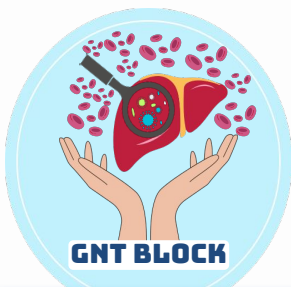


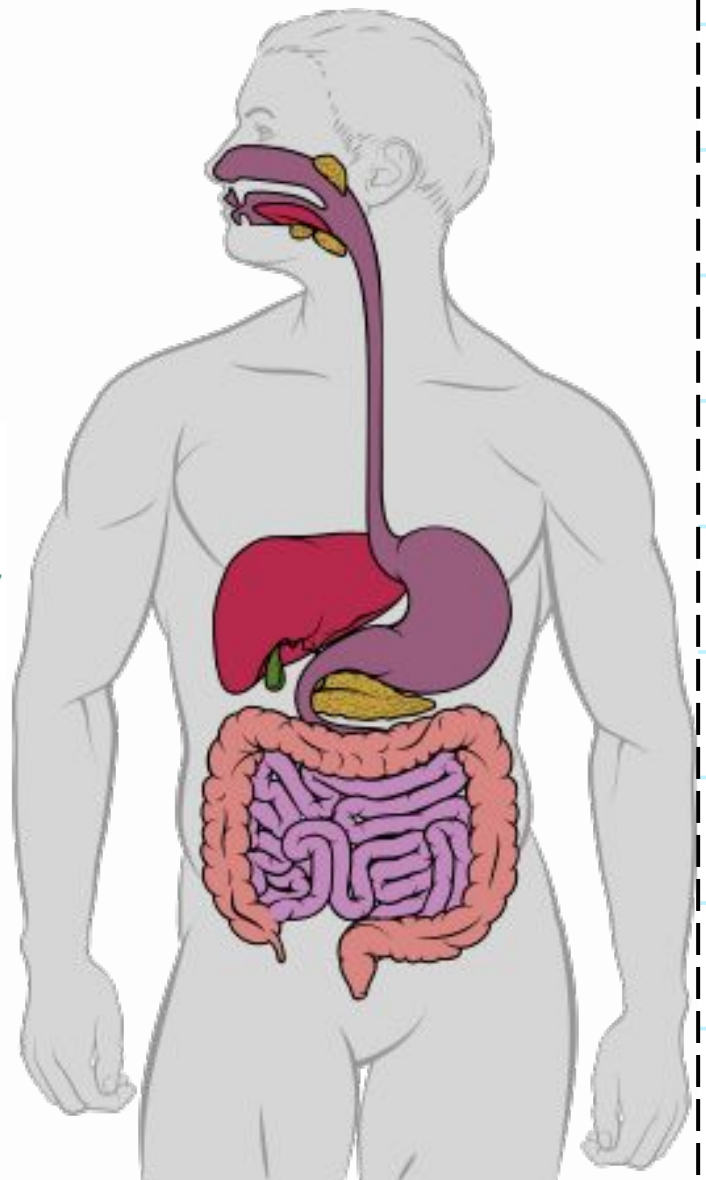
Liver and pancreas Neoplasm



Editing File

Color index :

- Main text (black)
- Female Slides (Pink)
- Male Slides (Blue)
- Important (Red)
- Dr's note (Green)
- Extra Info (Grey)



OBJECTIVES



Introduction



Describe clinical features and the pathological features of benign and malignant tumors of liver and pancreas



Describe most common liver malignancies: Hepatocellular and cholangiocarcinoma



Understand the frequency of metastatic disease of the liver



Recognise the rarity of primary liver neoplasms in children



Recognize all aspects of pancreatic carcinoma

THIS LECTURE WAS PRESENTED BY DR.WAJD ALTHAGAFI & DR.AHMED ALHUMAIDI



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Introduction

Malignant tumors occurring in the liver can be primary or metastatic.

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

Primary carcinomas of the liver are relatively uncommon.

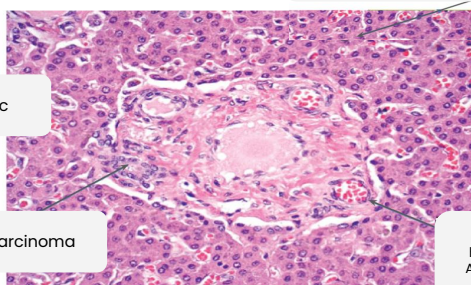
- Most primary liver cancers arise from hepatocytes and are termed:
 - Hepatocytes → hepatocellular carcinoma.
 - Bile duct (Much less common) → Cholangiocarcinomas.
 - Other rare forms of primary liver cancer: hepatoblastomas and angiosarcomas (mainly in children).

Liver tumors

Benign

-cavernous Hemangioma
-Hepatocellular Adenomas

Liver cell adenomas
Hepatocellular carcinoma
Hepatoblastoma



Metastatic

cholangiocarcinoma

hemangioma
Angiosarcoma

Malignant

Metastatic
(Most common
liver tumor)

Primary tumors:

-Hepatocellular carcinoma
-Cholangiocarcinoma
-Hepatoblastoma "rare"
-Angiosarcoma "rare"

Hepatocellular carcinoma (HCC)

Epidemiology

- Most common primary liver malignancy.
- There is a clear predominance of males with a ratio of 2.4 : 1.
- Peak incidence is between 20 and 40 years of middle age.
- More than 85% of cases of HCC occur in countries with high rates of chronic hepatitis B virus (HBV) infection.
- 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.
- Primary carcinomas of the liver are relatively uncommon in North America and western Europe.
- Incidence is highest in Asia (southeast China, Korea, Taiwan) and sub-Saharan Africa.
- Rarely manifests before 60 years of age, and in almost 90% of cases the malignancy emerges after cirrhosis becomes established.
- The third most frequent cause of cancer deaths.
- In ~50% of cases, it arises in non-cirrhotic livers. Accounts for approximately 5.4% of all cancers.

Etiology

Major etiologic factors associated with HCC have been established:

1. **Chronic viral infection (HBV, HCV):** More than 85% of cases of HCC occur in countries with high rates of chronic HBV infection.
2. **Cirrhosis:** the development of cirrhosis appears to be an important, but not requisite, contributor to the emergence of HCC.
3. Chronic alcoholism.
4. **Non-alcoholic steatohepatitis (NASH).** Accumulation of fat in the liver .e.g obese and diabetic
5. Food contaminants (primarily **aflatoxins**) Is a mycotoxin produced by Aspergillus species. from fungus
 - Contaminates staple food crops in Africa and Asia (in "moldy" grains and peanuts).
 - Metabolites are present in the urine of individuals who consume these foods, as are aflatoxin-albumin adducts in serum.Any food that contain aflatoxins especially in Africa and Asia could be risk of HCC.
- 6- **Tyrosinemia and hereditary hemochromatosis**

Other rare HCC risk factors:

1. Inherited disorders, particularly hereditary hemochromatosis, tyrosinemia and α 1 AT deficiency, and to a lesser degree Wilson disease.
2. Metabolic syndrome and its attendant obesity, diabetes mellitus, and NAFLD.

Hepatocellular carcinoma (HCC)

Male Slides

Pathogenesis

- Cell death, hepatocyte replication, and inflammation, seen in all forms of chronic hepatitis, are believed to be main contributors to **DNA damage**.
- Poor regulation of hepatocyte replication can occur by point mutations or overexpression or specific cellular genes such as B-catenin.

Female Slides

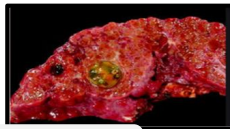
Morphology

HCC may appear grossly as:

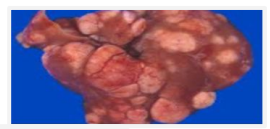
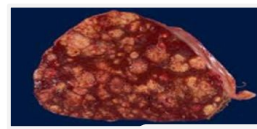
- Unifocal (usually one large)
- Multifocal, widely distributed multiple nodules of variable size and shape
- Diffusely infiltrative cancer.



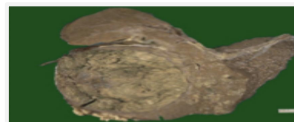
Unifocal nodule



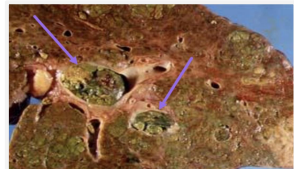
Multifocal nodule



Metastases are usually small, satellite tumor nodule around a larger primary mass .



Large and bulky mass, has a greenish cast because it contains bile. To the right of the main mass are small satellite nodules .



Venous invasion

Female Slides

Progression

- Intrahepatic metastasis by either vascular invasion or direct extension -> small satellite tumor nodules around a larger primary mass.
- In advanced cases: vascular invasion of hepatic venous system -> extrahepatic metastasis.
- 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 metastasis to the perihilar peripancreatic, and para-aortic nodes above and below the diaphragm can be present.
- Occasionally, invades vascular channels -> long, snake-like masses of intravenous tumor
- Portal vein -> portal hypertension
- Inferior vena cava -> extend up to the heart (right ventricle).

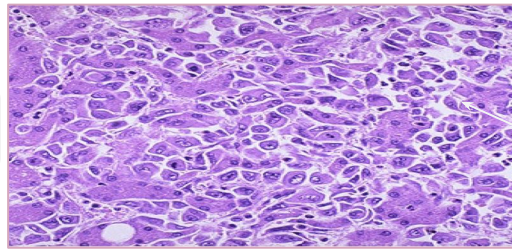
Hepatocellular carcinoma (HCC)

Microscopic

Microscopic Morphology:

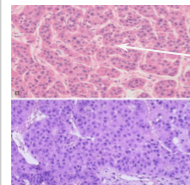
• Range from well-differentiated to highly anaplastic undifferentiated lesions.

Large hepatocytes



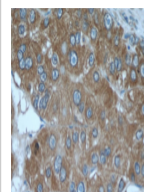
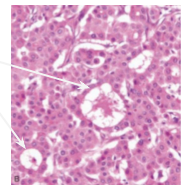
HCC are well s differentiated and interdigitate with normal

Malignant hepatocytes growing in distorted versions of normal architecture: large pseudoacinar spaces, essentially malformed.



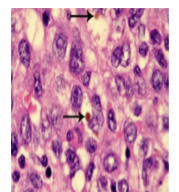
Thick trabeculae and Dilated bile canaliculi

Pseudoglands



The malignant cells may be positive for **alpha-fetoprotein (IHC)**

Bile pigment usually present (Intracellular bile)



Neoplastic cells of well-differentiated HCCs are recognizable as hepatocytic in origin and arranged in: **Thick trabeculae and pseudoglands**

Prognosis

Death occurs usually due to:

1. Cachexia. severe weight loss, weakness
 2. Gastrointestinal or esophageal variceal bleeding. **Vomit blood and die of hemorrhage**
 3. Liver failure with hepatic coma. **Because of the toxins that aren't detoxified by the liver**
 4. Tumor rupture with fatal hemorrhage
- Most common site of metastasis is **LUNG**.
-Prognosis is very bad; majority die within 2 years of DK



Deep Focus Question



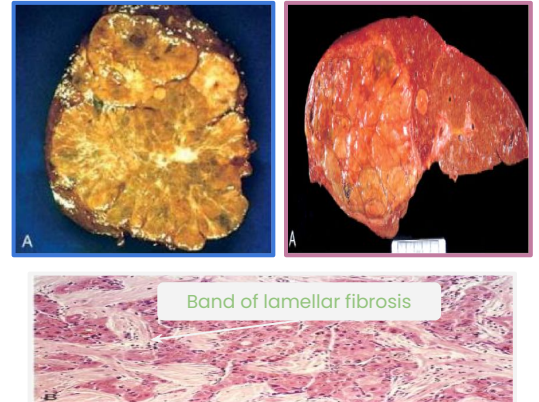
Which of the following tumor markers is characteristically increased in hepatocellular carcinoma?

- A. Alpha-fetoprotein
- B. CEA
- C. CA 19-9
- D. Beta HCG
- E. Inhibin

Answer: A

HCC variant- Fibrolamellar carcinoma

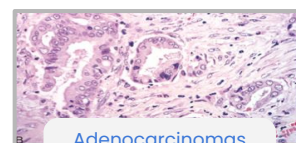
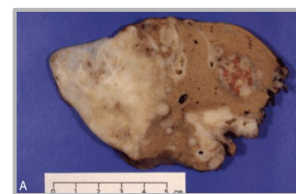
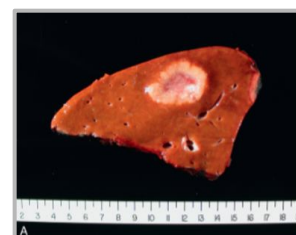
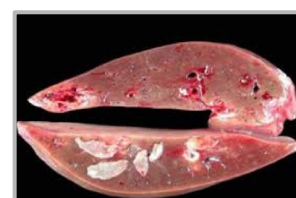
<p>Introduction</p>	<p>A distinctive variant of hepatocellular carcinoma It occurs in young male and female adults (20 to 40 years of age) with equal incidence . - No underlying chronic liver diseases (HBV or cirrhosis). it happens in people who have healthy livers. -Constitutes 5% of HCCs.</p>
<p>Morphology</p>	<p>- Composed of well-differentiated polygonal cells growing in nests or cords and separated by parallel lamellae of dense collagen bundles. -Single large, hard mass "scirrhou" tumor, with fibrous bands coursing through it. -The tumor cells have abundant eosinophilic cytoplasm and prominent nucleoli .</p>
<p>Clinical features</p>	<p>Ill-defined upper abdominal pain - Laboratory studies: Elevated levels of serum α-fetoprotein are found in 50% to 75% of patients with HCC.</p>
<p>Prognosis</p>	<p>Better prognosis than the conventional HCC.</p>



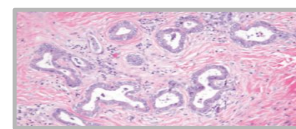
<p>Morphology</p>	<p>Occurs as a solitary, sharply demarcated mass up to 40 cm</p>
<p>Etiology</p>	<p>It is a complication of oral contraceptive use in women.</p>
<p>Complication</p>	<p>In about 30% of patients, the tumor tends to bleed into the peritoneal cavity, inducing hypovolemic shock that requires emergency treatment.</p>

Cholangiocarcinoma

<p>Introduction</p>	<ul style="list-style-type: none"> -Second most common primary malignant tumor of liver -Is a malignancy of biliary tree, Arises from Bile duct \ intrahepatic or \ and outside the liver extrahepatic bile ducts -50% to 60% of all CCAs are perihilar (Klatskin) tumors -20% to 30% are distal tumors -10% are intrahepatic
<p>Risk factor</p>	<ul style="list-style-type: none"> -Congenital fibropolycystic diseases of the biliary system (particularly Caroli disease and choledochal cysts) -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 <i>Opisthorchis sinensis</i> -Chronic inflammatory disease of large bile ducts (such as primary sclerosing cholangitis, IBD), hepatolithiasis & fibropolycystic liver disease. All → cholestasis & chronic inflammation -As with HCC, rates also are elevated in patients with hepatitis B and C and NAFLD
<p>Morphology</p>	<p>Gross funding of extrahepatic:</p> <ul style="list-style-type: none"> • Small lesions & discovered early due to obstruction of biliary tract. • Firm, gray nodules within the bile duct wall. • Can be diffusely infiltrative lesions. • Papillary, polypoid lesions. • Most are adenocarcinomas. <p>Gross funding of Intrahepatic:</p> <ul style="list-style-type: none"> • Occur in the noncirrhotic liver. • Track along the intrahepatic portal tract system to create a treelike tumorous mass within a portion of the liver. <p>Microscopic funding:</p> <ul style="list-style-type: none"> • Typically are mucinous- producing adenocarcinomas • Intrahepatic cholangiocarcinomas resemble adenocarcinomas arising in other parts of the body. • Most are well to moderately differentiated • Abundant fibrous stroma (desmoplastic stroma) • Common lymphovascular & perineural invasion with extensive extrahepatic & intrahepatic metastasis • Cholangiocarcinomas are rarely bile stained, because differentiated bile duct epithelium does not synthesize bile



Adenocarcinomas
Desmoplastic
stroma



Cholangiocarcinoma

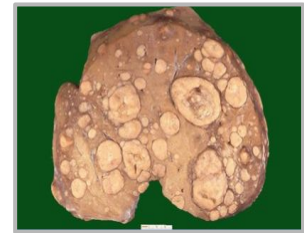
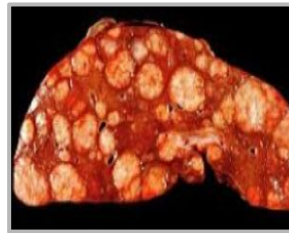
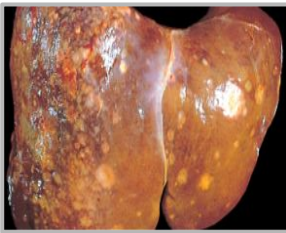
Clinical picture & prognosis

- Intrahepatic CCAs are not usually detected until late in their course and come to the attention because of obstruction of bile flow, or as a symptomatic liver mass
- Hilar and distal tumors present with symptoms of biliary obstruction, cholangitis, and right upper quadrant pain
- Prognosis is poor with survival rates of about 15% at 2 years after diagnosis
- The median time from diagnosis to death for intrahepatic CCAs is 6 months, even after surgery
- Alpha-fetoprotein is not elevated

Metastatic tumors

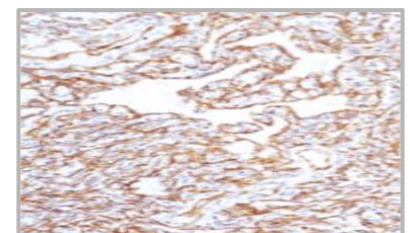
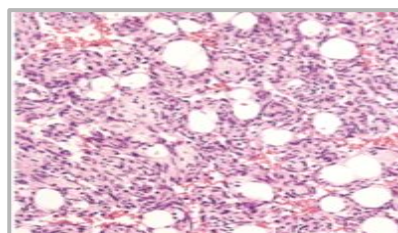
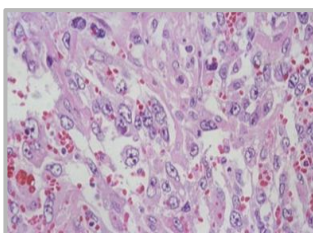
Far more common than primary neoplasia

- 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 can metastasize to liver.
- **Multiple nodular metastases** are found that often cause striking hepatomegaly and may replace over 80% of existent hepatic parenchyma.



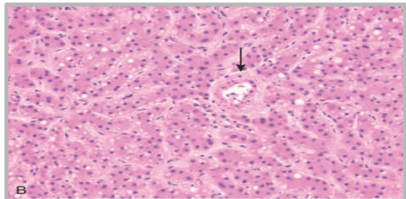
Angiosarcoma

- **Malignant tumor/** pleomorphic endothelial cells with large hyperchromatic nuclei, giant cells in frequent mitosis and form irregular anastomosing vascular channels. The cells may appear spindle shaped
- Cirrhosis is present in 20% to 40% of the cases
- These have also been linked to 2 kinds of toxins **vinyl chloride and thorotrast** exposure



Benign Hepatic Tumors: Hepatocellular Adenomas

Female Slides

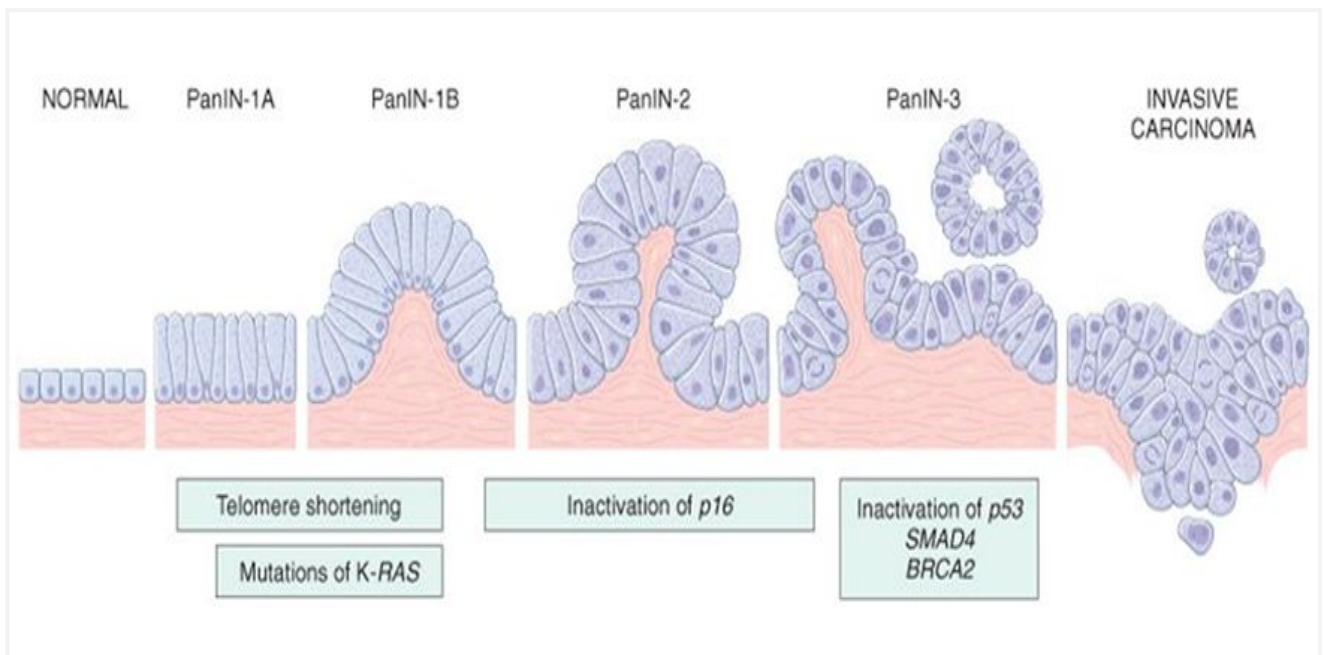
<p>General information</p>	<ul style="list-style-type: none"> • Benign neoplasms developing from hepatocytes, • Risk factor : Sex hormone (oral contraceptive pills & anabolic steroids) exposure → markedly increases frequency of occurrence • Cessation of exposure to sex hormones often “but not always” → tumor regression • The most common symptom is pain, occasionally rupture, an event that may lead to life-threatening intra-abdominal bleeding
<p>Molecular Subclassification</p>	<ul style="list-style-type: none"> • Low risk for malignant transformation • Intermediate risk for malignant transformation • High risk for malignant transformation
<p>Microscopic</p>	<ul style="list-style-type: none"> • Cords of hepatocytes, with an arterial vascular supply (arrow) and no portal tracts. 

Pancreas Carcinoma

<p>Pancreatic carcinoma</p>	<ul style="list-style-type: none"> • Acini ; Acinar cell carcinoma • Ducts ; Ductal cell carcinoma (most common) • islets of langerhan ; Endocrine tumors
<p>Epidemiology</p>	<ul style="list-style-type: none"> • 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 • 80% in persons 60-80 years of age • It occurs in the 6th to 8th decade, It is more common in blacks than in whites, diabetics more than non-diabetics. • Males more than females • Fourth leading cause of cancer deaths in the United States, preceded only by lung, colon, and breast cancers. • The strongest environmental influence is smoking its associated with a fivefold increased risk for adenocarcinoma of the pancreas. • Long-standing chronic pancreatitis and DM. • Familial clustering, e.g. germline mutation of familial breast/ovarian cancer gene BRCA2 are seen in 10% of cases.
<p>Pathogenesis</p>	<ul style="list-style-type: none"> • Arises from precursor lesions Pancreatic intraepithelial neoplasia (PanINs) (Pancreatic intraepithelial neoplasia, it has 3 grades) as result of progressive accumulation of inherited & acquired genetic mutations in pancreatic epithelium. • A K-RAS mutation is an early event in pancreatic carcinogenesis • Four genes are most affected by somatic mutations in this neoplasm: <ul style="list-style-type: none"> ○ KRAS, ○ CDKN2A/p16 ○ SMAD4 ○ TP53

Pancreatic Carcinoma

Pathogenesis of Pancreatic carcinoma



Progression model for the development of pancreatic cancer. It is postulated that telomere shortening and mutations of the KRAS oncogene occur at early stages, inactivation of the p16 tumor suppressor gene occurs at intermediate stages, and inactivation of the TP53, SMAD4, and BRCA2 tumor suppressor genes occurs at late stages. Note that while there is a general temporal sequence of changes, the accumulation of multiple mutations is more important than their occurrence in a specific order. PanIN, Pancreatic intraepithelial neoplasm. The numbers following the labels on the top refer to stages in the development of PanINs. (Modified from Maitra A, Hruban RH: Pancreatic cancer, *Annu Rev Pathol Mech Dis* 3:157, 2008.)

explained by the doctor

Deep Focus Question



Which of the following lesions in the liver is MOST commonly associated with long-term use of oral contraceptive pills?

- Dubin-Johnson syndrome
- Hepatoma
- Hepatic adenoma
- Cholangiocarcinoma
- Focal nodular hyperplasia

Answer: C

Deep Focus Question

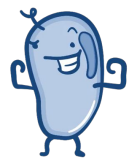


Which of the following medical conditions is the most significant risk factor for cholangiocarcinoma?

- Primary sclerosing cholangitis
- Hemochromatosis
- Autoimmune hepatitis
- Viral hepatitis
- Primary biliary cholangitis

Answer: A

Pancreatic Carcinoma



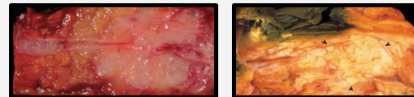
Gross morphology

1

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

2

Hard, gray-white, stellate, poorly defined masses, It is highly invasive, and it elicits an intense non-neoplastic host reaction called a "desmoplastic response".



Microscopic morphology

Female Slides

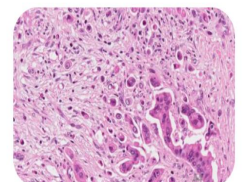
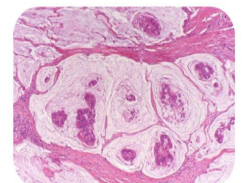
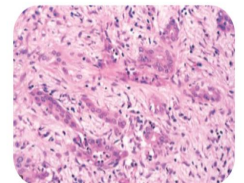
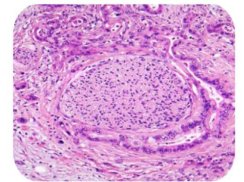
Majority of carcinomas are ductal adenocarcinomas.

Two characteristic features:

- Have prominent desmoplastic (stromal fibrosis) response.
- Highly invasive; often have invaded surrounding structures even early

Prominent perineural invasion & common lymphatic invasion

Peripancreatic, gastric, mesenteric, omental, and portohepatic lymph nodes are frequently involved. Distant metastases occur, principally to the lungs and bone.



Less common variant forms of pancreatic cancer include:

All from female slides except the bold ones. They are from both slides

Adenosquamous carcinoma

Hepatoid carcinoma.

Signet-ring cell carcinoma

Undifferentiated carcinomas with osteoclast-like giant cells

Colloid carcinoma

Medullary carcinoma

Undifferentiated carcinoma

Acinar cell carcinomas

Pancreatic Carcinoma

+ Clinical features

Remain silent until they invade into adjacent structures → (1st symptom) Erode the nerve fibers in retroperitoneum lead to pain

Tumors of the **head** of pancreas leads **obstructive jaundice** (**Painless jaundice** is a frequent initial symptom of pancreatic cancer)

Jaundice, Weight loss, anorexia, generalized malaise & weakness are signs of advanced disease

Migratory thrombophlebitis (Trousseau sign of **malignancy**) occurs in about 10% of patients due to platelet-aggregating factors and procoagulants from the carcinoma or its necrotic products the pancreatic cancer cells sometimes stimulate the platelets and the patient with have multiple thrombosis.

+ Prognosis

Female Slides

1 The clinical course of pancreatic carcinoma is rapidly progressive

2 Less than 20% of pancreatic cancers are resectable at the time of diagnosis

3 5-year survival is about 8%

Deep Focus Question

Which of the following should be screened for in a patient presenting with endocarditis without signs of infection?

- A. Hereditary colorectal carcinoma
- B. Bronchogenic carcinoma
- C. Small cell carcinoma of the lung
- D. Stomach cancer
- E. Mucus-secreting pancreatic carcinoma

Answer: E

Deep Focus Question

Which oncogene is primarily associated with pancreatic adenocarcinoma?

- A. C-kit
- B. K-ras
- C. p53
- D. PTEN
- E. Raf kinase

Answer: B

Keywords

Hepatocellular carcinoma	<ul style="list-style-type: none"> ● HBV or HCV infection ● Cirrhosis ● Chronic alcoholism ● Unifocal Or Multifocal distributed multiple nodules ● Thick trabeculae ● Pseudo Glands ● Intracellular bile ● Invasion of vascular channel ● Exposure to Aflatoxin ● Maybe + for alpha-fetoprotein
Fibrolamellar carcinoma	<ul style="list-style-type: none"> ● well-differentiated polygonal cells ● growing in nests or cords ● separated by parallel lamellae of dense collagen bundles. ● "scirrhous" tumor ● Elevated levels of serum α-fetoprotein (mostly with HHC in general)
Hepatic adenoma	<ul style="list-style-type: none"> ● solitary, sharply demarcated mass ● complication of oral contraceptive use ● May cause hypovolemic shock
Cholangiocarcinoma	<ul style="list-style-type: none"> ● malignancy of biliary tree ● exposure to Thorotrast ● Congenital fibropolycystic diseases Eg. Caroli disease and choledochal cysts ● liver fluke <i>Opisthorchis sinensis</i> Infection ● primary sclerosing cholangitis ● fibrous stroma (desmoplastic stroma) ● lymphovascular & perineural invasion ● Alpha-fetoprotein is not elevated
Metastatic Tumors	<ul style="list-style-type: none"> ● Multiple nodular metastases ● striking hepatomegaly
Angiosarcoma	<ul style="list-style-type: none"> ● Malignant pleomorphic endothelial cells ● vinyl chloride and thorotrast exposure
Pancreatic Carcinoma	<ul style="list-style-type: none"> ● Acinar cell carcinoma ● Ductal cell carcinoma (most common) ● smoking ● germline mutation of familial breast/ovarian cancer gene BRCA2 ● Arises from precursor lesions Pancreatic intraepithelial neoplasia (PanINs) ● Four genes are most affected : KRAS (early detection) , CDKN2A/p16 , SMAD4 , TP53 ● prominent desmoplastic (stromal fibrosis) response. ● obstructive jaundice (Painless jaundice)



IF YOU WANT A SUMMARY [CLICK HERE](#)

YOU **VS** MCQs

1

Which of the following is the most common primary liver malignancy?

A- Fibrolamellar carcinoma

B- Cholangiocarcinoma

C- Hepatocellular carcinoma

D- Hepatoblastoma

2

What is the main histopathological finding in fibrolamellar carcinoma?

A- Large hepatocytes

B- Thick trabeculae

C- Pseudoglands

D- Band of lamellar fibrosis

3

Which of the following oncogenic mutation in early stage of pancreatic carcinoma?

A- KRAS

B- p53

C- SMAD4

D- p16

4

A 34 year old women came to the ER with hypovolemic shock, and peritoneal cavity bleeding , she has a history of oral contraceptive. What does she mostly represent

A- Angiosarcoma

B- Hepatocellular carcinoma

C- Hepatic adenoma

D- Hepatitis C

1-C / 2-D / 3-A / 4-C



YOU **VS** MCQs

5

Ingestion of which of the following can cause Hepatocellular carcinoma?

A- Red meat

B- Alcohol

C- Aflatoxins

D- Smoking

6

What is the most common cancer in the liver ?

A- Hepatocellular carcinoma

B- Metastatic

C- Angiosarcoma

D- Hepatic adenoma

7

Which of the following is mostly has great elevation of Alpha-fetoprotein

A- Pancreatic adenoma

B- Angiosarcoma

C- Hepatocellular carcinoma

D- Cholangiocarcinoma

8

Patient has cancer in the head of the pancreas. Which of the following can be is least likely to be developed?

A- Steatorrhea

B- Bleeding

C- Malabsorption

D- Jaundice

5-C / 6-B / 7-C / 8-B



YOU **VS** CASES

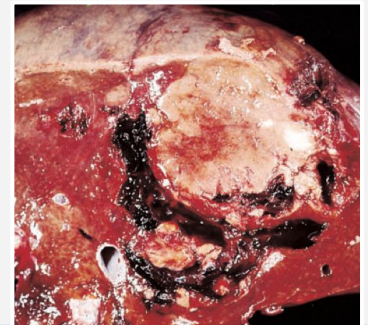
1. A 40-year-old woman presents with a long history of vague upper abdominal pain and frequent indigestion. Physical examination reveals an obese woman with jaundice and abdominal tenderness. Serum bilirubin is elevated (4.2 mg/dL). There is a mild increase in serum AST and ALT (62 and 57 U/L, respectively) and a moderate increase in alkaline phosphatase (325 U/L). Markers for viral hepatitis are negative. Abdominal ultrasound examination shows echogenic stone-like material within the gallbladder and thickening of the gallbladder wall. An intrahepatic mass is also visualized adjacent to the gallbladder. A cholecystectomy is performed. Histologic examination shows dense fibrous and glandular structures in the wall of the gallbladder. What is the most likely diagnosis?

- | | | | |
|---------------------------------|--------------------|--------------------|-----------------------------|
| A. Carcinoma of the gallbladder | B. Hemangiosarcoma | C. Hepatic adenoma | D. Hepatocellular carcinoma |
|---------------------------------|--------------------|--------------------|-----------------------------|

2. A 52-year-old recent immigrant from Vietnam complains of abdominal swelling, weight loss, and upper abdominal pain of 3 weeks in duration. His past medical history includes malaria and infection with the liver fluke *Clonorchis sinensis*. The liver is hard to palpation. An abdominal CT scan shows a hypoattenuated mass with lobulated margins in the liver. A biopsy discloses well-differentiated neoplastic glands embedded in a dense fibrous stroma. Which of the following is the most likely diagnosis?

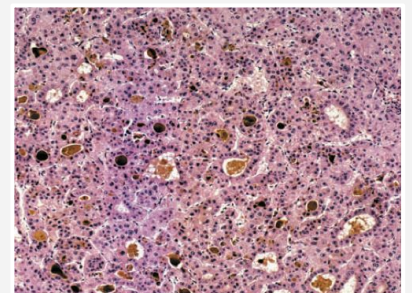
- | | | | |
|---------------------------------|-----------------------|--------------------|-----------------------------|
| A. Carcinoma of the gallbladder | B. Cholangiocarcinoma | C. Hemangiosarcoma | D. Hepatocellular carcinoma |
|---------------------------------|-----------------------|--------------------|-----------------------------|

3. A 25-year-old woman complains of sudden onset of acute abdominal pain. Physical examination shows abdominal distention. Her temperature is 37°C (98.6°F), respirations 22 per minute, heart rate 110 per minute, and blood pressure 70/50 mm Hg. A tap of the abdomen returns blood. A CT scan reveals a solitary 20-cm mass of the liver. A surgically resected portion of the liver is shown in the image. This patient's tumor was most likely associated with chronic exposure to which of the following?



- | | | | |
|-------------------------|--------------|----------------|------------------------|
| A. Carbon tetrachloride | B. Halothane | C. L-thyroxine | D. Oral contraceptives |
|-------------------------|--------------|----------------|------------------------|

4. A 68-year-old man complains of vague abdominal pain, intermittent fever, and a 20-lb (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. A needle biopsy is shown in the image. 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 |
|-------------------------|----------------------|----------------------|-----------------------------|



1-A / 2-B / 3-D / 4-B



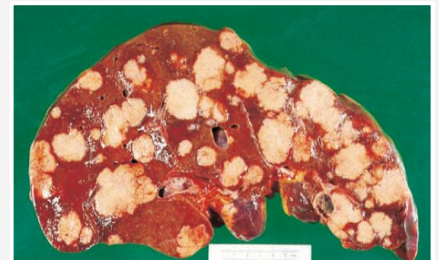
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YOU VS CASES

5. A 40-year-old woman complains of having severe back pain for about 3 months and recurrent fever. Her past medical history is significant for ulcerative colitis. On physical examination, the patient is thin and jaundiced. The liver edge descends 1 cm below the right costal margin and is nontender. Laboratory studies show normal serum levels of AST and ALT but elevated serum levels of alkaline phosphatase (420 U/L). Endoscopic retrograde cholangiopancreatography demonstrates a beaded appearance of the extrahepatic biliary tree. Which of the following diseases is a late complication of this patient's condition?

- | | | | |
|--------------------------------------|-----------------------|--------------------|-------------------------|
| A. Adenocarcinoma of the gallbladder | B. Cholangiocarcinoma | C. Hepatic adenoma | D. Hepatic angiosarcoma |
|--------------------------------------|-----------------------|--------------------|-------------------------|

6. A 69-year-old woman arrives in the emergency room complaining of weakness, abdominal pain, and a 9 kg (20 lb) weight loss during the past month. Physical examination reveals jaundice, conspicuous 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?

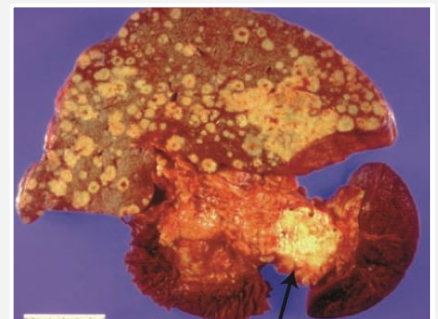


- | | | | |
|---------------------------------|--------------------------------------|-------------------------|----------------|
| A. Hemangiosarcoma of the liver | B. Metastatic carcinoma of the liver | C. Miliary tuberculosis | D. Primary HCC |
|---------------------------------|--------------------------------------|-------------------------|----------------|

7. A 60-year-old man presents with a 3-week history of weight loss, vague abdominal pain, and progressive yellowing of his skin and sclerae. He also reports the recent onset of intermittent pain in the upper and lower extremities. Laboratory studies show a serum bilirubin level of 15 mg/dL, mostly in the conjugated form. A CT scan of the abdomen reveals a mass in the head of the pancreas. The patient develops sudden shortness of breath and is diagnosed with pulmonary thromboembolism. Which of the following is the most likely cause of thromboembolism in this patient?

- | | | | |
|---|-------------------------------|-------------------------------|------------------------------|
| A. adenocarcinoma of the ampulla of Vater | B. Gastrinoma of the pancreas | C. Insulinoma of the pancreas | D. Pancreatic adenocarcinoma |
|---|-------------------------------|-------------------------------|------------------------------|

8. Despite best efforts at treatment, the patient described in Question 7 subsequently dies. The gross appearance of the pancreas and liver at autopsy is shown in the image. This patient's tumor most likely arose from which of the following types of cells?



- | | | | |
|-----------------|----------------|---------------|-----------------|
| A. Acinar cells | B. Alpha cells | C. Beta cells | D. Ductal cells |
|-----------------|----------------|---------------|-----------------|



5-B / 6-B / 7-D / 8-D



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9. A 65-year-old woman presents with a 5-week history of yellow skin and sclera, anorexia, and epigastric pain. Her past medical history is significant for insulin-dependent diabetes mellitus. She smoked one pack of cigarettes a day for the past 20 years. Physical examination reveals jaundice and a palpable gallbladder. Laboratory studies show a serum bilirubin level of 10 mg/dL, mostly in the conjugated form, and an elevated alkaline phosphatase (260 U/L). A CT scan of the abdomen discloses a mass in the head of the pancreas and multiple nodules in the liver measuring up to 3 cm. Which of the following is the most likely cause of jaundice in this patient?

- | | | | |
|-------------------|--------------|-------------------------------------|--------------|
| A. Cholelithiasis | B. Cirrhosis | C. Extrahepatic biliary obstruction | D. Hemolysis |
|-------------------|--------------|-------------------------------------|--------------|

10. Which of the following is the most important risk factor for the neoplasm arising in the patient described in Question 9?

- | | | | |
|------------------|-------------------|----------------------|------------------------|
| A. Alcohol abuse | B. Cholelithiasis | C. Cigarette smoking | D. Diabetes mellitus 1 |
|------------------|-------------------|----------------------|------------------------|

11. A 63-year-old woman presents with a 6-month history of recurrent epigastric pain and nausea. Abdominal ultrasound reveals a 13-mm hypoechoic lesion in the tail of the pancreas. Physical examination shows flushing of the face, periorbital edema, and hypotension (blood pressure = 90/50 mm Hg). Laboratory studies disclose normal serum levels of gastrin, amylase, insulin, and vasoactive intestinal polypeptide. Urinalysis demonstrates elevated levels of metanephrines (10 mg per 24 hours). Which of the following is the most likely diagnosis?

- | | | | |
|-------------------------------|----------------|---------------|-------------------------|
| A. Adenocarcinoma of pancreas | B. Glucagonoma | C. Insulinoma | D. Pancreatic carcinoid |
|-------------------------------|----------------|---------------|-------------------------|

12. A 60-year-old woman presents with several years of abdominal pain radiating to her back and a 5-day history of yellow skin and sclerae. She has lost 15 lb during the past several months, and her stools have become lighter in color. On physical examination, the patient is cachectic and jaundiced. The liver edge descends 1 cm below the right costal margin and is nontender. Her right calf is tender and erythematous. Serum AST and ALT are at the upper limits of normal, but alkaline phosphatase is increased to 430 U/L. A CT scan shows a mass in the head of the pancreas. What is the most likely cause of jaundice in this patient?

- | | | | |
|--------------------------|------------------------|---------------------------|-------------------------------------|
| A. Acute viral hepatitis | B. Alcoholic hepatitis | C. Drug-induced hepatitis | D. Extrahepatic biliary obstruction |
|--------------------------|------------------------|---------------------------|-------------------------------------|

LIVER TUMORS

- The liver is the most common site of metastatic cancers from primary tumors of the colon, lung, and breast.
- Hepatocellular adenomas** are benign tumors of hepatocytes. Most can be subclassified on the basis of molecular changes with varying degrees of malignant potential. They are associated with use of oral contraceptives and androgens.
- The two main types of malignant tumors are **hepatocellular carcinomas** and **cholangiocarcinomas**; HCCs are much more 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 HCC are hepatitis B and C, alcoholic cirrhosis, hemochromatosis, and exposure to aflatoxins. In the Western population, about 90% of HCCs develop in cirrhotic livers; in Asia, almost 50% of cases develop in noncirrhotic livers.
- The chronic inflammation and cellular regeneration associated with viral hepatitis are predisposing factors for the development of carcinomas.
- HCC may be unifocal or multifocal, tends to invade blood vessels, and recapitulates normal liver architecture to varying degrees.
- Cholangiocarcinoma is a tumor of intrahepatic or extrahepatic bile ducts that is relatively common in areas where liver flukes, such as *Opisthorchis* and *Clonorchis* species, are endemic.

SUMMARY

PANCREATIC NEOPLASMS

- Pancreatic cancer probably arises from noninvasive precursor lesions (most commonly, PanINs), developing by progressive accumulation of mutations of oncogenes (e.g., *KRAS*) and tumor suppressor genes (e.g., *CDKN2A/p16*, *TP53*, and *SMAD4*).
- Typically, these neoplasms are ductal adenocarcinomas that produce an intense desmoplastic response.
- Most pancreatic cancers are diagnosed at an advanced stage, accounting for the high mortality rate.
- Obstructive jaundice is a feature of carcinoma of the head of the pancreas; many patients also experience debilitating pain.
- Carcinomas of the tail of the pancreas are often not detected until late in their course.



9-C / 10-C / 11-D / 12-D



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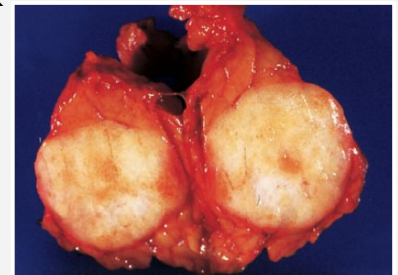
YOU **VS** CASES

EXTRA CASES MAY REQUIRE EXTRA INFO

1. A 35-year-old woman presents with 6-month history of skin rash and fatigue. Physical examination shows pallor and a necrotizing erythematous skin rash of her lower body. Laboratory studies reveal mild anemia and fasting blood glucose of 160 mg/dL. A CT scan of the abdomen demonstrates a 2-cm mass in the pancreas. Which of the following is the most likely diagnosis??

- | | | | |
|--------------------|---------------|----------------|---------------|
| A. Carcinoid tumor | B. Gastrinoma | C. Glucagonoma | D. Insulinoma |
|--------------------|---------------|----------------|---------------|

2. A 40-year-old woman comes to the physician with a 6-week history of episodic hunger and fainting spells. She is currently seeing a psychiatrist because she is irritable and quarreling with her family. Laboratory studies show a serum glucose concentration of 35 mg/dL. A CT scan of the abdomen demonstrates a 1.5-cm mass in the pancreas. The gross appearance of the bisected tumor is shown in the image. What is the most likely diagnosis?



- | | | | |
|-------------------|---------------|----------------|---------------|
| A. Adenocarcinoma | B. Gastrinoma | C. Glucagonoma | D. Insulinoma |
|-------------------|---------------|----------------|---------------|

3. A 67-year-old man comes to the clinic due to worsening fatigue and abdominal distension. The patient has lost 11 pounds in the last 2 months with minimal change in appetite. Past medical history is notable for chronic liver disease due to hepatitis B infection that was diagnosed 15 years ago. His most recent colonoscopy 1 year ago showed no abnormalities. His temperature is 37.0°C (98.6°F), pulse is 85/min, and blood pressure is 154/89 mm Hg. Physical examination reveals temporal wasting and scleral icterus. Palmar erythema and multiple spider angiomas are present. The abdomen is distended with shifting dullness to percussion. There is 2+ pitting edema of the lower extremities. Ultrasound shows a single homogenous liver mass with irregular borders. Which of the following best describes the tumor marker that is likely elevated in this patient?

- | | | | |
|---|--|--|---|
| A. Glycoprotein normally produced by the fetal yolk sac | B. Protein normally present in cells derived from the neural crest | C. Hormone produced by the placenta after embryonal implantation | D. Cell-surface glycoprotein found on Müllerian-type epithelium |
|---|--|--|---|



1-C / 2 -D/ 3-A

Pathology Team

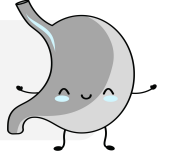
Leader

لمى العتيبي



Leader

زياد العتيبي



نورة المحيميد



عبدالرحمن المسّم



عائشة إبراهيم



ليان الرويلي



رغد المصلح



الدانة عبدالله



ريمز المحمود



فيصل الشويعر



ريما المطيري



عروب المحمود



سلطان البقمي



زياد حكمي



الجوهرة الوهبي



عبدالله الضويحي



خالد الرشيد



عبدالله الكودري



هيا الزير



لؤي الحديثي



إيلاف معتي



معاذ الحضيف



محمد السلامه



يزيد ال طلحه



ساره العجاي



يوسف بادغيش



رزان السطحي



رند ابا الخيل



أفنان الأحمرري



زياد السويلم



منصور العتيبي



هدى بن جدعان



عبدالرحمن الأحيدب



دانه المحيسن



محمد العرفج



عبدالمحسن الدايل



دينا المهوس



نوره المالك



شوق الخليفة

