The photomicrographs presented here are from five cases of hepatocellular carcinoma in the CAP Non-Gynecologic Cytopathology Program. Based on participants diagnoses all of these cases performed well. They represent typical patterns and cytologic features of hepatocellular carcinoma. While hepatocellular carcinoma is relatively uncommon in the United States, it is the most common primary malignant tumor of the liver worldwide, the highest incidence being in Asia and Africa.
Predisposing Conditions
- Chronic active hepatitis, both B and C
- Alcoholic cirrhosis
- Hemochromatosis
- Toxins
- Anabolic steroids
- Vinyl chloride
- Aflatoxins

Laboratory Findings
- Elevated alpha-fetoprotein (AFP)
  - Usually over 400 ng/ml (normal -5-10 ng/ml)
  - AFP levels often not available or drawn at the time of the biopsy
Hepatocellular Carcinoma - Cytologic Criteria

Cellularity of smears is high
Cells in trabeculae, clusters, acini
Endothelial cells at periphery or traverse cell groups
Polygonal cells, abundant cytoplasm, central nuclei
Cytoplasm granular, eosinophilic and/or vacuolated
Absence of bile duct epithelium
Hepatocellular Carcinoma - Cytologic Criteria

Nuclei round, round central nucleolus
Naked nuclei
Intranuclear cytoplasmic inclusions
Intracytoplasmic eosinophilic inclusions
Intracytoplasmic bile pigment, bile plugs between cells
Absence of bile duct epithelium
Cord and trabecular pattern of hepatocellular carcinoma
Small uniform malignant cells in hepatocellular carcinoma. Pale nuclei, very small inconspicuous nucleoli. Simulates neurodenodrine like tumor.
Eosinophilic intranuclear inclusion, lower left
Cytologic Criteria - Well Differentiated Hepatocellular Carcinoma

Cellularity of the smear - High

Arrangement of cells
- clusters and trabeculae
- borders of clusters, trabeculae are smooth
- peripheral wrapping of cell groups with endothelial cells

Cell Features
- smaller than normal hepatocytes
- bland appearance
- some increase in N/C ratio

Nuclei
- oval, placed centrally
- small nucleoli
Well differentiated hepatocellular carcinoma
Well differentiated hepatocellular carcinoma.
Vascular structures lower left of center
Cytologic Criteria - Moderately Differentiated Hepatocellular Carcinoma

Cellularity of the smear - High
Arrangement of cells
  long twisted trabeculae

Cell Features
  larger than normal hepatocytes
  abundant granular cytoplasm
  definite increase in N/C ratio
  naked nuclei

Nuclei oval, somewhat irregular
  Prominent nucleoli
  Definite chromatin abnormalities
Moderately differentiated hepatocellular carcinoma
Moderately differentiated hepatocellular carcinoma
Cytologic Criteria - Poorly Differentiated Hepatocellular Carcinoma

Cellularity of the smear - Very High

Arrangement of cells
  irregular aggregates, loosely cohesive cells

Cell Features
  large, pleomorphic, little resemblance to hepatocytes
  tumor giant cells, naked nuclei
  abundant granular cytoplasm
  high N/C ratio

Nuclei irregular, multiple
  very prominent nucleoli
  irregular chromatin, nuclear membranes
Poorly differentiated hepatocellular carcinoma.
Some clear cell features
Immunohistochemistry

Best performed on cell block material

Panel

Alfa-feto-protein
CEA - polyclonal only
Cytokeratins
  Cam 5.2
  AE 1,3
Immunohistochemistry Results

Alfa-feto-protein + most cases  
but negative does not rule out does not 
correlate with elevation in serum or absence 
there of.

Polyclonal CEA + (pattern)  
hepatocellular carcinoma - cannalicular metastatic tumors - diffuse cytoplasmic

Cytokeratin Cam 5.2 +  
Benign and malignant hepatocytes 
Most metastatic carcinomas

Cytokeratin AE1,3 +  
Only in metastatic carcinoma 
negative benign or malignant hepatocytes
Hepatocellular Carcinoma - Variants

Clear cell - cytoplasmic glycogen and or fat
Differential from metastatic clear cell tumors
kidney, adrenal, ovary, signet ring cell carcinomas

Acinar cell - prominent acinar formation
Differential from metastatic adenocarcinomas
mucin stain negative in acinar variant

Fibrolamellar - younger age group, not associated
with cirrhosis, negative AFP
Dissociated, frankly oncocytic frankly
malignant hepatocytes - maybe lowcellularity
REFERENCES


