A 74-year-old man from Barbados was admitted to the hospital for evaluation of progressive lethargy and confusion. His medical history was remarkable for diabetes mellitus, hypertension, alcohol abuse, and cirrhosis of the liver. He had not received any medical care for many years and was brought to the United States by his family 2 months before admission. At presentation, he was jaundiced and obtunded.

Physical examination documented grade III hepatic encephalopathy, ascites, hepatomegaly, and a bruit in the right upper quadrant. Laboratory evaluation was consistent with advanced liver failure; tests revealed an international normalized ratio (INR) of 3 (reference range, 0.8–1.0); serum albumin, 16 g/L (reference range, 35–50 g/L); and total bilirubin, 21.41 μmol/L (7.1 mg/dL) (reference range, 5–21 μmol/L [0.1–1.0 mg/dL]). Abdominal ultrasound revealed massive ascites and a mass in the right lobe of the liver. The patient’s serum a-fetoprotein level was 320 000 μg/L (reference range, 0–10 μg/L). The patient was treated with oral lactulose with minimal clinical improvement and died in the hospital 48 hours later.

At autopsy, the liver revealed a large, multinodular, and focally necrotic yellow mass replacing 90% of the right lobe and 40% of the left lobe. The tumor was extending and eroding into the lumen of the inferior vena cava (Figure 1). There was invasion and thrombosis of the portal and hepatic veins by the mass (Figure 2).

Microscopic examination confirmed hepatocellular carcinoma (HCC) arising in a background of micronodular cirrhosis (Figure 3). The tumor cells were arranged in trabecular and solid patterns with nuclear pleomorphism, prominent nucleoli, and scant basophilic cytoplasm. There was extensive invasion of intrahepatic vascular channels (Figure 4). Multiple metastatic nodules were identified within the lung parenchyma.

**COMMENT**

Hepatocellular carcinoma is considered to be one of the major malignant diseases worldwide, and more than 400 000 new cases are diagnosed every year. Its principal risk factors have been identified, and there is now a better understanding of the complex processes involved in its pathogenesis and prevention. Despite this progress, the results of treatment continue to be disappointing and the prognosis is poor.

Hepatocellular carcinoma runs a silent course in the early stages. Often the disease is advanced at the time the patient is first seen. The liver is almost invariably enlarged. An arterial bruit can be heard over the liver in 7% to 29% of patients and is thought to reflect the highly vascular nature of the tumor.

At presentation, 20% to 50% of patients have ascites. Ascites results either from portal hypertension secondary to cirrhosis, invasion of the portal or hepatic veins by tumor, or involvement of the peritoneum by direct invasion or metastatic spread. α-Fetoprotein is the most important tumor marker for the diagnosis of HCC. However, many HCCs do not produce α-fetoprotein or elevate its serum level only minimally, making early diagnosis difficult with this marker alone. Hepatocellular carcinoma may take 3 forms: nodular, massive, or diffuse. The nodular variety accounts for about 75% of HCCs and usually coexists with cirrhosis. The massive type of tumor is most common in noncirrhotic livers of younger patients. This type appears as a large circumscribed mass occupying a substantial portion of the liver, often with small satellite nodules. The diffusely infiltrating variety is rare. A large portion of the liver is homogeneously infiltrated with indistinct minute tumor nodules, which may be difficult to distinguish from regenerating nodules of cirrhosis.

The portal vein and its branches are occluded by tumor in as many as 70% of Japanese and black African patients. This complication is seen less often in the hepatic veins, but when the hepatic veins are occluded, the tumor may propagate into the lumen of the inferior vena cava and even into the right atrium. A size larger than 3 cm, high histologic grade, the presence of a fibrous capsule, necrosis, mitotic rate of more than 4 mitoses per 10 high-power fields, peliotic changes, the presence of tumor giant cells, high platelet count, and the absence of cirrhosis are all significantly correlated with portal venous invasion.

Ultrasonography can detect invasion of the portal and hepatic venous systems and can demonstrate flow patterns within the tumor. Computed tomography enhanced with the use of contrast material also shows the course, caliber, and patency of the hepatic and portal circulation.

Magnetic resonance imaging provides another way of distinguishing HCC from normal liver, as the use of contrast material increases the accuracy of detection of vascular invasion.
Despite the progress in detection of HCC using imaging techniques, the prognosis is extremely poor; cure is only possible with liver transplantation for an early tumor without extensive vascular invasion or extrahepatic spread. Encephalopathy and liver failure are always ominous signs.²

References