dilatation was marked and resembled those of peliosis hepatis. Focal changes of peliosis hepatis have rarely been seen in the hepatic cell adenoma (Gold et al. 1978).

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