Malignant liver tumors account for approximately 1.1% of all childhood tumors in the United States according to the Surveillance, Epidemiology, and End Results (SEER) program cancer registries, with an annual incidence rate of 1.8 cases per million children younger than 15 years. Two-thirds of all liver masses occurring in children are malignant.(1) Hepatoblastoma accounts for two thirds of liver tumors in children.(2) Other liver malignancies in children include hepatocellular carcinoma, sarcomas, germ cell tumors, and rhabdoid tumors. Benign tumors of the liver in children include avascular tumors, hamartomas, adenomas, and focal nodular hyperplasia. Liver cancer represented 2% of all malignancies in infants in the early 1980s with the incidence doubling to 4% 10 years later.(2)

Hepatoblastoma

It is the most common liver tumor in the pediatric population.(3) The cells in the hepatoblastomas are composed of cells resembling the pluripotent hepatoblasts in developing fetal and embryonic liver. The mean age of children presenting with this tumor is 18 months. Only 5% of hepatoblastomas develop after the age of 4 years. Histologically, these tumors can be divided into pure fetal, epithelial, mixed epithelial/mesenchymal tissue and the small cell undifferentiated type. Epithelial type is the most common while the small cell variety has the most dismal prognosis. Any child presenting with a liver lesion would require a triple phase abdominal CT Scan with a CT scan of the chest to stage the disease. Alfa feto protein levels would be required. Different groups have different protocols as regards the requirement of a biopsy prior to treatment. The SIOPEL group insists on a biopsy inspite of a high AFP level in a patient with a liver mass since they give neoadjuvant chemotherapy in all patients.(4) The Childrens Oncology Group protocol recommends upfront surgery if the imaging indicates resectability while those with borderline resectability are advised a biopsy prior to chemotherapy. The German group, however, regards biopsy as unnecessary in patients aged between 6 months and 3 years with unequivocal clinical findings, imaging and elevated alpha-fetoprotein (AFP) level. Current protocols favor image-guided needle biopsy with automated or semiautomated cutting needles (16- or 18-gauge) provide large cores of tumour. A coaxial approach is best, because this allows multiple cores to be obtained with a single puncture of both the liver and the tumour itself. The biopsy tract should be embolized through the outer needle at the end of the procedure, either with thrombogenic plugs of gelatin foam, or with a slurry of collagen. Since the European and American protocols differ, so do their staging systems.
Surgical resection forms the cornerstone of treatment in hepatoblastoma. Studies show that about 25% to 30% of hepatoblastomas are amenable to primary resection. Those with pure fetal histology have been cured without adjuvant chemotherapy. For all other histologies and for stage 2 disease (microscopic residual after surgery, 4 cycles of a combination of cisplatin, 5-fluorouracil, and vincristine (C5V) are given. (5) Primary resection should be attempted only if one is sure of the complete resectability. Positive margins are an adverse prognostic factor. If there are any doubts on the resectability, neoadjuvant chemotherapy must be given. For a tumor deemed unresectable at diagnosis or a patient with metastatic disease, current therapy in the United States consists of 4 cycles of chemotherapy, with either resection or liver transplantation after cycle 4, followed by 2 more cycles. The current recommendations of the Children’s Oncology Group are to start with C5V for 2 cycles. If there is poor response (little or no tumor shrinkage or an inadequate drop in serum alpha-fetoprotein), doxorubicin should be added to the regimen. Recently, a recommendation was made to add doxorubicin to C5V at the initiation of chemotherapy for stage IV patients and to consider it with stage III. Liver transplantation is recommended when complete tumor excision by partial hepatectomy is unlikely, such as cases involving PRETEXT IV tumors (unless clear downstaging of a unifocal tumor to PRETEXT III is shown after preoperative chemotherapy), multifocal PRETEXT III, and central tumors involving the inferior vena cava, all 3 hepatic veins, or the main portal vein or both its right left and right branches. Involvement of the major liver vessels does not contraindicate transplantation if all tumors can be excised at the time of hepatectomy. (1,4)
Hepatocellular carcinoma

Hepatocellular carcinoma (HCC) is the most common hepatic malignancy of adolescence. Hepatitis B virus can cause HCC as early as age 4 following perinatal transmission from infected carrier mothers. Vaccination and perinatal administration of hepatitis B immunoglobulin have already reduced the incidence dramatically. Surgery offers the best chance of cure for this condition. As in hepatoblastoma, a serum alpha fetoprotein and a triple phase CT abdomen would be required. Anatomical resection with a 1 cm margin would offer the best chance of cure. Most children with HCC would be cirrhotics. It is important to assess the functional quality of the underlying liver prior to deciding on the line of treatment. Resection would be an option only in Child A cirrhotics. If there is any doubt on the functional capacity of the remnant liver, a portal vein embolization may be carried out to assess the regenerative capacity of the liver. All other cirrhotics with HCC would be candidates for a Liver transplant if they fulfill the Milan criteria (a single tumor 5 cm or less in diameter or up to 3 tumors, each 3 cm or less in diameter; absence of macroscopic portal vein invasion; and absence of recognizable extrahepatic disease). For those who are beyond the criteria for transplant and are unresectable, options would include chemoembolization, radioembolization. Sorafenib may be considered in select cases. HCC included in the last Children’s Oncology Group liver tumor trial showed a 5-year overall survival rate for patients with stage 1 (resectable) tumors of 88%, whereas patients with stage 3 and 4 tumors had dismal rates of 23% and 10%.

Other liver tumors

Sarcomas in children take 1 of 3 forms: (1) rhabdomyosarcoma, which arises in relation to the larger bile ducts, typically in early childhood; (2) embryonal or undifferentiated sarcoma, which is usually detected in children between 6 and 10 years and occasionally is preceded by or occurs simultaneously with the benign mesenchymal hamartoma; and (3) angiosarcoma, which is extremely rare and even more rarely is antedated by a benign hemangioendothelioma in infancy. Biliary rhabdomyosarcoma presents a surgical challenge, and in a review of 25 patients over 26 years, gross total resection was achieved in only 6; only 2 of those had negative margins. However, the 5-year survival rate was 75% because of the tumor’s sensitivity to chemotherapy and radiation. Therefore, heroic resections or transplants are not generally recommended. Undifferentiated sarcoma recently has been successfully treated. In a series of 17 patients, 10 were alive in the first complete response after a combination of resection and chemotherapy. Angiosarcoma is a very aggressive tumor that often presents in both lobes, typically rendering complete resection highly unlikely. It is generally chemoresistant, but rare successes have been reported.

REFERENCES


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