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Infantile Hemangioendothelioma of the Liver
—A Case Report—

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A case of type 1 infantile hemangioendothelioma of the liver in a 3 month old male infant who had an abdominal mass incidentally noted at 40 days of age, is described. Grossly, the tumor showed a well circumscribed, pinkish gray and gelatinous mass with areas of central necrosis, multifocal thrombi and hemorrhages, and small cysts. Microscopically, the lesion consisted of numerous vascular channels of various size lined by a single layer of flat or plump endothelial cells. Areas of infarction, thrombosis and calcification, and formation of cavernous hemangiomatous foci were also noted in the lesion. Ultrastructurally, the cells had the characteristics of endothelium, including basal lamina, pinocytic vesicles, and Weibel-Palade bodies. Factor VIII-associated antigen was demonstrated in the tumor cells.

Key Words: *Hemangioendothelioma, vascular tumor, liver, infant, neoplasm*

INTRODUCTION

Although type 1 infantile hemangioendothelioma (IHE) of the liver described by Dehner and Ishak (1971) is the most common benign vascular tumor occurring in children, this tumor is still uncommon and less than 100 cases reported in the world's literature (Kunstadter, 1933; Keeling, 1971; Weinberg, 1983). To our knowledge, none have been reported in the Korean literature. The usual clinical manifestation is the characteristic triad of cardiac failure, hepatomegaly and cutaneous hemangioma (Touloukian, 1970). The clinical feature of high output cardiac failure, which is due to arteriovenous shunts within the tunor, is frequently noted in infantile hemangioendothelioma, and substantially contributes to its morbidity and mortality (Winters, 1954; Rosai, 1981).

Recently we had a chance to examine a case of infantile hemangioendothelioma of the liver in a 3 month old male infant who presented as an asymptomatic abdominal mass. We discussed the differential features of this tumor from mesenchymal hamartoma and angiosarcoma of the liver.

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CASE REPORT

A 3 month old male baby was admitted to the Seoul National University Children's Hospital for an evaluation and management of the abdominal mass, which was incidentally noted at 40 days of age. He had no symptoms or signs related to this mass. The mass

was hard, nontender and well demarcated on palpation. Abdominal sonography revealed a well defined, solid, exophytic mass, 5x7x7cm, in the right lower portion of the liver. He underwent hepatic segmentectomy under the impression of hepatoblastoma.

Resected specimen was a segment of liver in which a well circumscribed solid mass was seen. It measured 7.5x6.5x5cm. On section the mass was well demarcated, but not encapsulated with pale gray to pink color and with myxoid or gelatinous appearance. There were areas of central geographic necrosis with yellowish discoloration, multifocal hemorrhages and several thrombi within the mass (Fig. 1). The consistency was characteristically resilient and spongy. There were numerous small cystic spaces scattered in the mass. The surrounding hepatic parenchyma was unremarkable.

Microsopically, this lesion consisted of numerous vascular channels of varying size separated by intervening fibrous stroma containing elongated fibroblast-like cells (Fig. 2). The vascular channels were both irregularly dilated and small, compressed with lining of a single layer of flat and occasionally plump endothelial cells which had benign features. Mitotic activity and nuclear anaplasia were absent in both the endothelial and intervening elongated cells. The number and size of vascular channels varied in areas. Reticulin stain demonstrated that the tumor cells were endothelial cells located on the luminal side of the vascular reticulin sheath (Fig. 3). The central portions of this mass were fibrotic with areas of infarction resulting from vascular thrombosis and focal calcification. In those areas the vascular channels were composed mainly of compressed and delicated capillaries, and the stroma was fibromyxomatous (Fig.4). Small bile ducts of round shape were often seen in the fibrous stroma, mainly at the periphery of the mass. Areas reminiscent of cavernous hemangioma were also seen in the tumor (Fig.5).

Ultrastructurally, the tumor cells showed numerous irregular fine cytoplasmic process along the luminal

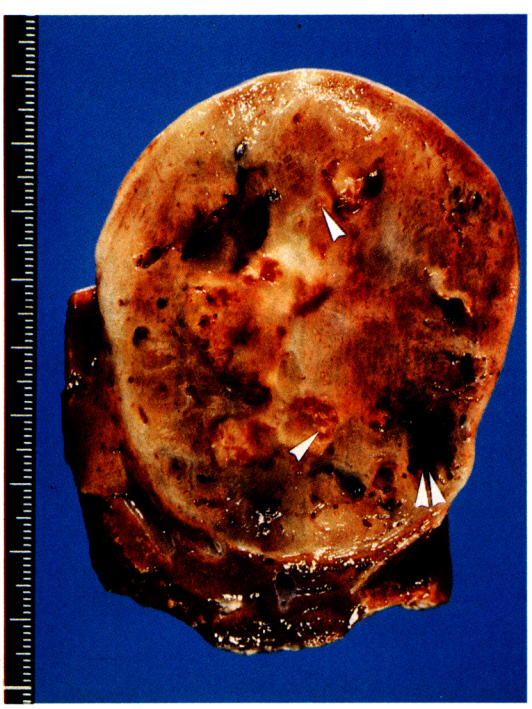

Fig. 1. Cut surface of the resected liver segment showing a well defined, gray to reddish tan hemorrhagic mass with gelatinous appearance and areas of central necrosis, punctate yellowish calcification (arrowhead) and thrombi (double arrowhead).

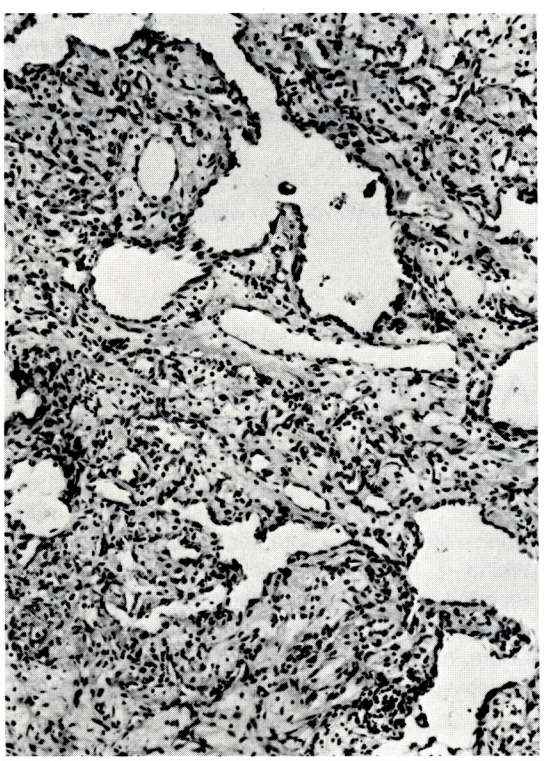

Fig. 2. Microscopically, the tumor consisting of suggestive intercommunicating vascular channels of various size with lining of a single layer of flat or plump endothelial cells (H&E. x100).

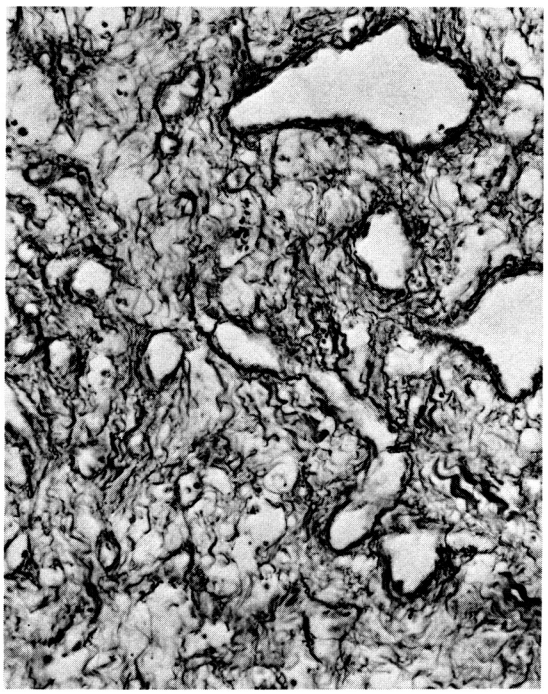

Fig. 3. Reticulum stain demonstrating presence of reticulin fibers outlining endothelial cells (x200).

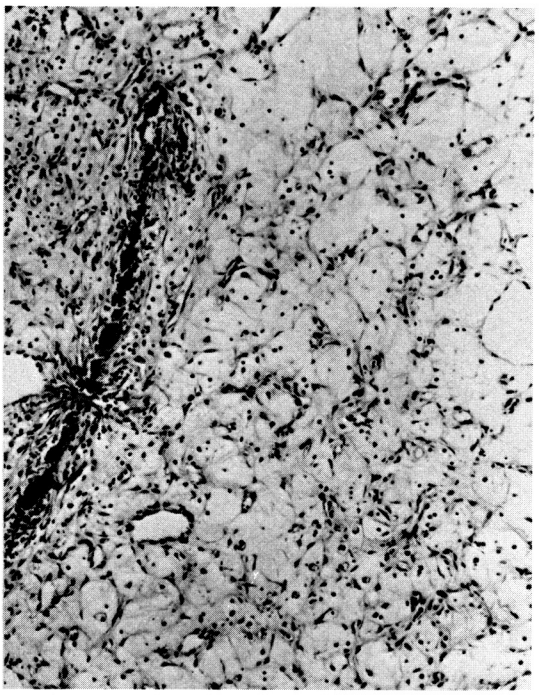

Fig. 4. This tumor showing areas of delicate blood vessels and loose myxoid stroma, simulating the mesenchymal hamartoma. Focal dystrophic calcification is seen. (H&E, x100).

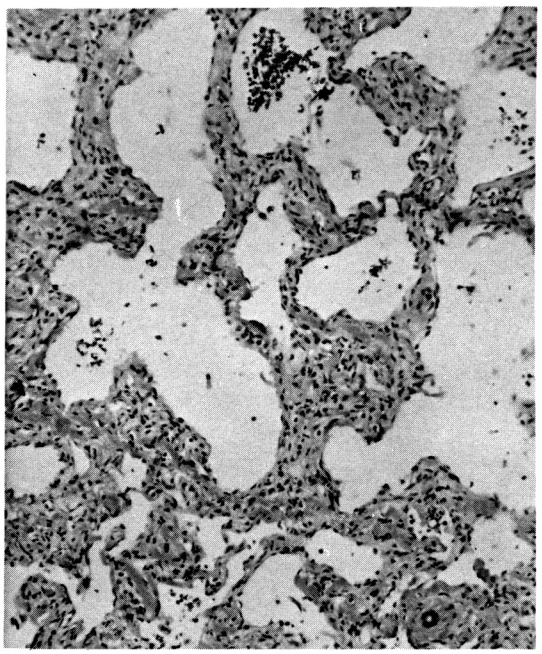

Fig. 5. Note the areas reminiscent of cavernous hemangioma in the tumor (H&E, x100).

surface, and were surrounded by the discontinous basal laminas and pericytes. Tumor cells had large numbers of cytoplasmic organelles including fine filaments, pinocytic vesicles, Weibel-Palade bodies, rough endoplasmic reticulum and mitochondria (Fig. 6). Intervascular spaces contained abundant collagen fibers.

Factor VIII-associated antigen (Peroxidase-anti-peroxidase technique, DAKO kit) was demonstrated in the tumor cells.

DISCUSSION

Vascular tumors are one of the most common mesenchymal neoplasms in childhood, and have a predilection for cutaneous and mucosal surfaces. In contrast, benign vascular tumors of the liver are uncommon and are divided into infantile hemangioendothelioma and cavernous hemangioma (Dehner, 1987). Cavernous hemangioma is less common in children than hamangioendothelioma. Dehner and Ishak (1971) reviewed twenty-three infantile hem-

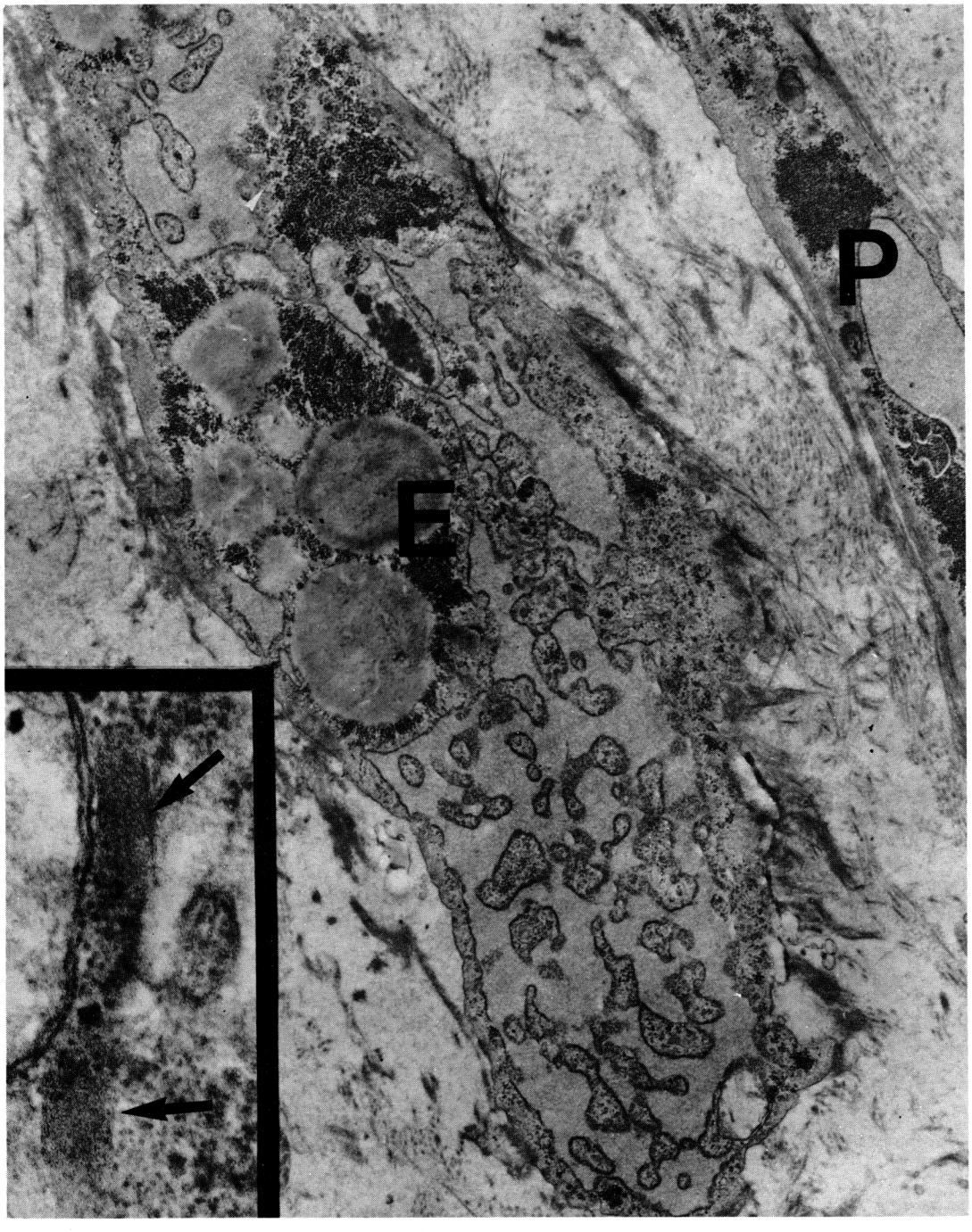

Fig.6. Ultrastructurally, the pericyte (P) and the endothelial cell (E) which has numerous cytoplasmic processes along the luminal surface, are in loose contact (x12,000). Inset: Note the Weibel-Palade bodies (arrow, x100,000).

angioendotheliomas in children ranging in age from the newborn to 4 years. Most of them (87%) occurred before the age of 6 months. One of the most symptoms were abdominal mass, and the mass was often detected as an incidental finding at physical examination. Approximately 50% of patient have one or more cutaneous angiomas. It is generally agreed that these skin lesion is not metastatic, but rather is a part of the multifocal process.

Grossly, the hemangioendothelioma are seen as solitary or multicentric nodules, and divided into two histological patterns (Dehner and Ishak, 1971). Type 1 is more mature in appearance, characterized by both irregularly dilated and small compressed vascular spaces lined by a single layer or less often, several layers of plump endothelial cells with bland cytologic appearance. Type 2 has a more aggressive light microscopic appearance, characterized by large hyperchromatic pleomorphic endothelial cells, arranged in irregular budding and branching structures.

Infantile hemangioendothelioma must be distinguished histologically from angiosarcoma and also from mesenchymal hamartoma of the liver. The angiosarcomas occur predominently in adult male and the mesenchymal hamartomas occur in children under two years of ago (Srouji, 1978). The angiosarcoma in adults shows a greater degree of cellular atypism, giant cell formation, solid sarcomatous foci, intrasinusoidal spread and invasion of portal and hepatic veins (Silverberg, 1983). Central regression and maturation, i.e. fibrosis, calcification and formation of cavernous hemangiomatous foci that are characteristic of infantile hemangioendothelioma are not seen in hemangiosarcoma.

Gross appearance of the present case and histologically myxoid stroma containing delicate blood vessels and bile ductules made us to consider the possibility of mesenchymal hamartoma. However, the dysmorphic features of bile ductules seen in mesenchymal hamartoma are not found in our case. The endothelium of the ectatic vascular spaces which is markedly attenuated in mesenchymal hamartoma, is predominent in infantile hemangioendothelioma. Furthermore hemorrhage, necrosis and calcification are rarely described in the mesenchymal hamartoma, whereas these findings are generally regarded as evidence of spontaneous regression in infantile hemangioendothelioma (Nguyen, 1982). Electron microscopic investigation of type 1 infantile hemangioendothelioma has been reported twice, with divergent findings (Balazs, 1978; Feldman, 1978). Our case is generally coinciding with those description. Ultrastructural features of tumor cells were similar to those of growing and recently formed blood vessels, i.e. larger size, increased number of organell and discontinuities of vessel wall.

Infantile hemangioendothelioma should not be considered entirely benign but as possessing a limited potential to metastasize. There were two reports of type 1 infantile hemangioendothelioma that evolved subsequently into angiosarcoma four and five years later in each (Kirchner, 1981; Strate et al. 1982).

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