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Benign hepatic tumors in childhood: surgical resection and outcomes

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Abstract

Background Primary hepatic neoplasms in pediatric age are rare entities. Clinical and survival data in children with benign liver tumors who were treated by surgery are still negligible. We aimed to present a tertiary oncological center experience regarding surgical management and outcomes of pediatric benign hepatic tumors.

Material and methods A retrospective chart review was performed including all children with benign liver tumors who were surgically managed at our institution from January 2014 to January 2022. Patients' demographics, presentations, imaging scans, pathological subtypes, operative details, complications that happened, and overall outcomes were discussed.

Results One-hundred ninety-three children with liver tumors were referred to our center, and 28 of them had benign tumors (14.5%). Ten patients were managed by medical therapy (all were IHH/hemangiomas), and the remaining 18 were treated by surgery. Of the 18 patients; there were 10 females (55.5%), and the median age at diagnosis was 24 months (range: 5–108 months). Palpable abdominal mass was the main symptom in 14 patients (77.8%). Eleven patients (61%) were PRETEXT II, while the remaining 7 (39%) were PRETEXT I. The median tumor size was 10.9 cm (range: 7.2–18 cm). Preoperative biopsy was conducted in 12 patients (66.7%). Seventeen patients had primary resection, while the remaining child with IHH/hemangioma underwent delayed surgery. Twelve cases had segmental resection or sectionectomy, and hemihepatectomy was performed in the remaining six. The resection rate of benign tumors versus all liver resections at our center during the study period was 12% (18/151). There were no intraoperative complications encountered in any patient. Only one patient developed biliary leakage on the 5th postoperative day which was managed conservatively. At a median follow-up time of 40 months, there were no deaths or recurrences among the included patients.

Conclusions Surgical resection is the principal modality of management for the majority of pediatric benign liver tumors, which constituted 12% of our hepatic resection rate. Complete excision with negative margins can be performed without significant morbidity for such tumors, and it achieves excellent clinical and long-term oncological outcomes.

Keywords Surgical resection, Children, Hepatectomy, Benign liver tumors, Outcome

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Background

Primary hepatic neoplasms in pediatric age are rare entities, as they represent approximately 5% of intra-abdominal tumors and about 0.5–2% of all childhood malignancies [1]. The annual incidence has been estimated to be 0.4–1.9 patients per one million children [2]. These tumors include benign and malignant lesions, and more than two-thirds of them are of malignant nature, with hepatoblastomas constituting the vast majority of such neoplasms [3].

Benign hepatic tumors in pediatric patients are less commonly encountered when compared to their malignant counterparts [4]. Focal nodular hyperplasia (FNH), mesenchymal hamartoma (MH), adenomas, infantile hepatic hemangioendothelioma (IHH), and hemangiomas are the most common pathological types as per previous reports in the pediatric literature [4–6]. Diagnosis is mainly based on clinical features and imaging criteria; however, in some patients, the differential diagnosis may be a challenge [5]. Due to the heterogeneity of such entities, management strategy includes a monitor-and-see policy, medical therapy, and interventional radiology in addition to surgical resection which is imperative for certain cases [4].

Hepatectomy in children is a complex procedure that requires a precise operative technique to define vascular anatomy, minimize blood loss and complications, and ensure tumor resection with adequate safety margins [7]. Despite several studies that have been published regarding surgical resection and an improved prognosis of hepatoblastomas [8–10], the clinical and survival data in children with benign liver tumors who were treated by surgery are still negligible. Thus, the current study reports a tertiary oncology center experience concerning surgical management and outcomes of pediatric benign hepatic tumors.

Methods

This is a retrospective review including all children with benign liver tumors who were surgically managed at Children's Cancer Hospital, Egypt, over 8 years (between January 2014 and January 2022). Our institution is the main center for pediatric oncology service in our country with a capacity of 360 beds. The institutional review board of our hospital has reviewed and approved the study design (Approval number: 46/2022). The written consents of the patients' guardians were waived due to the retrospective nature of the study.

Medical case records were reviewed to extract patients' demographics, presentations, radiological scans, pathological subtypes, operative details, complications that happened, and overall outcomes. All children underwent a complete clinical examination followed by an assessment of serum alpha-fetoprotein (AFP). Imaging studies included abdominal ultrasound and computed tomography (CT) to evaluate the origin, size, extent, and classic radiological characteristics of the tumor. Additionally, magnetic resonance imaging (MRI) was adopted to identify further data including vascular involvement in some cases. PRETEXT classification was applied to all patients for tumor staging before surgery [11]. Core-needle biopsy under ultrasound guidance was conducted to confirm the diagnosis in patients with equivocal imaging results.

All patients were presented and discussed in our weekly tumor board to establish a treatment decision. Children with small asymptomatic parenchymal nodules were observed for spontaneous regression. For symptomatic patients with IHH/hemangiomas, beta-blockers (propranolol 1.5–3 mg/kg/day) and steroids (prednisolone 2–5 mg/kg/day) were administered for 6 months. Follow-up imaging scans were conducted to evaluate the tumor size and response. Selective embolization procedures and/or surgical resection were performed on patients with persistent, large tumors. The anatomical extension of the lesion was the core base for surgical resection. The procedures were commenced with an injection of midazolam and fentanyl. Induction of general anesthesia was done with injection of propofol and rocuronium. Endotracheal intubation was performed using a cuffed Portex tube. Baseline arterial blood gases were obtained and a central line was secured. All vital parameters were monitored throughout the procedures. Hypothermia was avoided by using a warming system. Maintenance of anesthesia was conducted with oxygen 50%, fentanyl, and rocuronium infusions with Sevoflurane. Anatomical liver resections were performed in all patients (hemihepatectomy, sectionectomy, or segmental resection) using an ultrasonic aspirator or harmonic scalpel. Surgical ligation, argon laser, and/or bipolar cautery were used to achieve a bloodless field after tumor resection. The final pathological results of excised lesions were declared by our pathologists. The schedule of follow-up was; a visit every 3 months in the first two years and then every 6 months thereafter. Clinical assessment and imaging studies were adopted during monitoring visits, and follow-up data were collated till June 2022.

Results

During the study period, 193 children with hepatic tumors were presented to our tertiary, national institution. Out of them, there were 28 patients (14.5%) who were afflicted with benign liver tumors. Ten patients were successfully managed by medical therapy as aforementioned in the methods section, all of them were IHH/

hemangiomas. The remaining 18 cases were treated by surgical resection and enrolled for the analysis. The resection rate for all benign tumors was 64% (18/28). Figure 1 demonstrates all cases with hepatic tumors and their management strategies.

Of the 18 patients, there were 10 females (55.5%) and 8 males (44.5%). The median age at the time of presentation was 24 months (range: 5–108 months). Thirteen patients (72%) were less than 4 years of age. Fourteen patients (77.8%) were referred to our center due to a palpable abdominal mass and increased abdominal girth, whereas abdominal pain was the presenting symptom in the remaining 4 children (22.2%). None of the included cases were diagnosed incidentally, without any complaints. The duration of the presenting symptom ranged between 10 and 120 days, with a median of 45 days. According to PRETEXT classification; eleven patients (61%) were stage II, while the remaining 7 (39%) were PRETEXT I. The median level of AFP was 32 ng/ml (range: 2–2970 ng/ml). The tumors' sizes (measured by CT) ranged from 7.2 to 18 cm, with a median size of 10.9 cm. Ultrasound-guided tru-cut biopsy was conducted in 12 patients (66.7%), while the remaining 6 were diagnosed as per conclusive radiological criteria. There were no complications that occurred after imaging-guided biopsies, and the patients were discharged the next day. The final pathological types were as follows: FNH was demonstrated in 9 patients and MH in 6 cases. Adenoma was reported in 2 patients, and IHH/hemangioma in the remaining one. Table 1 summarizes patients' demographics, diagnosis, and surgical procedures for management.

Primary surgical resection was conducted in 17 patients, while the remaining child with IHH/hemangioma underwent surgery after failure of management using medical therapy and intervention angioembolization. All surgeries were performed by the same surgical team. Regarding the extent of the hepatic resection; 12 cases had segmental resection or sectionectomy (according to the tumors' location), and hemihepatectomy was performed in the remaining 6 cases as shown in Table 1. The total operative time ranged between 70 and 300 min, with a median of 210 min. The median level of blood loss was 105 ml (range: 80 and 320 ml), and only three patients received blood transfusions after resection. There were no intraoperative complications encountered in any patient. The resection margin was macroscopic and microscopic negative (R0) in 16 patients, whereas the remaining patient (IHH/hemangioma, 18 cm in diameter) had a microscopic positive margin (R1). The resection rate of benign tumors versus all liver resections at our center during the study period was 12% (18/151) as shown in Fig. 1. Imaging criteria and operative resection

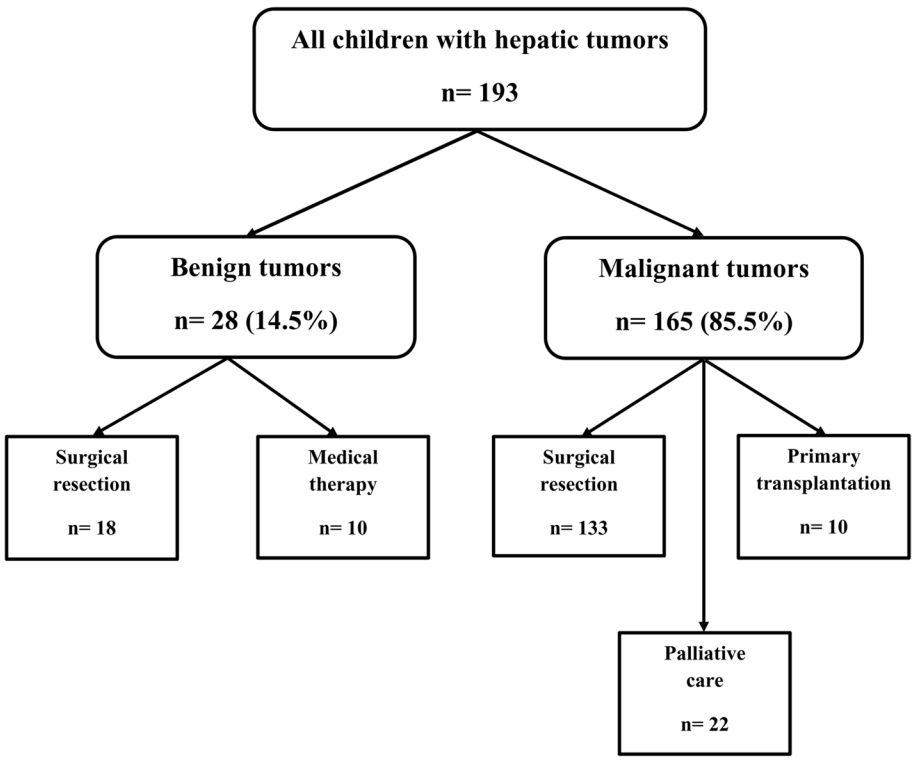

Fig. 1 All patients with hepatic tumors and their management strategies

Table 1 The clinical characteristics of all patients

Case *N*	[a]Age (m)	Gender	Presentation	Segments	PRETEXT	Tumor size (cm)	Diagnostic method	Pathological subtype	Extent of resection	Follow-up (m)
1	24	Female	Palpable mass	VI	I	7.2	Biopsy	FNH	Segmentectomy	88
2	24	Male	Palpable mass	V, VI	II	10.4	Imaging	FNH	Bisegmentectomy	80
3	17	Female	Palpable mass	V, VI, VII	II	15	Biopsy	MH	Segmental R	78
4	24	Female	Palpable mass	V, VI, VII, VIII	II	18	Biopsy	MH	Hemihepatectomy	71
5	10	Male	Abdominal pain	II, III, IV	II	12	Biopsy	Adenoma	Hemihepatectomy	68
6	72	Female	Palpable mass	III	I	7.5	Biopsy	Adenoma	Segmentectomy	60
7	84	Female	Palpable mass	II, III	I	11	Imaging	FNH	Left lateral S	53
8	11	Male	Abdominal pain	V, VI	II	13	Biopsy	MH	Bisegmentectomy	48
9	48	Female	Palpable mass	IVb, V	II	13	Biopsy	MH	Segmental R	43
10	60	Male	Palpable mass	V, VI, VII, VIII	II	18	Imaging	IHH	Hemihepatectomy	37
11	48	Male	Palpable mass	III	I	9.4	Imaging	FNH	Segmentectomy	33
12	5	Female	Palpable mass	VI	I	7.5	Biopsy	FNH	Segmentectomy	31
13	72	Female	Palpable mass	III	I	10.8	Biopsy	FNH	Segmentectomy	27
14	24	Male	Palpable mass	V, VI, VII, VIII	II	13.6	Imaging	MH	Hemihepatectomy	23
15	24	Female	Abdominal pain	V	II	10	Biopsy	FNH	Segmentectomy	18
16	108	Male	Abdominal pain	VI, VII	I	10	Biopsy	MH	Right posterior S	12
17	24	Male	Palpable mass	V, VI, VII, VIII	II	11	Imaging	FNH	Hemihepatectomy	10
18	24	Female	Palpable mass	II, III, IV	II	8	Biopsy	FNH	Hemihepatectomy	9

m, months; *MH*, mesenchymal hamartoma; *FNH*, focal nodular hyperplasia; *IHH*, infantile hemangioendothelioma; *R*, resection; *S*, sectionectomy

[a] The patients were arranged by a chronological manner regarding the time of presentation

of variable pathological subtypes were documented in Figs. 2, 3, and 4.

Regarding early postoperative morbidities; one patient developed biliary leakage on the 5th postoperative day that was managed conservatively. There were no other complications that happened among the patients. The postoperative hospital stay was as follows: median: 6 days, range: 5–12 days. One patient presented 7 months post-resection with a clinical picture of mechanical intestinal obstruction that was managed by laparotomy and adhesiolysis, without any oncological events. At the end of the follow-up duration (median: 40 months, range: 9–88 months), there were no deaths or recurrences among the included patients and all of them were alive and disease free.

Discussion

Hepatic tumors in the pediatric population are rare entities representing about 5% of all intra-abdominal masses in such age group. The presentation of benign and malignant tumors is quite similar with a palpable mass and/or abdominal pain as the chief complaints, as reported previously [6, 12]. Diagnosis is often based on radiological criteria and tumor markers or tissue biopsy in cases with doubtful imaging features.

The diagnosis of benign liver neoplasms is sometimes a challenge in spite of the advances in radiological studies in the recent era. In our study, only 33% of patients with benign lesions were diagnosed by classic imaging criteria. Similarly, Qureshi et al. reported that 38% of patients in their series were diagnosed as per radiological features [13]. In contradiction, Kochin et al. declared that definitive diagnosis using imaging was achieved in 58.5% of the patients in their study [14]. These data confirm that ultrasound-guided biopsy is imperative in cases with equivocal criteria to establish a precise tissue diagnosis for proper management. Serum AFP is often elevated in patients with hepatoblastoma and has a key role in the diagnosis of those patients [10]. In contrast, it is not elevated in the majority of children with benign tumors. However; serum AFP may be elevated in some patients with MH and the levels return to normal values within months after tumor resection [15, 16]. This was in line with our findings as three patients with MH were presented with elevated tumor marker at diagnosis that was normalized post-resection.

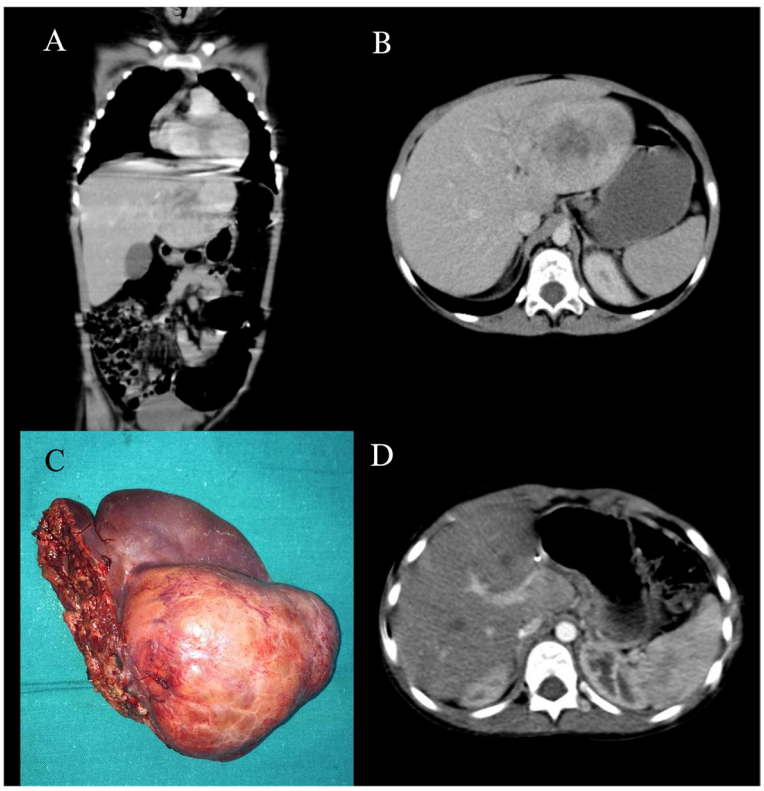

Fig. 2 **A** Initial CT (coronal view) shows an adenoma in segment III (7.5 cm). **B** Initial CT (axial view) of the same patient. **C** Segmental resection was performed with complete tumor resection. **D** Postoperative CT after 3 months (axial view) shows clear operative bed

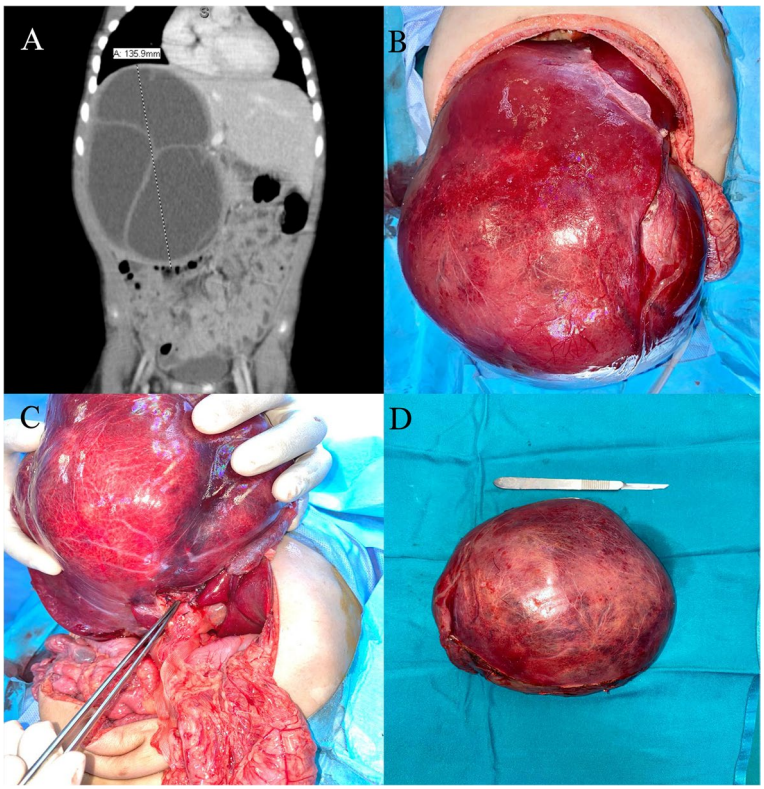

Fig. 3 **A** Initial CT (coronal view) of mesenchymal hamartoma in segments V, VI, VII, and VIII (13.6 cm). **B** Operative photo shows tumor exposure. **C** Operative photo shows hilar dissection. **D** Right hepatectomy was performed with complete tumor resection

Management of pediatric benign liver tumors includes several components, and hepatectomy is the sole modality in certain patients as documented by a recent report [4]. In the current study, operative resection was the treatment of choice for all pathological subtypes except IHH/hemangioma. Additionally, a patient with a huge IHH/hemangioma that did not respond to medical therapy or embolization technique was successfully managed by surgery. Our findings report that medical therapy is the first and an effective strategy for IHH/hemangioma as well as declared by Gnarra et al. [17]. However, surgery is reserved for cases with failed or progressive courses. Following IHH/hemangioma, MH is the second most commonly encountered benign liver tumor among children. Surgical resection is always performed for MH due to several causes as such tumors grow in sizes reaching huge sizes and malignant transformation to embryonal sarcoma could occur in addition to the rarity of spontaneous regression [16]. In our study, all patients with MH were exclusively managed by surgery and the same results were declared by others [1, 13, 14]. Liver adenoma is an extremely rare tumor in pediatric age. Intra-tumoral or intra-abdominal bleeding and malignant transformation can occur; consequently, operative management is fundamental in cases with adenomas more than 5 m in size [4]. In this study, the two patients with adenomas had tumor sizes of 12 and 7.5 cm, and both of them were treated by surgery to avoid the occurrence of the aforementioned complications. FNH is usually encountered in children between 7 and 14 years, with approximately 200 cases diagnosed per annum according to a literature report [4]. Surgical resection is the treatment of choice for symptomatic patients with FNH as documented by our study and others [1, 3, 13, 14]. Consequently, the authors of this study believe that surgery is a crucial modality of management for pediatric benign liver tumors as well as hepatoblastomas.

The complications of hepatectomy are several, and intraoperative or early postoperative bleeding is the most life-threatening complication [7]. This can be attributed to small blood volumes in pediatric patients in addition to the excision of tumors on normal liver tissue that leads to more hemorrhage when compared to adults with cirrhotic liver. In our study, none of the included patients had bleeding or other major complications, and only 3 cases received blood transfusion post-resection. Similar results regarding safe tumor resection without significant complications and reduced intraoperative blood loss

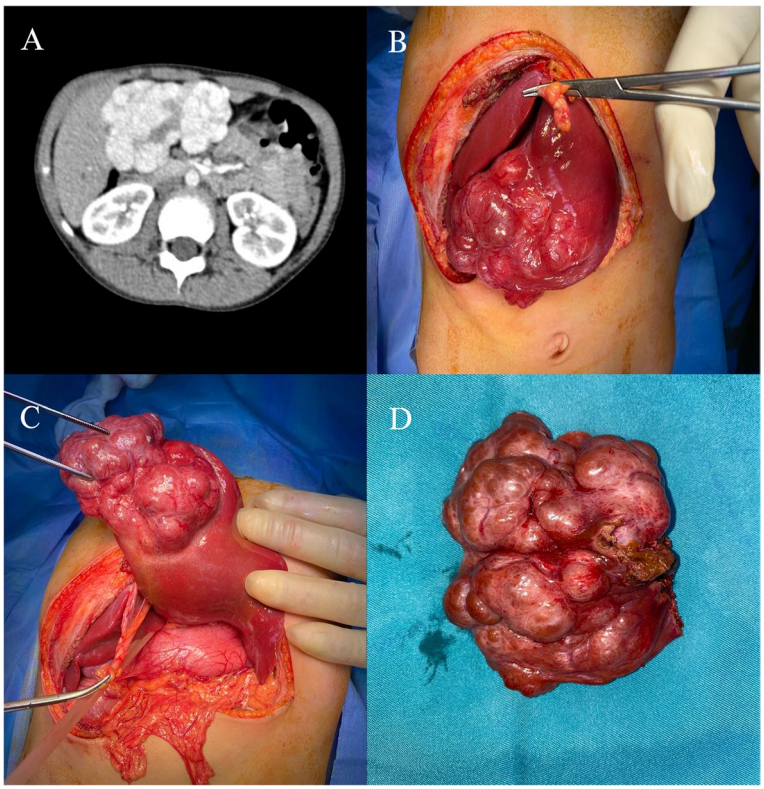

Fig. 4 **A** Initial CT (axial view) shows focal nodular hyperplasia in segment III. **B** and **C** Operative photo shows tumor exposure. **D** segmental resection was performed with complete tumor resection

were reported by previous studies [13, 18]. Definitely, the adoption of neoadjuvant chemotherapy in hepatoblastoma with huge sizes leads to tumor downsizing and easier resections [8, 9], which is not applicable in benign liver neoplasms. Therefore, surgical resection for benign hepatic tumors may be a critical procedure in some children with extensive lesions and we believe that tumor resection should be performed in dedicated centers with a high flow of pediatric liver surgeries. The outcomes of surgical resection for benign hepatic tumors are deficient in the pediatric literature. Nevertheless, few studies reported favorable results as well as our findings [1, 4, 13, 14].

Conclusions

Surgical resection is the principal modality of management for the majority of pediatric benign liver tumors, which represented 12% of our hepatic resection rate. Complete excision with negative margins can be performed without significant morbidity in such tumors, and it achieves excellent clinical and long-term oncological outcomes.

Abbreviations

CT	Computed tomography
MRI	Magnetic resonance imaging
R0	Complete resection
R1	Positive microscopic resection margin
MH	Mesenchymal hamartoma
FNH	Focal nodular hyperplasia
IHH	Infantile hemangioendothelioma

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Authors' contributions

Study design: AE. Data collection: AE and GA. Data analysis: AE and GA. Manuscript writing: AE. Manuscript critical review: AE, GA, and AY. All authors read and approved the final copy of the manuscript.

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Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on a reasonable request.

Declarations

Ethics approval and consent to participate

This study was reviewed and approved by the institutional review board and the research ethical committee of Children's Cancer Hospital, Egypt with an

approval number of 46/2022. A written consent was obtained from all study participants.

Consent for publication
Written informed consents were signed by all parents for surgery and data use in scientific purposes only at the time of management at our center. This consent was clearly stated in the manuscript in the methods section. All private data of patients such as name, address and phone number, or even identity photos will not appear in the research. The consents are in the patients' medical records.

Competing interests
The authors declare that they have no competing interests.

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