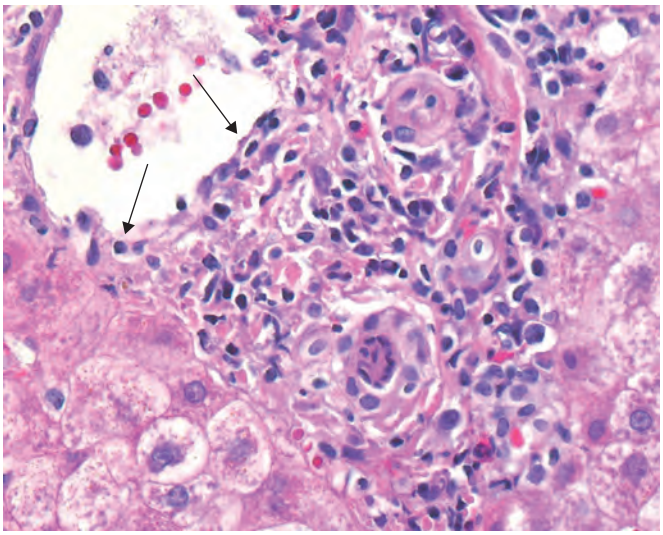

Figure 18-49 Transplanted liver with acute cellular rejection. Note the mixed inflammatory cell infiltration including eosinophils in portal tracts, bile duct damage, and endotheliitis. Arrows show subendothelial lymphocytes.

In a very small subgroup of pregnant women (0.1%), hepatic complications develop that are directly attributable to pregnancy. These disorders include preeclampsia and eclampsia, acute fatty liver of pregnancy, and intrahepatic cholestasis of pregnancy. In extreme cases, eclampsia and acute fatty liver of pregnancy may be fatal.

Preeclampsia and Eclampsia

Preeclampsia affects 3% to 5% of pregnancies and is characterized by maternal hypertension, proteinuria, peripheral edema, and coagulation abnormalities (Chapter 22). When hyperreflexia and convulsions occur, the condition is called *eclampsia* and may be life-threatening. Alternatively, subclinical hepatic disease may be the primary manifestation of preeclampsia, as part of a syndrome of *h*emolysis, *e*levated *l*iver enzymes, and *l*ow *p*latelets, dubbed the *HELLP syndrome*.

MORPHOLOGY

In preeclampsia, the periportal sinusoids contain fibrin deposits associated with hemorrhage into the space of Disse, leading to periportal hepatocellular coagulative necrosis. Blood under pressure may coalesce and expand to form a hepatic hematoma; dissection of blood under Glisson capsule may lead to catastrophic hepatic rupture in eclampsia (Fig. 18-50). Patients with hepatic involvement in preeclampsia may show modest to severe elevation of serum aminotransferases and mild elevation of serum bilirubin. Hepatic dysfunction sufficient to cause a coagulopathy signifies far advanced and potentially lethal disease. Mild cases may be managed conservatively. Termination of pregnancy is required in severe cases. Women who survive mild or severe preeclampsia recover without sequelae.

Acute Fatty Liver of Pregnancy

Acute fatty liver of pregnancy presents with a spectrum of disorders ranging from subclinical or modest hepatic dysfunction (evidenced by elevated serum aminotransferase levels) to hepatic failure, coma, and death. It is a rare disease affecting 1 in 13,000 deliveries. Affected women present in the latter half of pregnancy, usually in the third trimester. Symptoms are directly attributable to incipient hepatic failure, including bleeding, nausea and vomiting, jaundice, and coma. In 20% to 40% of cases, the presenting symptoms may be those of coexistent preeclampsia.

MORPHOLOGY

The diagnosis of acute fatty liver of pregnancy rests on biopsy identification of the characteristic diffuse microvesicular steatosis of hepatocytes. In severe cases there may be lobular disarray with hepatocyte dropout, reticulin collapse, and portal tract inflammation, making distinction from viral hepatitis difficult.

While this condition most commonly runs a mild course, women with acute fatty liver of pregnancy can progress within days to hepatic failure and death. The primary treatment is termination of the pregnancy. The pathogenesis of this disease is unknown, but mitochondrial dysfunction has been implicated. In a subset of patients, both mother and father carry a heterozygous deficiency in mitochondrial long-chain 3-hydroxyacyl coenzyme A (CoA) dehydrogenase. The homozygous-deficient fetuses fare well during pregnancy but cause hepatic dysfunction in the mother, because long-chain 3-hydroxylacyl metabolites produced by the fetus or placenta enter the maternal circulation and cause hepatic toxicity. This is a rare instance of the fetus causing metabolic disease in the mother.

Intrahepatic Cholestasis of Pregnancy

The onset of pruritus in the third trimester, followed in some cases (10-25%) by darkening of the urine and occasionally light stools and jaundice, heralds the development of this enigmatic syndrome. Serum bilirubin (mostly conjugated) rarely exceeds 5 mg/dL; alkaline phosphatase may be slightly elevated. The level of bile salts is increased greatly. The altered hormonal state of pregnancy seems to combine with biliary defects in the secretion of bile salts or sulfated progesterone metabolites to engender cholestasis.

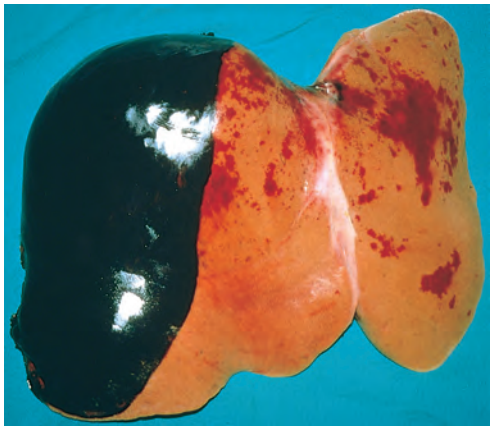

Figure 18-50 Eclampsia. Subcapsular hematoma dissecting under Glisson capsule in a fatal case. (Courtesy Dr. Brian Blackbourne, Office of the Medical Examiner, San Diego, Calif.)