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Hepatoblastoma of the adult: A systematic review of the literature

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ABSTRACT

Hepatoblastoma is the most common malignant liver tumor in children. On the other hand in the adult HB is very rare and characterized by unfavorable prognosis.

A review of the entire literature was performed: 58 articles and 63 cases of HB were found. The patient's data were collected and analyzed. No correlation with hepatitis virus was found and AFP was elevated in most cases. Usually HB forms a large single mass in the liver and presents aggressive behavior, with local invasiveness and metastatic spread. The current median survival time is 5 months, with a 1-year survival rate near 30%. Surgical resection is the only curative treatment. However major liver resections or extensive demolitions of the adjacent organs are necessary. There are no standardized protocols in the multimodal approach to this tumor.

1. Introduction

Hepatoblastoma is a rare tumor, but the most frequent liver tumor in childhood. It usually occurs in infants under 3 years of age and the 5-years overall survival rate in children with not disseminated tumors is close to 70% [1–4].

On the other hand, in the adult, hepatocellular carcinoma is the most common liver tumor, related to chronic hepatitis and cirrhosis.

Hepatoblastoma in adult is very rare and in literature only 63 cases have been described.

A recent study published in 2012 by RARECARE Working Group, collected data of embryonal cancers in Europe, from 89 European population-based cancer registries. Overall incidence rate for hepatoblastoma was reported less than 0.25 per million. From 1995 to 2002, authors calculated that 8% of HB occurred in adolescent or adults, with 14 cases observed over 15 of age versus 167 under 14 of age [5].

It is an aggressive neoplasm with a very poor prognosis [6]. The difficult management of these patients is due to the lack of standardized protocols of treatment.

2. Materials and methods

A systematic review of the literature was performed by two different investigators (A.C. and G. DA.), using MEDLINE, PubMed, EMBASE, and Google Scholar, from 1958 to June 2015.

The search terms included the following: “Hepatoblastoma”, “Adult Hepatoblastoma”, “Hepatoblastoma of the adult”, “Pediatric Hepatoblastoma”, “Hepatoblastoma of the children”, “ Hepatoblastoma in pediatric patients” and “Hepatoblastoma in children”. No search restrictions were imposed. References from selected articles were also reviewed. Preference has been given to English publications, but abstracts from other languages have been also included. All references in selected articles were further screened for additional publications. Articles were retrieved according to the Preferred Items for Reporting of Systematic Reviews and Meta-Analyses guidelines.

All cases in which histopathological diagnosis of Hepatoblastoma of the adult were included. All cases are collected considering demographic information, clinical findings, treatments modalities and outcomes. Survival of 43 cases, in which follow up was reported, was assessed by the Kaplan-Meier method and group comparison was performed using the long-rank test. SPSS 20.0 was the statistical software for the analyses. The search revealed only 58

Abbreviations: HB, hepatoblastoma; AFP, Alpha-fetoprotein; TACE, transarterial chemoembolization; HCC, hepatocellular carcinoma; HCV, hepatitis C virus; HBV, hepatitis B virus; RFA, radiofrequency ablation; RT, radiotherapy; TAE, transarterial embolization; NED, not evidence of disease; AWD, alive with disease; DOD, dead of disease; IVC, inferior vena cava; M, male; F, female; mets, metastasis.

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reports, with 63 patients (Fig. 1).

2.1. Demography

In adult HB is very rare, with an extremely poor prognosis [5–7]. In literature only 63 cases are described.

The ratio male: female was 1. Only in 49 articles sex was specified: 24 patients were male and 25 female. The mean age at the diagnosis was 42 years and the youngest patient was 16 years old and the oldest 84 years old. Most cases were upper 30 years old (38 vs 25 patients).

No difference between sexes is observed, even though some studies reported a slight female preponderance, but in this review this data has not been confirmed [8,9]. Most patients were older than 30 years, contrary to Wang XY [6] that reported most cases were in their 20s.

2.2. Presentation

Clinical symptoms were reported in 31/44 cases (70,5%) and pain, often in the presence of an abdominal mass, was the main manifestation.

Usually the presentation of HB was the right upper abdominal pain, often in presence of abdominal mass. In two cases, patients were admitted to emergency department for hemoperitoneum due to rupture of the tumor [10,11] and one for massive gastrointestinal bleeding [12].

2.3. Diagnosis

No cases of preoperative diagnosis without biopsy, surgery or autopsy are reported.

Imaging-diagnosis of HB was a real challenge, because several types of liver tumor, such as hepatic teratoma, carcinosarcoma, malignant mesenchymal tumor and HCC, presented similar characteristics [6,9,13]. Considering the literature, the preoperative imaging diagnosis were HCC in six cases [14–19], abdominal aortic aneurysm and neuroendocrine tumor in two cases respectively [20,21] and hepatic amoebic abscess in another case [22]. Anyway imaging remains essential in the definition of surgical planning. Sometimes, previous tumor biopsy for diagnosis has been done [13], but in the suspect of malignancy with a resectable lesion, biopsy should not be necessary and postoperative diagnosis is adequate. Considering that HBs are often large in dimension, hypervascular and exophytic, biopsy is high-risk procedure for bleeding or tumor rupture. Mondragon SR et al. [23] reported a case of patient's death after percutaneous biopsy of multinodular HB.

Sometimes the diagnosis of the tumor was a casual finding: during autopsy, or follow up for cancer, as our case, or post liver transplant, such as in the article of Dumortier J et al. [24].

AFP was elevated in 25 patients (62,5%) and normal in 15 (37,5%). The levels ranged widely from 30 to 1.873.000 ng/mL, perhaps expression of a different biological character of the tumors [19]. Anyway neither the imaging nor the AFP serum levels are useful to establish the proper diagnosis of HB in the adult without biopsy or surgical resection.

2.4. Pathology

Several studies described a correlation between viral hepatitis (B or C) and HB, for the possible role of the HCV-core proteins in the promotion of cell cycle progression in hepatoblastoma cell lines [18,25]. Despite that, this analysis fails to confirm this data: for a total of 44 cases, that reported the state of the liver, in 27 cases (60%), liver was normal and in 18 cases, liver disease was confirmed (40%).

In 48 cases HB was a single tumor (78,7%) and in 13 was multifocal (21,3%). In 24/50 patients (48%), HB was metastatic (Fig. 2).

The size of the tumors range from 1 cm, in the multifocal pattern, to 30 cm. Sometimes HB fills the entire right lobe, or produces a complete liver replace.

Considering the literature, in 51 cases tumor extension was reported: in 28 cases HB was confined to the liver, without metastases, in 23 cases metastatic spreading was described. In many

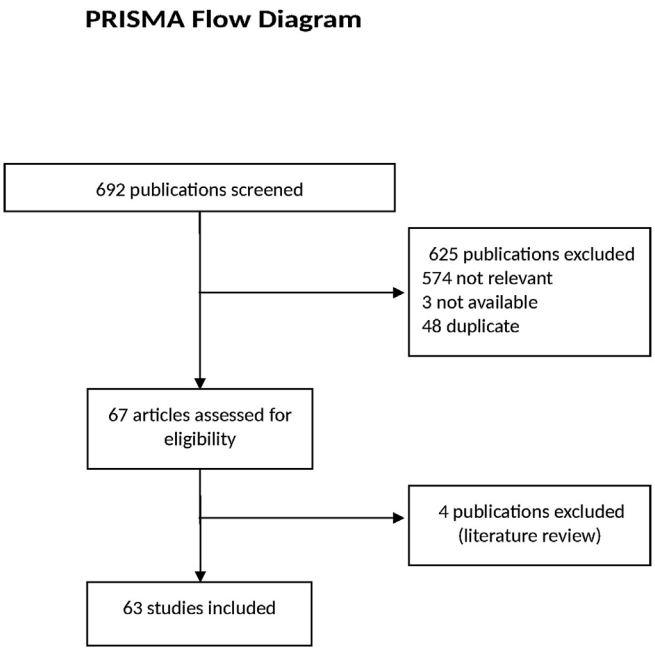

Fig. 1. Articles retrieval strategy, according to the Preferred Items for Reporting of Systematic Reviews and Meta-Analyses guidelines.

SITE OF METASTASIS	
Lymph nodes	[26, 27, 28]
Lungs	[23, 27, 41]
Pleura	[26]
Peritoneum	[8, 12, 19, 20, 27]
Pancreas	[55]
Ovaries	[33]
Ileum	[40]
Adrenal gland	[24]
Pericardium	[9, 12]
Rib	[42]

Fig. 2. Site of metastasis.