

Lecture 12

Cancer of the Liver and Pancreas



432 Pathology Team

Done By: Abdulmohsen Al-Meshari

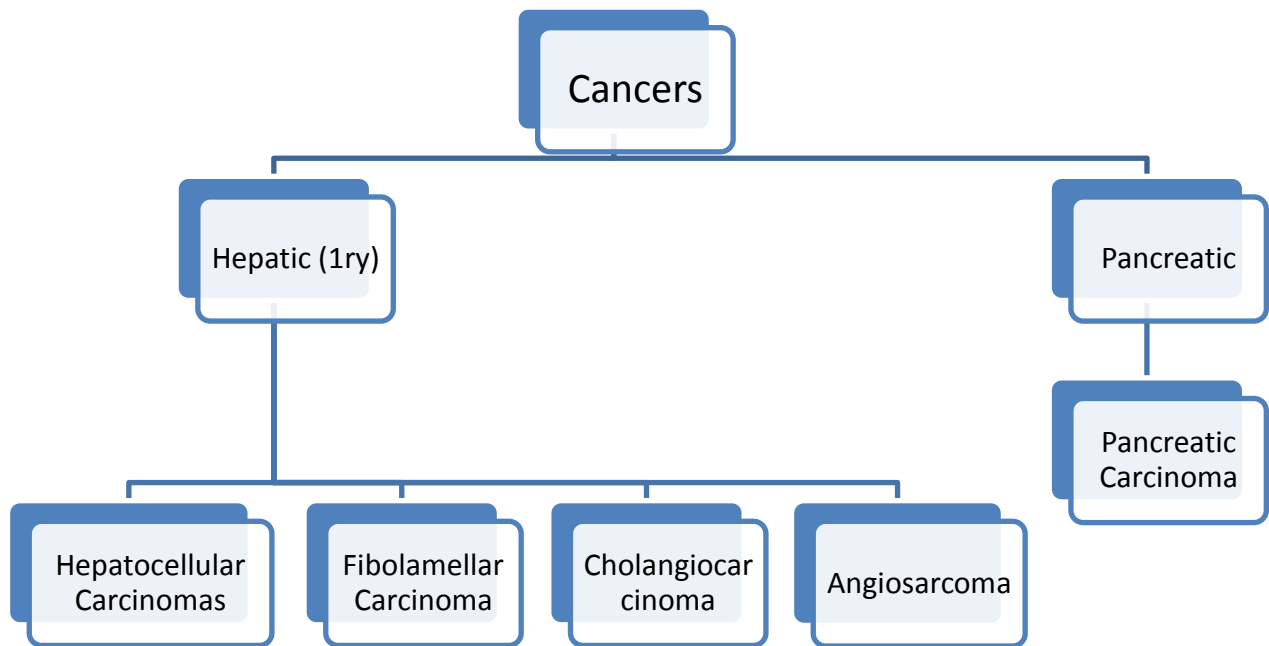
Reviewed By: Rihaf Al-Gain

GIT Block



Cancer of the Liver and Pancreas

Mind Map:



Introduction

Malignant Tumors of the liver

- The liver and lungs are the visceral organs that are most often involved by metastatic tumors.
- Metastatic involvement of the liver is far more common than primary neoplasia.
- Although the most common primaries producing hepatic metastases are those of the breast, lung, and colon, any cancer in any site of the body may spread to the liver, including leukaemia and lymphomas. (The most often site of Cancer that metastasizes to the liver is the GIT tract.)
- Typically, multiple nodular metastases are found that often cause striking hepatomegaly and may replace over 80% of existent hepatic parenchyma. The liver weight can exceed several kilograms.
- Primary carcinomas of the liver are relatively uncommon. Most arise from hepatocytes and are termed hepatocellular carcinoma (HCC).
- Much less common are carcinomas of bile duct origin, cholangiocarcinomas.
- The two rare forms of primary liver cancer are hepatoblastomas(in children) and angiosarcomas.

1RY CARCINOMAS OF THE LIVER

1) Hepatocellular Carcinoma (HCC)

(Also known as: Liver Cell Carcinoma or, Hepatoma)

Epidemiology:

1. Male predominance
2. More than 85% of cases of HCC occur in countries with high rates of chronic HBV infection. In these regions, the **HBV carrier state** begins in infancy following vertical transmission of virus from infected mothers, conferring a **200-fold increased risk** for HCC by adulthood.
3. In the Western world where HBV is not prevalent, **cirrhosis** is present in 85% to 90% of cases of HCC, usually in the setting of other chronic liver diseases.

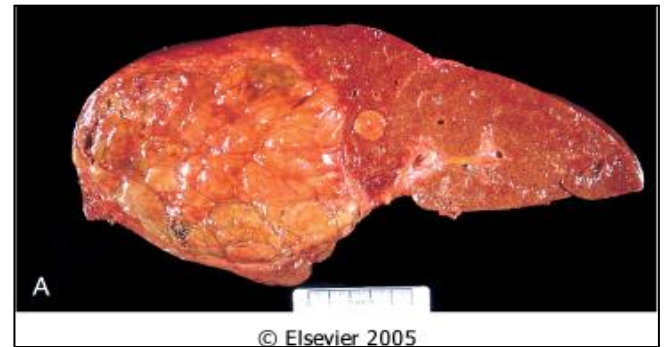
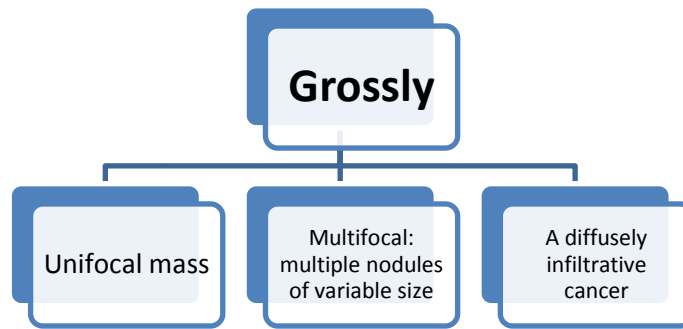
Pathogenesis:

The following have been implicated in human hepatocarcinogenesis:

- 1) **Viral infection (HBV, HCV)**: Extensive studies link chronic HBV and chronic HCV infection with liver cancer.
- 2) **Cirrhosis**: the development of cirrhosis appears to be an important, but not requisite, contributor to the emergence of HCC. (**HCC can be present without cirrhosis**).
- 3) **Chronic alcoholism**.
- 4) Food contaminants (primarily aflatoxins from aspergillus). High exposure to dietary aflatoxins derived from the fungus **Aspergillus flavus**. These highly carcinogenic toxins are found in "moldy" grains and peanuts.
- 5) Other conditions include tyrosinemia and hereditary hemochromatosis.

NOTE: Doctor mentioned that the first 3 are the most important

Morphology:



All three patterns may cause liver enlargement. All patterns of hepatocellular carcinomas have a strong propensity for invasion of vascular channels.

- Extensive intrahepatic metastases may occur.
- Has a greenish cast because it contains bile.
- Tumor may **invade the portal vein** (with occlusion of the portal circulation) or inferior vena cava, extending even into the **right side of the heart**.
- Lymph node metastases to the **perihilar (around hilum of lung), peripancreatic, and para-aortic nodes** above and below the diaphragm can be present.

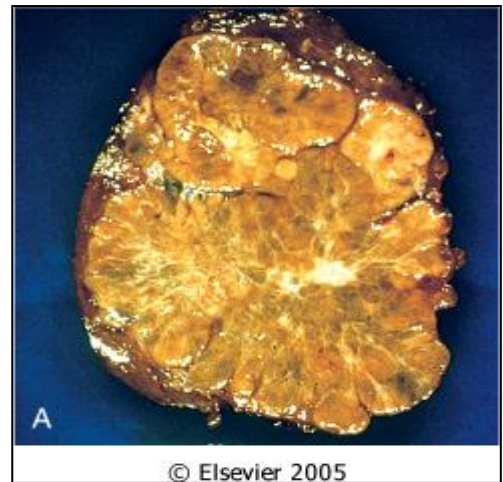
NOTE: If Multifocal, then probably it's a metastasis tumor NOT a primary.

Histologically: (Hepatocellular carcinomas range from well-differentiated to highly anaplastic undifferentiated lesions).

- In well-differentiated and moderately well-differentiated tumors, cells that are recognizable as hepatocytic in origin. Bile pigment is usually present. The malignant cells may be positive for **alpha-fetoprotein**. (1st test to be done when suspecting HCC) In poorly differentiated forms, tumor cells can take on a pleomorphic appearance with numerous anaplastic giant cells, can become small and completely undifferentiated cells. (Loss of architecture).

2) Fibrolamellar carcinoma

- A distinctive variant of hepatocellular carcinoma.
- This tumor occurs in young male and female adults (20 to 40 years of age), has no association with HBV or cirrhosis, and often has a better prognosis.
- It usually presents as single large, hard "scirrhous" tumor with fibrous bands coursing through it. On microscopic examination, it is composed of well-differentiated polygonal cells growing in nests or cords and separated by parallel lamellae of dense collagen bundles.



NOTE: It's different than HCC in: 1) Occurs in young. 2) No association with HBV or cirrhosis.

Clinical Features:

- Ill-defined upper abdominal pain, malaise, fatigue, weight loss, and feeling of abdominal fullness.
- In many cases, the enlarged liver can be felt on palpation. Jaundice and fever are uncommon.
- Laboratory studies: Elevated levels of serum α -fetoprotein (adult tumor marker) are found in 50% to 75% of patients with HCC.
- In HCC, Overall death usually occurs from :
 - (1) Cachexia: (also known as Wasting syndrome is characterized by: Loss of weight, muscle atrophy, fatigue, weakness, and significant loss of appetite.)
 - (2) Gastrointestinal or esophageal variceal bleeding.
 - (3) Liver failure with hepatic coma.
 - (4) Rupture of the tumor with fatal hemorrhage.

3) Cholangiocarcinoma

Cholangiocarcinoma is a malignancy of the biliary tree, arising from bile ducts within and outside of the liver. (An adenocarcinoma)

Risk Factors:

1. **Primary sclerosing cholangitis (Autoimmune Disease)** (is a disease of the bile ducts that causes inflammation and subsequent obstruction of bile ducts both at an intrahepatic and extrahepatic).
2. Congenital fibropolycystic diseases of the biliary system (particularly **Caroli disease** (is a rare inherited disorder characterized by dilatation of the intrahepatic bile ducts) and choledochal cysts).
3. Previous exposure to **Thorotrast** (formerly used in radiography of the biliary tract).
4. In the Orient, the incidence rates are higher, and it is due to chronic infection of the biliary tract by the liver fluke **Opisthorchissinensis** (parasite).

Morphology:

- **Intrahepatic cholangiocarcinomas** occur in the non-cirrhotic liver and **may track along the intrahepatic portal tract system** to create a treelike tumorous mass within the liver or a massive tumor nodule. Lymphatic and vascular invasion are common.
- By microscopy, cholangiocarcinomas resemble adenocarcinomas arising in other parts of the body. Most are well to moderately differentiated. Cholangiocarcinomas **are rarely bile stained**, because differentiated bile duct epithelium does not synthesize bile.
- Mixed variants occur, in which elements of both hepatocellular carcinoma and cholangiocarcinoma are present.
- Hematogenous metastases to the lungs, bones (**mainly vertebrae**), adrenals, brain. Lymph node metastases to the regional lymph nodes are also found.

Clinical Features:

- Intrahepatic cholangiocarcinoma is usually detected late in its course, either as the result of obstruction to bile flow through the hilum of the liver or as a symptomatic liver mass.
- **Prognosis is poor. The median time from diagnosis to death is 6 months (Because we discover it lately in its course).** Aggressive surgery remains the only treatment offering hope for long-term survival.
- **Alpha-fetoprotein is not elevated.**

4) Angiosarcoma

- This consists of pleomorphic endothelial cells with large hyperchromatic nuclei, giant cells in frequent mitosis and irregular anastomosing vascular channels. The cells may appear spindle shaped and cirrhosis is present in 20% to 40% of the cases. These have also been linked to **vinyl chloride** and **thorotrast** exposure.

REMEMBER:

- Thorotrast exposure can also lead to Cholangiocarcinoma

Pancreatic Carcinoma (Death sentence)

Introduction:

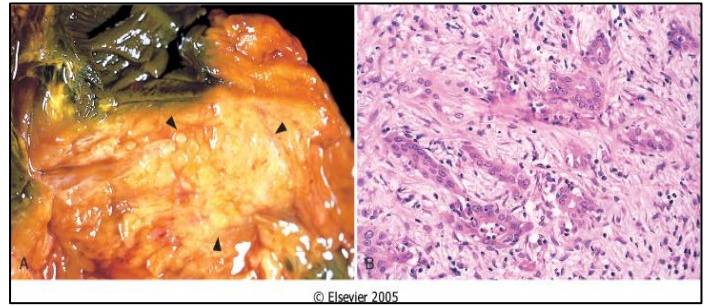
Pancreatic cancer has one of the **highest mortality rates** of any cancer (it usually comes back after surgery and chemotherapy). It is carcinoma of the exocrine pancreas. It arises from ductal epithelial cells. (Most painful cancer ever).

Risk Factors:

It occurs in the 6th to 8th decade, blacks more than whites, males more than females, diabetics more than non-diabetics. (obesity)

Morphology:

- Approximately 60% of cancers of the pancreas arise in the head of the gland (could give an acute presentation due to its close location to the gall bladder), 15% in the body, and 5% in the tail; in 20%, the neoplasm diffusely involves the entire gland.
- Carcinomas of the pancreas are usually hard, stellate, gray-white, poorly defined masses
- Majority of carcinomas are **ductal adenocarcinomas**. Two features are characteristic: It is highly invasive (also has potential to metastasize), and it elicits an intense non-neoplastic host reaction called a "**desmoplastic response**".
- Peripancreatic, gastric, mesenteric, omental, and portahepatic **lymph nodes are frequently involved**. Distant metastases occur, principally to the **lungs** and **bones**.
- Less common variants of pancreatic cancer include **acinar cell carcinomas**, **adenosquamous carcinomas**, and **undifferentiated carcinomas with osteoclast-like giant cells**. (The doctor said not to worry about the less common variants)



Clinical Features:

Jaundice (If it was head of pancreas that was involved; due its proximity to the gallbladder), **weight loss**, **pain**, **massive metastasis to liver** and **migratory thrombophlebitis**.

Summary (from Robbins Basic Pathology):

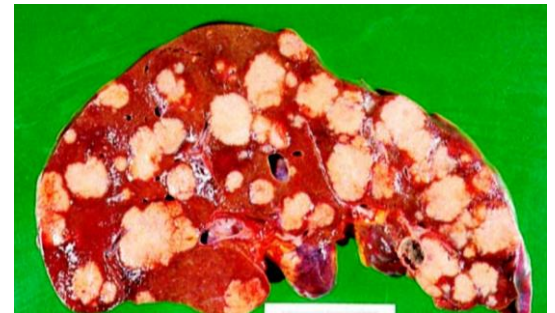
- The liver is the most common site of metastatic cancers from primary tumors of the colon, lung, and breast.
- The main primary tumors are hepatocellular carcinomas and cholangiocarcinomas; hepatocellular carcinomas are by far the most common.
- HCC is a common tumor in regions of Asia and Africa and its incidence is increasing in the United States.
- The main etiologic agents for hepatocellular carcinoma are hepatitis B and C, alcoholic cirrhosis, hemochromatosis, and rarely, Tyrosinemia.
- The chronic inflammation and cellular regeneration associated with viral hepatitis may be predisposing factors for the development of carcinomas.
- HCC may be unifocal or multifocal, tend to invade blood vessels and recapitulate normal liver architecture to varying degrees.

Questions

1/ A 68-year-old man complains of vague abdominal pain, intermittent fever, and 9-kg weight loss over the past 6 months. For the past 12 years, he has suffered from chronic hepatitis B. On physical examination, the patient shows diffuse abdominal tenderness, hepatomegaly, and mild jaundice. A CT scan of the abdomen reveals a diffusely nodular liver, with a dominant mass measuring 3 cm in diameter. Which of the following serum markers is useful for monitoring the progression of disease in this patient?

- (A) Alkaline phosphatase
- (B) Alpha-fetoprotein
- (C) Anti-HBc antibody
- (D) Carcinoembryonic antigen

2/ A 69-year-old woman arrives in the emergency room complaining of weakness, abdominal pain, and a 9kg weight loss during the past month. Physical examination reveals jaundice, hepatomegaly, and ascites. The patient expires, and a section of liver is examined at autopsy (shown in the image). Which of the following is the most likely diagnosis?



- (A) Hemangiosarcoma of the liver
- (B) Metastatic carcinoma of the liver
- (C) Miliary tuberculosis
- (D) Primary hepatocellular carcinoma

Answers:

- 1- B
- 2- B

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If there is any mistake or feedback please contact us: 432PathologyTeam@gmail.com

