PATHOLOGY TEAM

Cancers

of the liver and pancreas

Done by:

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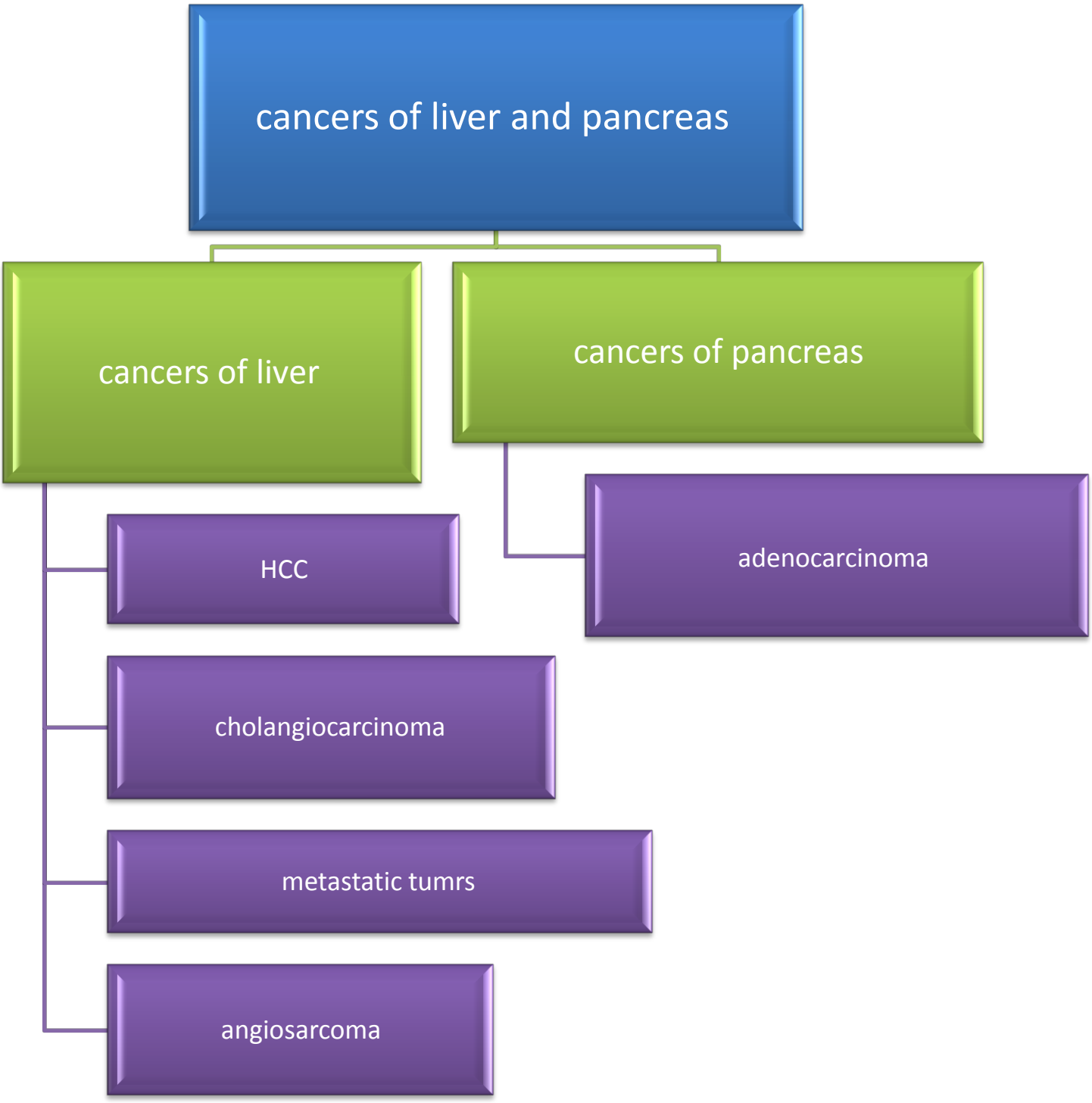


Malignant tumors of the liver

The liver and lungs are the visceral organs that are **most often involved by metastatic tumours**.

Primary carcinomas of the liver are relatively uncommon.

Most arise from hepatocytes and are termed hepatocellular carcinoma (HCC). Much less common is carcinomas of bile duct origin: cholangiocarcinoma.

There are two rare forms of primary liver cancer hepatoblastomas and angiosarcomas

Hepatocellular carcinoma is the most common and important cancer in the liver.

From the biliary tree adenocarcinoma (glandular) can arise

hepatoblastomas :- a childhood hepatocellular tumour. ROBBINS:- Page 663

Hepatocellular Carcinomas

Male predominance

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.

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 of HCC

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.

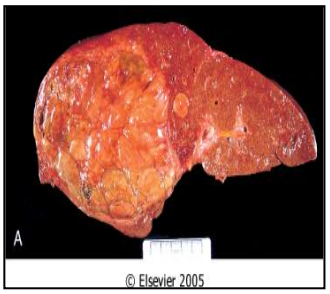
HCV or HBV not necessary pass to cirrhosis to become carcinogenic could transform to HCC during inflammation

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.

Morphology of HCC



Grossly it may be

(1) a unifocal mass

(2) multifocal, multipe nodules of variable size;

(3) a diffusely infiltrative cancer.

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

Primary tumour often is unifocal mass . If it is multiple nodules it will be one major mass with smaller nodules

Metastatic tumour is often multiple nodules

Extensive intrahepatic metastases may occur

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.

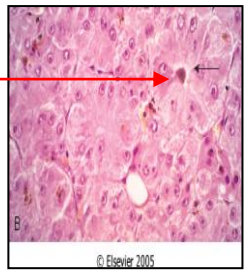
Lymph node metastases to the perihilar, peripancreatic, and para-aortic nodes above and below the diaphragm can be present.

Hepatocellular carcinomas range from well-differentiated to highly anaplastic undifferentiated lesions.

When it invade the regional lymph nodes it start usually with perihilar lymph nodes and then it can extend to peripancreatic, biliary tree ,and para-aortic lymph nodes.If it invade the portal system this is very advanced stage and probably it is too late to treat the patient

Hepatocellular carcinomas range from well-differentiated:-morphologically and functionally (can produce bile)

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**.



In poorly differentiated forms, tumor cells can take on a pleomorphic appearance with numerous anaplastic giant cells, can become small and completely undifferentiated cells.

If a patient has liver mass and positive for alpha-fetoprotein this is most likely (because not all HCC will have positive for alpha-fetoprotein) hepatocellular carcinoma

fibrolamellar carcinoma

A distinctive variant of hepatocellular carcinoma is the fibrolamellar carcinoma.

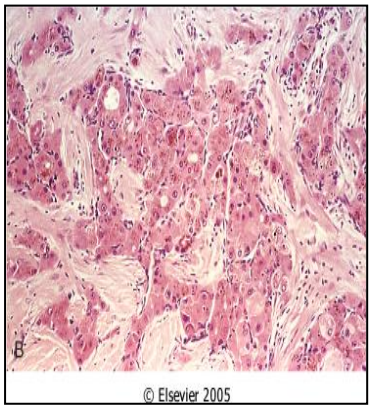
This tumor occurs in young male and female adults (20 to 40 years of age), has no association with HBV or cirrhosis, and often has a better prognosis.

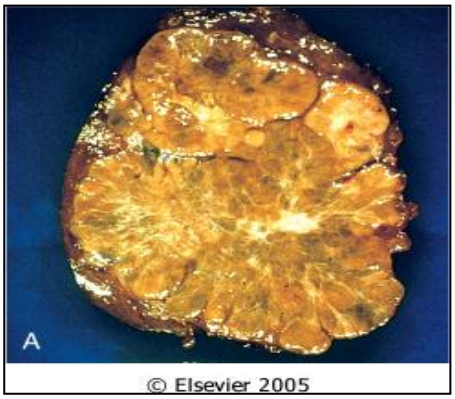
It usually presents as single large, hard "scirrhous" tumor with fibrous bands coursing through it. On microscopic examination, it is composed of well-differentiated polygonal cells growing in nests or cords and separated by parallel lamellae of dense collagen bundles.

fibrolamellar carcinoma: rich in fibrous tissue and collagen tissue

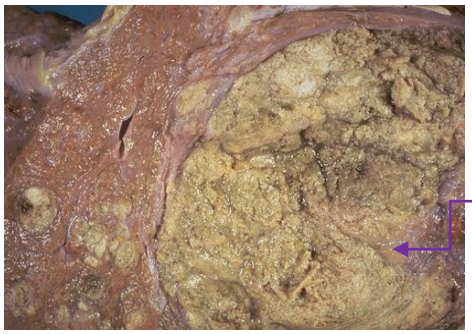
The fibrolamellar carcinoma:- usually present with big single solitary mass very fibrotic very hard with central scar

Easiest to diagnose as pathologist





Hepatocellular carcinoma. Such liver cancers arise in the setting of cirrhosis. Worldwide, viral hepatitis is the most common cause, but in the U.S., chronic alcoholism is the most common cause. The neoplasm is large and bulky and has a greenish cast because it contains bile. To the right of the main mass are small



The satellite nodules of hepatocellular carcinoma

Clinical Features

Ill-defined upper abdominal pain, malaise, fatigue, weight loss, and feeling of abdominal fullness.

Clinical Features :- vague like any cancer

In many cases, the enlarged liver can be felt on palpation. Jaundice and fever are uncommon. Maybe you find it like cirrhosis in some patient

Laboratory studies: Elevated levels of serum α-fetoprotein are found in 50% to 75% of patients with HCC.

Jaundice :- usually is not from the early feature because in the beginning there is no obstruction to the bile duct and biliary system

Hepatocellular Carcinoma

Overall, death usually occurs from

(1) cachexia

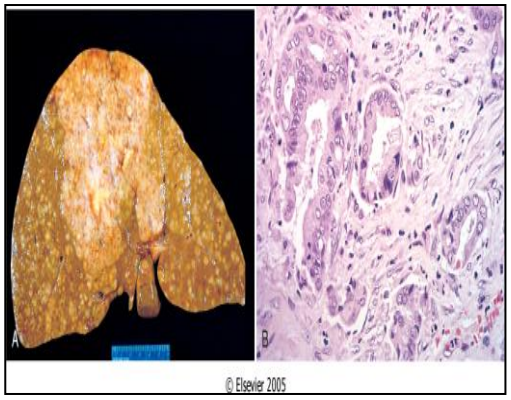
(2) gastrointestinal or esophageal variceal bleeding

(3) liver failure with hepatic coma

(4) rupture of the tumor with fatal hemorrhage

cachexia :- cancer patients suffer progressive loss of body fat and lean body mass, accompanied by profound weakness , anorexia , referred to as cachexia (for further information ROBBINS Basic Pathology , 8th edition , chapter 6 , page 218)

Cholangiocarcinoma



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

The risk conditions for development of cholangiocarcinoma include:-

Primary sclerosing cholangitis,

Congenital fibropolycystic diseases of the biliary system (particularly Caroli disease and choledochal cysts),

Caroli disease: dilatation of intrahepatic bile ducts
Choledochal cyst: dilataion of bile ducts

Previous exposure to **Thorotrast** (formerly used in radiography of the biliary tract).

In the Orient, the incidence rates are higher, and it is due to **chronic infection of the biliary tract by the liver fluke Opisthorchis sinensis.**

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.

cholangiocarcinomas :- any place in the biliary tree (intra hepatic or extra hepatic)

By microscopy, cholangiocarcinomas resemble adenocarcinomas :- like any adenocarcinoma which is glandular formation tumour with invasive and desmoplastic reaction around it

The carcinoma at the left has a glandular appearance. Cholangiocarcinomas do not make bile, but the cells do make mucin, and they can be almost impossible to distinguish from metastatic adenocarcinoma on biopsy or fine needle aspirate

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. Aggressive surgery remains the only treatment offering hope for long-term survival.

Alpha-fetoprorein is not elevated.

Clinical Features:- in the beginning vague symptoms

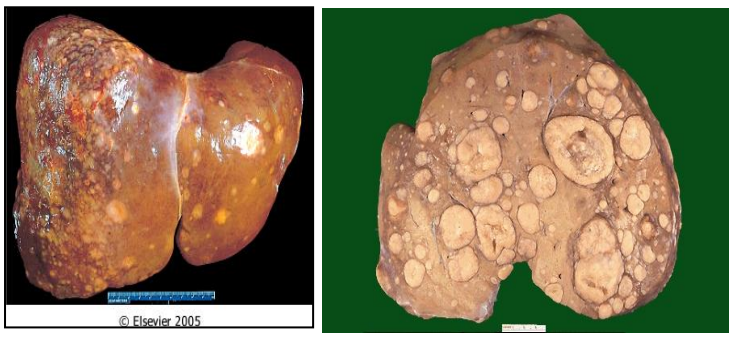
Tumour of the biliary tree and pancreas usually have poor prognosis

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 leukemias and lymphomas.

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.



Numerous mass lesions of variable size. Some of the larger ones demonstrate central necrosis. The masses are metastases to the liver

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 thorostrast exposure.**

(the doctors wants us to know from angiosarcoma its risk factors)

Hepatic angiosarcoma are associated with carcinogenic exposures,including arsenic (arsenical pesticides) thorotrast (a radioactive contrast agent formerly used for radiologic imaging), and polyvinyl chloride (PVC; widely used plastic)

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is a malignant neoplasm (cancer) of endothelial-type cells that line vessel walls. This may be in reference to blood (hemangiosarcoma) or lymphatic vessels (lymphangiosarcoma).

PANCREATIC CARCINOMA

Pancreatic cancer has one of the highest mortality rates of any cancer. It is carcinoma of the exocrine pancreas. **It arises from ductal epithelial cells**.

It occurs in the 6^{th} to 8^{th} decade, blacks more than whites, males more than females, diabetics more than non-diabetics.

PANCREATIC CARCINOMA Morphology

Approximately **60% of cancers of the pancreas arise in the head of the gland**, 15% in the body, and 5% in the tail; in 20%, the neoplasm diffusely involves the entire gland.

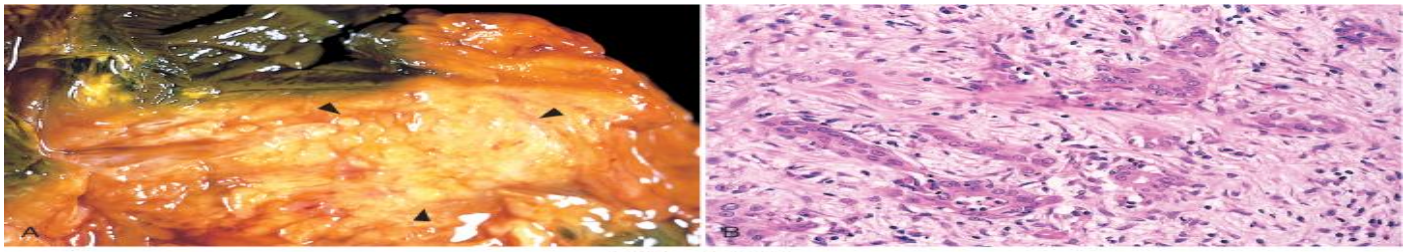
Carcinomas of the pancreas are usually hard, stellate, gray-white, poorly defined masses.

Majority of carcinomas are ductal adenocarcinomas. Two features are characteristic: It is **highly invasive**, and it elicits an intense non-neoplastic host reaction called a "**desmoplastic response**".

Most of pancreatic carcinoma arise in the head of pancreas

Cancer arise in the head of pancreas can be discovered earlier than cancer that arise in tail of pancreas because Head of the pancreas is more likely to produce symptoms (Cancer that arise in the head of pancreas will let the patient usually come with obstructive jaundice)

Cancers of the pancreas arise in the tail has the worst prognosis



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.

PANCREATIC CARCINOMA: CLINICAL FEATURES

Jaundice, weight loss, pain ,massive metastasis to liver and migratory thrombophelebitis

> Why the pancreatic cancer is so painful ?
>
> Because it is a retroperitoneal organ in posterior abdominal wall near to the nerves

Summary:

Liver tumors :

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 but HCC are the commonest among primary tumors.

The main etiologic agents for HCC are HBV , HCV , alcoholic cirrhosis , hemochromatosis , and more rarely tyrosinemia .

The chronic inflammation and cellular regeneration associated with viral hepatitis may predispose to carcinoma.

HCC may be unifocal or multifocal , tend to invade blood vessels and normal liver architecture to varying degrees

Pancreatic tumors :

Usually it is diagnosed after it is deeply invasive , it is an aggressive malignancy with a very high mortality

Obstructive jaundice is a feature of the carcinoma of the head of the pancreas

Which one of the following is most commonly associated with very high elevation of alpha-fetaprotien?

a-Cholangiocarcinoma
b- hepatocellular carcinoma
c- pancreatic cancer
d- colorectal cancer

regarding hepatocellular carcinoma :
a-there is a female predominance
b- more than 80% of cases are in countries with high rates of chronic HBV
c- chronic alcoholism doesn't contribute to the formation of HCC
d- none of the above

which one of the following feature is commonly seen in cases of carcinoma of the head of pancreas ?
a-Obstructive jaundice
b-thrombosis of mesenteric artery
c- megaloblastic anemia
d-weight loss

a 36 year old man present with jaundice and pruritus. Physical examination finds a diffuse yellow discoloration to his skin. Laboratory examination reveals markedly elevated serum levels of alkaline phosphatase, but neither antinuclear nor antimitochondrial antibodies are present. A liver biopsy revealed reactive hepatocytes and fibrosis in the sinusoids. The portal tract showed marked fibrosis around the bile ducts. But no granulomas were seen. While waiting for a liver transplant he developed a malignancy and died. Which of the following tumors is most closely associated with his liver disease?
a-Cholangiocarcinoma
b-Hepatoblastoma
c-Pancreatic carcinoma
d-Gallbladder carcinoma

b-b-a-a