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Callow and Vernal-Hepatoblastoma

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Editorial

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Introduction

Hepatoblastoma configures as a malignant, primary hepatic neoplasm constituted of a blastomatous component wherein the neoplasm appears reminiscent of embryological stages of hepatic development. Neoplasm is commonly encountered within the paediatric population. Tumefaction expounds varying combinations of epithelial and mesenchymal components and configures an epithelioid pattern or mixed epithelioid and mesenchymal pattern. Neoplasm is appropriately staged with PRETEXT which is designated as PRE-Treatment Extent of tumour classification. Majority (~90%) of neoplasms emerge between 5 months to 6 years of age. However, prenatal lesions or tumours implicating neonates and older children may be discerned. Tumour occurrence within adults is extremely exceptional. A mild male predilection is observed [1,2].

Hepatoblastoma preponderantly incriminates hepatic parenchyma and is preferentially discerned within right lobe or may commence within the right hepatic lobe. Currently, hepatoblastoma is posited to be engendered from primary hepatoblasts or multipotent hepatic progenitor cells [1,2].

Hepatoblastoma preponderantly emerges as a sporadic neoplasm. Few neoplasms are associated with familial adenomatous polyposis with concurrent genomic mutations within adenomatous polyposis coli (APC) gene, Beckwith-Wiedemann syndrome or trisomy 18. Neoplasm is intensely concordant with parental tobacco consumption as smoking or low birth weight and is predominantly observed in neonates < 1,000 grams birth weight [1,2].

Evaluation of gene expression profile appears advantageous for stratification of hepatoblastoma. Neoplasms with significant possible emergence of malignant metamorphosis depict upregulation of NFE2L2 activity, elevated levels of LIN28B, HMGA2, SALL4 and alfa fetoprotein (AFP) and enhanced expression of oncofetal proteins with stem cell markers [1,2]. Tumefaction demonstrating minimal possible occurrence of malignant metamorphosis exhibit LIN28B and let-7 expression along with significant activity of HNF1A gene [1,2]. Generally, hepatoblastoma represents with abdominal enlargement, abdominal tumefaction or pain along with anorexia and weight loss. Hyper-bilirubinaemia is uncommon [2,3].

Cytological examination is contingent to clinical concurrence of hepatic tumefaction arising within paediatric population associated with elevated serum alfa fetoprotein (AFP) and application of precise immunohistochemistry [2,3]. Neoplastic cellular elements of advanced grade appear admixed with mesenchymal component. Foci of necrosis, mitotic activity and apoptotic figures appear to indicate an embryonal or small cell undifferentiated tumour configuration [2,3].

Grossly, a singular or multinodular tumour with well-defined perimeter is exemplified. Cut surface appears tan to brown, especially within the foetal subtype. Small cell undifferentiated subtype enunciates a variegated countenance. Following therapy, focal necrosis and haemorrhage may be discerned. Foci of osteoid delineate a firm and gritty texture of the neoplasm [2,3]. Upon microscopy, as per International Paediatric Liver Tumour Consensus Classification, hepatoblastoma is categorized as ~epithelial hepatoblastoma which may enunciate various configurations denominated as foetal, embryonal, small cell undifferentiated (SCUD), cholangioblastic or macro-trabecular wherein aforesaid tumour patterns may appear singularly or in combination [3,4].

- Foetal pattern is composed of attenuated trabeculae or nests of miniature to intermediate cells simulating

hepatocytes of developing foetal liver. Tumour cells are pervaded with clear or finely granular cytoplasm, variable quantities of glycogen and lipids, miniature spherical nucleus and an indistinct nucleolus. Foci of extramedullary haematopoiesis are discerned. Typically, mitotic activity is minimal wherein the neoplasm is designated as a well differentiated hepatoblastoma. A subset of neoplasms exhibit elevated mitotic activity, decimated cytoplasmic glycogen and pleomorphic nuclei wherein the variant is designated as mitotically active hepatoblastoma [3,4].

- Embryonal pattern simulates developing liver upon 6 weeks to 8 weeks of gestation. Tumefaction is composed of solid cellular nests, glandular pattern or acinar articulations demonstrating papillae and pseudo-rosettes. Tumour cells are pervaded with dark, granular cytoplasm devoid of glycogen or lipids and enlarged nuclei with coarse chromatin, reminiscent of blastemal cells. Extramedullary haematopoiesis is absent. Mitotic figures are enhanced [3,4].
- Small cell undifferentiated pattern is composed of solid sheets of dis-cohesive miniature cells wherein the neoplasm configures as a small, round blue tumour. Mitotic activity, apoptotic bodies and focal necrosis are plentiful.
- Macro-trabecular pattern is constituted of dense trabeculae of 5 cells to 12 cells thick. The trabeculae may be comprised of foetal, embryonal, pleomorphic or hepatocellular carcinoma-like tumour cells [3,4].
- cholangioblastic pattern is articulated of miniature ducts disseminated within or circumscribing hepatocellular components.

Mesenchymal pattern is constituted of mature and immature fibrous tissue wherein osteoid or osteoid-like tissue is abundantly exemplified following chemotherapy (Figures 1 & 2). Foci of hyaline cartilage may be discerned. A subset of neoplasms may exhibit teratoid features with component of endodermal cells, neuroectodermal tissue as neuronal cells, glial tissue and melanin producing cells admixed with complex tissue as striated muscle [3,4].

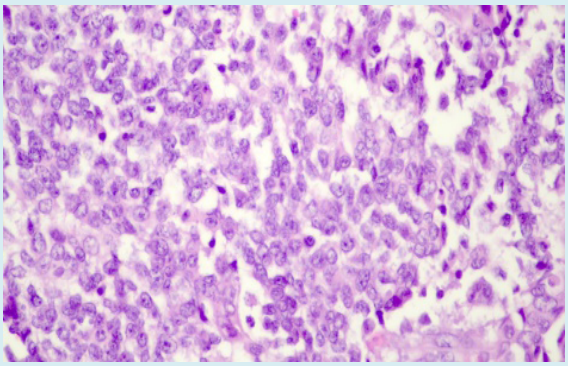

Figure 1: Hepatoblastoma delineating aggregates and trabeculae of immature hepatoblasts impregnated with abundant granular cytoplasm, intracytoplasmic glycogen, miniature nuclei and indistinct nucleoli [5].

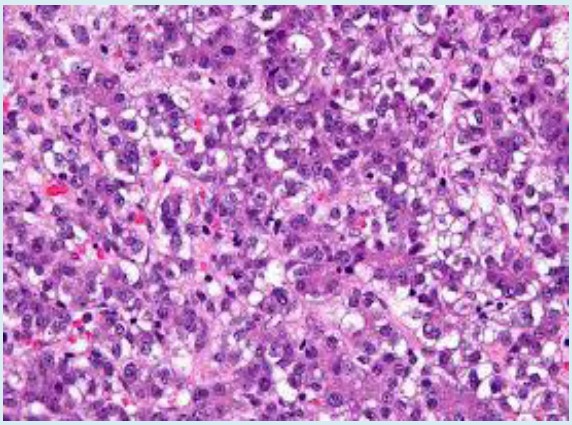

Figure 2: Hepatoblastoma exemplifying trabeculae and cell nests of immature hepatoblasts imbued with granular cytoplasm, intracytoplasmic glycogen, miniature nuclei and indistinct nucleoli [6].

Cogent staging of hepatoblastoma designated as PRETEXT or PRE-Treatment EXTent of tumour is recommended by the Pediatric Hepatic International Tumour Trial (PHITT) and denominates features as extent of tumour incriminating hepatic parenchyma and quantifiable surgical resection of the neoplasm. Appropriate tumour staging is obtained with surgical tissue sampling. The PRETEXT group of tumour stage I, stage II, stage III and stage IV is indicative of hepatic parenchymal incrimination by the neoplasm. Enhancing PRETEXT stages are associated with inferior prognostic outcomes [3,4]. PRETEXT factors enunciate extra parenchymal neoplastic characteristics as ~V representing incrimination of vena cava, three hepatic veins or a combination of aforesaid vascular articulations ~P representing incrimination of portal bifurcation, right and left portal veins or an amalgamation of aforesaid vascular articulations ~E representing extrahepatic contiguous tumour extension ~F representing multifocal hepatic neoplasm ~R representing tumour rupture upon initial tumour detection ~M representing tumours with distant metastasis [3,4].

Epithelial/ foetal hepatoblastoma appears immune reactive to β catenin or glutamine synthetase whereas well differentiated neoplasms with minimal mitosis or tumours with mesenchymal configuration appear immune non reactive. Besides, tumour cells appear immune reactive to alpha fetoprotein(AFP), HepPar1, polyclonal carcinoembryonic antigen(pCEA), glypican 3, pan-cytokeratin, CK7, CK19 and integrase interactor1 (INI1) or SMARCB1 [7,8].

Subset of small cell undifferentiated hepatoblastoma appear immune non reactive to integrase interactor 1(INI1) or SMARCB1 and depict inferior prognostic outcomes [7,8]. Hepatoblastoma requires segregation from neoplasms such as rhabdoid tumour, well differentiated hepatocellular carcinoma, focal nodular hyperplasia, hepatic adenoma, malignant lymphoma or hepatic metastases from various primary carcinomas [7,8]. Hepatoblastoma can be appropriately ascertained upon assessment of clinical features, biochemical assay and radiological features. Certain neoplasms may require evaluation with fine needle aspiration cytology (FNAC) or tissue sampling of surgical specimens. Majority (-90%) of subjects depict significantly elevated levels of serum alfa fetoprotein (AFP) [7,8].

Upon ultrasonography, tumefaction represents as a solid, hyperechoic mass traversed by hypoechoic fibrous tissue septa, in contrast to adjacent hepatic parenchyma. Epithelial hepatoblastoma configures a homogeneous tumefaction. Mixed epithelial and mesenchymal tumours represent as heterogeneous neoplasms on account of discernible components of osteoid, cartilaginous and fibrous tissue. Frequently, tumours display echogenic calcification with acoustic shadows and anechoic foci indicative of focal haemorrhage or necrosis [7,8]. Computerized tomography exhibits a well defined, hypo-attenuating tumefaction with uniform perimeter, in contrast to adjacent hepatic parenchyma. Upon administration of contrast medium, diffuse, heterogeneous image enhancement is commonly encountered. An estimated 50% neoplasms appear lobulated or traversed by fibrous tissue septa, especially upon contrast enhanced imaging [7,8].

Hepatoblastoma is appropriately alleviated with cogent and comprehensive surgical eradication of the neoplasm. Besides, chemotherapy may be adopted with curative intent. Notwithstanding, liver transplantation may be imperative in certain instances.

- **Therapeutic options applicable to diverse tumour stages are represented as:**

- Stage I may be subjected to comprehensive surgical resection of the neoplasm
- Stage IIa may be treated with comprehensive macroscopic surgical resection and is associated with intrahepatic residual microscopic disease
- Stage IIb may be managed with comprehensive macroscopic surgical resection and is associated with extra hepatic residual microscopic disease
- Stage IIIa may be treated with incomplete surgical resection and is associated with macroscopic residual disease and/or significant spill of tumour cells and/or metastasis into regional lymph nodes
- Stage IIIb exemplifies neoplasms which are unamenable to surgical resection
- Stage IVa exhibits neoplasms demonstrating distant metastasis wherein primary tumour is subjected to comprehensive surgical resection
- stage IVb exemplifies neoplasms delineating distant metastasis wherein primary tumour is incompletely eradicated with surgical intervention [7,8].

Contingent to factors such as tumour staging, occurrence of distant metastases and serum alfa fetoprotein (AFP) levels, hepatoblastoma is segregated into definitive prognostic groups wherein group I exhibits superior prognosis and group V is associated with inferior prognosis. Superior prognostic outcomes are encountered with PRETEXT stage I and stage II neoplasms. However, PRETEXT stage IV tumefaction is associated with inferior prognostic outcomes [7,8].

- **Factors contributing to prognostic outcomes occur as:**

- Incrimination of hepatic venous structures or inferior vena cava ~incrimination of portal venous articulations

- Extrahepatic disease dissemination
- Multifocal tumefaction
- Tumour rupture
- Incrimination of caudate lobe of liver
- Appearance of regional lymph node metastases
- Occurrence of distant metastases [7,8].

- **Factors contributing to inferior prognostic outcomes emerge as:**

- Multifocal disease
- Extrahepatic lesions
- Neoplasm unamenable to surgical resection
- Incrimination of vascular articulations
- Rupture of tumefaction
- Occurrence of distant metastasis upon initial tumour discernment
- Age of tumour emergence >6 years
- Normal or decimated levels of serum alpha fetoprotein (afp) and small cell undifferentiated morphological subtype delineate an aggressive clinical course [7,8].

- **Following therapeutic intervention, factors delineating unfavorable prognostic outcomes emerge as:**

- Inferior response to chemotherapy
- Disease progression upon chemotherapy
- Tumour confined to surgical margins
- Tumour reoccurrence [7,8]. Superior prognostic outcomes are associated with
- Age of tumour emergence <1 year
- Declining serum alfa fetoprotein (afp) levels during therapy indicative of response to treatment
- Histological subtype of pure foetal pattern with minimal mitotic activity [7,8].

References

1. Musick SR, Smith M, Rouster AS, Babiker HM (2023) Hepatoblastoma. Stat Pearls International. Treasure Island, Florida.

2. DeRenzi AD, Bowen A (2023) A Case Report and a Review of Pediatric Hepatoblastoma. HCA Healthc J Med 4(5): 377-382.

3. Cao Y, Wu S, Tang H (2023) An update on diagnosis and treatment of hepatoblastoma. Biosci Trends.

4. Espinoza AF, Patel KR, Shetty PB, Whitlock RS, Sumazin P, et al. (2023) Navigating relapsed hepatoblastoma: Predictive factors and surgical treatment strategy. Cancer Med 12(23): 21270-21278.

5. Figure 1: Courtesy: Pathology outlines.

6. Figure 2: Courtesy: Wikipedia.

7. Tian Y, Chen X, Yu F, Feng J, Huang G, et al. (2023) Neoadjuvant chemotherapy or upfront surgery in hepatoblastoma: A multicenter retrospective study. Pediatr Blood Cancer e30470.

8. Srinivasan S, Prasad M, Parambil BC, Shrimal A, Gollamudi VRM, et al. (2023) Treatment outcomes and prognostic factors in children with hepatoblastoma using a risk-stratified approach. Pediatr Blood Cancer 70(7): e30302.