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Infantile Hepatic Hemangioendothelioma with Subsequent Malignant Degeneration

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Abstract. A 4 year old child was seen because of an enlarging epigastric mass and a rapidly falling hematocrit 3½ years following steroid treatment for multiple hepatic hemangioendotheliomas. Technetium 99 m sulfur colloid liver scan and hepatic angiography confirmed the presence of a large, vascular mass involving the left lobe of the liver. A left hepatic lobectomy was performed and histopathology showed angiosarcoma. As children with hemangioendotheliomas of the liver begin to survive for longer periods of time, surveillance for the possible development of neoplastic disease is recommended.

Key words: Hemangioendothelioma, hepatic – Hemangioendothelioma, malignant degeneration – Angiosarcoma, hepatic – Neoplasm, hepatic

Juvenile hepatic hemangioendothelioma is a vascular tumor which is often multicentric in origin. In spite of its benign histology, death frequently occurs as a result of congestive heart failure [3], consumptive coagulopathy, hemorrhage, pressure on vital structures or tumor replacement of the liver [4]. This report describes a patient with multiple hemangioendotheliomas who was treated successfully with prednisone [4] and who subsequently developed hepatic angiosarcoma.

Case Report

A 6 month old girl was admitted to Vanderbilt University Hospital because of hepatomegaly, multiple cutaneous hemangiomas and poor weight gain. At that time, Technetium 99m sulfur colloid liver scan demonstrated hepatomegaly and 2 localized areas of decreased activity. Celiac angiography showed changes typical of multiple hepatic hemangioendotheliomas (Fig. 1 A and B), and microscopic sections (Fig. 2) of tissue obtained at open liver biopsy confirmed that diagnosis. Treatment with prednisone, 2 mg/kg every other day, was begun at 7½ months of age because of a continually enlarging liver. At no time was there evidence of arteriovenous shunting or congestive heart failure. After 4 months of treatment the steroid therapy was tapered and then discontinued as the liver was no longer palpable. A technetium 99m sulfur colloid liver scan was normal, and the child showed normal growth and development at 22 months of age.

At 4 years of age, the child was seen again with an enlarging epigastric mass and a rapidly falling hematocrit. A technetium 99m sulfur colloid liver scan (Fig. 3) revealed hepatomegaly and several areas of decreased activity in the left lobe. Selective celiac and hepatic angiography (Fig. 4) was then performed. A hypervascular mass occupying and enlarging the left hepatic lobe was outlined. Pooling of contrast and stretching of vessels were prominent features of the angiogram.

A left hepatic lobectomy was performed and microscopic sections (Fig. 5) of the surgical specimen were diagnostic of angiosarcoma. The child was treated with vincristine, cytoxan, adriamycin, 5-fluorouracil, and radiation therapy. At age 4½ years, laparotomy, for lysis of abdominal adhesions was performed and no residual tumor was found. At 6 years of age the patient remains clinically free of tumor.

Discussion

Juvenile hepatic hemangioendothelioma, although a benign lesion of the liver, is now usually managed aggressively to avert the often fatal complications of the disease which may occur prior to the natural regression of the lesions. The patient reported here was successfully treated with steroids [4], but other therapeutic modalities have been described. These include hepatic artery ligation [3], radiation therapy [1, 8], cytotoxic drugs [1, 10], and balloon embolization [5]. Because of the diffuse nature of the hemangioendotheliomas, hepatic lobectomy is usually not applicable to this lesion [3, 11].

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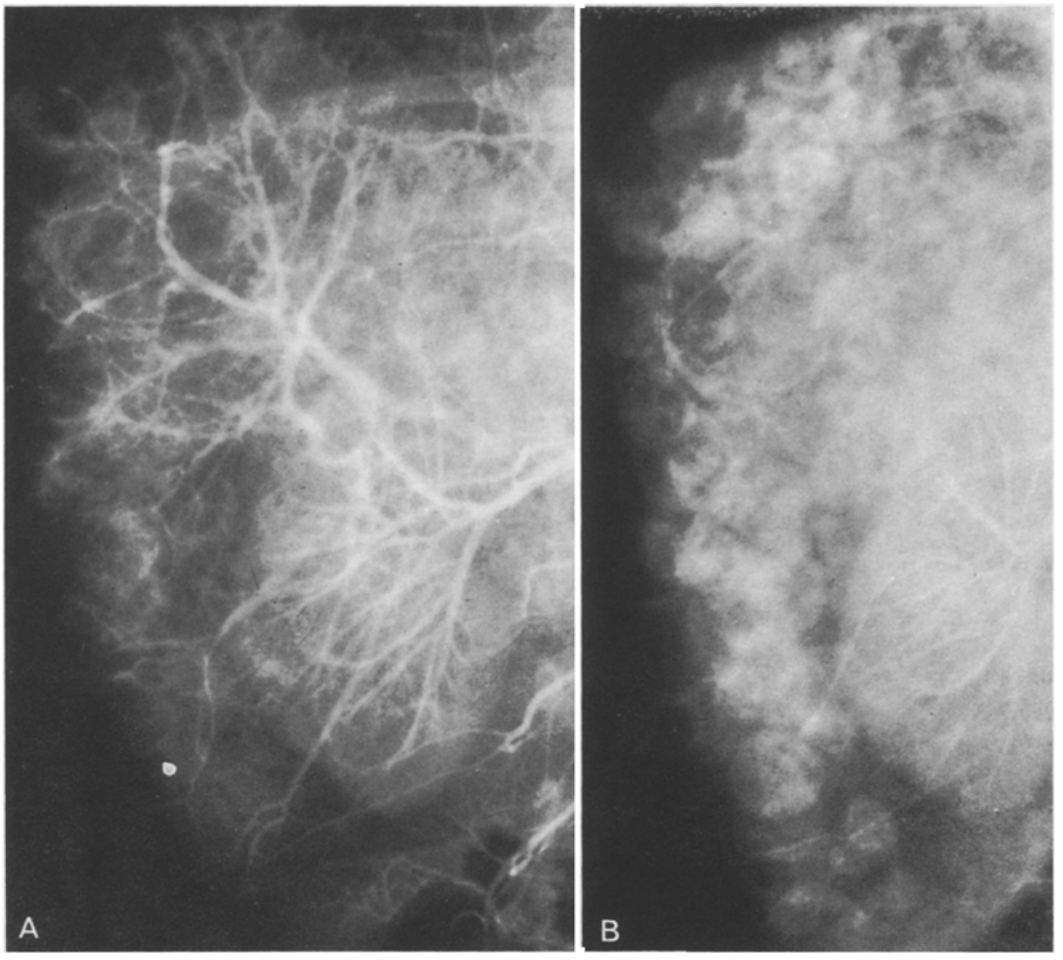

Fig. 1 A and B. At age 6 months, selected films of early **A** and late **B** phases of celiac angiogram, coned to the right lobe of the liver, show findings typical of juvenile hepatic hemangioendotheliomas. Multiple nodules which displace the hepatic arterial branches are present. On the late phase some nodules show only a rim of contrast opacification while others seem to be more uniformly dense

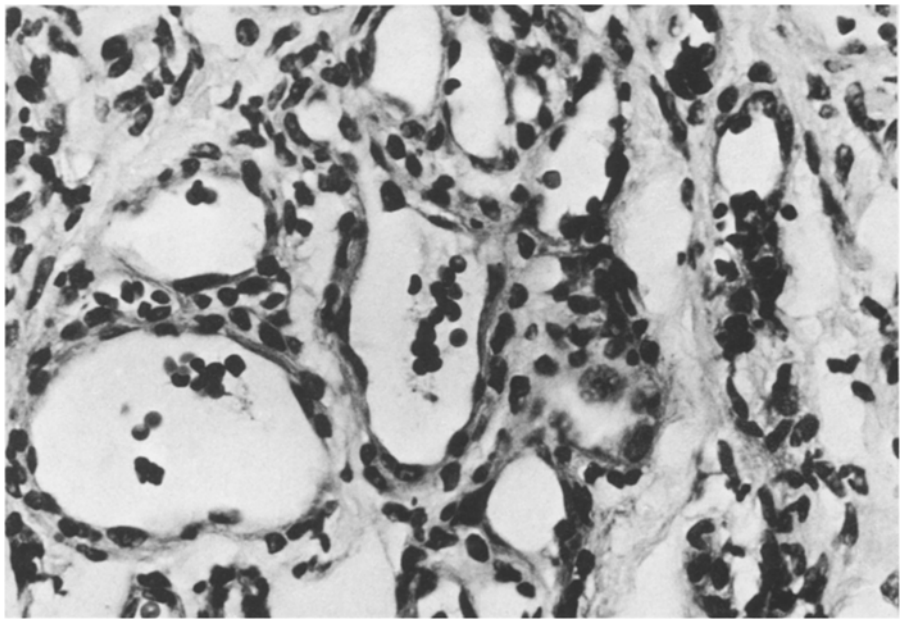

Fig. 2. Biopsy at 6 months. Microscopic section (490 ×, hematoxylin-eosin) shows dilated vascular spaces lined by endothelial cells characteristic of juvenile hepatic hemangioendothelioma

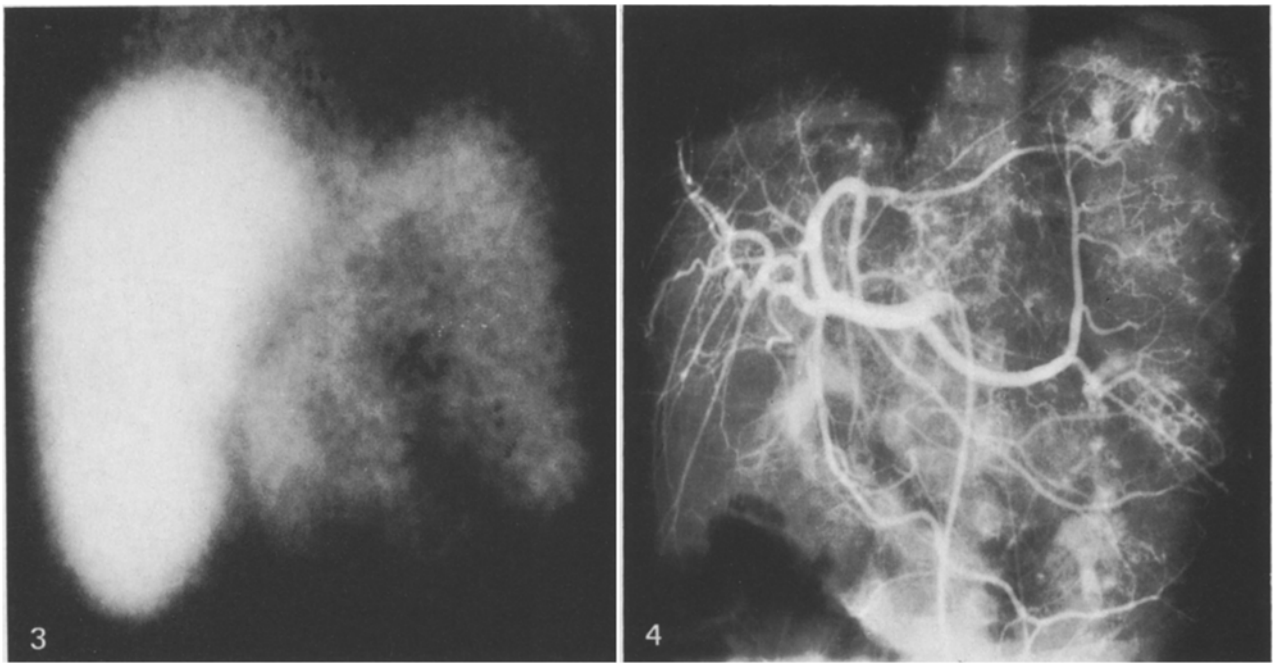

Fig. 3. At age 4 yrs. anterior view of 99 m Tc sulfur colloid liver scan demonstrates hepatomegaly which particularly involves the left lobe. Several mottled areas of decreased uptake are present

Fig. 4. At age 4 yrs. selected film from early phase of celiac angiography reveals a large mass in the left lobe of the liver. Vascular displacement and pooling of contrast media are present

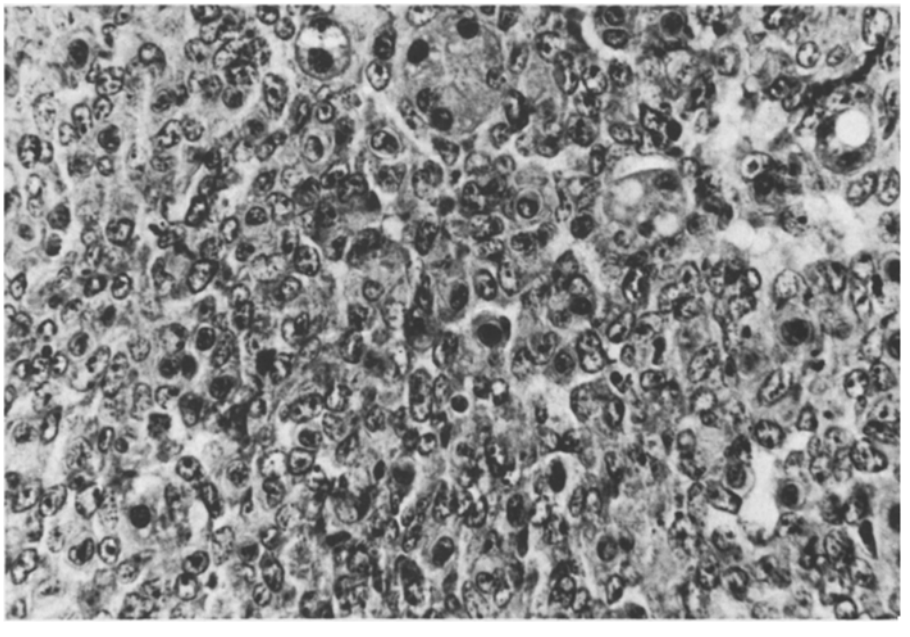

Fig. 5. Biopsy at 4 yrs. Microscopic section (490 ×, hematoxylin-eosin) of the hemorrhagic mass shows angiosarcoma with anaplastic endothelial cells. Invasion into surrounding liver was present

The child described in this report is important because of the development of hepatic angiosarcoma $3^1/_2$ years following initiation of steroid therapy and approximately 2 years after clinical evaluation and radionuclide imaging showed the liver to be normal. At age 4 years, the patient presented with an enlarging epigastric mass and a falling hematocrit. It is of interest, that the angiogram performed at this time was vastly different from the initial study which showed features characteristic of juvenile hepatic

hemangioendothelioma [5, 9]. A hypervascular mass with stretching of vessels and puddling of contrast material was detected. Unfortunately, the differentiation of benign from malignant hepatic hemangiomas and neoplasms is not always possible by angiography [7] or other imaging modalities [6]. Angiosarcoma was proven in this case because of the necessity of surgery to control hemorrhage.

Search of the English literature has thus far revealed only one other instance of malignant behavior of juvenile hemangioendothelioma initially felt to be benign by microscopic inspection [2]. That patient was first seen at 18 months of age, the hemangioendothelioma was a solitary lesion in the left lobe of the liver and treatment consisted of lobectomy followed by postoperative radiation therapy.

The obvious question which must be raised by these two patients is: Will we begin to see malignant degeneration in children with juvenile hepatic hemangioendothelioma who are successfully managed with the treatment modalities now available? Although juvenile hemangioendotheliomas probably more typically regress with age, malignant behavior may also be an eventual result [2]. Until more children with this disease are observed over longer periods of time, surveillance for the possible development of neoplastic disease is recommended. The appropriate method and time frame for follow-up can only be conjecture. The radionuclide liver scan and ultrasonography are recommended as accurate, noninvasive means of screening the liver for space occupying lesions, while the determination of alpha-fetoprotein levels in the blood might prove to be a useful laboratory screen for malignant degeneration.

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