Infantile Hemangioendothelioma of the Liver in an Adult

—Report of a Case—

Toshinori HARADA
First Division, Department of Internal Medicine, Yamaguchi University School of Medicine Ube, Japan
Yoshiteru NISHIAKI, Masaharu MAKISAKA, Hiroshi MATSUURA, and Tatsuo MATSUBRA
Department of Internal Medicine, Kokura Memorial Hospital, Kitakyushu, Japan
Futoshi MATSUBARA
First Department of Pathology, Yamaguchi University School of Medicine Ube, Japan
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Primary hemangioendothelioma of the liver is an extremely rare tumor[1,2,3,9,12,13]. Hemangioendotheliomas of the liver in infants usually differ in the histological structure of the tumor tissue and its mode of growth from those encountered in adults. The former presents features of benign tumors and the latter malignant[6].

This report describes the case of a male adult who was found to have marked hepatomegaly and ascites over a prolonged period of time and died after frequent episodes of hematemesis and melena, and in which the postmortem examination revealed a hepatic hemangioendothelioma with histopathological features characteristic of an infantile hemangioendothelioma.

CASE REPORT

The male patient, aged 24, was admitted to the kokura Memorial Hospital on November 2, 1972, with the chief complaints of lassitude and a sensation of epigastric fullness. He had been in normal health until he began to complain of lassitude, anorexia and a feeling of upper abdominal distension early in July, 1972. In the middle of August, 1972, the patient noted generalized pruritus and on September I, 1972, he consulted a physician who told him of the presence of marked hepatomegaly with mild liver function impairment for which, therefore, he was treated at the clinic until his admission to this clinic.

Physical examination on admission revealed a moderately nourished man of average stature with no evidence of jaundice of the bulbar conjunctivae or skin, eruption, spider angioma or lymphnode swelling. On auscultation and percussion there was no abnormality noted of the heart or lungs. The liver was palpable seven fingerbreadths below the right costal margin in the mid-clavicular line and was rigid, non-tender with a somewhat irregular surface. Either kidney was not palpable. Neither a fluid wave nor varicosities were demonstrable on examination of the abdomen. All findings in the neurological examinations were within normal limits.

Laboratory data on admission: Hemoglobin was 15.6 g/dl; red blood cells, 5110,000 per cu. mm; white blood cells, 7,400 per cu. mm with a differential count of 48% neutrophils, 7% eosinophils, 3% basophils, 37.9% lymphocytes and 3% monocytes. The serum total bilirubin was determined to be 1.5 mg/dl; serum alkaline phosphatase, 9.0 Bod. units; serum cholesterol, 185 mg/dl; S-GPT, 81 Karmen units; S-GOT, 93 Karmen units; serum lactic dehydrogenase, 220 units (normal: $<$400 units); serum leucine aminopeptidase, 480 units (normal: $<$170 units); serum γ-glutamyl transpeptidase, 204 units (normal: $<$40 units); serum total protein, 7.6 g/dl; serum albumin, 3.4 g/dl; and serum γ-globulin, 1.8 g/dl. Immunological tests for hepatitis B antigen, α-fetoprotein and rheumatoid factor were all negative. The BSP test showed 30.8% retention of injected dye at 45 minutes, and the erythrocyte sedimentation rate was 2 mm in I hour. There was no evidence of hemorrhagic diathesis and liver scintigram revealed a filling defect in the area corresponding to the left hepatic lobe. Microscopic examination of the liver tissue specimen obtained by needle biopsy disclosed a moderate connective tissue proliferation and round cell infiltration in the portal tract of the right lobe, and an extensive loss of liver parenchyma which had been displaced by proliferation of connective tissue in the left lobe.

Hospital course: During the initial course of his admission he continuously showed a slight elevation of serum alkaline phosphatase level and minimal jaundice. In about March, 1973, he developed ascites which subsequently became more pronounced with marked abdominal varicosities. The patient had frequent episodes of hematemesis and melena from April that year and, in September, a transient disturbance of consciousness. The ascites was so marked that the use of diuretics completely failed to reverse this manifestation, and these circumstances necessitated frequent abdominal paracentesis. With the clinical course characterized by circulatory disturbances of the portal system the patient succumbed after the seventh episode of hematemesis and melena in June,

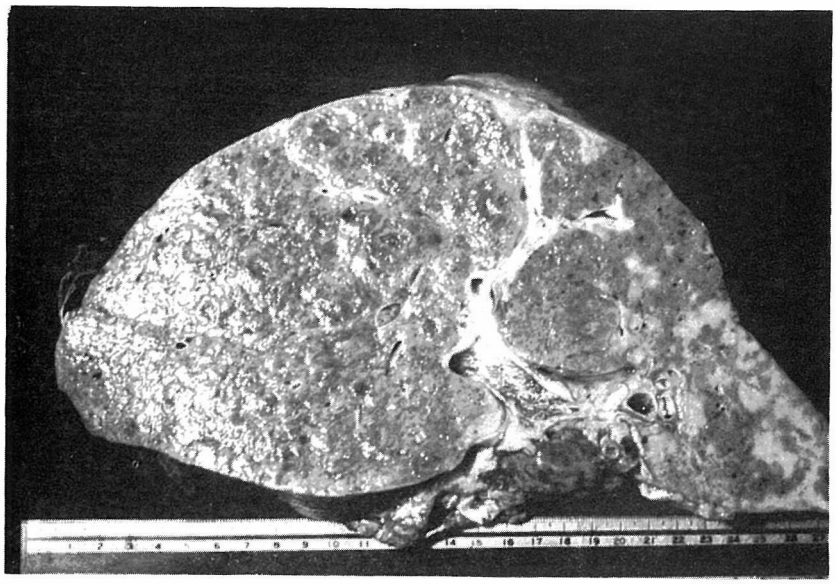

Fig. 1. Cut surface of the liver showing a number of nodules, reddish-purple in the center and grayish-white at the periphery, distributed throughout the entire liver. Note a mosaic arrangement of greyish-white scars and residual liver parenchyma in the left lobe.

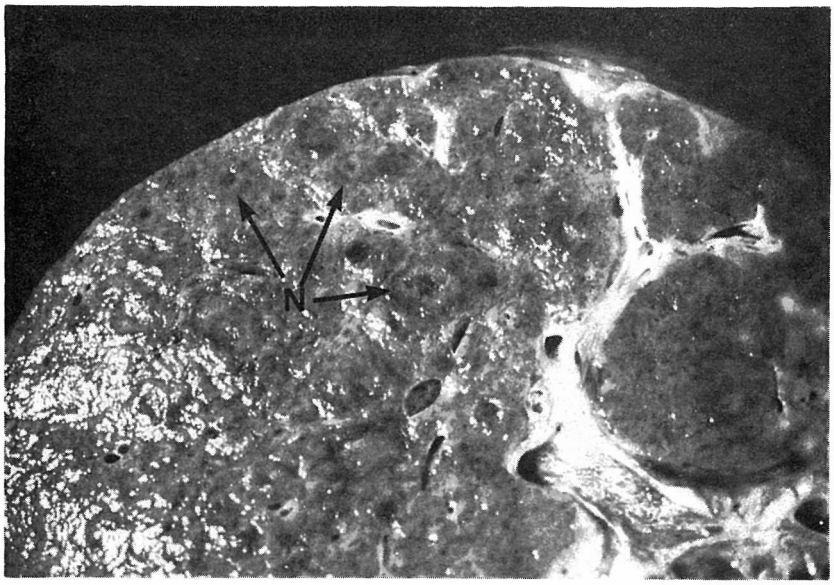

Fig. 2. Higher magnification of Fig. 1. Nodules (N) are noted to have central umbilicus-like depressions.

1974, about 2 years after the onset of his illness or about 16 months after the development of ascites.

Postmortem findings: Gross pathology:- The liver weighed 3590 gms. Sections through the right lobe revealed a number of nodules of 0.5 to 1.5 cm in diameter, reddish-purple in the center and greyish-white at the periphery, distributed throughout the entire lobe. Such nodules were found only in a limited area of sections through the left lobe. Most of the remaining part showed a mosaic arrangement of greyish-white scars and residual liver parenchyma (Fig. 1). Larger nodules were noted to have central umbilicus-like depressions (Fig. 2). There were several lymphnodes as large as the tip of the little finger with a dark red medullary appearance of their cut surfaces, distributed over the area extending from the portal region to the head of the pancreas. An accessory spleen approximately I cm. in size was found to be present in the vicinity of the tail of the pancreas. Fresh hemorrhage was noted in the lower esophagus.

Histopathology:- In the nodular lesions of the liver, microscopic features of a hemangioendothelioma were observed, characterized by polymorphic, plump endothelial cells forming anastomosing small vascular lumens and densely proliferating toward these vascular spaces (Fig. 3).

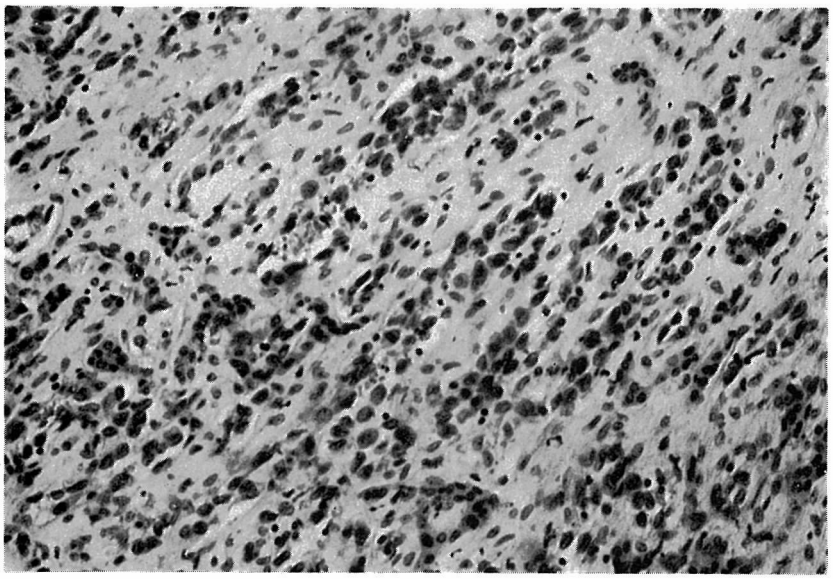

Fig. 3. Anastomosing vascular lumens, lined with one or more layers of plump endothelial cells. Hematoxylin and eosin stain; ×370.

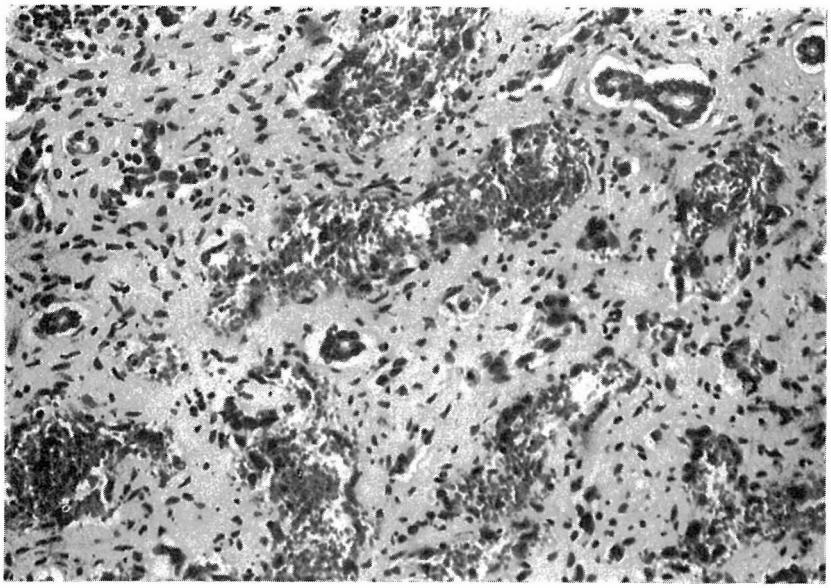

Fig. 4. Large thin-walled and blood filled spaces lined by a single layer of flattened endothelial cells in the central portion of a tumor nodule. Hematoxylin and eosin stain; ×350.

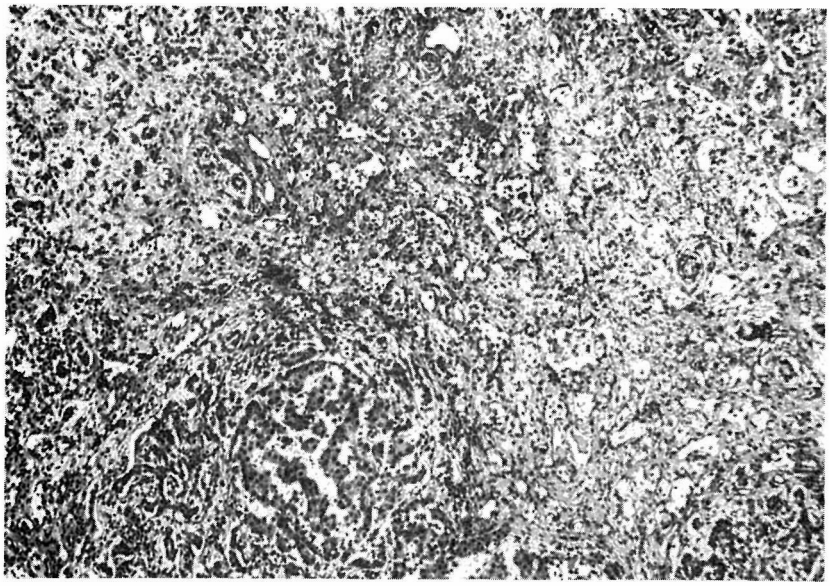

Fig. 5. Small island of liver parenchyma surrounded by a large zone of blood spaces lined by endothelial cells. Note the proliferation of endothelial cells in the left upper quadrant. Hematoxylin and eosin stain; ×370.

Occasional lesions presented histological features of a cavernous hemangioma in the centrinodular area (Fig. 4). The nodules were not encapsulated and, in some areas, irregular tumor extensions were seen infiltrating the adjacent liver parenchyma. The endothelial cells themselves, however, showed only mild atypism and mitotic figures were not prominent (Fig. 3). These findings are well in accord with the histopathological findings described for the so-called infantile hemangioendothelioma[6,9,12]. As for unnodulated areas, moderate proliferation of connective tissue with round cell infiltration was noted in the portal region, but there was virtually no evidence of degeneration or necrosis of the liver cells. In cicatricated areas of the left lobe the liver parenchyma was extensively replaced by proliferation of connective tissue in which hemangioendotheliomatous growths were observed (Fig. 5) as well as in the accessory spleen and in the above-described lymphnodes.

DISCUSSION

It has been described by Foote[8] that hemangioendotheliomas of the liver in infants are congenital and invariably present at birth and, in most cases, symptoms develop ranging from 36 hours to 4½ years of age. This tumor is histologically benign but, since it grows rapidly, death usually follows in less than 6 months after the onset of illness[6]. There has been no clear view set forth as to whether or not such benign hemangioendotheliomas of the liver occur in adults as well, however. In fact, there is as yet no report of these tumors in adults to our knowledge. Therefore, the male adult with a hemangioendothelioma of the liver described herein with histopathological features characteristic of the so-called infantile hemangioendothelioma is considered to be an extremely rare case. The findings of the liver and the remarkably prolonged clinical course noted in this case, and the fact[6,7,10,11] that spontaneous regression or even complete cure very rarely occurs in this neoplasm would suggest, though by mere coujecture, that the tumor did not develop after the patient had grown into manhood but existed already at birth and grew thenceforth very slowly or remained latent over the decades.

Abdominal enlargement or an abdominal mass is the earliest manifestation of the disease and, as the tumor expands, consequent pressure symptoms on the gastrointestinal or respiratory systems, anemia and signs of congestive heart failure[4,10,14] caused by arteriovenous anastomosis within the tumor[5] become manifest. However, the marked ascites as seen in this case is usually rare[9]. Rare involvement of the venous

system in an infantile hemangioendothelioma of the liver[6] may be one of the reasons for this. In this case the development of marked ascites is considered to be due to a disturbance of the inflow of portal blood caused by the multiple neoplastic growths in the entire liver and associated connective tissue proliferation (with partial cicatrization). In addition, it seems also probable that the presence of arterio-venous (arterio-portal) anastomosis within the tumor which brough about abnormalities in the hemodynamic homeostasis facilitated the development of marked ascites.

SUMMARY

A case of primary hemangioendothelioma of the liver with histopathological features characteristic of an infantile hemangioendothelioma of the liver, in a 24-year-old male, was reported. The patient was found to have marked hepatomegaly and ascites over a prolonged period of time and succumbed with hematemesis and melena about 2 years after the onset of his illness or about 16 months after the development of ascites. Multiple tumor nodules of 0.5 to 1.5 cm in diameter, reddish-purple in the center and greyish-white at the periphery, were found throughout the liver with pronounced cicatrization on limited area of the left lobe at autopsy. Hemangioendotheliomas of the liver in infants are congenital and many of the patients develop symptoms ranging from 36 hours to 4½ years of age. Although these tumors are histologically benign, most patients die within 6 months following the onset of their illness because of a rapid growth of the neoplasm. The findings noted in the case described herein would suggest that, in rare instances, hemangioendotheliomas of the liver in infants may grow very slowly or remain latent over a prolonged period of time.

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