

Hepatocellular carcinoma: [HCC]

→ It is malignant tumor derived from hepatocytes or their precursors.

Etiopathogenesis:

- multistep process

3 major etiological factors Risk

Major → chronic hepatitis B, C → NAFLD

(ABCL) code

Alcoholic cirrhosis → Aflatoxin C

Minor → Wilson's disease, α_1 -Antitrypsin def, psal/contraceptives, cigarette, hemochromatosis, GSD. (Associated with HCC)

⇒ chronic hepatitis → HCV & HBV is 3 times higher than either alone

⇒ The genome of HBV is integrated into the host DNA of liver cells

Active proto oncogenes → oncogenes.

→ X gene of HBV encodes HBV X-protein which is transcriptional

Activator of many genes. It is an inactivator of Tumor

suppressor gene → cause

cell transformation

→ HCV → HCV core protein interact with many cellular proteins to cause HCC

via injection

⇒ Aflatoxin B₁ (chemical carcinogen)

→ produced by *Aspergillus flavus* (in many)

They bind covalently with cellular DNA of hepatocytes & cause mutation of TP53 Tumor suppressor gene.

Molecular Basis of HCC:

Genetic RANKA
DATE / /
PAGE

epigenetic.

Genetic Alterations: (Aneuploidy, point mutation, loss of gain of chromosomal components)

1) Mutation in tumor DNA Repair gene.

Risk factors
(HBV, HCV, cirrhosis)

Reflected, cycle of liver cell death,
Regeneration of Repair → lead to mutation
in DNA Repair gene.

2) Activation of oncogene

- KRAS - p-cadherin (Tumor signaling)
- TP53 (TSG)

Activation ↓

• X proteins of hep B show oncogenic effect.

by Integration of HBV genome into hepatocyte genome.

Epigenetic Alterations:

1) CHC Amplification

2) Telomerase - cell become immortal

These factor if occur in low frequency then:

Lead to → Hepatocellular Adenoma → benign tumor of liver
(p-cadherin Mutation)

Intermediate frequency

→ cellular dysplasia

small cell change

large cell change

} premalignant
↑ N:C
Ratio

high frequency

→ Dysplastic nodules

PCN

LDN

Low grade dysplastic nodules

High grade dysplastic nodules

HADN

HCC

↑ DNA
Activation
↑ KRAS
↑ TP53

Tumor

1944 1001 -

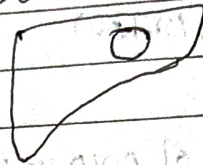
NON - HODKIN LYMPHOMA

MORPHOLOGY: HCC

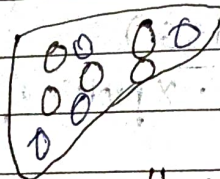
⇒ HCC - Bile production by neoplastic cell is half made
GROSS:

Nodules and Area of Necrosis & Hemorrhage

→ Unifocal (large unencapsulated single tumor mass)



→ Multifocal (Multiple nodules of varying shape & size)



→ Diffusely infiltrative

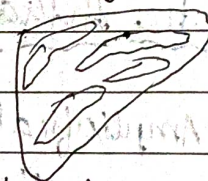
Homogeneous tumor nodules

large part / Entire liver

(Indistinct tumor nodules)

Diff. Elements

Diff. necrosis



Color → light Brown, yellowish or gray in color, Production of Bile by tumor cell → greenish brown dissolution of the tumor.

Diff. tumor cell Bile

NOTES: Lectin fraction 3 of AFP

→ Highly specific HCC

Indicator of poorly diff HCC

Unfavorable Prognosis

Hep - par 1 (hepatocyte paraffin-1)

(1) marker for normal & neoplastic hepato

• Dysplastic nodules → diff from normal nodules in size, color, shape, number & location, may be seen.

DCH

MICROSCOPY:

Earliest Alteration

large cell change

small cell change

- Hepatocytes larger than normal
- enlarged multiple prominent nuclei
- No ↑ in N:C Ratio
- smaller than normal
- mild nuclear chromatin pleomorphism.
- ↑ N:C Ratio.

Family differentiated: pleomorphic cell (shape & size variation)

HCC

moderately differentiated HCC

- solid variety: Tumor cell is small no bile production
- scirrhus variety: Malignant cell separated by abundant fibrous stroma
- clear cell variety: clear cell due to glycogen or fat

Well differentiated: Bile production by tumor cell
↓
Hallmark of HCC (Malignant hepatocyte)

Tumor cell two Arrangement

Tubular

Acinar

→ Resemble gland

hepatocellular tumor cells (pseudo glands)

- polygonal cells
- Abundant cytoplasm
- large nuclei hyperchromatic
- prominent nucleoli

Note:

Globular hyaline structure is seen in cytoplasm of hepatocellular carcinoma

Spread: more to vessels

1) Bihapatic metastases (locally) → distal metastasis
(common in diaphragm)

2) Lymphatic spread HCC → portal lymph node
pericardial nodes
para Aortic nodes

3) Blood spread → portal circulation
IVC - Rt side of heart
→ lungs

Occasionally invade the portal vein metastasize to the lungs.

Clinical features → upper Abdominal pain

malaise, fatigue, weight loss

Ass with paraneoplastic syndrome → polycythemia, hypoglycemia,
hypercalcemia, electrolyte imbalances

Lab findings

→ Alpha fetoprotein (↑ level)

→ α -1-fetoprotein

→ Serum des α -carboxy prothrombin ↑ level

A

→ The Risk for → Esophageal
→ Chronic Hep
→ Nematode infestation
→ Liver cancer

NOTE

→ Staining for glycogen 3 is used to distinguish early HCC from dysplastic nodules