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Review article

Fetal and neonatal hepatic tumors

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Abstract

Background/Purpose: Although hepatic tumors are uncommon in the perinatal period they are associated with significant morbidity and mortality in affected patients. The purpose of this review is to focus on the fetus and neonate in an attempt to determine the various ways liver tumors differ clinically and pathologically from those found in the older child and adult and to show that certain types of tumors have a better prognosis than others.

Methods: The author conducted a retrospective review of perinatal hepatic tumors reported in the literature and of patients treated and followed up at Children's Hospital San Diego and Children's Hospital Los Angeles. Only fetuses and infants younger than 2 months with adequate clinical and pathologic data ere accepted for review. The period of patient accrual was from 1970 to 2005. Length of follow-up varied from 1 week to more than 5 years. Elevated α-fetoprotein level was defined as one significantly higher than that of the reporting institution's normal level for age group; laboratory values for this protein vary from one institution to the next and therefore it was not possible to assign one figure as a standard reference number. Discussion of the differential diagnosis and pathologic findings of hepatic tumors in the fetus and neonate are described elsewhere and will not be discussed here in detail (Perspect Pediatr Pathol 1978;4:217; Weinberg AG, Finegold MJ. Primary hepatic tumors in childhood. In: Finegold M, editor. Pathology of neoplasia in children and adolescents. Philadelphia, PA: WB Saunders, 1986; Am J Surg Pathol 1982;6:693; Pediatr Pathol 1983;1:245; Arch Surg 1990;125:598; Semin Neonatol 2003;8:403; Pediatr Pathol 1985;3:165; Isaacs H Jr. Liver tumors. In: Isaacs H Jr, editor. Tumors of the fetus and newborn. Philadelphia, PA: WB Saunders, 1997; Isaacs H Jr. Liver tumors. In: Isaacs H Jr, editor. Tumors of the fetus and infant: an atlas. Philadelphia, PA: WB Saunders, 2002).

Results: One hundred ninety-four fetuses and neonates presented with hepatic tumors diagnosed prenatally (n = 56) and in the neonatal period (n = 138). The study consisted of 3 main tumors: hemangioma (117 cases, 60.3%), mesenchymal hamartoma (45 cases, 23.2%), and hepatoblastoma (32 cases, 16.5%). The most common initial finding was a mass found either by antenatal sonography or by physical examination during the neonatal period. Overall, hydramnios was next followed by fetal hydrops, respiratory distress, and congestive heart failure, which were often related to the cause of death. Half of the fetuses and neonates with hepatoblastoma had abnormally elevated serum α-fetoprotein levels compared with 16 (14%) of 117 of those with hemangioma and 1 neonate with mesenchymal hamartoma. There were 76 (65%) examples of solitary (unifocal) hemangiomas and

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41 (35%) of multifocal (which included the entity diffuse hemangiomatosis) with 86% and 71% survival rates, respectively. Of 45 patients with mesenchymal hamartoma, of the 29 (64%) who had surgical resections, 23 (79%) survived. Patients with hepatoblastoma had the worst outcome of the group, for only 8 (25%) of 32 were alive. Half of patients with either stage 1 or 3 hepatoblastoma died; no patient with stage 4 survived. There was some relationship between histologic type and prognosis. For example, half of the patients with the pure fetal hepatoblastoma histology survived compared with those with fetal and embryonal histology where 30% survived. Fifteen of 32 hepatoblastoma patients received surgical resection with or without chemotherapy, resulting in 7 (47%) of 15 cures. The 56 fetuses and 138 neonates with hepatic tumors (hemangioma, mesenchymal hamartoma, and hepatoblastoma) had survival rates of 75%, 64%, and 25%, respectively. The overall survival of the entire group consisting of 194 tumors was 125 or 64%.

Conclusions: The study shows that clinical findings in fetuses and neonates with hepatic tumors are less well defined than in older children. Survival rates are much lower as well. When the clinical course is complicated by associated conditions such as stillbirth, fetal hydrops, congestive heart failure, severe anemia, or thrombocytopenia, the mortality rate is much greater. If the patient is mature enough and in a clinical condition where he or she can be operated on, survival figures approach those of the older child. Some hepatic tumors have a better prognosis than others. Neonates with focal (solitary) hepatic hemangiomas have the best outcome and fetuses with hepatoblastoma the worst. Although infantile hemangioma undergoes spontaneous regression, it may be life threatening when congestive heart failure and/or consumptive coagulopathy occur. Mesenchymal hamartoma is a benign lesion best treated by surgical resection, which usually results in cure. However, there are fatal complications associated with this tumor, ie, fetal hydrops, respiratory distress, and circulatory problems owing to a large space occupying abdominal lesion and sometimes stillbirth, all contributing to the death rate. Hepatoblastoma, the major malignancy of the fetus and neonate, is treated primarily by surgical resection. Pre- or postoperative chemotherapy is reserved for those patients with unresectable tumors or metastatic disease. The survival rate is much lower than that reported by multigroup prospective trials. Patients die from the mass effect caused by the tumor, which lead to abdominal distension, vascular compromise, anemia, hydrops, respiratory distress, and stillbirth. Metastases to the abdominal cavity, lungs, and placenta are other causes of death. Because of the danger of labor-induced rupture of the tumor and potentially fatal intraabdominal hemorrhage, cesarean delivery is recommended when a hepatic tumor is found on prenatal ultrasound.

Hepatic tumors seldom occur in the perinatal period. They comprise approximately 5% of the total neoplasms of various types occurring in the fetus and neonate [1-9]. Infantile hemangioma is the leading primary hepatic tumor followed in order by mesenchymal hamartoma and hepatoblastoma [1,4,5,10,11]. All 3 present clinically as an abdominal mass and are detected by antenatal sonography [7,9,12-14]. Including the total surgical and necropsy specimens, most hepatic tumors are metastatic rather than primary [1,4]. Neuroblastoma is the neoplasm that metastasizes most often to the liver in the fetus and neonate followed in rank by leukemia and renal tumors. Yolk sac tumor, rhabdomyosarcoma, and rhabdoid tumor are examples of other malignancies metastasizing to the liver in this age group [1,4]. During the first year of life, hepatoblastoma rather than hepatocellular carcinoma is the principal primary malignant hepatic tumor; less than 10% of hepatoblastomas occur in the perinatal period [1,4,15,16]. Hepatocellular carcinoma is rarely noted in patients younger than 6 years where often there is an associated underlying condition such as cirrhosis or congenital metabolic storage disease [4,15,16].

The classification of liver tumors and tumorlike conditions is listed in Table 1.

1. Results

One hundred ninety-four fetuses and neonates presented with hepatic tumors diagnosed antenatally (n = 56) and in the neonatal period (n = 138). The most common initial finding was a mass detected either by antenatal sonography or by physical examination during the neonatal period. Overall, a maternal history of hydramnios was next followed by fetal hydrops, respiratory distress, and congestive heart failure. One hundred sixty-two tumors (83.5%) were classified as histologically benign and 32 (16.5%) as malignant. One hundred seventeen fetuses and neonates presented with hepatic hemangioma diagnosed antenatally (n = 33) and at birth (n = 84). The most common initial finding in the fetus was a hepatic mass detected by antenatal sonography followed in rank by anemia, hydrops, hydramnios, congestive heart failure, thrombocytopenia, and disseminated intravascular coagulation, which contributed to its demise. In the neonate, hepatomegaly was the leading finding. Congestive heart failure, cutaneous hemangiomas, a murmur (bruit), respiratory distress, cardiomegaly, thrombocytopenia, and hepatic mass were next. α-Fetoprotein levels were elevated in 5 fetuses and in 11 neonates (16/117 or 14%) with