Benign Liver Cell Adenoma Associated With Use of Oral Contraceptive Agents

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A benign hepatic adenoma in a young woman taking oral contraceptives for 7 years is reported. The diagnosis must be suspected in any young woman taking oral contraceptive agents who develop signs and symptoms of acute cholecystitis with hepatomegaly or mass, or when signs and symptoms of non-traumatic intra-abdominal hemorrhage are present. Rupture of the tumor is a life-threatening complication. Treatment should be either hepatic lobectomy or wide local resection.

A VARIETY of complications associated with the use of oral contraceptive agents have been described.[1,9,11] Since the report by Baum et al.[2] in 1973 of 7 cases of benign hepatoma in young women taking oral contraceptive agents, there have been isolated case reports of such tumors.[3,7,10]

This paper reports another case of hepatic adenoma which developed in a 31-year-old woman taking oral contraceptive agents for 7 years.

Case Report

A 31-year-old Caucasian woman was admitted to the City Hospital Center at Elmhurst because of an acute onset of right upper quadrant abdominal pain associated with nausea, vomiting and fever on November 6, 1974. The pain was colicky and was radiated to the back. There was no history of fatty food intolerance, jaundice or melena. However, one year prior to admission on routine physical examination she was told that her liver was slightly enlarged and liver function was normal. She had been taking oral contraceptive agent (Ortho Novum 2 mg.) for the past 7 years. Physical examination on admission showed a well developed, well nourished female in acute distress complaining of severe right upper quadrant abdominal pain. Blood pressure was 160/90 mmHg. Body temperature was 100.6 F and pulse was 82 per minute. Positive findings were confined to the abdomen. There was tenderness in the right upper quadrant and a poorly defined mass was palpable 8 to 10 cm below the right costal margin. Laboratory tests showed; hemoglobin 12, hematocrit 37%, WBC 13,400 cumm with a shift to left. Alkaline phosphatase 167 mu/ml, LDH 460 mu/ml, SGOT 250 mu/ml, bilirubin 1.0 mg%, amylase 117 dye units, prothrombin time was 12.2/11/5 seconds.

The clinical diagnosis was acute cholecystectomy. She was treated with intravenous fluids and systemic antibiotics over the following 30 hours in the hospital; despite this, temperature rose to 103.2F and abdominal pain increased. Hematocrit dropped to 28% from 37%, and WBC count rose to 17,000 cumm with a shift to left. Oral cholecystography visualized a normal gallbladder without stones. Intravenous pyelography revealed a normal collecting systems, but showed downward depression of the right kidney probably by an enlarged liver. Intra-abdominal hemorrhage was suspected, and emergency laparotomy disclosed a large vascular tumor in the liver replacing the right lobe. There was no evidence of bleeding into the free peritoneal cavity. As the nature of the tumor was not clear, further surgery was postponed. During the immediate postoperative period, ^{198}Au colloid liver scan showed a filling defect involving most of the right lobe of the liver. The early phase of technetium scan showed pooling of isotope in the right lobe of the liver; then a large defect developed in this area at a later phase. Celiac and selective hepatic angiogram confirmed these findings demonstrating a large mass involving most of the right lobe of the liver with clearly defined margins. A peripheral arterial blood supply with penetrating central vessels was seen. No venous lakes or arteriovenous shunts were present and there was no evidence of portal or hepatic vein involvement by the tumor (Fig. 1). Alpha fetoprotein and hepatitis associated antigen were negative. Liver biopsy was not performed.

At laparotomy, one week after the initial surgery, a well circumscribed, non-encapsulated tumor was found in the right lobe of the liver which extended into the pelvis.

The tumor was highly vascular with blood vessels on the surface (Fig. 2). The porta hepatis was not involved by the tumor. There was no lymph node enlargement; the left lobe of liver was completely free from the tumor. Following right hepatic lobectomy and cholecystectomy, the patient had an uneventful recovery.

On cross section, the specimen consisted of a tumor with a large necrotic central area filled with blood clots (Fig. 3). The tumor measured 18 × 16 × 12 cm. The margins of resection were free of tumor. There was no

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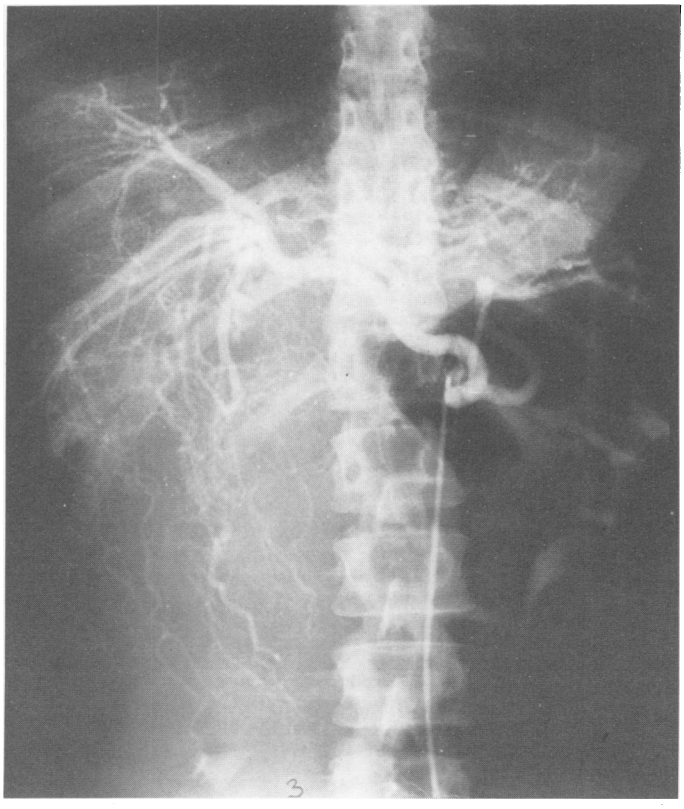

FIG. 1. Celiac angiogram shows a large highly vascular mass in the right lobe of the liver supplied by a branch from the right hepatic artery.

tumor thrombus in the major blood vessels. Microscopically, the tumor consisted of well differentiated liver cells with single or double liver cell cords or occasionally compacted liver cell arrangement. No normal lobular architecture or portal traits could be identified in the tumor tissue. Nuclear atypism was occasionally seen, but no mitoses were found. There was no vascular or direct invasion into the normal liver tissue. This tumor was described as a liver cell adenoma (Fig. 4).

Discussion

It has been shown that administration of steroid compounds causes a variety of effects on liver parenchyma[4]; androgenic steroids are known to be closely associated with hepatocellular carcinoma.[6,8,12] Hepatic adenoma is a rare tumor. Increasing number of reports in recent years of benign hepatic adenoma arising in the livers of young women taking oral contraceptives strongly suggest association between oral contraceptives and benign hepatic adenoma.

Hepatic adenomata vary in size, shape and appearance. Usually, the tumor is well circumscribed and not encapsulated. Some are hardly distinguishable from normal liver in color and texture. Others are well demarcated and are green from retained bile. Marked vascularity is often noted but may not be present. On cross section, it is common to find necrotic foci filled with clotted blood. Microscopically, they are comprised of normal looking hepatocytes forming cords and sinuses. Lobulation is absent as are portal triads and central veins. Peliosis hepatis is often present.[11] All but two of the reported cases involved women in their twenties and thirties with a several year history of taking oral contraceptive agents, not always consecutively, nor of the same dosage. One woman took the oral contraceptive agents for only 6

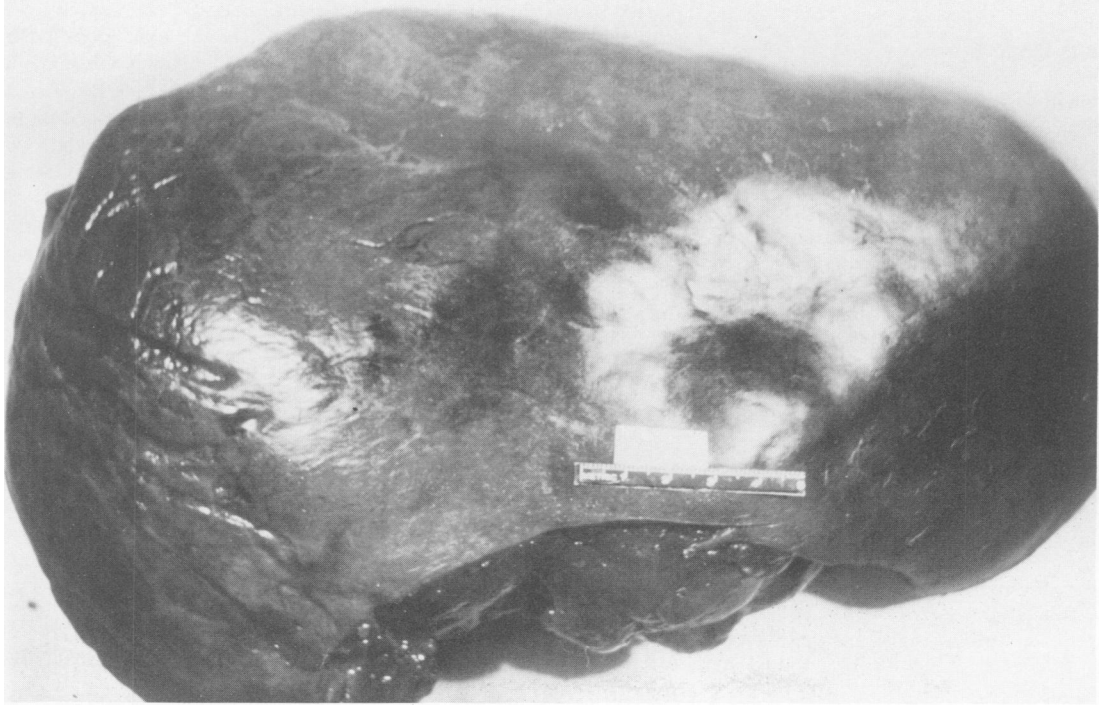

FIG. 2. Gross specimen showing shiny encapsulated tumor. Note the many vessels.

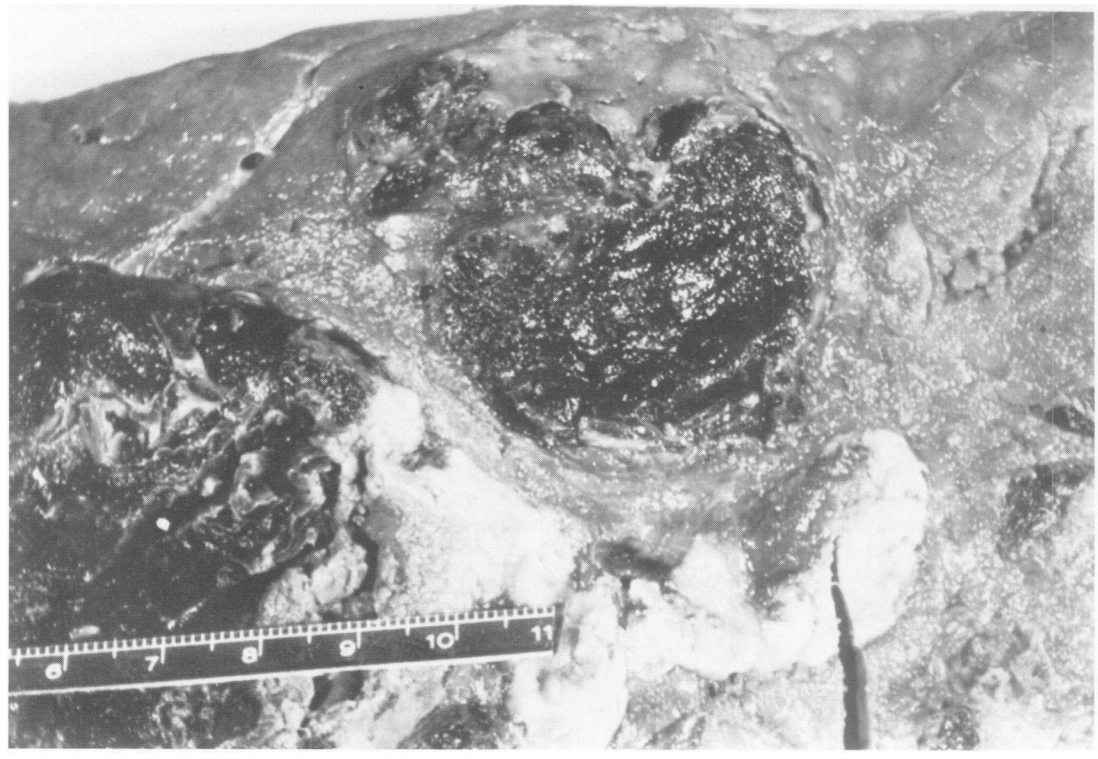

FIG. 3. The cut section showing a well circumscribed and encapsulated tumor mass with central necrotic area filled with clotted blood.

months,[2] while another had never used oral agents and was 9 months pregnant at the time of death from rupture of the tumor.[3] Considering the number of women using oral contraceptive agents, the incidence of this tumor is very low.

The presenting symptoms vary and can be divided into three groups: (1) signs and symptoms of acute cholecystitis. Signs are usually minimal and progressive. One woman treated as an outpatient died within several hours from tumor rupture.[5] (2) signs and symptoms of an acute

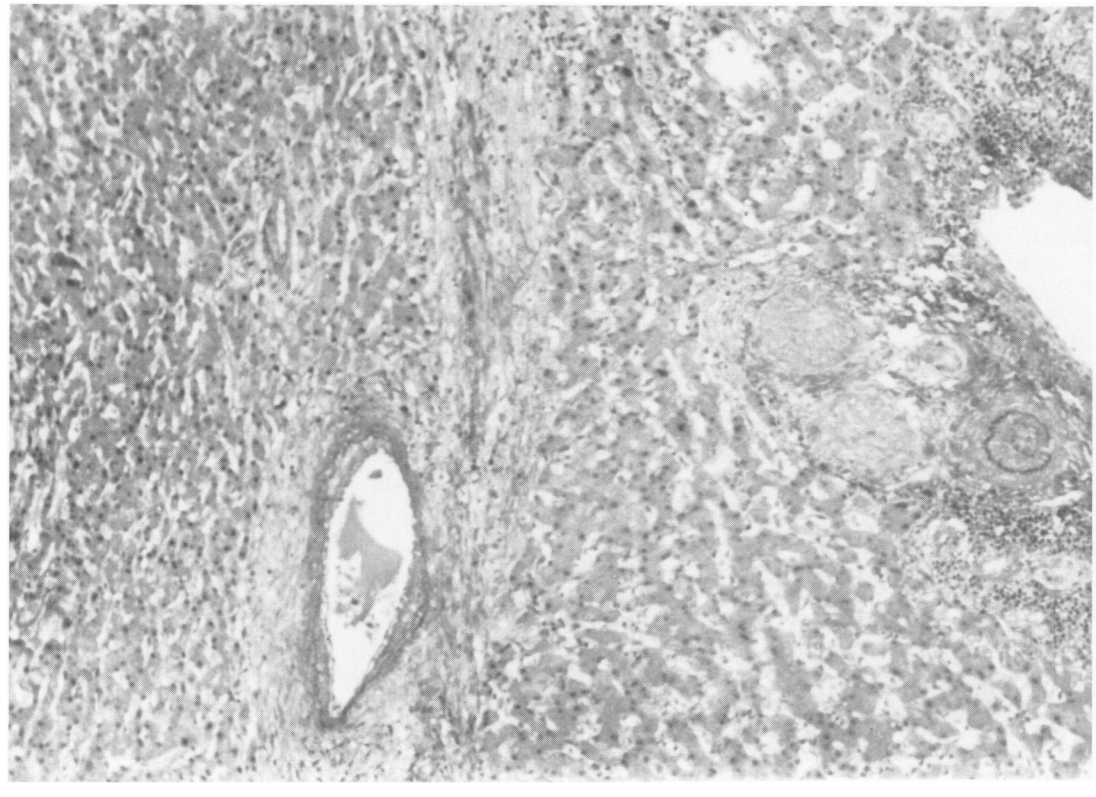

FIG. 4. Microscopic picture shows well-differentiated liver cells arranged in cords. Note the absence of tubular architecture of the liver.

abdomen with existing or impending shock as a result of hemorrhage from the tumor; (3) patients who are asymptomatic with an enlarged liver discovered on routine examination. Patients in the first group often progress into the second group. Approximately one third of the reported cases died on arrival to the hospital or during the preoperative period as a result of hemorrhagic shock from non-traumatic rupture.

Diagnosis is difficult. Hepatic scanning and antiography are most helpful but may not be conclusive. Any form of liver biopsy is to be avoided, since this tumor is highly vascular.

Treatment is the removal of tumor whenever possible.

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