An 18-Year-Old Man With Abdominal Pain, Weight Loss, and Liver Cyst

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An 18-year-old obese man without significant past medical history presented to an outside hospital complaining of 2 months of sharp, nonradiating right upper quadrant pain and 7-kg weight loss. Two weeks prior to admission the pain increased in intensity and he was unable to sleep. He denied fever, chills, nausea, vomiting, jaundice, diarrhea, or hematochezia. The patient's travel, social, and family histories were unremarkable. An abdominal computed tomographic scan revealed a large cystic lesion nearly replacing the right lobe of the liver. A percutaneous drain was placed, evacuating 2 L of dark fluid. Cytologic and microbiologic studies were unrevealing. The patient was transferred to the University of Illinois at Chicago Medical Center for further treatment.

Physical examination revealed a 126-kg young man in no acute distress. The abdomen was soft with mild right upper quadrant tenderness on deep palpation. Laboratory evaluation was significant for hypochromic microcytic anemia (hemoglobin, 10.9 g/dL; hematocrit, 35.1%; mean corpuscular volume, 77.1 fL), with reactive thrombocytosis (platelets, 472 $\times$ $10^3/\mu L$), low serum albumin (2.4 g/dL), and a prolonged prothrombin time with international normalized ratio of 1.650. A repeat computed tomographic scan showed a 20 $\times$ 16-cm cystic lesion in the right lobe of the liver (Figure 1). The patient underwent right lobectomy (trisegmentectomy), which resulted in brisk hemorrhage and a large amount of blood loss.

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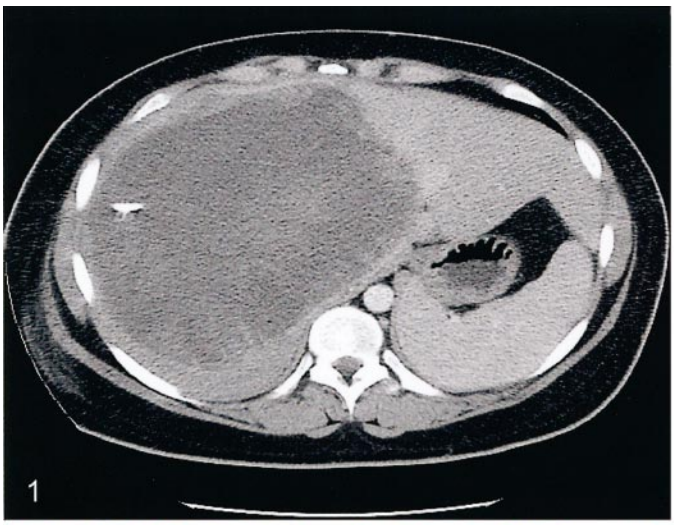
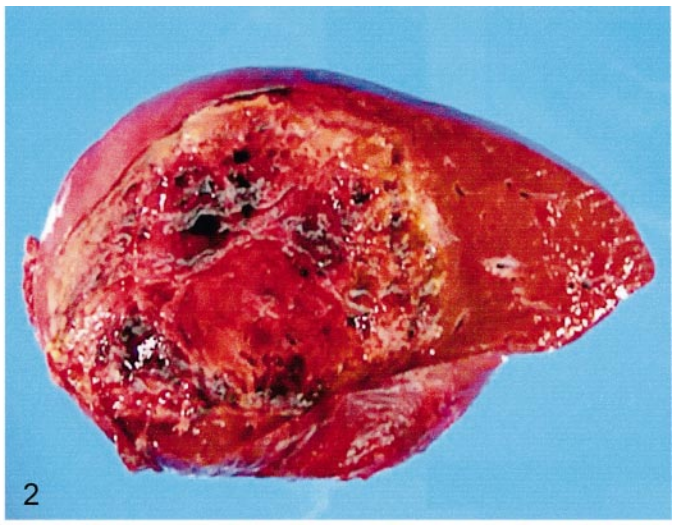
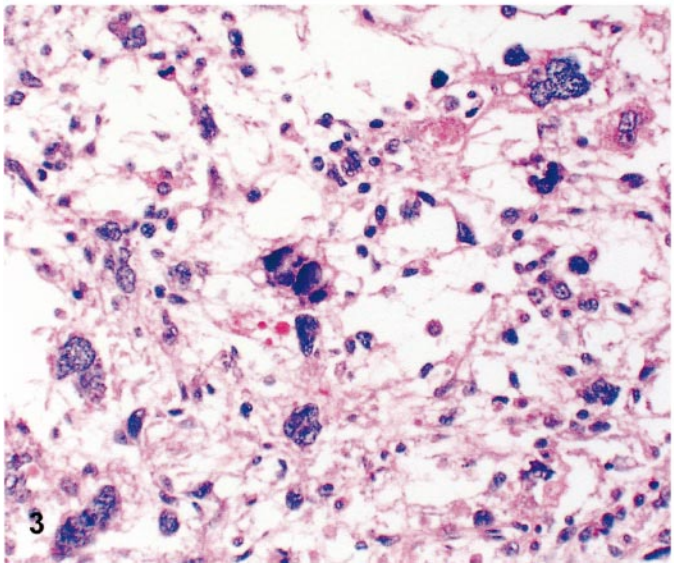
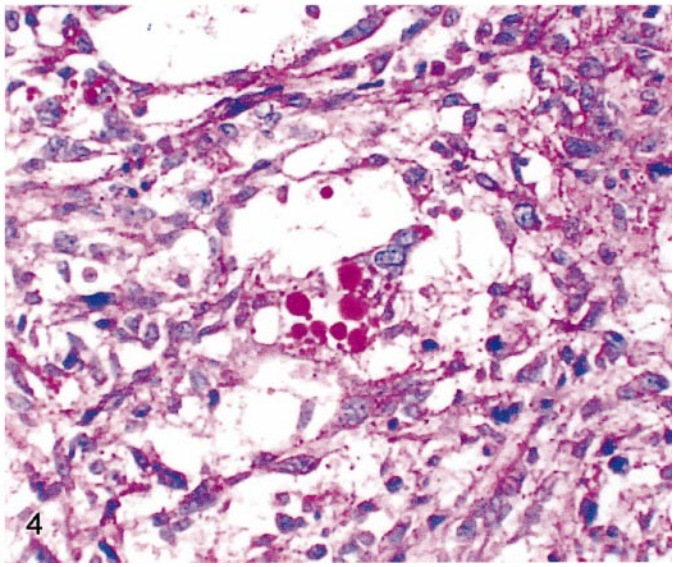
A 3.5-kg right hepatic lobectomy specimen was received, measuring 36 $\times$ 28 $\times$ 13 cm. A 23 $\times$ 14 $\times$ 13-cm, well-demarcated but nonencapsulated cystic lesion with incomplete septations and cavities filled with necrotic and hemorrhagic material occupied approximately 80% of the specimen. The cut surface of the lesion was variegated, with solid, gray-white tumor alternating with gelatinous transparent to green mucoid material, red lakes of hemorrhagic fluid, and yellow necrotic debris (Figure 2). The tumor was located 0.1 cm from the closest surgical resection margin and abutted the liver capsule. Microscopically, the lesion had a fibrous pseudocapsule separating the tumor from the compressed adjacent liver parenchyma. The periphery contained entrapped bile ducts and hepatic parenchymal elements. The tumor was composed of atypical spindle to stellate cells with variable amounts of myxoid stroma (Figure 3). We noted marked variation in cell size, nuclear pleomorphism, hyperchromasia, numerous mitotic figures, and bizarre multinucleated giant cells. Intracytoplasmic and extracellular pink eosinophilic globules were present. The globules were positive with periodic acid–Schiff and resistant to diastase digestion (Figure 4) and were strongly immunoreactive for α_1-antitrypsin. The tumor cells were positive for vimentin and α_1-antitrypsin, focally positive for smooth muscle actin, and focally weakly positive for desmin. Reactions for myogenin and myoglobin were negative. The proliferation marker Ki-67 was positive in 30% to 40% of tumor cells, and p53 was expressed in 60% of tumor cells. The tumor lacked immunoreactivity for α-fetoprotein, HepPar-1, carcinoembryonic antigen, cytokeratins 7 and 8/18, epithelial membrane antigen, CD31, CD34, CD45, CD68, neuron-specific enolase, and S100. Electron microscopy revealed primitive mesenchymal cells with irregular nuclei, peripherally condensed chromatin, and inconspicuous nucleoli. The cytoplasmic organelles were very scant, represented by dilated endoplasmic reticulum.

What is your diagnosis?









Pathologic Diagnosis: Undifferentiated Embryonal Sarcoma of the Liver

Undifferentiated (embryonal) sarcoma of the liver (UESL) is a rare neoplasm that occurs predominantly in children and young adolescents. The typical age of presentation is 6 to 10 years; it constitutes 15% of all primary hepatic neoplasms in patients aged 5 to 20 years.[1] Cases occurring in adulthood have also been reported. There is no sexual or racial predilection. The tumor typically presents as an abdominal mass with or without pain and weight loss of relatively short duration. Most tumors are confined to the right liver lobe; however, left lobe involvement as well as extrahepatic and inferior vena cava invasion may occur. Results of serum α-fetoprotein and liver function tests are usually normal. Radiologically, the tumor is described as a cystic and solid mass; computed tomographic scan usually shows a hypodense lesion with a hyperdense rim and septations. Angiographically, it is a poorly vascularized lesion, deriving its blood supply from the hepatic arterial system.

Grossly, the tumor is a large single mass (10–30 cm) with an incomplete capsule. It has a soft, gelatinous, necrotic, and hemorrhagic appearance with variegated color. Microscopically, the tumor is composed of spindle and stellate cells with ill-defined outlines and scant cytoplasm suspended in an abundant mucopolysaccharide matrix. The cells have remarkable anisonucleosis. Mitotic activity is brisk, atypical mitoses are easily found, and apoptotic bodies are abundant. Cells with bizarre nuclei, multinucleated giant cells, and extramedullary hematopoiesis may be present. Eosinophilic hyaline globules are present both intracellularly and extracellularly. These globules are positive with periodic acid–Schiff and are resistant to diastase digestion. They are thought to represent lysosomal globules, composed of apoptotic bodies phagocytosed by the tumor cells. Compressed hepatocytes and entrapped cystically dilated bile ducts are frequently found at the interface with the adjacent liver. Ultrastructurally and immunohistochemically, the tumor cells have shown divergent differentiation, including a mixture of cells with fibroblastic, histiocytoid, fibrohistiocytoid, myofibroblastic, and primitive mesenchymal phenotypes.[2] Immunohistochemically, the neoplastic cells are variably positive for vimentin, α_1-antitrypsin, and α_1-antichymotrypsin. Cytokeratins may be seen focally and desmin staining is variable. The tumors consistently lack staining for myoglobin, neuron-specific enolase, S100, muscle-specific actin, carcinoembryonic antigen, factor VIII, and α-fetoprotein.[3]

Differential diagnostic considerations include hepatic angiosarcoma, embryonal rhabdomyosarcoma, sarcomatoid hepatocellular carcinoma, anaplastic small cell hepatoblastoma, malignant fibrous histiocytoma/undifferentiated pleomorphic sarcoma, and mesenchymal hamartoma.

Little is known of the etiology of UESL. It is well accepted that this is a mesenchymal tumor, which may display partial differentiation. The possibility of it being the malignant counterpart of mesenchymal hamartoma of the liver was first suggested in 1973.[4] To our knowledge, a total of 3 cases of embryonal sarcoma arising from preexisting mesenchymal hamartoma have been reported to date.[5–7] The translocation t(19q)(13.4) has been associated with mesenchymal hamartoma of the liver.[6] This translocation has been found in only 2 cases of UESL. Cytogenetic analysis of UESL, on the other hand, has demonstrated complex karyotype, including gains of chromosomes 1q, 5p, 6q, 8p, and 12q, and losses of 9p, 11p, and 14.[8] DNA ploidy studies of UESL found some tumors to be diploid and others aneuploid.[3]

Undifferentiated (embryonal) sarcoma of the liver is a rapidly growing tumor. Complete resection with a multimodal approach, including chemotherapy and radiation, are necessary for significant disease-free survival. Local recurrences as well as distant metastases are common. Traditionally considered to have a grim prognosis, a recent report has shown more promising results.[9]

Our patient developed massive hepatic necrosis due to a left hepatic vein thrombosis with severe intra-abdominal hemorrhage. Despite 3 surgical interventions, the patient died while awaiting liver transplantation. Postmortem examination of the remaining liver showed massive necrosis and hemorrhage. There was no evidence of residual or metastatic tumor.

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