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Histomorphologic Patterns of Hepatoblastoma Observed in a Tertiary care hospital

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Author`s Contribution

[1]Concept/research design, data collection, and takes the responsibility and accountable. statistical analysis and manuscript writing, [2,3]Project management, and critical revision of the manuscript for important intellectual content [4]Provided concept/research design, and data collection, - 7[5]concept/research design, data collection, and project management. [6]Statistical analysis and manuscript writing

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ABSTRACT

Background: Hepatoblastoma is one of the most common malignant childhood tumors with diverse histologic patterns. Recent advances in imaging, pathologic evaluation, risk stratification, neo-adjuvant treatment and surgical interventions have remarkably improved the survival status of these patients in the developed world. In developing countries like Pakistan successful outcome with limited resources is still challenging for the clinicians and pathologists. Histopathology plays an important role in timely correct diagnosis leading to prompt clinical management and survival.

Methodology: 34 cases of hepatoblastoma of both genders were recorded. Clinical presentation, radiology, serum AFP level , histopathologic diagnosis and outcome data were collected and analyzed.

Results: Out of 34 cases,24 were male and 10 were female with median age of diagnosis was 3 years. Most children were presented with abdominal distension 19 cases and right sided hepatic lesion 21 cases. The most common histopathologic type was mixed mesenchymal and epithelial 35% followed by fetal type(20%),epithelial type (17%),embryonal and small cell types(6%),macro trabecular type (11%) and pleomorphic type(2%). Elevated AFP level was observed in more than 90% of cases.

Conclusion: The most common histopathologic type was mixed epithelial and mesenchymal with male predominance was observed.

Key words: hepatoblastoma, fetal, histomorphology

Introduction

Hepatoblastoma (HB) , a pediatric malignant tumor of the liver accounts for 1 % of all childhood tumors and is usually seen in children less than 5 years of age. It constitutes to 66% of the malignant hepatic neoplasms in childhood , with an annual incidence of 1.2–1.5 cases per million population.[1-3]

Hepatoblastoma has a sporadic as well as association with various syndromes like familial adenomatous polyposis syndromes, Li-Fraumeni syndrome, Wilms tumor-associated syndromes (such as Beckwith Wiedemann syndrome and Edward syndrome) (1). Upregulation in Wnt/β-catenin pathway can be seen in 70–80% cases of HB(4). In addition to mutational changes there are some other contributory risk factors associated with hepatoblastoma like it is seen more commonly in children with low birth weight and prematurity, maternal risk factors are smoking, alcohol consumption, and use of oral contraceptives. [3,4]

Clinically patients with hepatoblastoma most commonly present with either raised levels of serum alpha feto-protein, palpable abdominal mass, sometimes fever and abdominal pain is the only clinical symptom noted. The metastatic deposits of HB usually go to the lungs. Hematogenous lymph nodal metastases are documented.

Morphologically hepatoblastoma can show a variable heterogeneous features both macroscopically and histopathologic ally.[5]. HB is classified into 2 broad categories: epithelial and mesenchymal type. The majority of HB are of the epithelial type ([6]). The epithelial variety is further divided into six patterns: small-cell undifferentiated, embryonal, pleomorphic, cholangioblastic, fetal, and macro trabecular. It is important to be aware of various morphological patterns associated with it to distinguish it from other childhood tumors ([4]). Histomorphology and immunohistochemical stains (such as HepPar 1, B-Catenin, CyclinD1 and Glutaminase Synthetase)are essential for the diagnosis of the different HB types ([6, 7]).

Histopathology of HB is of utmost importance since it has been included as an important risk stratification variable in the Children's Oncology Group (COG) protocols for planning treatment. All Histomorphologic patterns have a distinct histology and specific clinical associations. Hence correct Pretreatment Extent of Tumor (PRETEXT) staging and risk status along with correct histological subtype diagnosis of hepatoblastoma is essential for patient treatment, outcome and overall disease free survival (8).

The management of HB has changed markedly over the last three decades. Serum Alfa- feto protein (AFP) is the main tumor marker for diagnosis , treatment and follow up. International collaborative efforts have led to the implementation of the Pre - Treatment Extent of the Disease PRETEXT staging system consensus classification to assess upfront resect ability (7, 9).

Neoadjuvant chemotherapy followed by surgery is the main treatment modality followed by surgical oncologists. If the tumor is completely resectable, the prognosis is highly favorable, primarily because it responds well to adjuvant chemotherapy. If complete removal is not possible due to late diagnosis and presentation, the prognosis is far less favorable (10, 11).

Prognosis is based on numerous factors, including age at the time of diagnosis, metastases, alpha fetal protein (AFP) levels, histologic subtype, completeness of resection, and clinical stage of the disease (7).

The study aims to classify HBs on histopathological examination into its different subtypes and correlate with serum alpha-fetoprotein levels.

Methodology

It was a descriptive study carried out in The Children hospital Lahore during the period of 1 and a half year started from 1st January 2023 to 30th June 2024.Total 34 patients of Hepatoblastoma including both male and female were included in the study. All detailed clinical information such as name, age, gender , serum alpha fetoprotein levels (AFP), follow up data on survival/response to therapy were recorded and filled in the Performa. PRETEXT staging was assigned using contrast computed tomography (CT). Histological data regarding gross features were collected ,hematoxylin and eosin stain slides were examined, and results were entered on Performa for analysis. SPSS version 24 was used for data analysis. Ethical approval was obtained from the Institutional

Results

A total of 34 cases of Hepatoblastoma were evaluated. The male to female ratio is 71% and 29% respectively showing male predominance. The mean age of patients is 4.43 representing earlier age presentation. The most common presentation of children was abdominal mass 60%, followed by abdominal pain 32% and only 11.8% cases presented with fever. Involvement of right sided lobe of liver is more frequent in our study with 64% involvement as compared to left side liver lobe involvement 23%, only 11.8% cases were multifocal.

Table I: Characteristics of study cases	
Gender	
male	24 (70.6%)
female	10 (29.4%)
Age	4.432±3.0
Clinical presentation	
Abdominal swelling	19(55.9%)
Pain	11 (32.4%)
Fever	4(11.8%)
Gross features	
Right side lesion	22(64%)
Left side	8 (23.5%)
multifocal	4 (11.8%)

The most common histologic subtype in our study is mixed epithelial and mesenchymal 35.3% followed by fetal morphology 20%, macro trabecular 11.8%, embryonal and small cell having equal frequency of almost 6% and the least common histologic type is pleomorphic with only 2.9% reported case. The overall prevalence of epithelial morphology is almost 17.6%.

Table II: Frequency of various Histomorphologic subtypes of Hepatoblastoma		
Morphological Subtypes	**N**	**(%)**
Fetal type	07	20.6
Epithelial	06	17.6
Mixed epithelial and Mesenchymal	12	35.3
Embryonal	2	5.9
Small cell	2	5.9
Macro trabecular	4	11.8
Pleomorphic	1	2.9
Total	34	100

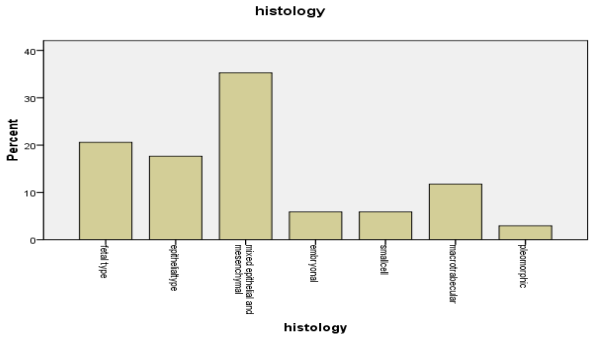

Figure 1. Histogram representing histology patterns.

Discussion

Liver masses are uncommon in infants and children, comprising 15% of all primary abdominal tumors, two-third are malignant, and HB is the most common one(11). HB is commonly seen in males as solitary liver mass (80–85%), often affecting the right lobe of the liver(4). In our current study the same finding was observed with right side lobe involvement more frequent (64%) as compared to left one 23%. Out of 34 , 24 were male patients and 10 were female with a ratio of 2.4:1 (Male : Female).

Serum AFP, a very sensitive marker is elevated in 90% of HB patients and almost all patients in our study had an elevated AFP at presentation (12, 13). In one of the studies carried out at Archana the most common clinical presentation is an abdominal mass or distention , which is in in concordance with our study(12). The histopathological subtypes included primarily of epithelial origin followed by mixed epithelial and mesenchymal (12), that also correlated with our study finding of mixed epithelial and mesenchymal subtype being the most common(35.3%).

With advancing age from 5years onward, the diagnosis of hepatoblastoma versus hepatocellular carcinoma should be seriously considered as in our study we have not observed any significant correlation between the age of the patient and occurrence of various histologic patterns of HB while the incidence of hepatocellular carcinoma approaches and overtakes that of HB with advancing age. (14, 15).

The subtypes can be determined based on distinct morphological features. However, immunohistology can aid in the diagnosis of cases with indeterminate morphology (16). Prognosis is based on numerous factors, including age at the time of diagnosis, metastases, alpha fetal protein (AFP) levels, histologic subtype, completeness of resection, and clinical stage of the disease(7, 16).

As prognosis and treatment may differ according to the morphological subtype, the use of immunohistochemistry in future may improve standardization of treatment stratification according to tumor histopathology(12). In one of the studies conducted by Rowland JM the most common morphologic pattern observed was mesenchymal(45%) then comes the fetal (30%), embryonal (20%), and macro trabecular (5%) patterns under epithelial type and mixed epithelial, there was only one case diagnosed having features of teratoid differentiation.(1). Hepatoblastoma most commonly expressed chromosomal aberrations of the beta-catenin and WNT signaling pathway in around 80% of cases (2).

Clinically HB patients can be classified into high risk and low risk as per SIOPEL risk stratification protocol that depends on the following features:

Standard risk: Patients with no evidence of metastasis, invasion of blood vessels and localized liver lesions are categorized as PRETEXT I, II, and III while the High Risk patients are those with evidence of rupture of hepatic capsule, blood vessel invasion and serum alpha feto protein level less than 100ng/ml. All these patients are categorized as PRETEXT IV. (17,18)

Histomorphologic patterns of hepatoblastoma are not included in the above risk stratification protocol. (17) In our study it was found that the presence of mixed epithelial and mesenchymal histology has clinically associated with high mortality and poor prognosis. HB is known to be associated with disorders such as Beckwith-Wiedemann syndrome, familial adenomatous polyposis, and congenital anomalies like hemihypertrophy and cleft palate, Wilms' tumor, and glycogen storage diseases (19). Hepatoblastoma has also shown association with germline mutations as well as with Edward syndrome that is also associated with Wilms tumor (1). Upregulation in Wnt/β-catenin pathway can be seen in 70–80% cases of HB(4).

Although the stage of tumor at diagnosis remains the key factor in determining prognosis, various clinical and

histological factors have also been implicated in prognostication.

Diagnosing hepatoblastoma is challenging for a general pathologist even in specialized institutions owing to its rarity, histological diversity as well as a lack of a current international consensus on its classification (20). Histology is very important because it is incorporated as a risk stratification parameter in the Children's oncology group (COG) protocols for planning treatment. It is seen that each of the histological parameters have distinct clinical associations(17).

Conclusion

Considering the patient's age, exact location, and nature of the lump, the HB shall be considered as differential diagnosis for abdominal mass in children. Clear knowledge of its various Histomorphologic subtypes is essential for correct diagnosis that also decides patient's prognosis and survival .

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