Hepatocellular carcinoma

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Abstract

Hepatocellular carcinoma (HCC) is a very rare pediatric tumor. Primary hepatic tumors as a whole represent about 1-1.5% of all pediatric neoplasms with an incidence of 1.5 cases per million children aged less than 15 years. Hepatoblastoma is the most frequent primary hepatic tumor 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.
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 also be associated with 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 (Czauderna 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 (Czauderna 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; Czauderna, 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% (Czauderna, 2002; Katzenstein et al, 2002).

Unresolved questions
Due to its extreme chemoresistance, the high rate (60-70%) of tumour'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).

References


http://www.orpha.net/data/patho/GB/uk-Hepatocellularcarcinoma.pdf