Pathological Case of the Month

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A 7-YEAR-OLD white girl was admitted to the hospital with vomiting and anorexia of 3 weeks' duration. During this time she had also had a weight loss of 3 kg. A physical examination revealed diffuse hepatomegaly. A laboratory study disclosed the following values: aspartate aminotransferase, 889 U/L (reference range, 5-40 U/L); alanine aminotransferase, 503 U/L (reference range, 5-42 U/L); alkaline phosphatase, 613 U/L (reference range, 90-380 U/L); γ-glutamyl transpeptidase, 408 U/L (reference range, 10-50 U/L); lactate dehydrogenase, 971 U/L (reference range, 200-270 U/L); serum uric acid, 0.54 µmol/L (reference range, 0.15-0.45 µmol/L); and calcium, 3.37 mmol/L(13.4 mg/dL) (reference range, 2-2.63 mmol/L[8-10.5 mg/dL]). The remaining values, including serum α_1-fetoprotein, immunoreactive parathyroid hormone, and calcitriol and vitamin D were within normal limits. A computed tomographic scan confirmed the presence of a large lobulated intrahepatic mass. The tumor was hypodense and showed areas of necrosis and calcification (**Figure 1**). Small, peripheral nodular lesions in the lower pulmonary lobes were interpreted as metastasis. No brain, renal, or skeletal pathologic condition was present.

Exploratory laparotomy with tumor biopsy was performed (**Figure 2** and **Figure 3**). Neoplastic cells also expressed epithelial membrane antigen. An ultrastructural study was also performed (**Figure 4**).

Chemotherapy was started with a combination of carboplatin, vincristine sulfate, and epirubicin hydrochloride. Despite treatment, progressive neurologic deterioration ensued and the patient died 22 days after her admission to the hospital.

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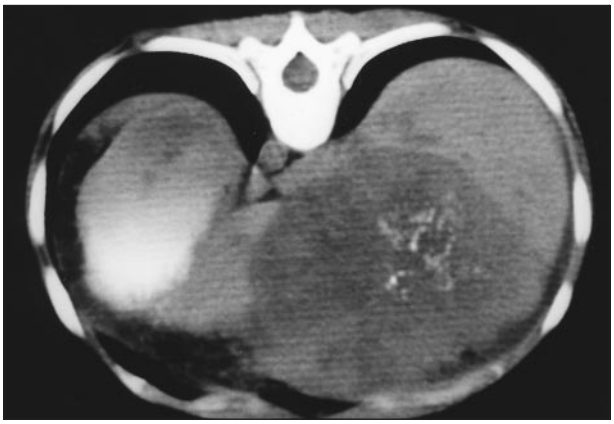

Figure 1.

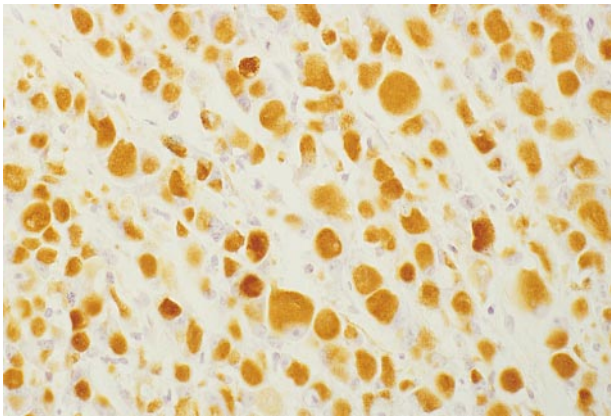

Figure 2.

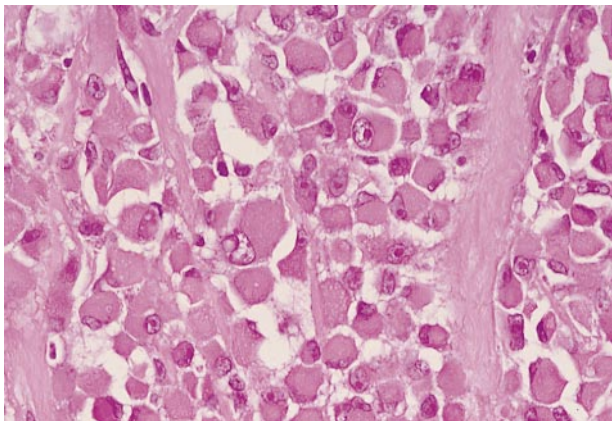

Figure 3.

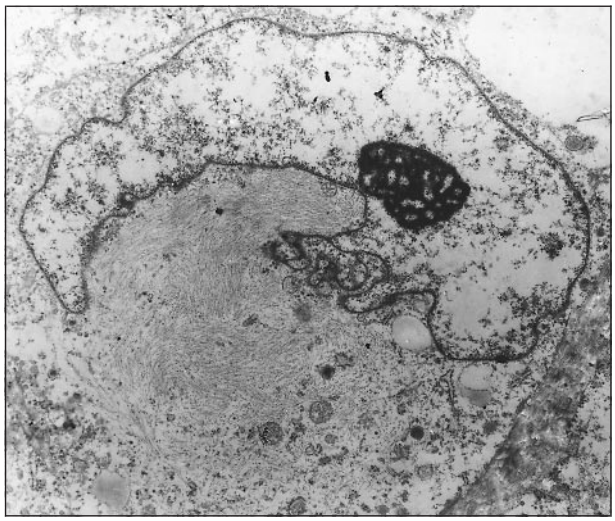

Figure 4.

Diagnosis and Discussion

Primary Hepatic Malignant Tumor With Rhabdoid Features

Figure 1. *Abdominal computed tomographic scan showing a large hypodense liver mass with irregular calcifications.*

Figure 2. *A solid sheet of round to polygonal cells with vesicular nuclei, prominent nucleoli, and abundant eosinophilic cytoplasm (hematoxylin-eosin, original magnification ×100).*

Figure 3. *Neoplastic cells demonstrate an intense intracytoplasmic immunoexpression for vimentin (peroxidase, original magnification ×100). Epithelial membrane antigen was expressed and no reaction to muscle specific actin cytokeratins, and S100 proteins were noted.*

Figure 4. *Electron microscopy showing a rhabdoid cell with large nucleoli and paranuclear aggregates of intermediate filaments (original magnification ×3900).*

Rhabdoid tumor was originally described as a distinctive, highly malignant renal neoplasm of the infant.[1,2] Extrarenal rhabdoid tumors, like those arising in the kidney, usually present in early infancy and have an aggressive behavior. Nevertheless, it is unclear whether extrarenal rhabdoid tumors are only "pseudorhabdoid" and represent a morphologic phenotype or whether they really are distinct clinicopathologic entities.[2-4] The histogenesis of these tumors remains unknown, and the term *primitive malignant tumor with rhabdoid features* (MTR) was introduced to describe neoplasms with a rhabdoid phenotype, particularly those occurring outside the kidney.[4,5]

Primary hepatic MTR are rare, and less than 20 cases have been reported.[6] They present in early infancy, as an abdominal mass. Hepatic MTR, α_1-fetoprotein levels are normal. Unlike hepatoblastoma, do not respond to treatment and have an ominous prognosis. Pathological diagnostic features include: (1) Sheets of large polygonal cells with eccentric vesicular nuclei, prominent nucleoli, and abundant eosinophilic cytoplasm; (2) Immunohistochemical expression of vimentin and epithelial markers and sometimes other antigens; and (3) Ultrastructural demonstration of cytoplasmic inclusions composed of whorled intermediate filaments.

Hypercalcemia, although rarely associated, is a well-established complication of renal rhabdoid tumors.[7-9] It is not caused by bony metastases but may be caused by neoplastic cells' secretion of parathyroid hormone, parathyroid hormone-like proteins, or prostaglandins. Hypercalcemia was a constant laboratory finding in our patient. The reason for the hypercalcemia was unrelated to skeletal metastases and serum levels of immunoreactive parathyroid hormone, calcitriol, and vitamin D were within normal limits. We were unable to find a similar phenomenon in the 18 previously reported cases of hepatic MTR.

Hepatoblastoma and hepatocarcinoma account for most malignant hepatic tumors of children. Both neoplasms, as well as the less common undifferentiated embryonal sarcoma and rhabdomyosarcoma, have been well-characterized cytologically.[10] However, no previous cytologic reports concerning hepatic MTR are available. Our cytologic findings were identical to those reported in rhabdoid tumor of the kidney.[9] So identical, that the possibility of a metastasizing renal tumor should always be considered and a renal scan should always be performed. Although hepatic MTR is rare, we believe that cytologic findings are characteristic enough to permit its recognition. A specific diagnosis is only obtained after immunohistochemical and ultrastructural evaluation. The decision whether primary hepatic or metastatic tumor is present requires a complete clinical and physical examination of the patient.

Hepatic MTR is an uncommon neoplasm with distinct pathological features. It should enter the differential diagnosis of pediatric primary hepatic tumors with normal levels of α_1-fetoprotein and of malignant neoplasms associated with hypercalcemia. Whether it represents a well-defined clinicopathologic entity remains unknown. However, its recognition is important since it does not respond to therapy and its prognosis is fatal.

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