ANNALS of Hepatology

CASE REPORT

October-December, Vol. 9 No.4, 2010: 465-467

Clear cell hepatocellular carcinoma arising 25 years after the successful treatment of an infantile hepatoblastoma

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ABSTRACT

Primary liver tumors in children are rare with hepatoblastoma (HB) being the most common malignancy. Clear cell carcinoma, a variant of hepatocellular carcinoma (HCC), is another rare tumor of the liver that tends to affect adults. We describe the diagnosis and management of the only known documented case of a primary clear cell HCC arising twenty-five years after the patient was successfully treated with chemotherapy and surgical resection for a malignant HB as an infant. While some evidence has shown a genetic link between HB and various types of HCC, other research has shown distinct chromosomal alterations and molecular mechanisms unique to both. Further knowledge of liver tumorigenesis will help elucidate the complicated genetic, molecular, and environmental factors involved in the development of these two rare hepatic malignancies.

Key words. Clear cell hepatocellular carcinoma. Hepatoblastoma. Radioembolization. Yttrium-90 labeled microspheres. Liver tumorigenesis.

A 28-year-old man presented with several months of abdominal pain, lower extremity edema, and a 25 pound weight loss. His past medical history was notable for a right lobe hepatoblastoma (HB) that was successfully resected and treated with adjuvant chemotherapy over 25 years ago. Physical examination was notable for mild tenderness in the right upper quadrant with a liver edge palpated 4 cm below the costal margin. He had a well-healed surgical scar across his abdomen, but the remainder of his exam was unremarkable. His bilirubin was 1.6 mg/dL, aspartate transaminase was 29 U/L, alanine transaminase was 60 U/L, and his alkaline phosphatase was 293 U/L. Viral serologies, anti-mitochondrial antibodies, anti-smooth muscle antibodies, and anti-nuclear antibodies were negative. Ceruloplasmin, iron studies, and immunoglobulins were normal. An alpha-fetoprotein was 15,308 ng/mL. A magnetic resonance scan of his abdomen revealed a 7.1 cm x 6.4 cm x 5.7 cm heterogenous mass within segment 4B with additional scattered masses throughout the remainder of the liver (Figure 1). A computerized tomogram of his chest revealed small nodules consistent with metastatic disease.

Multiple small core needle biopsies were taken of the liver mass and demonstrated a uniform po-

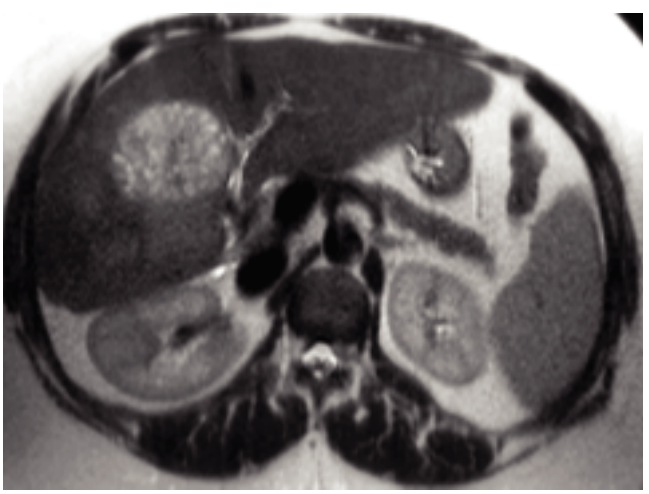

Figure 1. *T2-weighted MRI with a 7.1 x 6.4 x 5.7 cm hyperintense mass centered in segment 4B.*

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Manuscript received: July 15, 2010
Manuscript accepted: September 26, 2010.

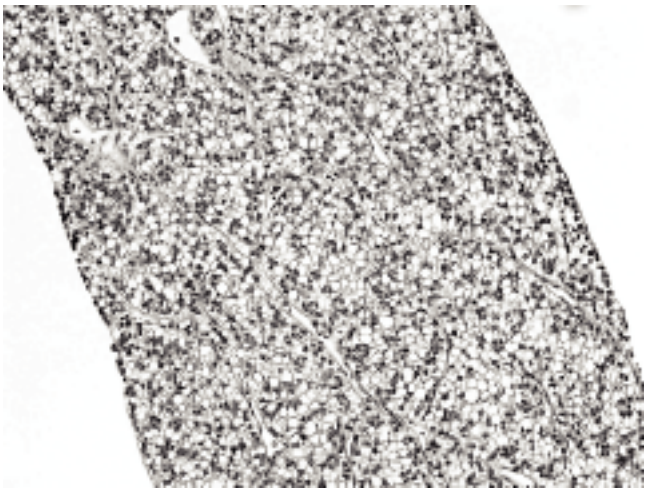

Figure 2. Hematoxylin-eosin (H & E) staining of liver mass showing hepatocellular carcinoma comprised of a uniform population of polygonal cells with clear cytoplasm and monomorphic, eccentric nuclei (100x).

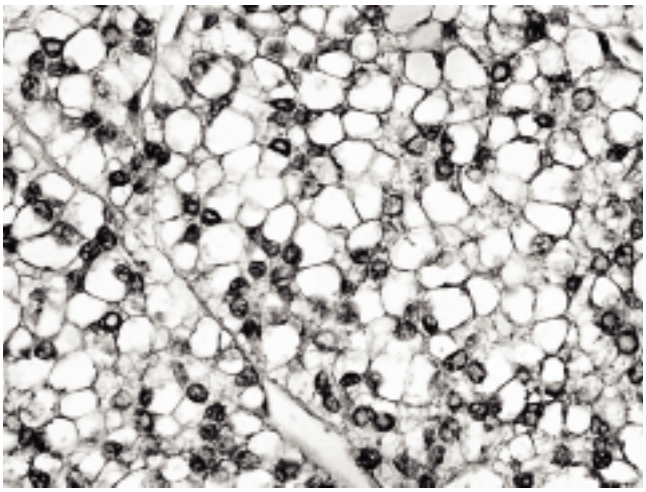

Figure 3. Hematoxylin-eosin (H & E) staining of liver mass showing hepatocellular carcinoma comprised of a uniform population of polygonal cells with clear cytoplasm and monomorphic, eccentric nuclei (400x).

pulation of polygonal cells with clear cytoplasm and hyperchromatic monomorphic nuclei growing in large masses in a macrotrabecular array (Figures 2 and 3). There were no stromal or ductal elements, or evidence of primitive or embryonal differentiation. Mitoses were absent and necrosis was not a feature. The surrounding liver parenchyma was without cirrhosis. Immunohistochemistry was negative for HMB-45, AFB, CD-15, HepPar-1, SMA, Vimentin, and polyclonal CEA. The findings were felt to be most consistent with well-differentiated hepatocellular carcinoma (HCC) with clear cell features, and not a recurrent HB. The dominant mass was treated with Yttrium-90 labeled microspheres. Post-procedure magnetic resonance imaging showed no interval decrease in tumor size, but further palliative radioembolization is planned.

We describe the diagnosis and management of a clear cell HCC arising 25 years after the patient was successfully treated for HB as an infant. HB is the most common childhood primary liver tumor, but it is exceptionally rare with only about 100 cases documented each year. The peak incidence is between six months and three years of age.[1,2] In patients with limited-extension HB, surgical resection and adjuvant multi-agent chemotherapy with cisplatin-based regimens remains the gold standard of treatment. Chemoembolization, radiofrequency ablation, and liver transplantation have been used for surgically unresectable tumors. Primary clear cell carcinoma of the liver, a histopathological variant of HCC, is also rare and accounts for 7.5-12.5% of liver cancers.[3] Compared to HCC, primary clear cell carcinoma has a better prognosis and does better with surgical resection.

The genetic basis of liver tumors continues to be debated. Recent research suggests that some HCCs may develop from maturation arrest of liver stem cells instead of dedifferentiation of mature hepatocytes. Due to the fact that HB is a stem-like cell carcinoma and similar overlapping groups of upregulated and downregulated genes exist in both HCC and HB, HB may be an early form of some types of HCC.[4] Other data from microsatellite analysis and comparative genomic hybridization has suggested that despite common involvement of a few distinct chromosomes, the patterns of chromosomal alterations and molecular mechanisms are unique among HCC and HB.[5] A better understanding of the molecular, genetic, and clinicopathological basis of these two rare hepatic malignancies will help shed light on the etiology and risk factors involved in liver tumorigenesis.

ACKNOWLEDGEMENTS

The authors would like to thank Dr. Milton J. Finegold at Texas Children's Hospital, Dr. Louis Dehner at Washington University School of Medicine, and Dr. Julia C. Iezzoni at the University of Virginia Medical Center as well as their staff for their histotechnological support and pathological expertise.

CONFLICTS OF INTEREST

The authors disclose no conflicts of interest.

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