World Journal of Advanced Research and Reviews
eISSN: 2581-9615 CODEN (USA): WJARAI
Cross Ref DOI: 10.30574/wjarr
Journal homepage: https://wjarr.com/

(CASE REPORT)

Hepatoblastoma: Experience of the paediatric haematology and oncology department, Hassan II university hospital of Fez.

V. KASHAMA *, G. OVIEBO ANDO, S. BOURAMDANE, K. ELMKADDEM, H. HBIBI and S. BENMILOUD.

Department of paediatrics, Hassan II University Hospital, University Sidi Mohammed Ben Abdellah, Fez, Morocco.

World Journal of Advanced Research and Reviews, 2024, 22(02), 185–189

Publication history: Received on 16 March 2024; revised on 01 May 2024; accepted on 03 May 2024

Article DOI: https://doi.org/10.30574/wjarr.2024.22.2.1363

Abstract

Introduction: Hepatoblastoma is the most common malignant hepatic tumour in children. However, it is a rare disease, representing approximately 2% of childhood tumours. The treatment combines chemotherapy with surgical excision. The objective of this study was to describe the epidemiological, clinical, therapeutic and progressive aspects of hepatoblastoma treated in the paediatric haematology and oncology department at the University Hospital Hassan II of Fès.

Patients and Methods: This was a descriptive and retrospective study conducted over a 11-year period. All patients aged 0 to 15 years who were admitted and treated for hepatoblastoma were included.

Results: 24 patients met the study criteria, including 9 boys and 15 girls. The average age at diagnosis was 11.52 months ± 4.9. The most common reason for consultation was abdominal distension. Hepatomegaly was observed in 50% of cases. The average tumour size was 116 mm. At the time of diagnosis, one-third of patients had pulmonary metastases, and all patients were classified as high risk. Therapeutically, 19 patients (79.17%) received chemotherapy and 16 (66.67%) underwent surgery. On the evolutionary level, we observed a recovery without events in 10 (41.67%) patients.

Conclusion: hepatoblastoma is a rare tumour, but remains the most common hepatic tumour in children. Despite progress in diagnostic and therapeutic means, the mortality rate is significant.

Keywords: Hepatoblastoma; Alpha Foeto-Protein; Chemotherapy; Hepatectomy.

1. Introduction

Hepatoblastoma (HB) is the most common hepatic malignancy in children, with an incidence that is increasing approximately 5% per year. However, it is rare and represents approximately 2% of childhood tumours (1,2,3). It mainly affects children under 3 years old, without underlying hepatic pathology. Despite the lack of a clear etiology, there are genetic predisposition factors (4,5,6,7,8).

The diagnosis is rapidly established based on the association of a liver mass with a high serum alpha-fetoprotein (AFP) level. Imaging plays a role in the diagnostic and extension assessment, as well as in patient monitoring (6,9,10). Pathology and tissue markers will confirm the diagnosis and allow the establishment of histoprognostic criteria.

A number of signalling pathways involved in liver development have been identified, which has enabled the identification of new therapeutic targets and the establishment of a classification of HB (6,7,8). Treatment combines

* Corresponding author: V. KASHAMA

platinum-based chemotherapy with surgical excision of the tumour, which may in certain cases require liver transplantation (6). Early and adequate treatment allows for an overall survival of around 80% at three years.

The objective of this study was to describe the epidemiological, clinical, therapeutic, and progressive aspects of hepatoblastoma in children treated in the pediatric hemato-oncology department at the University Hospital Hassan II of Fez.

2. Methodology

This was a descriptive and retrospective study conducted over a period of 11 years, from 1 January 2011 to 31 December 2023. All patients aged between 0 and 15 years who were admitted and treated for hepatoblastoma at our training facility were included in the study. Data on the patients' epidemiological, clinical, radiological and therapeutic characteristics were collected and analysed, with particular attention paid to the progressive aspects of the patients' conditions.

The data was entered and analysed using the Epi Dada software. Quantitative variables are presented as an average with standard deviation and confidence interval, while qualitative variables are presented as a percentage proportion. The Helsinki ethical principles, to which our institution adheres, were respected throughout the study.

3. Results

During the study period, 24 patients met the criteria for inclusion. The mean age at diagnosis was 11.52 months ± 4.9.

3.1. Clinical data

The reason for consultation was, in order of frequency, abdominal distension (87.5%), the alteration of the general condition (43.75%), fever (37.5%), abdominal pain (25%), and jaundice (6.25%). The consultation time ranged from 5 days to 6 months. Hepatomegaly was identified on clinical examination in 12 patients (50%) and no signs of early puberty were observed.

Radiological examination revealed that all patients underwent an abdominal CT scan. This revealed a right hepatic tumour in more than half of the cases, with an average size of 116 mm and an average tumour volume of 300 cm3 (86-1384 cm3). Vascular involvement was observed in 18 patients (75%) and exhibited a multi-segmental topography. Two cases were classified as PRETEXT 1 (8.33%), 17 cases were classified as PRETEXT 2 (70.83%), four cases were classified as PRETEXT 3 (16.67%), and one case was classified as PRETEXT 4 (4.17%).

The extension assessment revealed pulmonary metastases in seven patients, representing 29.2% of the total. Alpha-fetoprotein (AFP) was elevated in 22 patients, or 95.8%, with values ranging from 1008 to 1744000 ng/ml. All patients were classified as high risk.

Therapeutically, 19 patients (79.17%) received chemotherapy, while 16 (66.67%) underwent surgery. Among the latter group, 14 patients underwent a partial hepatectomy, while two patients underwent a lumpectomy.

On the evolutionary level, we observed a recovery without events in 10 (41.67%) patients with a follow-up of 4 years and 8 months (8 months to 8 years). One patient developed T lymphoblastic lymphoma 3 years and 7 months after the end of treatment. Thirteen patients (54.17%) died. Among these deaths, seven were due to tumour progression, two patients died as a result of relapse, two patients died before the start of chemotherapy, one patient died intraoperatively and one patient died postoperatively.

4. Discussion

The objective of this study was to describe the epidemiological, clinical, therapeutic and progressive aspects of hepatoblastoma in children treated in the paediatric haematology-oncology department at the University Hospital Hassan II of Fès.

HB is a rare disease. The incidence of hepatoblastoma in France is estimated to be between 0.5 and 1.5 per million per year. This figure varies considerably between countries, with England reporting a rate of 0.2 per million per year and Hong Kong reporting a rate of 2.1 per million per year. The incidence of hepatoblastoma decreases rapidly with age,

with rates of 4.6 per million for children under five years old and 0.01 per million for adolescents over 15 years old. (11) Over the course of 13 years, 24 cases were recorded in our series, representing a hospital frequency of 1.7% of admissions for paediatric cancer.

The average age of our patients is comparable to that reported in the literature (1.12). However, there is no absolute predominance of one sex over the other. We found a female predominance (1,2,3,12).

The etiology of HB differs from that of hepatocellular carcinoma by the absence of viral hepatitis or cirrhosis, and the association with certain congenital syndromes. However, this remains exceptional. Similarly, familial cases of HB are rare. (13) According to recent studies, there are several environmental risk factors associated with HB. Prematurity and low birth weight could be associated with the later appearance of HB. The risk is approximately 20 times higher in children with a birth weight < 1500 g and the risk is double in those with a moderately low birth weight (1,500-2,500 g). (14) Hepatoblastoma is characterised by the proliferation of immature hepatic epithelial cells (embryonal or fetal hepatoblasts), often associated with components of mesenchymal origin (osteoid, chondroid, adipocyte) or even occasionally teratoids. This tumour could therefore originate at a very early stage of hepatic differentiation. Our clinical and biological results are consistent with data from the literature (2,10,15,16,17). The rare tumours secreting β-hCG or testosterone are associated with early puberty (18). None of our patients exhibited these signs. At the time of diagnosis, 22/24 of our patients had pulmonary metastases, representing a 95.8% prevalence. This proportion is notably higher than that reported by D. Yassine (12.5%) and even higher than that observed in certain series (10, 11, 19, 20, 21).

It is evident that surgical intervention remains a crucial component of the treatment plan for hepatoblastoma (HB), given that no documented cases of a cure have been reported in the absence of tumour excision.

The criteria for determining the suitability of a patient for surgical intervention are as follows: (16) the possibility of completely removing the tumourous liver, the preservation of a sufficient volume of healthy parenchyma (at least that of a left lobe), the maintenance of the arterial and portal blood supply, as well as the biliary and suprahepatic drainage.

Liver transplantation represents a potential alternative in cases where partial hepatectomy is contraindicated. The most significant advancement in the treatment of children with hepatoblastoma has been the discovery of effective chemotherapy. Its objective is to reduce the tumour mass, making the surgical procedure easier, and to prevent metastases. (19) In our series, 66.67% of patients underwent surgery and 79.17% underwent chemotherapy. In the study by Y Lahraoui (9), almost all patients received neoadjuvant chemotherapy, with only one undergoing surgery from the outset. In our study, 19 patients received preoperative chemotherapy, which resulted in a reduction of the tumour mass to approximately 40%. Cisplatin (CDDP) is the most effective agent, having been used in all major studies conducted by different cooperation groups (20, 21, 22). Currently, the paediatric oncology department of Fes treats children suffering from HB according to the protocol of the SIOPEL 3 group (23). In our patients, chemotherapy allowed a tumour reduction of 40%.

The other significant strength of our study is the long-term follow-up of up to 8 years. This allowed us to note a complete remission in 41.67% of cases. This result remains lower than that reported in the literature, which ranges from 50% to 65%. (20, 24, 25).

Hepatoblastoma is more prevalent in standard risk forms than in high risk forms, which are characterised by the presence of at least one of the following factors: the presence of metastases, diffuse liver damage, a normal alpha-fetoprotein level, tumour rupture, vascular invasion or an age of the child greater than or equal to 8 years.

5. Conclusion

Hepatoblastoma is a rare tumour, but remains the most common hepatic tumour in children. The diagnosis is straightforward in the case of a child under the age of five with an elevated alpha-fetoprotein (AFP) level. The treatment involves a combination of chemotherapy and surgery, in accordance with the protocols established by the relevant study groups. Despite the progress that has been made in diagnostic and therapeutic techniques, the mortality rate remains significant.

Compliance with ethical standards

Disclosure of conflict of interest

No conflict of interest to be disclosed.

Statement of informed consent

Informed consent was obtained from all individual participants included in the study.

References

[1] Lack EE, Neave C, Vawter GF. Hepatoblastoma: a clinical and pathological study of 54 cases. Am J Surg Pathol 1982 Dec;6(8):693-705.

[2] Gonzales-Crussi F, Upton MP, Maurer HS. Hepatoblastoma: an attempt at the characterisation of histologic subtypes. Am J Surg Pathol. 1982 Oct;6(7):599-612.

[3] JT Store. Hepatoblastoma. Semin Diagn Pathol. 1994 May;11(2):136-43.

[4] Laurence Bruges, Sophie Branchereau, Véronique Milkman. Primary malignant tumours of the liver in children. Cancer Bulletin, Volume 99, Issue 2, February 2012, Pages 219-228.

[5] BH to berle, U Bode, D von Schweinitz. Differentiated treatment protocols for high- and standard-risk hepatoblastoma: an interim report of the German Liver Tumor Study HB99. Klin Padiatrist 2003 May-Jun;215(3):159-65. doi:10.1055/s-2003-39375.

[6] Jörg Fuchs. Pretreatment prognostic factors and treatment results in children with hepatoblastoma: a report from the German Cooperative Pediatric Liver Tumor Study HB 94. Cancer 2002 Jul 1;95(1):172-82. doi: 10.1002/cncr.10632.

[7] Anthony D DeRenzi , Audrey Bowen. A case report and a review of paediatric hepatoblastoma are presented in this article.HCA Healthc J Med. 2023 Oct 30;4(5):377-382. doi:10.36518/2689-0216.1095. eCollection 2023.

[8] Monica Fabre. Hepatic tumours in children: Experience with 245 tumours and review of the literature. Annals of Pathology, Volume 24, Issue 6, December 2004, Pages 536-555.

[9] Barbara E Wildhaber, Ernesto Montaruli, Florent Guérin, Sophie Branchereau, Hélène Martelli, Frédéric Gauthier. A diagnosis of mesenchymal hamartoma or embryonal sarcoma of the liver in childhood can be challenging prior to complete surgical excision. This is due to the lack of specific clinical and imaging features that would allow for an accurate diagnosis. A case report published in the Journal of Pediatric Surgery in September 2014 (10.1016/j.jpedsurg.2014.04.005) describes a patient who presented with a similar clinical picture. The patient underwent surgical excision of the tumour, which was histologically diagnosed as mesenchymal hamartoma.

[10] Y. Lahraoui, HAS. Ammor, H. Benhadou, A. Oulahyane, HAS. Bouhafs, Mr. Kisra et al. (2010). Hepatoblastoma in children: 16 cases. Pediatric Archives, 17(6), 17.

[11] D. Yassine. Hepatoblastoma in children: approximately 17 cases. Faculty of Medicine and Pharmacy, Rabat - Medicine thesis 2018 [5750].

[12] Gustave Roussy. [Pediatric liver tumors [Internet]. [cited April 29, 2024]. Further information can be found at: https://www.gustaveroussy.fr/fr/tumeurs-du-foie-pediatrics

[13] Ortega JA, Krailo MD, Haas JE, King DR, Ablin AR, Quinn JJ, et al. Effective treatment of unresectable or metastatic hepatoblastoma with cisplatin and continuous infusion doxorubicin chemotherapy: a report from the Children's Cancer Study Group. J Clin Oncol. December 1991; 9(12): 2167-76.

[14] Fraumeni Jr. JF, Rosen PJ, Hull EW, Barth RF, Shapiro SR, O'Connor JF. Hepatoblastoma in infant sisters. Cancer. 1969; 24(5): 1086-90.

[15] Spector LG, Birch J. The epidemiology of hepatoblastoma. Pediatric Blood Cancer. Nov 2012;59(5):776-9.

[16] C Armengol, S Cairo, M Fabre, CA Renard, L Brugières, V Laithier, et al. CA3-Classification of hepatoblastoma by microarray study of the gene expression profile. Doi: GCB-8-9-2005-29-8-0399-8320-101019-200515089.

[17] Masson E. Benign liver tumours [Internet]. EM-Consult. [cited 27 April 2024]. Further information can be found at: https://www.em-consulte.com/article/23176/tumeurs-benignes-du-foie

[18] von Schweinitz D, Glü er S, Mildenberger H. Liver tumours in neonates and very young infants: diagnostic pitfalls and therapeutic problems. Eur J Pediatr Surg. Apr 1995;5(2):72-6.

[19] Galifer RB, Sultan C, Margueritte G, Barneon G. Testosterone-producing hepatoblastoma in a 3-year-old boy with precocious puberty. J Pediatr Surg. Dec 1985;20(6):713-4.

[20] von Schweinitz D. Hepatoblastoma: recent developments in research and treatment. Semin Pediatr Surg. Feb 2012;21(1):21-30.

[21] Pizzo PA, Poplack DG. Principles and Practice of Pediatric Oncology. Wolters Kluwer Health/Lippincott Williams & Wilkins; 2011. 1531 p.

[22] von Schweinitz D. Management of liver tumours in childhood. Semin Pediatr Surg. Feb 2006;15(1):17-24.

[23] Chemotherapy for Childhood Hepatoblastoma and Hepatocellular Carcinoma. SpringerLink [Internet]. [cited April 20, 2023]. Available at: https://link.springer.com/chapter/10.1007/978-3-642-14504-9_12.

[24] Zsíros J, Maibach R, Shafford E, Brugieres L, Brock P, Czauderna P, et al. Successful Treatment of Childhood High-Risk Hepatoblastoma With Dose-Intensive Multiagent Chemotherapy and Surgery: Final Results of the SIOPEL-3HR Study. JCO. 20 May 2010;28(15):2584-90.

[25] Hishiki T, Matsunaga T, Sasaki F, Yano M, Ida K, Horie H, et al. Outcome of hepatoblastomas treated using the Japanese Study Group for Pediatric Liver Tumor (JPLT) protocol-2: report from the JPLT. Pediatr Surg Int. Jan 2011;27(1):1-8.

[26] Häberle B, Schmid I, Schweinitz D. Does the HB99 study identify a high-risk subgroup in childhood hepatoblastoma? A subgroup analysis of the GPOH study HB99. Pediatric Blood Cancer. 1 Nov 2010;55.