Mixed Hepatoblastoma in an Adult
- A case report and literature review -

Hepatoblastoma is thought to originate from embryonal hepatic tissue, and most of these tumors occur in children under the age of 2 years. Hepatoblastoma in adults is extremely rare, and the prognosis is much worse than the mixed hepatoblastoma of childhood. We experienced a case of mixed hepatoblastoma in a 51 year old female patient. She had been suffering from a mild pain and a palpable lump in the epigastric area. Serum AFP was 43,850 ng/ml. Computerized tomography and selective abdominal angiography showed a large low-density mass. With a suspicion of hepatocellular carcinoma of the left lobe, a left lateral segmentectomy was performed. The external surface showed a huge protruding mass and the capsule was previously ruptured. On section, the tumor was a 11×7 cm sized expanding mass which had a variegated surface composed of yellow-white friable tissue with multifocal hemorrhagic areas. Microscopic examination revealed a tumor consisted of epithelial and mesenchymal elements. The mesenchymal cells were spindle in shape and proliferated over the whole tumor with focal osteosarcomatous differentiation. The epithelial components showed well-differentiated hepatocellular carcinoma-like areas, poorly differentiated acinar or tubular structures.
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INTRODUCTION

Hepatoblastomas are the most common tumors of the liver in early childhood under the age of 2 years (1). Most of these tumors arise in the embryo during the developmental phase of the liver, hence it seems to be unusual that hepatoblastomas occur in adults. The literature of mixed hepatoblastoma in adults has been confused because the various names used by different authors to describe their cases, such as hepatic embryonic mixed tumor (2), carcino-osteochondromyxosarcoma (3) and rhabdomyosarcohepatoma (4). The most common pseudonym is malignant mixed tumor (5~9), but not all cases described as 'malignant mixed tumor' may represent hepatoblastoma. Hepatoblastoma was adopted in adults for the first time by Bartok (10) and then by Carter (11). There has been 32 cases in world literature and we report the first adult case of hepatoblastoma in Korea.

CASE PRESENTATION

The patient was a 51 year old female who was referred to our hospital with the impression of pancreatic pseudocyst from the local clinic. She had been suffering a mild pain and a palpable lump in epigastric area for one month. Her previous medical history was not remarkable and there was no family history of liver disease. Laboratory studies showed the following values : AST, 42 U/L; ALT, 25 U/L; serum amylase, 377 U/L; urine amylase, 749 U/L; lipase, 661 U/L; serum α-fetoprotein (AFP), 43,850 ng/ml; carcinoembryonic antigen, <0.5 ng/ml; hepatitis B surface antigen, positive; hepatitis B surface antibody, negative. Computerized axial tomography of the upper abdomen demonstrated a 10×8×14 cm-sized huge low-density mass in the lateral segment of the left lobe of liver (Fig. 1-A). Selective celiac arteriogram revealed stretching of the lateral segmental branch of the left hepatic artery with a faint tumor blush and faint tumor staining from the splenic artery (Fig. 1-B). Based on the above findings, a clinical diagnosis was made of hepatocellular carcinoma and the left lateral segmentectomy was performed. After surgery, the serum AFP level went down to 1,592 ng/ml, but she died about 2 months after operation.

Pathological findings

The liver was markedly enlarged (15×9×2 cm). The

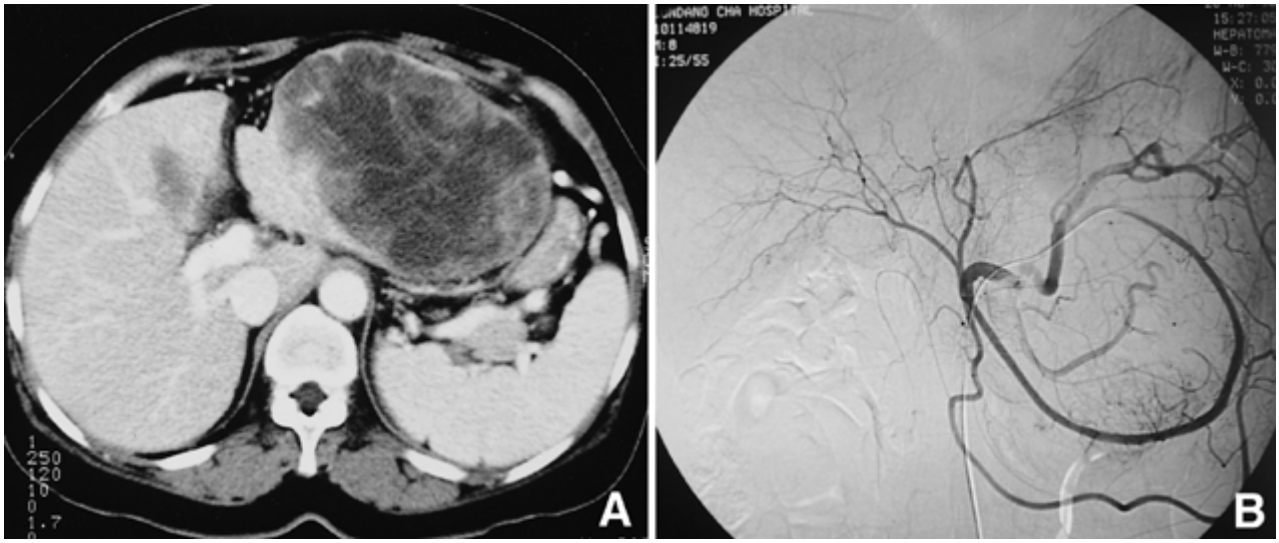

Fig. 1. A : Abdominal computerized tomography after contrast enhancement ; About 13x8cm sized huge mass with exophytic growth is noted in the lateral segment of left lobe of liver. **B :** Celiac arteriography ; In arterial phase, stretching of lateral segmental branch of left hepatic artery with faint tumor blush, and faint tumor staining from splenic artery is noted. The mass is hypovascular due to necrotic nature of tumor.

capsule was ruptured previously and showed a huge exophytic mass. On section, it was a well-defined expanding mass (11×7 cm), which had a variegated appearance consisting of yellow-white, friable tissue with multifocal hemorrhage and necrosis (Fig. 2). The remaining nontumorous area appeared as macronodular cirrhosis. On microscopic examination, the tumor was composed of mainly two components which were intermingled ; epithelial and mesenchymal elements (Fig. 3-A). The epithelial elements had two types of cells. The one was a more large polygonal cell with dark hyperchromatic round nucleus and abundant eosinophilic or clear cytoplasm, which resembled tumor cells seen in hepatocellular carcinoma (Edmondson's grade II, Fig. 3-B). The other was smaller than the former and had a more hyperchromatic, elongated nucleus and scanty cytoplasm, which appeared more primitive, fetal-type cells. These cells arranged as cords or trabeculae, and sometimes showed acinar or ductular differentiation (Fig. 3-C). The mesenchymal elements mainly took the form of spindle shaped cells with elongated tapering nuclei, which showed marked pleomorphism with increased mitotic activity. These cells haphazardly arranged and intermingled with epithelial component in some areas (Fig. 3-A). In other areas, these cells formed interlacing short bundles surrounding epithelial components. There were areas resembling osteosarcoma consisting of lace-like osteoid materials surrounded by atypical osteoblast-like cells (Fig. 3-D). Nowhere was there evidence of fibrosarcoma, chondrosarcoma or rhabdomyosarcoma. On the ground of above histological findings, the diagnosis of mixed hepatoblastoma was made.

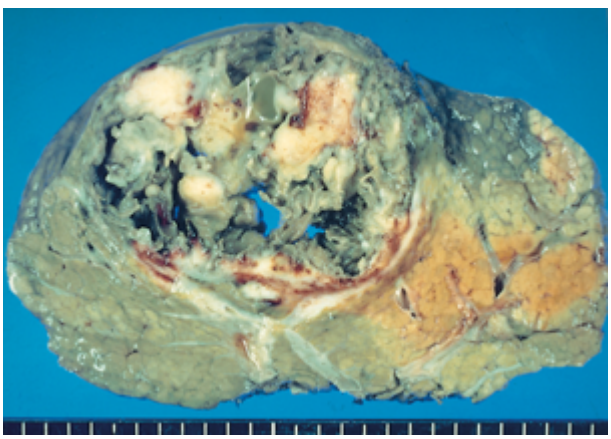

Fig. 2. The cut surface of the liver. The tumor is a mass of expanding type composed of gray white friable tissue with multifocal hemorrhage and necrosis. The surrounding parenchyme shows macronodular cirrhosis.

DISCUSSION AND LITERATURE REVIEW

Hepatoblastoma accounts for 0.2~5.8% of total malignancies and for 25~45% of primary hepatic tumors in childhood (12). The vast majority, 83~92%, occur under 5 years of age and 66% of the cases occur in the first 2 years of life. Adolescents or young adults are seldom affected and only 32 cases have been recorded up to middle age and even in old age (13~15). The usual

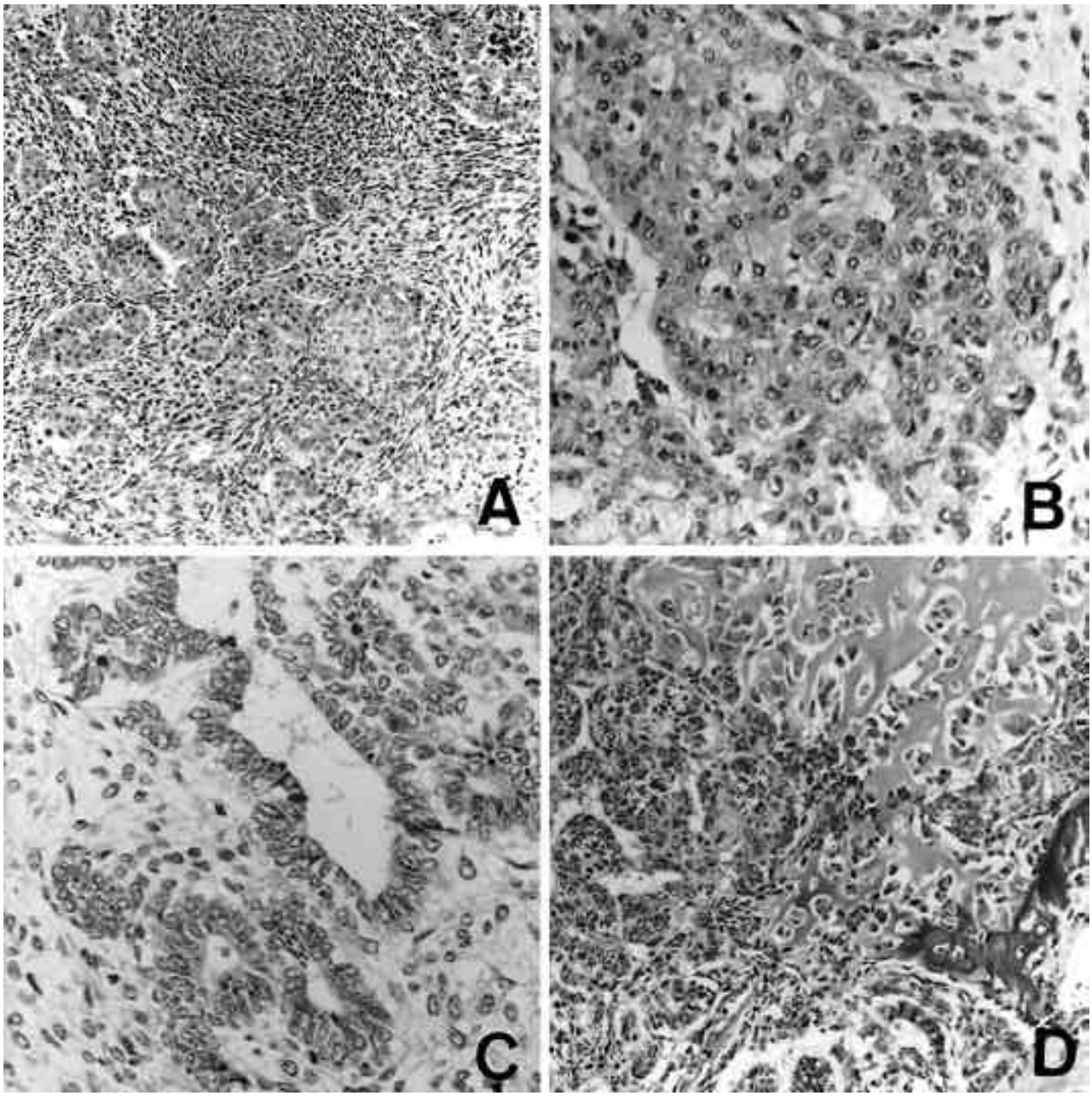

Fig. 3. The microscopic findings of the tumor. **A :** The epithelial and mesenchymal cells are intermingled. The whorling pattern of more primitive cells are noted in the center. **B :** Hepatocellular carcinomatous area composed of large polygonal cells with dark hyperchromatic round nucleus. **C :** Tubular or glandular differentiation of more primitive fetal type cells in the background of myxoid mesenchymal cells. **D :** Osteosarcomatous area in the proximity of clusters of epithelial cells with sinusoidal pattern (H & E).

presentation is failure to thrive, loss of weight and a rapidly enlarging upper abdominal mass. The serum AFP level is almost invariably high. It is difficult to distinguish clinically hepatoblastoma from hepatocellular carcinoma without histological examination. In the patient reported here, symptoms and physical and radiological findings were not different from those of the usual hepatocellular carcinoma.

Ishak and Glunz (16) divided 35 cases of hepatoblastoma in infancy and childhood into two morphological groups. One is the epithelial type, which is predominantly composed of epithelial tumor cells of varying degrees of maturity. The other is the mixed type with epithelial and mesenchymal elements. The epithelial elements include areas resembling embryonic liver, e.g., cords and clusters of cells separated by sinusoid-like clefts maybe seen together with glandular spaces lined by cuboidal epithelium, which represent bile duct differentiation.

Table 1. Summary of hepatoblastoma in adults

Case No.	Reference	Sex/Age	Gross finding	Histologic Type	Author's Diagnosis	Survival
1	Barnett[17] (1958)	M/35	8500 g	Mixed	Embryonic tumor	Died 1 month after surgery
2	Alexander[5] (1961)	F/68	Uninodular (15 cm)	Mixed	Primary mixed tumor	Postmortem
3	Ojima[18] (1964)	M/48	3800 g	Mixed	Malignant mixed tumor	Postmortem
4	Kerr[2] (1966)	M/56	Uninodular micronodular cirrhosis	Mixed	Hepatic embryonic mixed tumor	Sudden death
5	Blanding[6] (1968)	M/84	3000 g Multinodular (8cm)	Mixed	Malignant tumor	Died after biopsy
6	Carter[11] (1969)	M/78	2200 g Multinodular (19×13×6 cm) no cirrhosis	Mixed	Hepatoblastoma	1 month after surgery
7	Goldman[4] (1969)	F/65	3500 g Uninodular (25×15×10 cm)	Mixed	Rhabdomyo-sarcohepatoma	Sudden death
8	Meyer[19] (1974)	F/19	1900 g Uninodular (19 cm)	Mixed	Hepatoblastoma	ND[a]
9	Ludwig[7] (1975, case 1)	F/53	2515 g Multinodular, no cirrhosis	Mixed	Mixed malignant tumor	Died after surgery
10	Ludwig[7] (1975,case2)	M/40	4500 g Multinodular, no cirrhosis	Mixed	Mixed malignant tumor	Postmortem
11	Jameson[20] (1978)	F/51	Uninodular (12×10×10 cm)	Mixed	Hepatoblastoma	Postmortem
12	Yoshida[13] (1979)	M/60	1800g Multinodular (6×6 cm) chronic hepatitis	Mixed	Hepatoblastoma	Died 2 months after surgery
13	Honan[14] (1980)	F/27	4510g Uninodular (25 cm) no cirrhosis	Mixed	Mixed Hepatoblastoma	Postmortem
14	Kishimoto[9] (1984)	M/60	2350 g Multinodular, cirrhosis	Mixed	Malignant mixed tumor	Died 2 days after surgery
15	Kawarada[21] (1985, Case 1)	M/43	4000 g Uninodular (15×12 cm)	Mixed	Nonhepatocytic malignant mixed tumor	Alive for 32 month after surgery
16	Kawarada[21] (1985, Case 2)	M/49	3000 g Multinodular	Mixed	Hepatocytic malignant mixed tumor	Postmortem
17	Sugino[22] (1989)	M/22	Uninodular (6.5×6×6 cm) no cirrhosis	Epithelial	Hepatoblastoma	Died 9 months after surgery
18	Altmann[15] (1992, case1)	M/73	Uninodular (18×18×10 cm) cirrhosis	Mixed	Hepatoblastoma	ND[a]
19	Altmann[15] (1992, case2)	F/35	ND[a]	Epithelial	Hepatoblastoma	ND[a]
20	Harada[23] (1995)	M/24	720 g (6×5×3 cm)	Mixed	Hepatoblastoma	Died 16 months after surgery
21	Present case (1997)	F/51	Uninodular (11×7 cm) micronodular cirrhosis	Mixed	Hepatoblastoma	Died 2 months after surgery

ND[a] ; Not described

Areas of adenocarcinoma (11) and hepatocellular carcinoma (2, 4, 7, 11) may be seen. Mesenchymal elements include myxoid connective tissue resembling primitive mesenchyme and areas resembling fibrosarcoma (11), chondrosarcoma (7, 11), osteosarcoma and rhabdomyoblasts (4, 11) may be found. Fat, smooth muscle and neural elements are very unusual and if found, an alternative diagnosis should be considered. The case presented here was categorized as the mixed type because the tumor was composed of not only small polygonal, poorly differentiated embryonal cells with hepatocellular carcinoma-like areas, but also primitive mesenchymal cells with osteoid formation. In some areas, primitive epithelial cells showed intermingling with primitive connective tissue. There were small hepatocellular islands in the midst of extensive mesenchymal areas or in close proximity of bony trabeculae, which tend to suggest that the indifferent mesenchymal elements may change to epithelial cells or that the hepatoblastic cells may differentiate into both epithelial and primitive mesenchymal cells. That the mesenchymal elements are pluripotent is certain as the formation of bony and vascular structures, cross-striated muscle and even nervous tissue in the previously documented cases. But the question for the pathogenesis still remains whether the hepatoblastic cells are as a precursor of the mesenchymal elements, or whether there are two different pathways of differentiation originating in a common mother cells (15). We also cannot conclude the pathogenetic pathway only in histological aspect and the electron-microscopic examination of the primitive epithelial and mesenchymal cells may be helpful. The clinical and pathological features of adult hepatoblastoma were summarized in Table 1, including the present and previously reported cases which were available for the review in the English literature. The mean age of 21 cases was 50 years old and a male preponderance (M : F=13 : 8) was noted. The surrounding parenchyme revealed cirrhotic change in 4 cases (19%) including the present case and chronic hepatitis in 1 case. The tumors in 10 cases were uninodular whereas multinodular in 7 cases. Histologically the tumors were mostly the mixed type (90%) with the exception of 2 cases of epithelial types. The patients had lived for 1 month to 32 months after surgery with the mean survival time of 3.5 months, whereas long-term survival of 15~35% was recorded in childhood.

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