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## GELLIS & KAGAN'S

# CURRENT PEDIATRIC THERAPY

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## SPONTANEOUS BACTERIAL PERITONITIS

Spontaneous bacterial peritonitis may occur in patients in whom cirrhosis is complicated by ascites. Symptoms and signs include fever, lethargy, poor feeding, vomiting, diarrhea, diffuse abdominal pain, abdominal distention and rigidity, and diffuse rebound tenderness. In up to 15 per cent of patients, however, the condition may be asymptomatic. Diagnostic paracenthesis is indicated in all suspected cases. The ascitic fluid should be assessed for cell count and differential, total protein, lactate, pH (with concomitant capillary or arterial pH), and microbiologic studies, including a Gram stain and both aerobic and anaerobic cultures. Antibiotic therapy should be initiated in all patients with an ascitic fluid polymorphonuclear leukocyte count of more than 500 cells/mm$^3$ or in any patient with signs of peritonitis and polymorphonuclear leukocytes of more than 250 cells/mm$^3$. Before sensitivity is known, ampicillin (200 mg/kg/day), gentamicin (7.5 mg/kg/day), and clindamycin (30 mg/kg/day) should be started. Decreased ascitic fluid pH and increased lactate may help in establishing the diagnosis; however, awareness of the condition remains the key to diagnosis.

## LIVER TRANSPLANTATION

Unfortunately, in many patients with chronic liver disease and in hepatic failure, orthotopic liver transplantation may be the only remaining consideration. Poor prognostic signs indicative of the need for liver transplantation include (1) serum bilirubin greater than 10 to 15 mg/dl, (2) serum albumin less than 2.5 g/dl, (3) presence of hepatic encephalopathy, (4) prothrombin time greater than 5 seconds above control, (5) presence of the hepatorenal syndrome, (6) recurrent episodes of cholangitis, (7) spontaneous bacterial peritonitis or septicemia, (8) intractable ascites, and (9) the development of focal hepatocellular carcinoma. In the past, the requirement for a size-matched donor liver had contributed to the difficulty in obtaining organs for pediatric recipients. Currently, the use of segmental transplantation has increased the proportion of candidates transplanted and reduced the overall mortality.

# TUMORS OF THE LIVER

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Increasing numbers of hepatic mass lesions are found incidentally by advanced imaging technology. Although most of these "incidental" tumors are histologically benign and do not require any therapy, they must be thoroughly investigated. Modern imaging technology is quite efficient in detecting small lesions but is not effective in producing pathognomonic findings of many hepatic lesions other than hemangiomas and cysts. Percutaneous needle biopsy often fails to establish a definitive diagnosis because of its limited sampling, and it can cause serious hemorrhage when unwisely performed for vascular lesions.

Major hepatic resections can now be performed with minimum operative risk (less than 5 per cent), but no surgeon should explore a hepatic mass without having the competence to perform all of the major resections, including a right and left trisegmentectomy.

## BENIGN TUMORS

Most of the benign tumors of the liver are asymptomatic and are found incidentally during studies for other disorders or during abdominal operations. The general approach to a small incidental tumor (less than 3 cm in diameter) that is considered benign is close observation after "thorough" investigation. When the tumor changes its imaging characteristics or increases in size during close observation, it must be immediately excised. Larger incidental tumors, other than asymptomatic cavernous hemangiomas, deserve excisional therapy unless unequivocal benignity is confirmed.

Hemangiomas are the most common benign tumors of the liver. Giant cavernous hemangiomas should be treated by surgical excision, particularly when they are symptomatic (e.g., pain, mass-related complaints) or are found to have a necrotic center inside. The majority of giant cavernous hemangiomas require lobectomies or trisegmentectomies of the liver, but some located on the surface of the liver or pedunculated can be enucleated along pseudocapsular margins without significant loss of normal liver tissue. Ligation or embolization of the feeding hepatic artery and radiation therapy may be hazardous and do not have long-standing effects on the course of giant cavernous hemangiomas.

Infantile hemangioendotheliomas are most often seen in infants during the first 6 months of life and are distinct from cavernous hemangiomas. The lesions should be excised by anatomic hepatic resection whenever possible. Treatment with prednisone, diuretics, and digoxin can be used initially when the patient's condition prohibits surgery or the lesion is too extensive for resection. Response to prednisone may allow surgery to be performed safely in a few weeks. In extensive lesions, radiation to the liver may be used after pathologic diagnosis is confirmed. Favorable responses to steroids, radiation, and hepatic artery ligation or embolization have been reported. The treatment should be vigorous, because complete regression and cure are possible.

Other benign tumors include liver cell adenoma, focal nodular hyperplasia, hematoma, mesenchymoma, teratoma, and fibroma. Radiologic differentiation of these benign tumors from malignant tumors is unreliable. Pathologic confirmation of benign tumors is mandatory for each lesion. Large benign tumors should be treated by surgical excision, particularly when they are symptomatic. Adenoma has a tendency to rupture and cause life-threatening hemorrhage. Some adenomas cannot be easily differentiated from low-grade hepatocellular carcinoma by needle biopsies. If the diagnosis is uncertain, the lesion should be excised with an adequate margin without delay.

Congenital hepatic cysts are usually asymptomatic and do not require any therapy. Although aspiration, internal drainage, marsupialization, fenestration, and sclerotherapy have all been recommended for symptomatic congenital cysts, these approaches are no longer justifiable for the treatment of single or localized multiple cysts because hepatic resections can be performed quite safely now.

## MALIGNANT TUMORS

The most common primary malignant tumor of the liver in children is hepatoblastoma. Hepatocellular carcinoma is the second most common and usually occurs in older children. Sarcomas of the liver, such as rhabdomyosarcoma and angiosarcoma, are rare. None of these has a favorable outlook, but fibrolamellar hepatocellular carcinoma, which is common in older children and young adults, has a better prognosis than other types of malignancy.

The treatment for all malignant liver tumors is complete surgical excision by anatomic hepatic resection. Hepatic resections of more than the right or left lobe of the liver can be performed quite safely. For example, a large tumor occupying the right lobe of the liver and the medial segment of the left

lobe can be resected by right hepatic trisegmentectomy, leaving only the left lateral segment of the left lobe (to the left of the falciform ligament), or a large tumor occupying the left lobe and the anterior segment of the right lobe can be resected by left hepatic trisegmentectomy, leaving only the posterior segment of the right lobe (posterior to the right hepatic vein). These major hepatic resections can now be performed by experienced surgeons with less than a 5 per cent operative mortality.

We have found that computed tomography scan or magnetic resonance imaging is most useful in assessing the extent of the tumor, but findings can be misleading, particularly when a large tumor distorts normal anatomic boundaries. If the resectability is uncertain after extensive preoperative investigation, the patient should be referred to a surgeon who is experienced in major hepatic resection rather than undergo exploratory celiotomy by someone who is unprepared to undertake a definitive procedure.

After curative hepatic resection, we usually recommend that patients receive adjuvant chemotherapy for at least 1 year. We have been using combination chemotherapy with doxorubicin, dactinomycin, vincristine, and cyclophosphamide, and often mitomycin or cisplatin. The value of this approach has not been validated in randomized trials, but the patients who have received adjuvant chemotherapy after curative resections of large tumors have seemed to have longer tumor-free survival.

In general, liver transplantation (total hepatectomy and liver replacement) cannot offer good long-term results when applied to large malignant tumors that cannot be removed by subtotal hepatectomy. However, liver transplantation can result in a cure (more than 5-year survival) on more than isolated occasions. The most favorable lesions for transplantation, just as with resection, are the fibrolamellar hepatoma and epithelioid hemangioendothelial sarcoma. On the other hand, most of the patients who have received liver transplantation for other end-stage liver diseases, such as tyrosinemia and alpha$_1$-antitrypsin deficiency disease, and whose malignant tumors were small and incidental, survived tumor-free for several years.

The most common metastatic liver tumors in children are neuroblastoma and Wilms' tumor. Although chemotherapy and radiation therapy may be helpful in treating these metastatic tumors, the lesion should be excised whenever possible, particularly if it is localized to part of the liver. Hepatic resections for metastatic tumors are much safer than those for primary malignancy.

# PORTAL HYPERTENSION

JOHN T. BOYLE, M.D.

Portal hypertension in childhood may be classified as *intrahepatic* or *extrahepatic*. Intrahepatic portal hypertension results from cirrhosis, which in the United States is most commonly caused by biliary atresia, chronic viral or autoimmune hepatitis, or alpha$_1$-antitrypsin deficiency. Extrahepatic portal hypertension is most commonly caused by portal vein thrombosis (cavernous transformation of the portal vein) or by hepatic venous or inferior vena caval obstruction (Budd-Chiari syndrome). The etiology in individual patients is usually suggested by real-time ultrasonography and Doppler flowmetry. Although anatomy of the portal circulation is best defined by angiography, information such as site of portal vein obstruction, distribution of collaterals, and dynamics of portal flow is of therapeutic importance only when shunt surgery is being contemplated.

Portal hypertension results in splenomegaly and esophageal varices. Clinical presentations include asymptomatic splenomegaly (with or without laboratory evidence of thrombocytopenia, anemia, or neutropenia), upper gastrointestinal (GI) bleeding from ruptured esophageal or gastric varices, or, rarely, ascites or bleeding hemorrhoids. In patients who present for the first time with upper GI bleeding, the possibility of bleeding esophageal varices is primarily suggested by a past history of jaundice, hepatitis, blood transfusion, sepsis, shock, chronic right-sided heart failure, pulmonary hypertension, exchange transfusion, omphalitis, or umbilical vein catheterization.

Because there are few reports in the pediatric literature regarding the management of variceal bleeding, therapy is based primarily on the adult experience. It is important to emphasize that there is no consensus on management policy in pediatric patients before, during, or after variceal bleeding.

## TREATMENT

### Management of Splenomegaly in Patients with Portal Hypertension

Every effort should be made to ensure that a child with portal hypertension leads as normal a life as possible. Normal school activity should be allowed with the exception of contact sports and physical education activities involving prolonged running or jumping. Oftentimes, education of school officials is required to explain signs and symptoms of bleeding.

Although hypersplenism is a common complication of splenomegaly in patients with portal hypertension, bleeding and infection related to thrombocytopenia and neutropenia are rare. Hypersplenism is not an indication for splenectomy in such patients. Nevertheless, the presence of fever in a patient with portal hypertension demands immediate and careful evaluation to identify a source of infection. It is my practice to recommend pneumococcal immunization to patients with cirrhosis and hypersplenism.

### Prophylactic Management to Prevent the First Variceal Bleed

Patients should avoid nonsteroidal anti-inflammatory agents, which may cause GI inflammation or ulceration. Coughing associated with upper respiratory infections should be treated with antitussive agents.

The risk of first-time variceal bleeding in children with known portal hypertension is unknown. In adults, only 25 to 30 per cent of patients with esophageal varices will experience variceal hemorrhage. Therefore, the risk-benefit ratio is widely believed to be against the use of repeated sclerotherapy and shunt surgery as prophylactic therapy prior to the first variceal bleed. In adults, a number of randomized, double-blind trials have now reported a statistically significant reduction in the frequency of variceal bleeding for patients while on chronic beta-blocker therapy. Results have been best in patients with Child Class A or B (an index of liver dysfunction based on serum albumin, serum bilirubin, prothrombin time, and the presence of ascites and encephalopathy).

The main argument for prophylactic use of beta-blockade therapy is that there is little to lose. In the absence of cardiac decompensation, heart block, and reactive airway disease, propranolol appears to have a wide margin of safety in pediatric patients. It is imperative to remember that during acute bleeds propranolol may mask compensatory hemodynamic changes, a fact that must be taken into account during resuscitative efforts.

Patients with documented portal hypertension should undergo endoscopy at least every 2 years. In patients judged likely to be compliant, a decision to use prophylactic propran-