

Hepatocellular carcinoma¹

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Creation date: July 2004

Editor: Professor Riccardo Riccardi

¹Adapted from the Childhood Liver Tumours Strategy Group (SIOPEL)

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Abstract

Hepatocellular carcinoma (HCC) is a very rare pediatric tumour. Primary hepatic tumours as a whole represent about 1-1,5% of all pediatric neoplasm with an incidence of 1.5 cases per million children aged less than 15 years. [Hepatoblastoma](#) is the most frequent primary hepatic tumour in this age group followed by HCC. HCC tends to occur in adolescents. In adults, HCC constitutes the most common liver cancer. Main symptoms are palpable hepatic mass, abdominal pain and also cachexia and jaundice in advanced cases. Serum alpha-fetoprotein levels are frequently elevated. In the pediatric population, HCC can complicate liver cirrhosis due to viral hepatitis, - especially in endemic areas (sub-Saharan Africa, East Asia, Native Eskimos of Alaska) - or metabolic diseases. HCC arising in otherwise healthy liver are more common in the pediatric population than in adults. Current treatment of HCC is largely inefficient due to its extreme chemoresistance and to usually advanced disease at diagnosis. Overall survival at 3 years remains below 25%.

Keywords

Hepatocellular carcinoma, pediatric epithelial liver tumour, serum alpha-fetoprotein

Disease name and synonyms

- Hepatocellular carcinoma (HCC)
- Hepatoma
- Primary liver cell carcinoma
- Hepatocarcinoma
- Liver cancer

Definition

HCC is a carcinoma of the liver derived from well-differentiated hepatocytes.

Differential diagnosis

Differential diagnosis involves all kinds of liver masses including other malignant (*i.e.* [hepatoblastoma](#), transitional liver tumours (Prokurat *et al*, 2000) undifferentiated sarcoma, [rhabdomyosarcoma](#), [teratoma](#),) or benign (*i.e.* hemangioma, hemangioendothelioma, focal nodular hyperplasia, hepatoma, hepatic cysts: post-traumatic, congenital or echinococcal) masses.

Etiology

HCC is traditionally linked to liver cirrhosis and to ongoing process of liver necrosis/regeneration. Liver cirrhosis may be due to hepatitis B and C (although it usually takes 10-15 years to develop) or metabolic diseases like tyrosinemia. HCC can be also associated with an intake of food contaminated by aflatoxines, which is commonly the case in Africa. Viral hepatitis itself and inclusion of parts of viral genomic material into structural genome of the hepatocytes may by itself contribute to increased chance of development of HCC (Ganem *et al*, 2004). However, all above-mentioned reasons are true mainly in endemic HCC areas: sub-Saharan Africa and East Asia (China, Taiwan). On the contrary in Europe, only about 30% of pediatric HCC cases are linked to liver cirrhosis; others are *de novo* cases, whereas in adults, in which HCC constitutes the most common liver cancer, 85% of cases arise on the background of the liver cirrhosis (Czuderna *et al*, 2002).

Clinical description

Main symptoms are palpable hepatic mass, abdominal pain and, in advanced cases, cachexia and jaundice. Symptoms and signs of liver insufficiency can be present. Tumour can be unifocal or multifocal. Peritoneal implants and lymph nodes involvement at *porta hepatis* are not uncommon. Main metastatic sites are lungs. HCC is commonly associated with elevated alpha-fetoprotein levels (AFP).

Diagnostic methods

Diagnosis is mainly based on imaging. Initial step usually consists of abdominal ultrasonography. It allows not only to make primary diagnosis but also to assess intrahepatic tumour extent.

Other standard investigations include:

- Contrast enhanced computed tomography (CT) of the abdomen or magnetic resonance imaging (MRI).
- X-ray and/or CT of the chest to rule out eventual pulmonary metastases.
- Serum AFP levels.

The final diagnosis depends upon histologic assessment

Epidemiology

HCC is a very rare primary pediatric tumour. Primary hepatic tumours as a whole represent about 1-1,5% of all paediatric neoplasm with an incidence of 1.5 cases per million children aged less than 15 years. Hepatoblastoma is the most frequent primary hepatic tumour in this age group followed by HCC (Czuderna *et al*, 2002).

Management

Treatment of pediatric HCC has traditionally been incorporated in pediatric hepatoblastoma (HB) protocols, which consist of cisplatin-based chemotherapy associated with tumour resection or liver transplantation (Perilongo *et al*, 2004). The current treatment of HCC, including liver transplantation, is largely inefficient due to its extreme chemoresistance and usually advanced disease at diagnosis (Colombo and Sangiovanni, 2002; Boucher *et al*, 2002; Klintmalm, 1998; Qin and Tang, 2002; Reyes *et al*, 2000; Ringe *et al*, 1991; Roayaie *et al*, 2002). Overall survival at 3 years remains below 25% (Chang, 1998; Czuderna, 2002; Katzenstein *et al*, 2002). Liver transplantation in HCC remains a limited option due to the very strict Milano criteria used to select patients. Moreover, even complete tumour resection does not guarantee survival. Recurrence rate after complete HCC resection is in the range of 40-50% (Czuderna, 2002; Katzenstein *et al*, 2002).

Unresolved questions

Due to its extreme chemoresistance, the high rate (60-70%) of tumor's unresectability at diagnosis and the limitations of liver transplantation, HCC remains a tremendous therapeutic challenge. Hence HCC requires completely new therapeutic approach, which will be different than that used for HB, while these two entities were treated similarly in the past (Cusnir and Patt, 2004).

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