HAMARTOMA OF THE LIVER

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HAMARTOMA OF THE LIVER, a distinctly rare entity, if judged by the paucity of cases reported, deserves mention when encountered because it represents a resectable and curable tumor in an organ commonly involved by hopeless neoplasms.

Hamartoma (*ἁμαρτία*, error or defect; and *-ωμα*, tumor) is a term coined by Albrecht[1] in designation of certain tumors which cannot be classified with the true neoplasms, which have a relative quantitative disproportion of tissue elements normally comprising the organ, but which have not attained the complete pattern of the organ. These tumors are congenital and of a teratoid nature, with retention of some embryonal characteristics; they are more or less encapsulated, do not contain mitotic figures and do not metastasize. In the indexed titles of the literature of the past ten years the term, hamartoma, has been used in connection with tumors of the skin, tympanum, brain, choroid plexus, thyroid, lung, bronchi, spleen, heart, mediastinum, and liver. Hamartoma of the liver is generally found in the infant. Ladd and Gross[5] described an hamartoma of the liver, weighing 400 Gm., successfully removed from an infant of eight months. Benson and Penberthy,[3] in 1942, excised a similar tumor, weighing 60 Gm., from the liver of an infant seven months of age with recovery.

Case Report.—No. 18591: R. O., white, female, age 16.5 months, was admitted on the Pediatrics Service of Memorial Hospital by Dr. J. Keller Mack, September 15, 1946, because of enlargement of the abdomen. She had been born by cesarean section because of postpoliomyelitic deformities of the mother, and had always appeared in normal health, though her abdomen was always noted to be large. No abnormality was detected by her family doctor until he found an abdominal mass about two weeks before admission.

Physical Examination: A well-developed child, weighing 24 pounds, and standing with moderate irreducible protrusion of the abdomen (Fig. 1). A rounded, partially lobulated, firm mass extended from the right costal margin into the iliac fossa, filled the right flank and extended across to the left nipple line, occupying about two-thirds of the abdomen. Examining fingers could be inserted beneath the costal margin, but the upper border of the mass was indefinite; the lower border was freely palpable, and the tumor could be moved slightly, with no apparent pain; it was less well-palpated through the flank.

Laboratory Data: Hemoglobin 11.5 Gm. (74 per cent); R. B. C. 3.99 million; W. B. C. 8,600; lymph. 58, seg. 32, stab. 21, eosin. 4, mono. 4. Urinalysis was normal.

Roentgenograms showed a large homogeneous mass in right side of abdomen. After barium enema the mass was seen to displace the proximal colon downward and posteriorly (Fig. 2). Intravenous pyelogram showed no dye in right kidney, but retrograde examination showed normal pelvis and calyces on right.

Course: After preliminary blood transfusion, and with a diagnosis of probable mesenteric cyst, operation was performed, September 21, 1946, under vinyl and ethyl ether inhalation anesthesia. Through a long right rectus incision the tumor was immediately encountered and delivered (Fig. 3). It measured 8 x 7 x 4 inches *in situ,* and in shape, size, consistency and color bore a striking resemblance to a beef heart; the base was broadly incorporated into the right lobe of the liver, and the medial border lay immediately adjacent to the gallbladder; the apex felt cystic; large veins coursed beneath the serosa of the tumor into the liver. Complete excision required resection of nearly half of the right lobe of the liver, which was accomplished without great difficulty by preliminary placement of mattress sutures of No. 1 chromic catgut; the lateral half of the resection was facilitated by temporarily compressing the liver with a rubber-shod intestinal clamp. The capsule of the tumor did not completely enclose the base where the tumor tissue blended with normal liver, but it was considered to have the gross characteristics of a benign lesion. Mild shock ensued during traction on the liver despite blood replacement; it was estimated that less than 200 cc. of blood was lost, but a similar amount was probably contained in the tumor. The raw stump was allowed to retract above the mesocolon without reperitonealization. The wound was closed with No. 0 chromic catgut for peritoneum and No. 30 cotton for fascia. A small Penrose drain was left inlying to the stump.

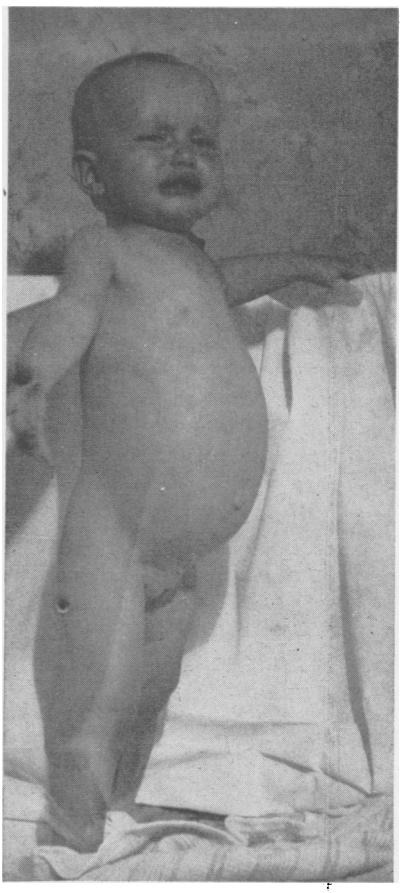

FIG. 1.—Preoperative photograph demonstrating enlarged abdomen.

The patient developed a rectal temperature of 104.2° F. eight hours after operation, and this gradually decreased to normal by the 8th day, when the drain and sutures were removed. Adequate urinary output was assured by intravenous solutions. Abdominal distention was present for three days. She was discharged on the 11th postoperative day. Examination five months after operation disclosed that her physical development had proceeded normally and there was no evidence of recurrence of the tumor.

Pathologic Examination (Dr. A. Vass).—*Gross:* A heart-shaped mass 17 x 17 x 9.5 cm., weighing 1,575 Gm. (Fig. 4A). On section (Fig. 4B), the entire mass consists of roughly lobulated, firm but elastic yellowish-pink tissue; the lobules measure from 2 to 5 mm. in diameter and are separated by septa less than 1 mm. in width. In the distal portion is a roughly spherical 8-cm. cyst containing clear yellowish fluid and lined by a smooth pinkish-gray transparent membrane with incomplete septa. Several similar but smaller cysts were found on further section. At the base a 3 to 4 mm. layer of reddish-brown liver tissue is noted to be well-demarcated from the adjoining tumor tissue.

Microscopic: The liver tissue present at the proximal end of the specimen appears to be quite normal. Very slight infiltration by round cells is present in periportal connective tissue. However, in the zone of the liver which adjoins the tumor mass (Fig. 4C) the periportal connective tissue contains rather irregularly-shaped glandular structures which

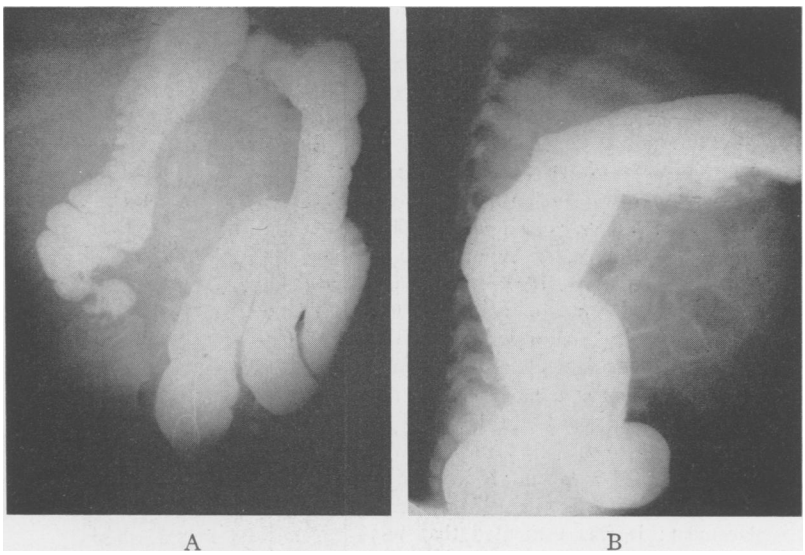

FIG. 2.—Roentgenograms, A. anteroposterior, and B. lateral, demonstrating inferior and posterior displacement of right colon.

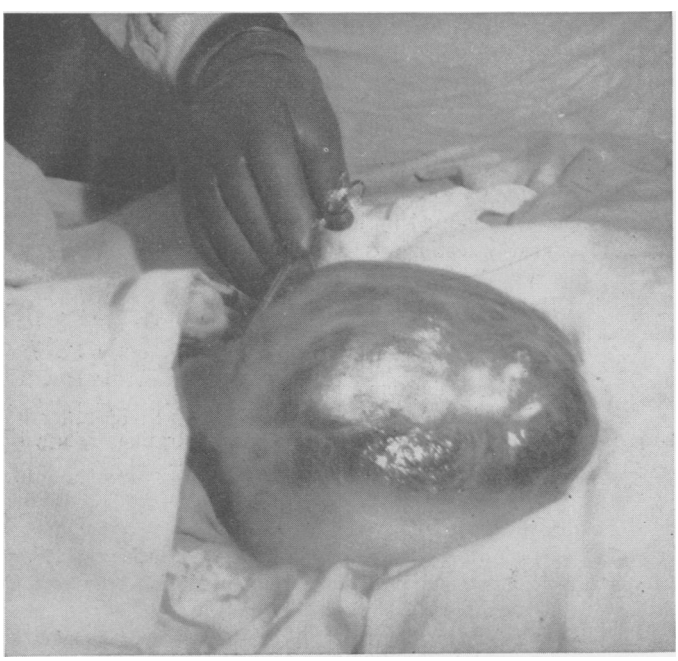

FIG. 3.—Appearance of tumor at operation. Hemostat indicates attachment to liver.

are more or less haphazardly arranged. They are lined by a single to double layer of cuboidal epithelial cells most of which possess vesicular and only occasionally hyperchromatic nuclei. Often these structures are surrounded by groups of lymphocytes and a few eosinophilic polymorphonuclear leukocytes. The structures are not always confined

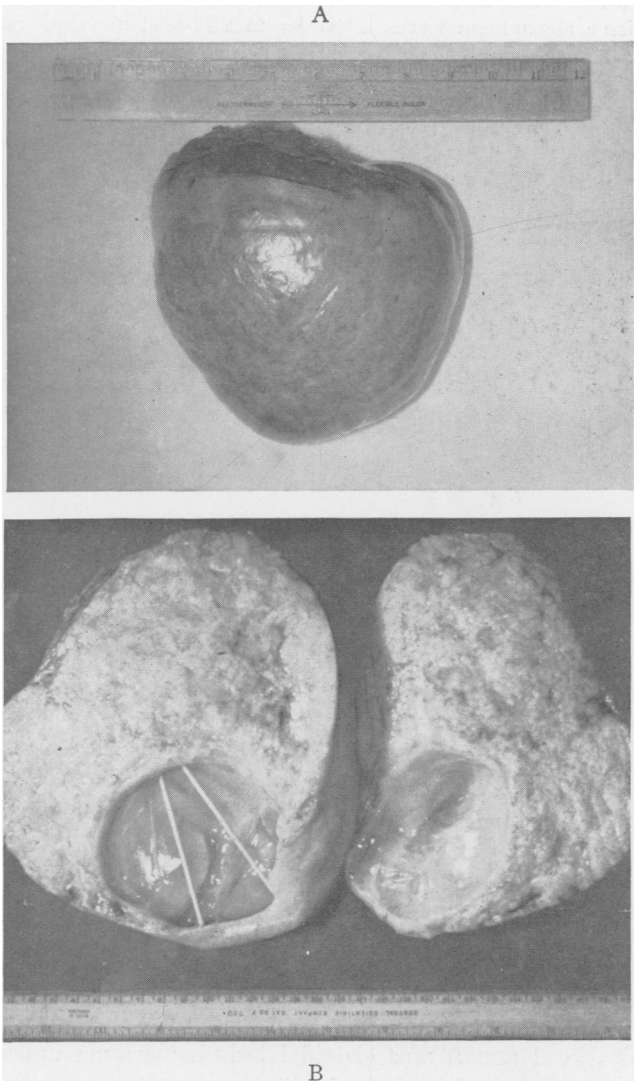

FIG. 4.—Gross specimen: A. after excision, and B. after section, demonstrating cyst at apex.

to the periportal connective tissue but are also found between the adjoining liver cords. The structures are not infrequently surrounded by apparently newly-formed moderately cellular connective tissue. These structures resemble bile ducts in a general way. Sections from the periphery of the tumor (Fig. 4D) reveal it to consist of rather abundant, somewhat edematous, hyalin connective tissue forming the stroma into which are embedded

numerous glandular structures similar to those described above except that they are more irregular in shape and are somewhat distended. They contain traces of pinkish-staining homogeneous material. Occasionally there are papillary projections of connective tissue into the lumina. These projections are covered with cuboidal cells similar to those lining the lumina elsewhere. There are also a large number of rather distended capillary blood spaces lined with a single layer of flat endothelial cells. Occasionally the arrangement of connective tissue about these spaces is similar to that seen in veins. Small islands of polygonal, moderately large cells, possessing somewhat hyperchromatic moderately large nuclei and somewhat eosinophilic cytoplasms, are scattered throughout the section. These

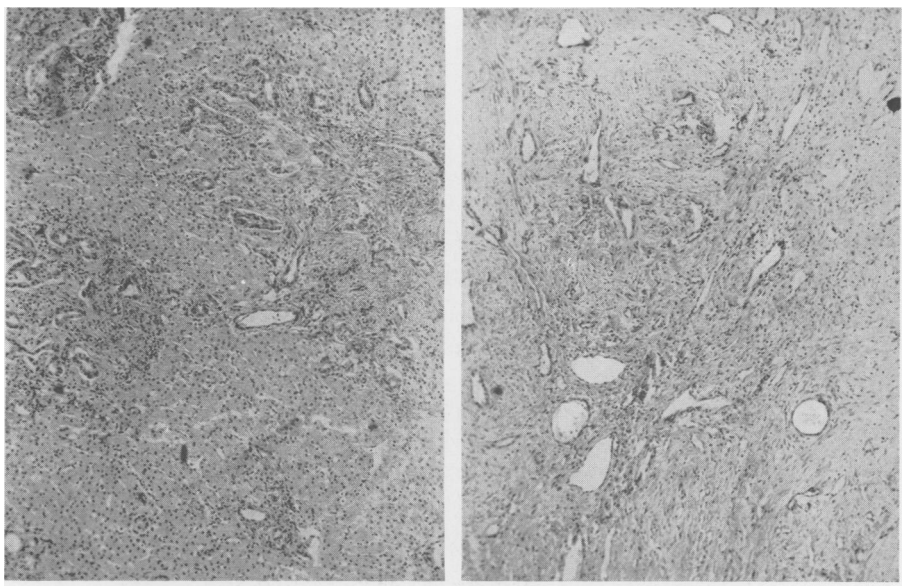

FIG. 4C FIG. 4D

FIG. 4. (Cont'd.)—Photomicrographs demonstrating C. liver-like tissue near base of tumor, and D. fibrocystic appearance near apex.

resemble liver cells and sometimes are continuous with the above mentioned glands. *Pathologic Diagnosis:* Hepatoid hamartoma. A tumor of complex embryonal origin, probably arising from the multivalent liver cell, and possibly malignant.

DISCUSSION.—Sections from this tumor were reviewed by another pathologist* who agreed that it was classifiable as hamartoma under the present usage of the term, considered it benign but preferred a more descriptive term such as "benign mixed cystic teratoid tumor."

In a classification of true primary tumors of the liver, Warvi[10, 11] considtred hamartomas to be indistinguishable from adenoma of the liver, a more common and usually benign tumor. His opinion was based on review of material demonstrating a preponderance of liver cords without bile ducts or

* Dr. Carl V. Weller, Director of Department of Pathology, University Hospital, Ann Arbor, Michigan.

portal triads, a type of tissue not exactly comparable to our case nor to that of Benson and Penberthy who permitted the author to study their sections which resemble the proximal portion of the tumor here reported. Further case studies should be reported to permit a more precise classification of these tumors and to define their relationship to other benign tumors composed of hepatoid elements. It is possible that the variable criteria for the diagnosis of adenoma of the liver may have resulted in the classification of hamartomas with adenomas in other series.[8]

It would appear inaccurate to liken the tumor in our case to adenoma, cystadenoma or cholangiohepatoma as the proportions of liver cells, bile ducts and fibrous tissue varied within the tumor itself, there being, at the base (Fig. 4C), a less mature but more liver-like tissue than at the apex (Fig. 4D) where liver cells were scarce and fibrocystic tissue predominated. A comparable tumor removed from the liver of a 13-months-old infant and weighing 4.5 pounds was described by Lee[6] as "large solitary bile-cell fibro-adenoma of the liver." It is this abnormally great development of supporting connective tissue that is described by Albrecht[2] in his discussion of hamartoma and hamartoblastoma. In a former article[1] he regarded the two main possibilities of the manner of origin of fibrocanalicular hamartomas as: (a) abnormally abundant formation of connective tissue as a result of increased anlage or greater localized power of proliferation of mesenchyme cells; and (b) abnormal relative activity between the canaliculi-forming and the supporting tissue cells.

The tumor in our case weighed 1575 Gm., nearly five times the weight of the average liver of this age, which is said to be 331 Gm.;[4] and composed one-seventh of the patient's total weight.

These tumors apparently occur most often in the right lobe of the liver. Characteristic displacement of the colon downward and posteriorly, but not forward as in the more common Wilm's tumor, a normal pyelogram and a tumor of the upper right abdomen more easily palpable anteriorly than in the flank should suggest the possibility of a primary liver tumor in an infant. Hamartoma cannot be distinguished from adenoma without exploration.

The technic of resection of the liver is fairly well-standardized.[7, 9, 11] Improved anesthesia and restorative therapy now permit resection of liver tumors with increased safety. Fibrin foam or gelatin sponge with thrombin should be useful hemostatic adjuncts. The febrile postoperative course of our patient was not adequately explained but may have been the result of liver trauma.

SUMMARY

Hamartoma of the liver is a structurally variable but benign and resectable tumor of the liver which occurs predominantly in infants. Despite the frequency of malignant liver tumors, surgical exploration is considered justifiable because of the occasional occurrence of hamartoma or other benign tumor, in which case a good prognosis may be given if the tumor is totally removed.

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