Focal Liver Lesions

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Primary Malignant Tumors

- Hepatocellular Carcinoma
- Intrahepatic Cholangiocarcinoma
- Hepatoblastoma
- Hemangiosarcoma
- Epithelioid Hemangioendothelioma
- Undifferentiated (Embryonal) Sarcoma
- Liposarcoma
- Lymphoma
- Rhabdomyosarcoma

Hepatocellular Carcinoma

Hepatocellular Carcinoma

- Most common primary malignant tumor of liver
- 5th most common in men; 8th most common in women
- 4th in annual cancer mortality rates
- Incidence higher among Asians
- Men are generally more susceptible than women

Hepatocellular Carcinoma

Symptom	Frequency (%)
Abdominal pain	59-95
Weight loss	34-71
Weakness	22-53
Abdominal swelling	28-43
Nonspecific GI symptoms	25-28
Jaundice	5-26

Sign	Frequency (%)
Hepatomegaly	54-98
Ascites	35-61
Fever	11-54
Splenomegaly	27-42
Wasting	25-41
Jaundice	4-35
Hepatic bruit	6-25

Paraneoplastic Syndrome

- Rare and uncommon
- **Type A Hypoglycemia**
  - Mild form of glycopenia that occurs in the terminal stages
  - Inability of the liver to keep up with the demands for glucose by a large and rapidly growing tumor
- **Type B Hypoglycemia**
  - Less than 5%
  - Severe hypoglycemia early in the course of the disease
  - Defective processing by malignant hepatocytes of the precursor to insulin-like growth factor II (pre-IGF II)

Hepatocellular Carcinoma

Paraneoplastic Syndromes Associated with HCC
Carcinoid syndrome
Hypertrophic osteoarthropathy
Neuropathy
Osteoporosis
Polymyositis
Porphyria
Systemic arterial hypertension
Thyrotoxicosis
Thrombophlebitis migrans
Watery diarrhea syndrome

Diagnosis

- **Serum Tumor Markers**
  - **Alpha Fetoprotein**
    - Sensitivity of 25-65%; Specificity 79-95%
    - α_1-globulin normally present in high concentrations in fetal serum but only in minute amounts thereafter
    - Reappearance of high serum levels of AFP strongly suggests the presence of HCC or hepatoblastoma
    - Tumors of endodermal origin, nonseminomatous germ cell tumors and pregnancy
    - Levels affected by ethnicity, underlying cause of liver disease, and tumor stage

Diagnosis

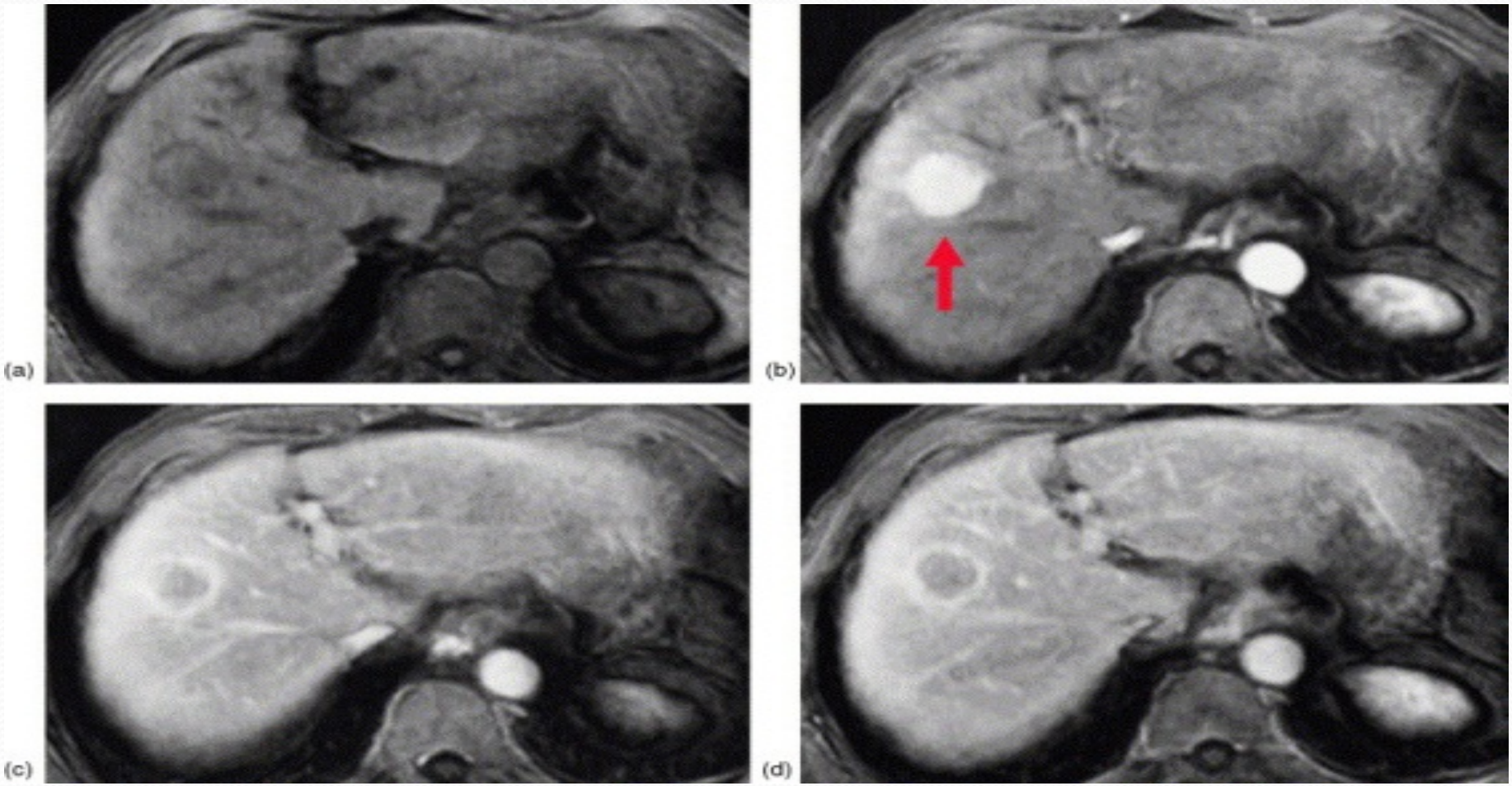
- **Serum Tumor Markers**
  - AFP-L3
  - Des-γ-Carboxy Prothrombin (DCP)
  - Glypican 3
  - Golgi protein 73
  - Hepatocyte growth factor
  - IGF-1
  - TGF-β1
  - Surface-Enhanced Laser Desorption/Ionization Time of Flight (SELDI-TOF)

Imaging

- **Ultrasonography**
  - Sensitivity 48%; Specificity 97%
  - Detects most HCC but may not distinguish from other solid lesions
  - Sensitivity increases with increasing size of lesion
  - **Advantage**: Safe, availability, and cost effective
  - **Disadvantage**: nonstandardized, examiner-dependent, and body habitus
- **Multiphase Computed Tomography**
  - Sensitivity 67.5%; Specificity 92.5%
  - Imaging technique of choice for diagnosis
  - Noncontrast, arterial, portal venous, and delayed phases

Noncontrast

Arterial

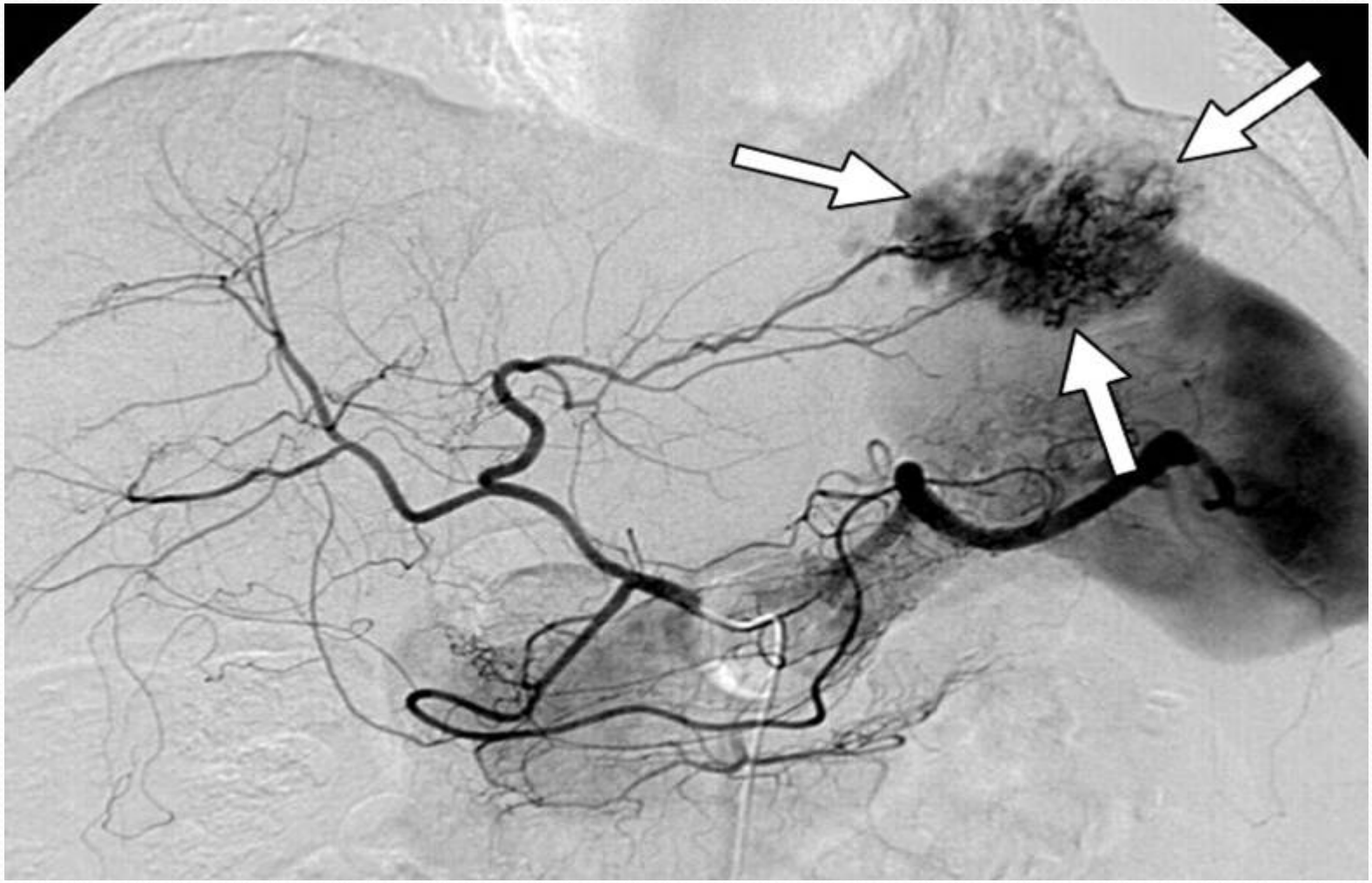


Portal Venous

Delayed

Imaging

- **Magnetic Resonance Imaging (MRI)**
  - Sensitivity 80.6%; Specificity 84.8%
  - Slightly superior to CT
- **Hepatic Angiography**
  - Diagnostic role has decreased since advent of CT and MRI
  - Helpful for recognizing small hypervascular HCC but may miss early, well-differentiated hypovascular tumors
  - Essential for delineating the hepatic arterial anatomy in planning embolization or chemoembolization of the tumor or infusion of cytotoxic drugs directly into the hepatic artery or its branches



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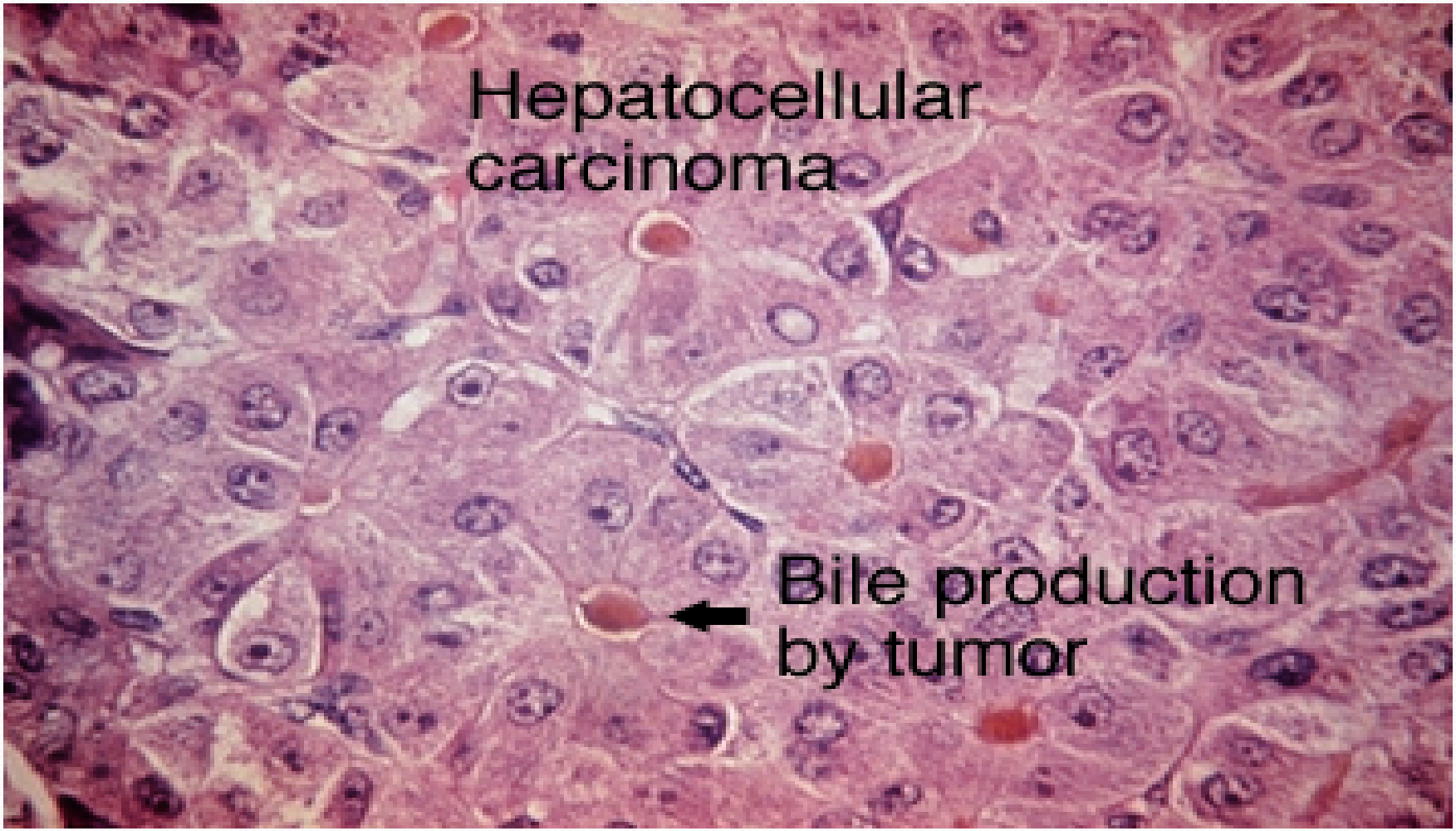


http://www.pathology.med.umich.edu/greensonlab/hcc4.jpg

Treatment

- **Surgical Resection**
  - Best chance for cure
  - Confined to one lobe of the liver, favorably located, and the nontumorous liver tissue should not be cirrhotic
  - Feasible in only approximately 15% of patients
- **Liver Transplantation**
  - Ideal therapy
  - Performed in patients with nonresectable tumor but confined to the liver

Treatment

- **Local Ablation**
  - Potentially curative with small tumors (3-5cm)
  - Survival rates similar to surgical resection but higher recurrence rates
  - **Percutaneous Ethanol Injection (PEI)**-safe and effective (<2-3cm); multiple sessions; complications rare; possible tumor seeding
  - **Radiofrequency Ablation (RFA)**-more effective (3-5cm); fewer sessions; similar complication rates to PEI
  - PEI favored when lesions are adjacent to major vessel or large bile ducts
- **Chemoembolization (TACE)**
  - Palliative
  - Can be considered if waiting time for transplant > 6 months or tumor size near acceptable limit
  - Theoretically can be used to reduce size to make resection or transplantation possible; studies show mixed results

Treatment

- **Chemotherapy**
  - **Sorafenib**-inhibitor of Raf kinase and tyrosine kinase activity of vascular endothelial growth factor receptors (VEGRFs) and platelet-derived growth factor receptor (PDGFR)
  - Considered for patients with intact hepatic function and portal vein thrombosis, extrahepatic tumor, or failures of other therapies

- **Alternative Therapies**
  - Cyroablation
  - Microwave ablation
  - Laser ablation
  - Stereotactic radiotherapy
  - Radioembolization with ^{90}Y microspheres

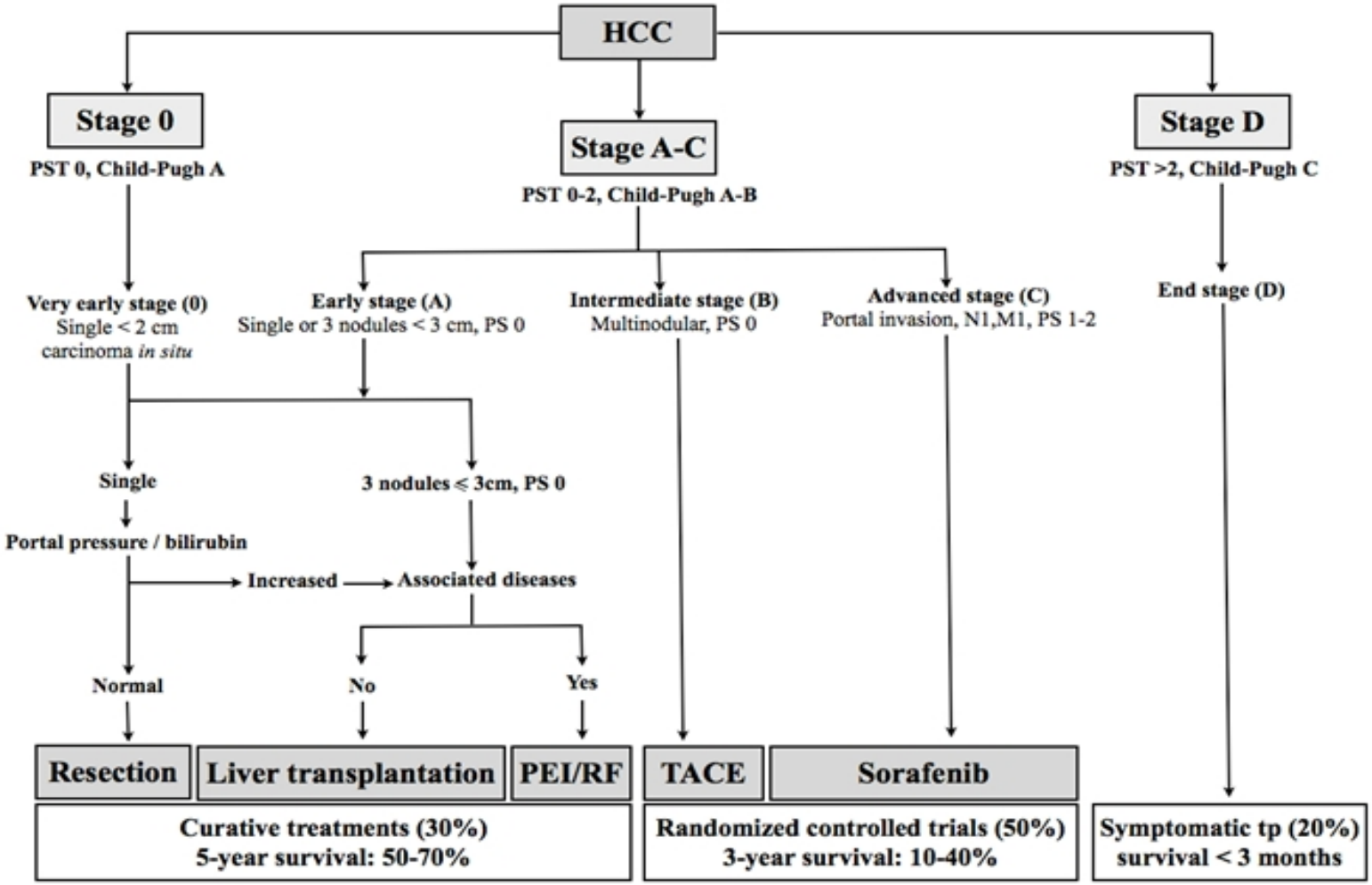


Figure 1. Barcelona Clinic Liver Cancer (BCLC) staging classification (modified from Bruix J and Sherman M[77])

Intrahepatic Cholangiocarcinoma

Intrahepatic Cholangiocarcinoma

- **Name based on particular portion of biliary tree involved**
  - Small intrahepatic bile ducts (Peripheral cholangiocarcinoma)
  - Hepatic duct bifurcation (Perihilar cholangiocarcinoma or Klatskin tumor)
  - Extrahepatic bile ducts (Bile duct carcinoma)

- **Epidemiology**
  - 10-20% of all primary liver cancers
  - Age at presentation > 65 years
  - Highest prevalence in Asia (Thailand, Hong Kong, China, Japan, and Korea); likely thought to be due to chronic infection of liver fluke (*Opisthorchis viverrini*)
  - 0.85/100,000 with a 1.5-fold higher rate in men than women in the US
  - Radiographic contrast agent thorium dioxide (Thorotrast); banned in 1950s
  - PSC, biliary atresia, von Meyenburg complexes, Caroli's disease, choledochal cysts, and intrahepatic cholelithiasis

Intrahepatic Cholangiocarcinoma

- **Pathogenesis**
  - Malignant transformation of the bile duct cells generally in the setting of inflammation and/or cholestasis
  - Mutations of the *K-ras* gene, gene for IL-6, and allelic loss or mutations of *TP53* and *p16*
- **Clinical Features**
  - Similar to HCC; seldom produces symptoms until tumor is advanced

Diagnosis

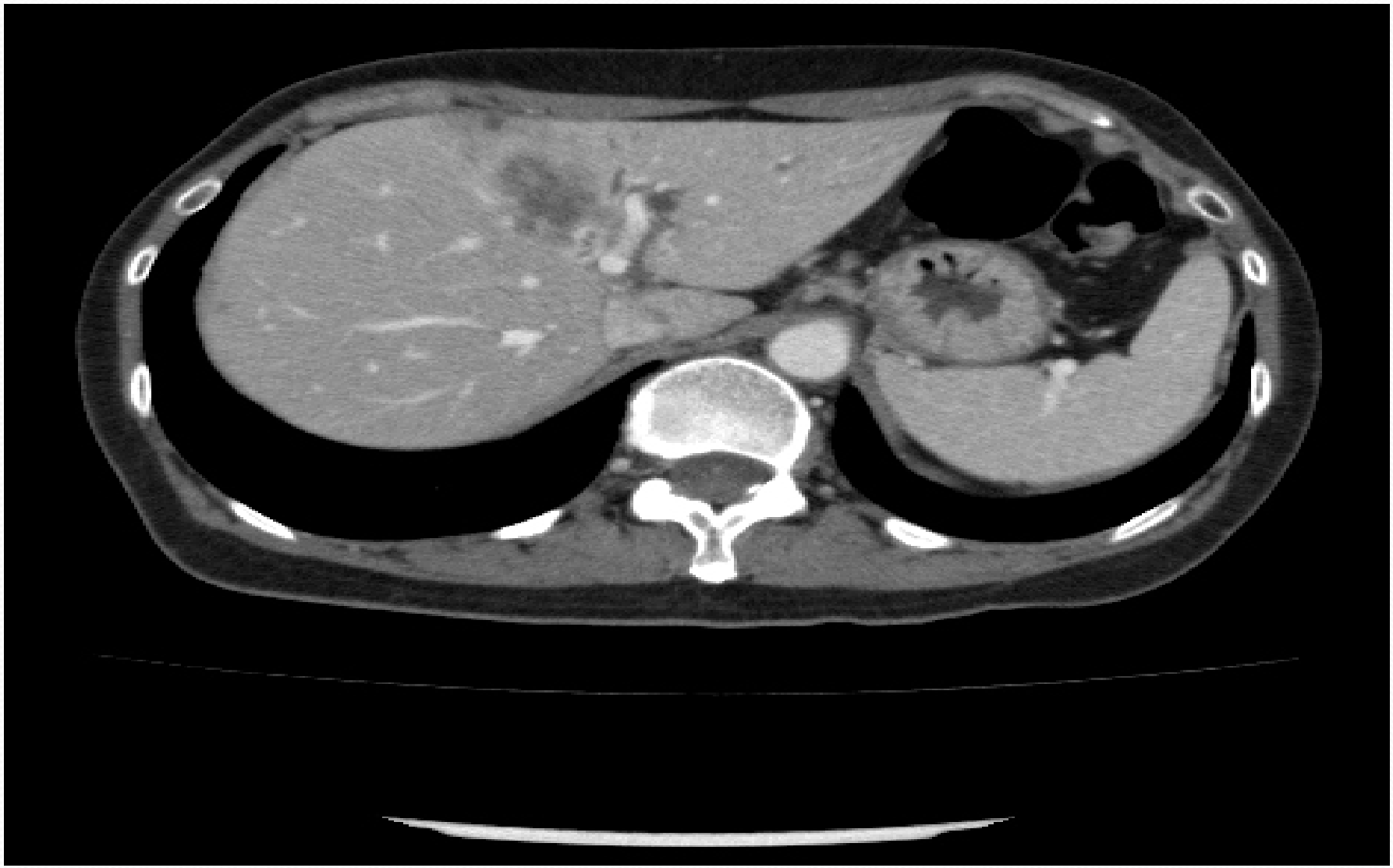
- Often only AP elevated
- CA19-9 is most frequently used but has significant limitations; always undetectable in 7% of the population that is Lewis blood group-negative
- Initial imaging with U/S helps identify biliary obstruction
- CT and MRI can help localize the lesion and determine possibility of resection
- MRCP is a superior modality; higher sensitivity than CT for detecting and localizing lesion

Diagnosis

- ERCP for localization of tumor, sampling of tissue and bile, and relief of biliary obstruction if the tumor is unresectable
- Cytology 30% sensitivity; improves to 40-70% with addition of brushings and biopsies
- EUS with FNA has advantage of improving sensitivity and specificity for diagnosis of primary lesion and nodal metastasis but can cause peritoneal seeding; avoid all biopsies if surgical resection contemplated

Appearance

- Large and solitary tumor, but it may be multinodular
- Poorly vascularized
- Rarely bleeds internally or ruptures
- Most tumors are well-differentiated
- Distinguishing the tumor from metastatic adenocarcinoma may be difficult



http://atlasgeneticsoncology.org/Tumors/IntraCholangioCarID5330.html

Treatment and Prognosis

- Early diagnosis is unusual
- Long term survival after diagnosis is dismal; one-year 28% and five-year <5%
- Surgical resection is only opportunity for cure
- Criteria for resection include absence of **all** the following:
  - Evidence of extrahepatic mestastasis
  - Main portal vein or hepatic artery invasion or encasement
  - Bilateral segmental bile duct involvement
  - Contralateral hepatic lobar atrophy

Treatment and Prognosis

- Endoscopic or percutaneous drainage appears to improve symptoms and survival if resection is not possible
- Expandable metal stent preferred if expected survival >3-6months
- Rates of response and survival following radiation therapy and chemotherapy are modest
- Liver transplantation alone results in unacceptably high recurrence rates and limited survival

Hepatoblastoma

Epidemiology

- In children, 3rd most common malignant tumor and most common malignant hepatic tumor
- Almost exclusively in the 1st three years of life
- Boys affected twice as often as girls

Clinical Features

- Most present with abdominal swelling
- Failure to thrive, weight loss, poor appetite, abdominal pain, irritability, and intermittent vomiting and diarrhea
- Rarely rupture
- Distant metastasis evident, usually in lungs (20%), abdominal LN, and brain
- Occasionally cause isosexual precocity in boys as a result of ectopic production of HCG

Diagnosis

- AFP is present in high concentrations in 80-90% and useful clue to diagnosis
- Low serum AFP appear to have worse prognosis
- Ultrasound is used for initial imaging
- CT and MRI are used to define the extent of the tumor and plan definitive surgery
- Avascular mass on hepatic angiography
- Tumors are well-circumscribed and solitary with diameter 5-25cm

http://www.humpath.com/spip.php?article8015

Pathogenesis

- Unclear
- May occur sporadically or in association with hereditary syndromes (FAP or Beckwith-Wiedemann Syndrome) therefore suggesting possible role for chromosomes 5 and 11
- Possible mutations in FAP gene or β-catenin gene

Treatment and Prognosis

- Rapidly progressive
- Surgery is often curative if solitary and sufficiently localized to be resectable
- 5-year survival as high as 75%
- Current practice is to pretreat patient with cisplatin and doxorubicin
- If tumor is inoperable, neoadjuvant chemotherapy may reduce the size and may permit resection
- Encouraging results with liver transplantation with bilobar multifocal tumors without extrahepatic extension
- If surgery is not possible or tumor recurs after surgery then prognosis is generally poor

Hemangiosarcoma

Epidemiology

- Rare
- Most common malignant mesenchymal tumor of the liver
- Most prevalent in the sixth and seventh decades of life
- Men are affected 4x as often as women

Clinical Features

- Most common presenting symptom is upper abdominal pain
- Duration of symptoms generally ranges from one week to six months
- Liver almost always enlarged and usually tender
- Approximately 15% of patients present with acute hemoperitoneum following tumor rupture

Appearance

- Hallmark is presence of blood-filled cysts, although solid growth is also seen
- Fairly well circumscribed but not encapsulated
- Distant metastases are present in 50% of tumors

Pathogenesis

- Specific risk factors have been identified:
  - Exposure to thorium dioxide
  - German vintners who used arsenic-containing insecticides and drank wine adulterated with arsenic
  - Potassium arsenite used to treat psoriasis
  - Workers exposed to vinyl chloride monomer (VCM)

Treatment and Prognosis

- Grows rapidly and prognosis is poor, death ensues within six months
- Operative treatment usually is precluded by the advanced stage of the tumor
- Even with surgery, survival only 1-3 years
- Results of irradiation and chemotherapy are poor

Epithelioid Hemangioendothelioma

- **Epidemiology**
  - Rare whose incidence is not known
  - Case series of 137 cases where 2/3 were female and occurred at all ages in adulthood
- **Diagnosis**
  - Highly vascular mass
  - Case reports indicate that the tumor can be visualized with PET
  - Requires histologic examination via biopsy (stain + for factor VIII-related antigen, CD34 or CD 31)
- **Appearance**
  - Multiple and may be diffuse throughout the liver

- **Treatment and Prognosis**
  - Low-grade malignant potential; but still can metastasize
  - Must be distinguished from hemangiosarcoma because much better prognosis
  - Primary treatment is surgical resection or transplantation
  - Transplantation appears to be effective even in the presence of advanced or even metastatic disease
  - Not sensitive to radiation or chemotherapy

Undifferentiated (Embryonal) Sarcoma

Embryonal Sarcoma

- Rare primary malignancy of the liver
- Occurs in both children and adults
- Aggressive but long-term survival can be achieved with radical surgery and chemotherapy

Question

A 57 y/o man with CPC B cirrhosis due to chronic HCV infection is found to have a 3cm HCC in the right lobe on MRI. There is an enhancing thrombus in the right portal vein. Which of the following is the most appropriate approach to treatment of this patient?

A) Chemoembolization followed by transplantation
B) Liver transplantation
C) RFA or ethanol injection
D) Surgical resection

Answer C

HCC with extension to the portal vein is not considered an indication for liver transplantation given the very high risk of recurrence. Chemoembolization is relatively contraindicated due to portal vein thrombosis. Surgical resection is reserved for HCC in patients without cirrhosis. Local ablative therapies would be most appropriate in this case. Sorafenib, an inhibitor of Raf kinase and the receptor tyrosine kinase activity of vascular endothelial growth factor receptors and platelet-derived growth factor receptor is the first of these new agents to be shown to modestly improve survival compared with supportive care. It should be considered for patients with intact hepatic function (Child A) and portal vein thrombosis, extrahepatic disease, or failure of other therapies.

Benign Tumors

Benign Tumors

- Hepatocellular Adenoma
- Cavernous Hemangioma
- Infantile Hemangioendothelioma
- Angiomyolipoma
- Bile Duct Adenoma
- Biliary Cystadenoma
- Biliary Adenofibroma

Hepatocellular Adenoma

Epidemiology

- Extremely rare before the use of OCP
- Risk is still small even with OCP use but increases with duration of use (25x with use for longer than 9 years)
- Increases in size during pregnancy
- Occasional regression and even disappearance of the tumor after cessation of OCP
- May also occur with long-term use of anabolic androgenic steroids and certain inherited metabolic disturbances

Pathogenesis

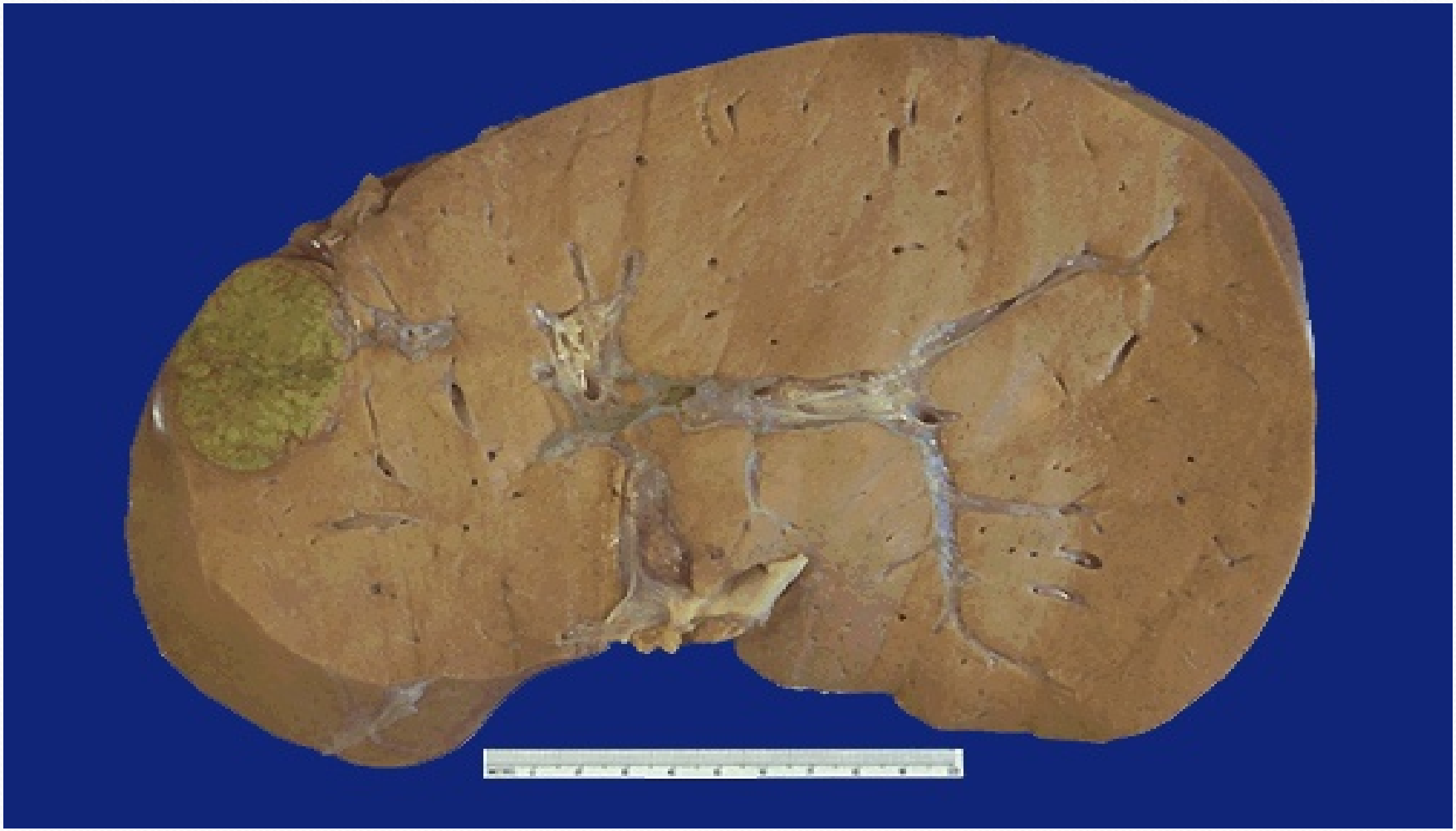
- **Genetic alterations:**
  1. Bilallelic mutations of the TCF1 gene that codes for hepatocyte nuclear factor 1α (HNF-1α) found in 60% of patients with adenoma
  2. β-Catenin activation via wnt pathway confers a higher risk of malignant transformation
  3. Acute inflammatory responses

Clinical Features

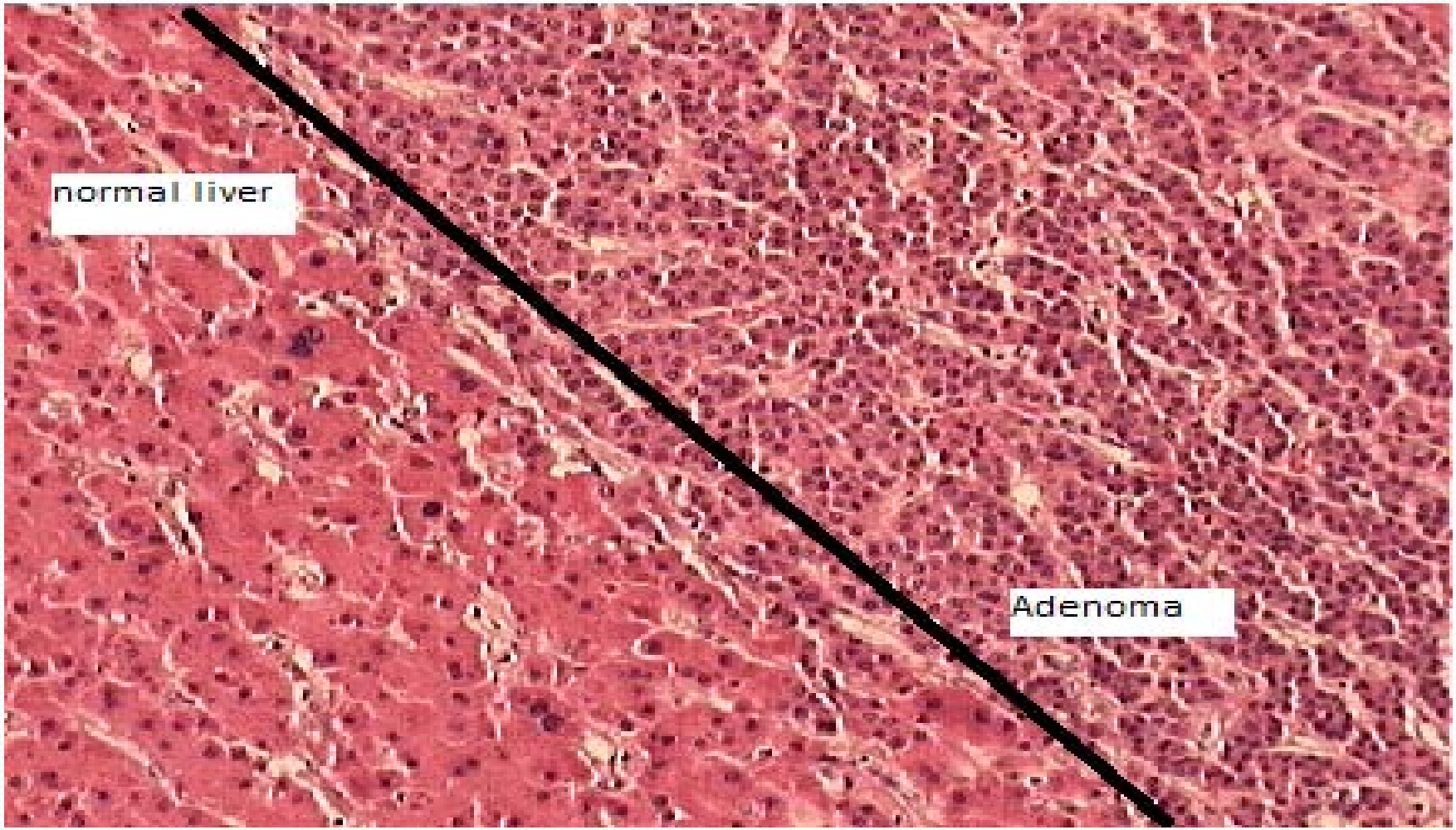
- 25% experience right hypochondric or epigastric pain
- Most alarming presentation is acute hemoperitoneum following rupture of the adenoma. Not uncommon.
- Tumors that rupture are generally large and solitary
- Most important determinant of rupture is a superficial location
- Often, affected woman is menstruating at the time of rupture and may also occur during pregnancy

Diagnosis

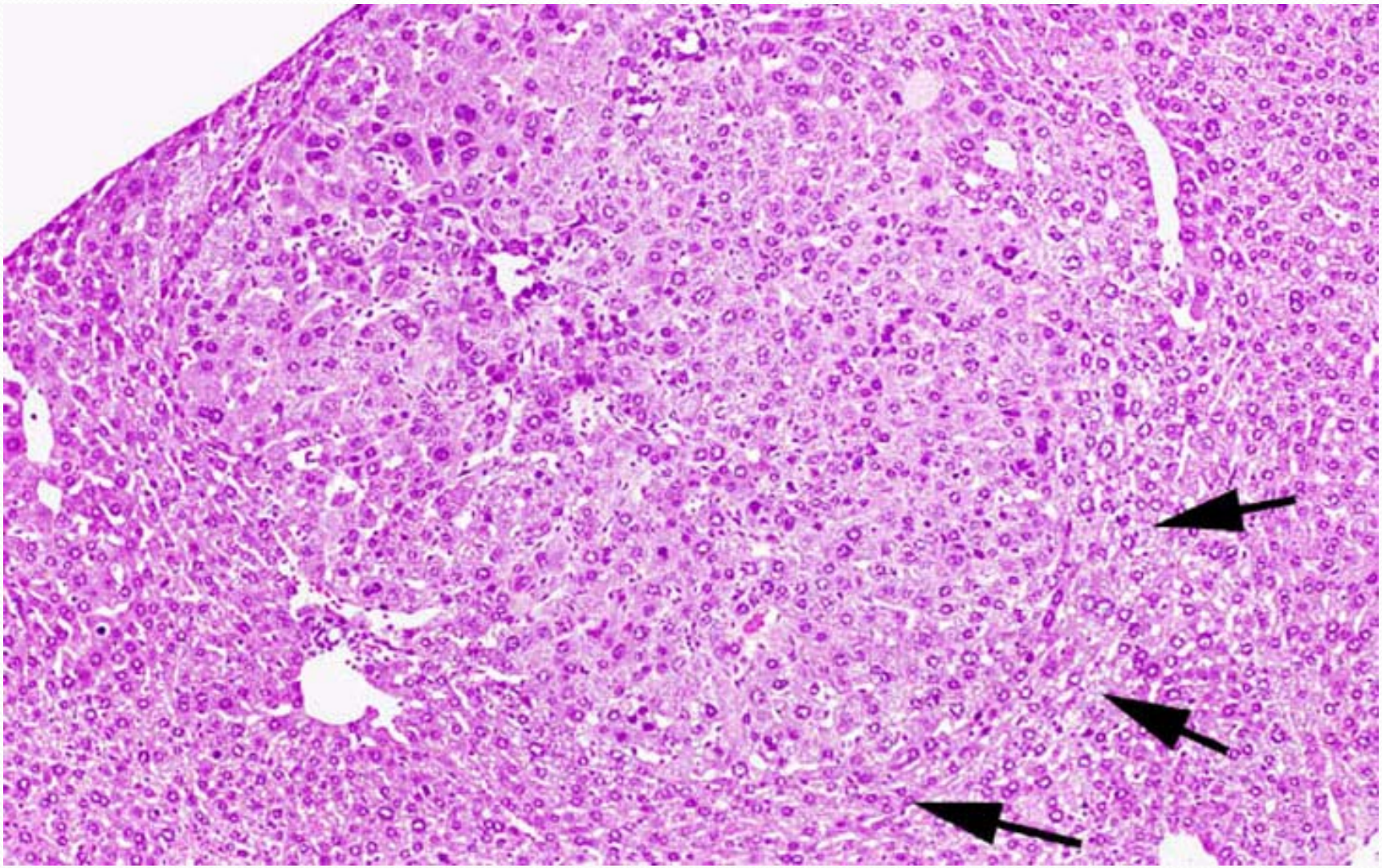
- Serum AFP are normal
- Clearly defined margin and often has parallel vessels entering it from the periphery (spoke wheel appearance)
- Sharply circumscribed but does not have a true capsule
- Mimic normal liver tissue microscopically, therefore needle biopsy and FNA may be of limited diagnostic value



http://library.med.utah.edu/WebPath/NEOHTML/NEOPL021.html



http://pathcases4u.blogspot.com/2012/11/n3a.html



http://www.niehs.nih.gov/research/atniehs/labs/assets/images/b_d/do4hepatocellular_adenoma.jpg

Treatment and Prognosis

- Due to danger of rupture, surgical treatment is recommended
- Emergency resection should be performed in the event of rupture if possible, otherwise the hepatic artery should be ligated
- Patients must refrain from taking OCP and pregnancy should be avoided in an unresected adenoma
- Role of liver transplantation is not clear at present
- Questionable risk of malignant transformation

Cavernous Hemangioma

Epidemiology

- Most common benign tumor; found in as many as 7% of autopsies
- Thought to be congenital malformation or hamartoma that increases in size
- Affect persons of all ages
- Manifest most often in the 3rd-5th decade
- Women affected 4-6:1
- May increase in size with pregnancy or the administration of estrogens
- More common in multiparous than nulliparous women

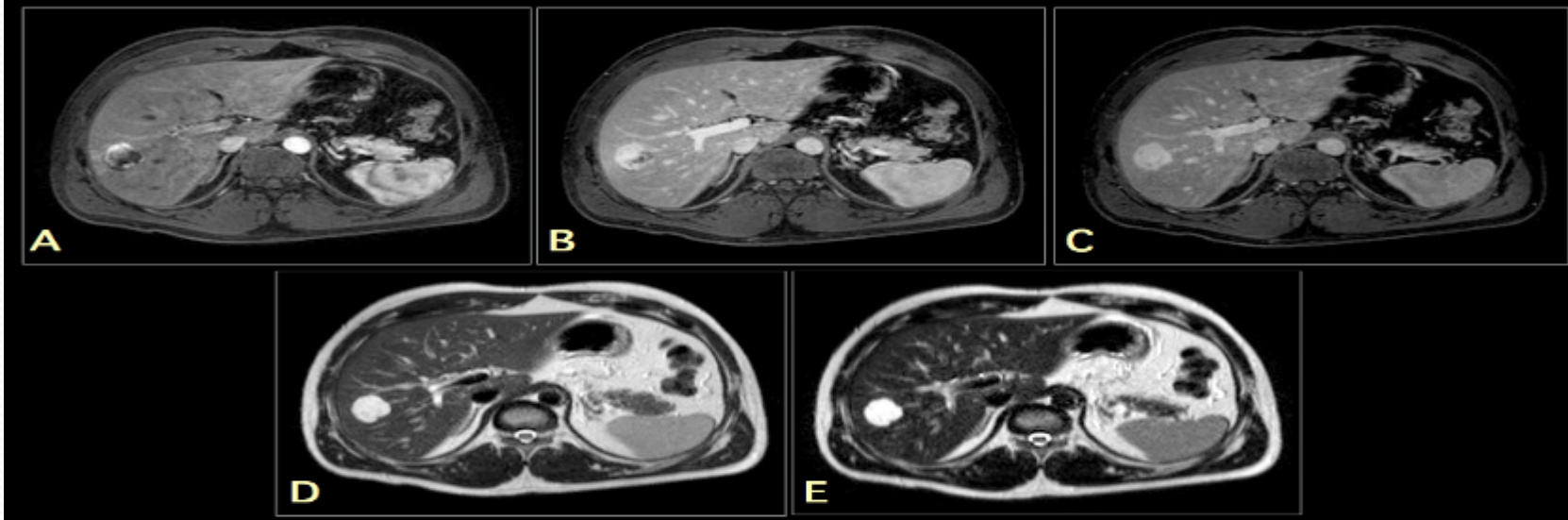
Clinical Features

- Large or multiple lesions produce symptoms
- May become as large as 27cm
- Upper abdominal pain is the most common complaint and results from partial infarction of the lesion or pressure on adjacent tissues
- Occasionally rupture

Diagnosis

- U/S appearance is variable and nonspecific; but lesion usually echogenic
- Single Photon Emission CT (SPECT) with tagged RBC shows highly vascular lesion
- MRI has a high degree of specificity and a central role in the diagnosis of small hemangiomas
- Needle biopsy is of limited value and also risk of severe bleeding
- Solitary lesions and are well circumscribed but seldom encapsulated

Hepatic Cavernous Hemangioma



CE 3D FS T1W GRE in arterial (A), venous (B) and delayed phases (C) demonstrate characteristic peripheral pooling or puddling enhancement with centripetal fill in over time. This pattern is pathognomonic for benign cavernous hemangioma. T2W images show the lesion to be as bright as CSF at both echo times, 80 msec (D) and 140 msec (E). This excludes the possibility of hepatoma which may be hyperintense on less heavily T2W images of TE=80 msec.

http://limpeter-mriblog.blogspot.com/2009/12/hepatic-cavernous-hemangioma.html

Treatment

- Majority can be left untreated
- Resection should be considered if large and causing incapacitating symptoms
- If ruptured, then would need embolization or clamping of the hepatic artery

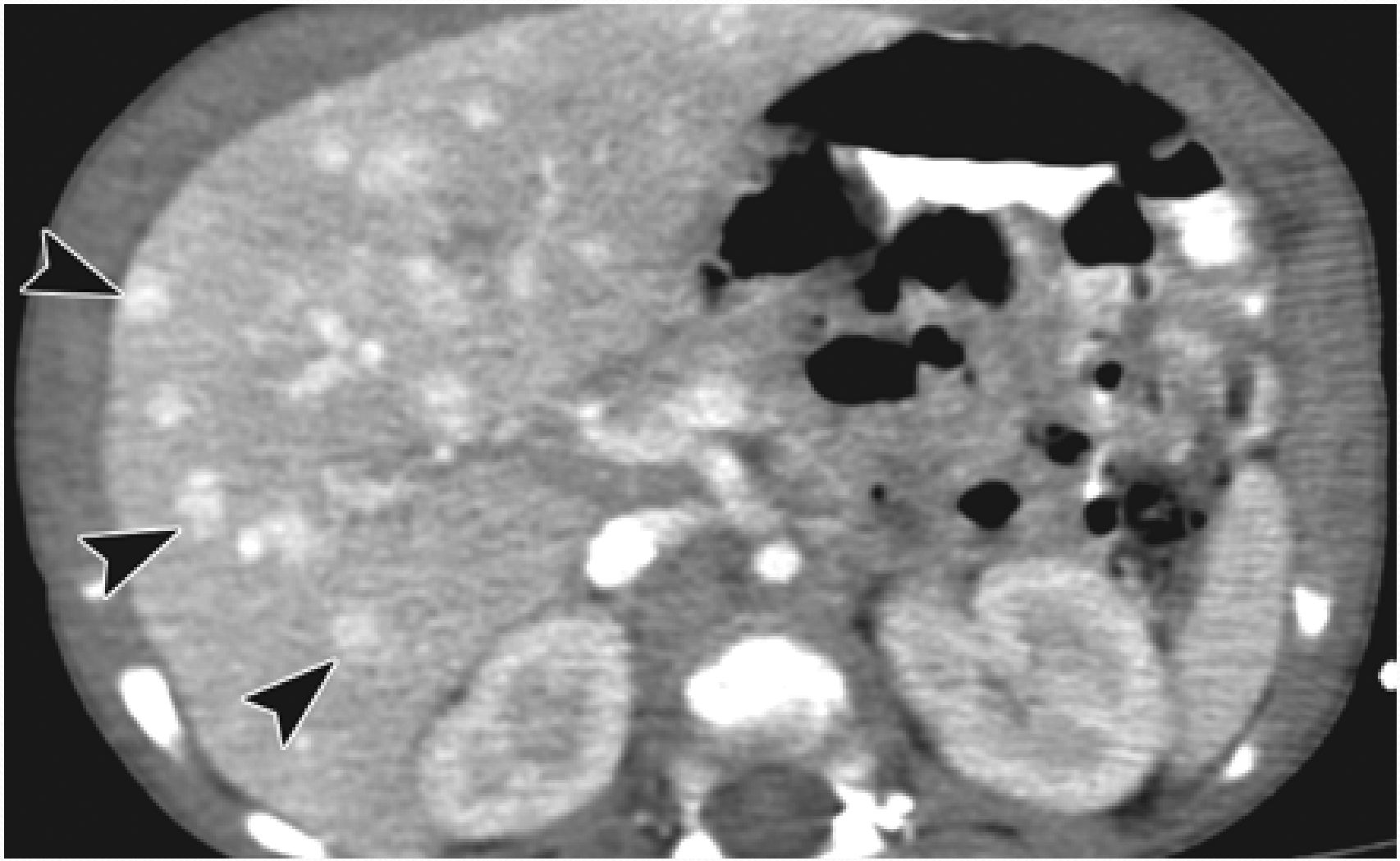
Infantile Hemangioendothelioma

- **Epidemiology**
  - Most common tumor of liver in infants; rare
  - High incidence of congestive heart failure resulting in high mortality rate
  - Manifests within first six months of life and twice as common in girls
  - Often coexists with hemangiomas in other organs, especially the skin (50% of patients)

- **Clinical Features**
  - Usually asymptomatic
  - Large lesions usually recognized clinically by diagnostic triad: enlarged liver, high-output cardiac failure, and multiple cutaneous hemangiomas
  - Malignant change is a rare complication

- **Diagnosis**
  - Percutaneous biopsy is contraindicated because of the danger of bleeding

- **Pathology**
  - Multifocal; well demarcated but not encapsulated
  - **Two Types:**
    1. **Type I Lesions**-calcified; fibrous stromal separations with bile ductules
    2. **Type II Lesions**-more malignant and disorganized-appearing endothelial cell lining and no stromal bile ductules



- **Treatment and Prognosis**
  - Dependent on tumor growth during early months of life
  - If child survives the life threatening aspects such as HF, consumptive coagulopathy, or rupture then tumor completely involutes
  - Treat HF via conventional means but if fails then aggressively treat the tumor
  - When tumor is confined to one lobe, resection is curative even in the presence of HF

Question

A 38 y/o woman who has been taking OCP for 12 years undergoes and abdominal ultrasound scan because of a bout of right upper quadrant pain and a mass is seen. She is otherwise well. Her only medication is OCP. MRI shows a brightly enhancing 6-cm mass in the periphery of the right lobe of the liver. The mass has a "spoke wheel" appearance but no central scar. Which of the following is most appropriate for managing this patient's condition?

A) Arterial embolization
B) Exploratory laparoscopy
C) Radiologic percutaneous biopsy
D) Repeat MRI in six months
E) Surgical resection

Answer E

The lesion in question is a hepatic adenoma, a benign tumor, but one that may rupture, especially if, as in this case, it is located peripherally. Because adenomas mimic normal liver tissue microscopically, needle biopsy and fine-needle aspiration may be of limited diagnostic value. Surgical resection is the recommended treatment for such tumors, whenever feasible. Arterial embolization should be reserved for lesions not amendable to surgical resection. Because of the risk of rupture and reports of malignant transformation, observation by repeat imaging is not an appropriate way to manage these tumors. Whether or not the tumor is removed, the patient must refrain from taking OCP. If the adenoma is not resected, pregnancy should be avoided.

Question

A 41 y/o woman who is undergoing an ultrasound scan for infertility evaluation is noted to have a 3-cm hyperechoic mass in the left lobe of her liver. She is otherwise well and has no risk factors for or physical exam findings consistent with chronic liver disease. Liver function test results and serum AFP levels are normal. Which is the most appropriate next step in the care of this patient?

A) Hepatic artery embolization
B) Contrast-enhanced MRI
C) No further treatment or testing
D) Radiography-guided biopsy of the mass
E) Surgical resection of the mass

Answer B

The incidentally discovered mass is likely to be a cavernous hemangioma, the most common benign tumor of the liver. Although the ultrasonographic appearance of this tumor is variable, the lesion is usually echogenic. Contrast-enhanced CT or MRI is diagnostic. Biopsy is unnecessary, and, in fact some reports on series of patients with this tumor have suggested that biopsy in these cases is associated with an increased risk of bleeding. Hemangioma rarely requires resection, which is usually only performed when a patient has severe symptoms or hemorrhage.

Tumor-Like Hepatic Lesions

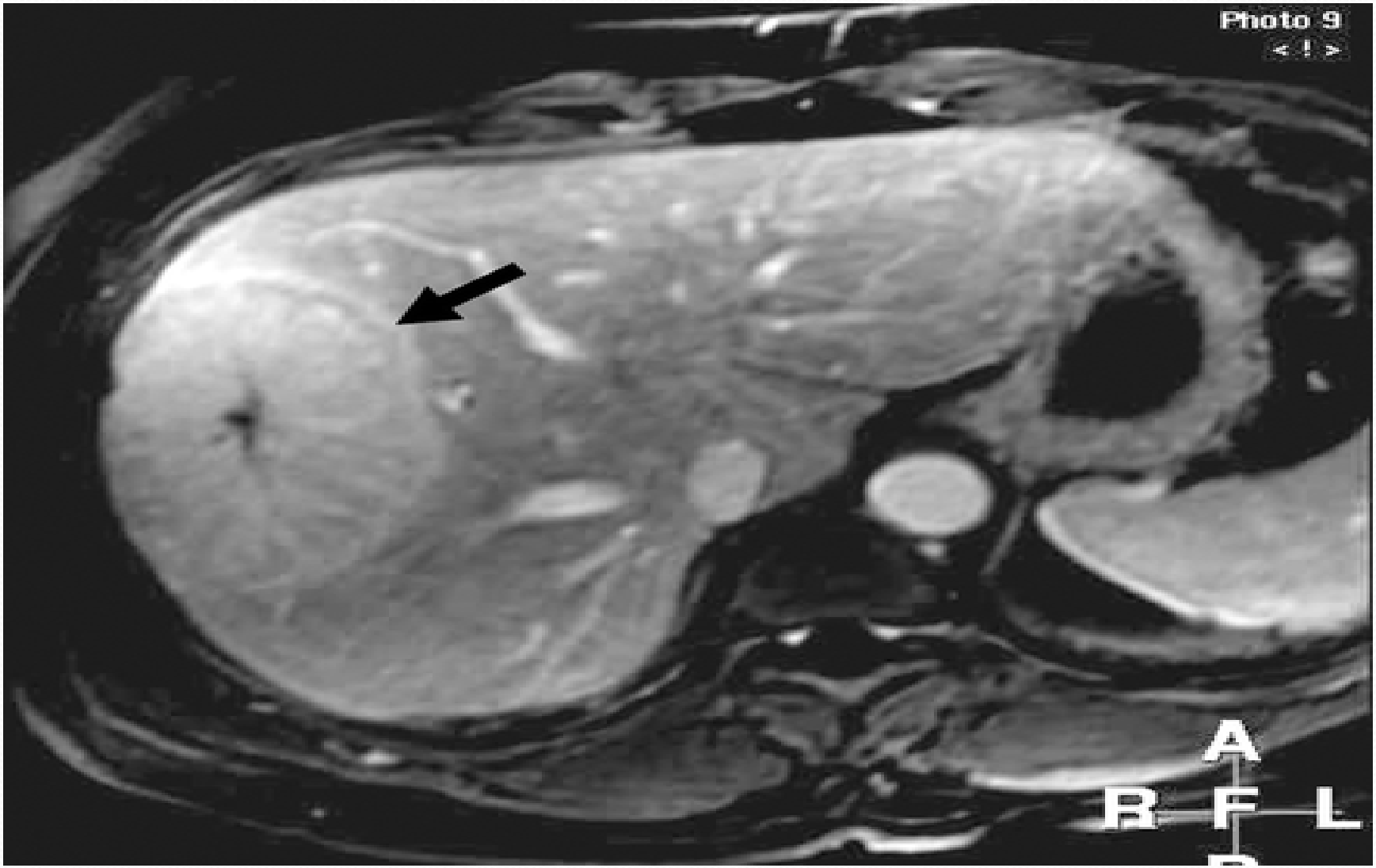
Tumor-Like Hepatic Lesions

- Focal Nodular Hyperplasia (FNH)
- Nodular Regenerative Hyperplasia (NRH)
- Macroregenerative Nodules
- Inflammatory Pseudotumor

Focal Nodular Hyperplasia

- **Epidemiology**
  - More common than hepatocellular adenoma
  - Seen more often in women
  - Occurs at all ages but mostly in 3rd and 4th decades of life
- **Pathogenesis**
  - Cause is unknown
  - Possible vascular malformation due to abnormalities seen in arteries of small and medium-sized portal tracts
  - Sometimes occurs with other vascular lesions
  - May be hormone-dependent; ?role of OCP but has been disputed
  - Rarely rupture
- **Clinical features**
  - Most do not produce symptoms and found incidentally
  - May experience mild pain with bleeding into or necrosis of the lesion

- **Diagnosis**
  - AFP levels are normal
  - CT is not specific unless the central scar and feeding artery are seen
- **Pathology**
  - Variable size with a dense, central stellate and radiating fibrous septa that divide the lesion into lobules
  - Closely resembles a focal form of inactive cirrhosis microscopically
- **Treatment**
  - Large symptomatic or complicated lesions should be resected
  - Recurrence after resection is rare
  - Recommend to stop OCP if not resected
  - Periodic u/s if firm diagnosis of FNH has not been made



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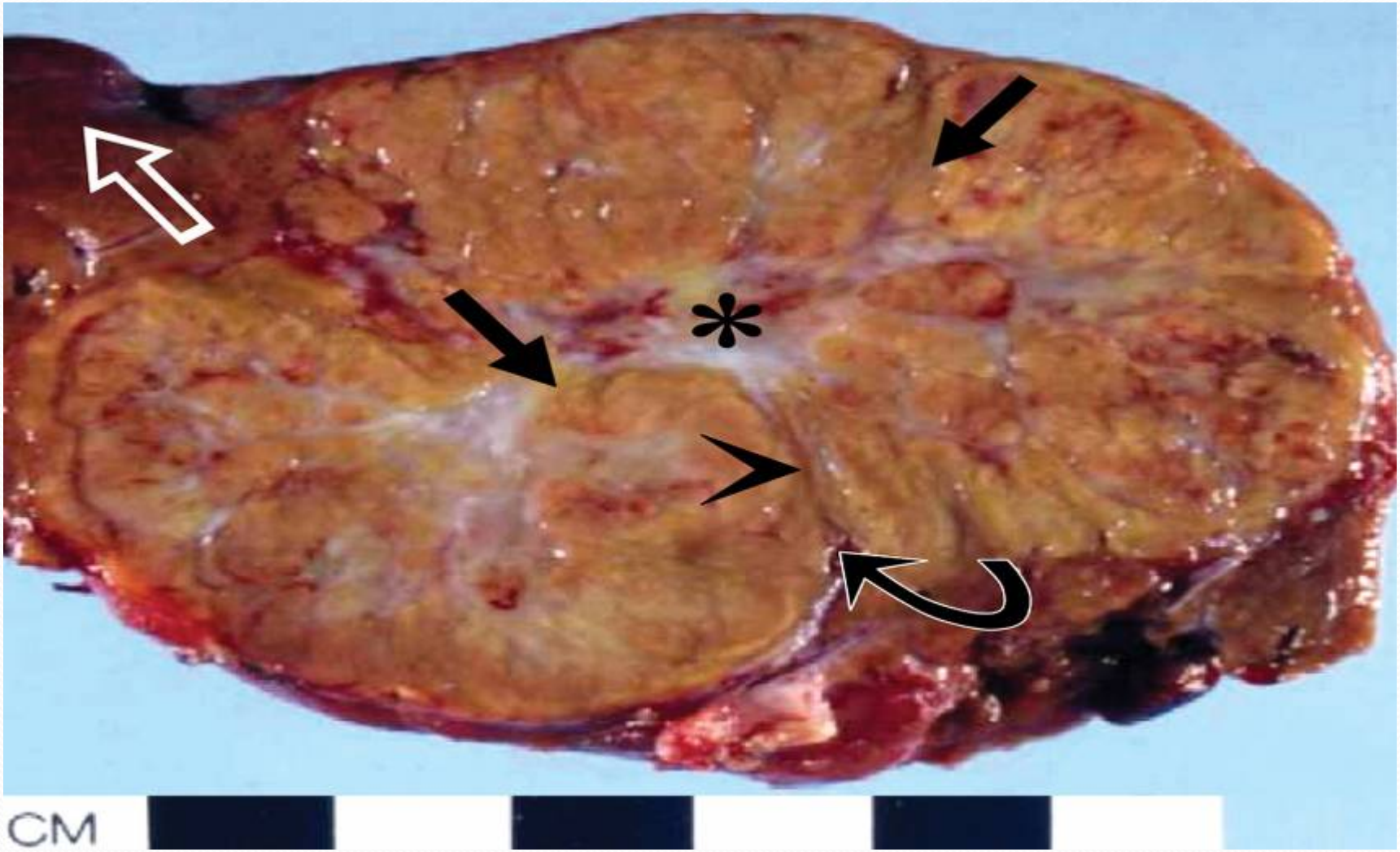

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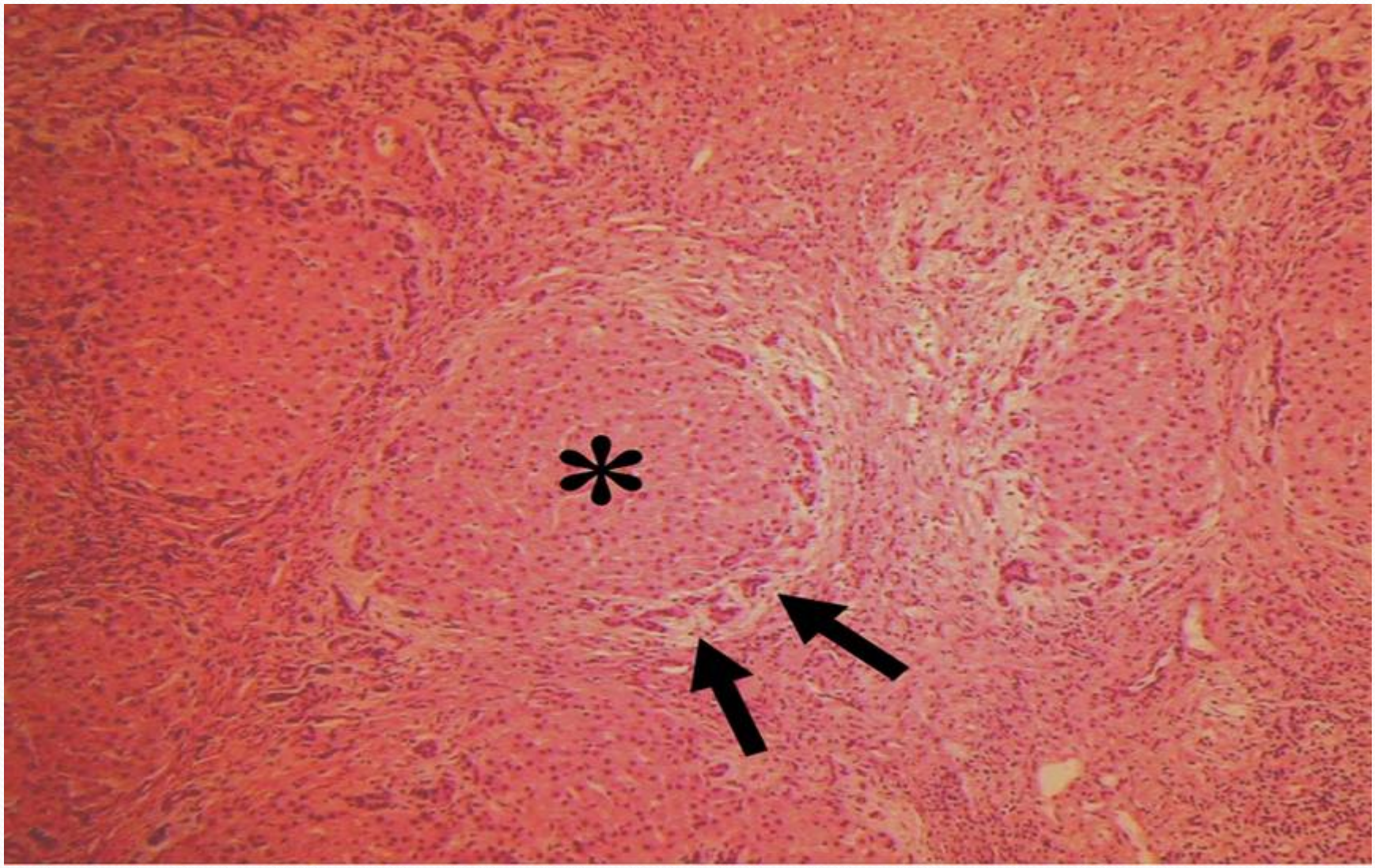


http://radiographics.rsna.org/content/24/1/3.figures-only

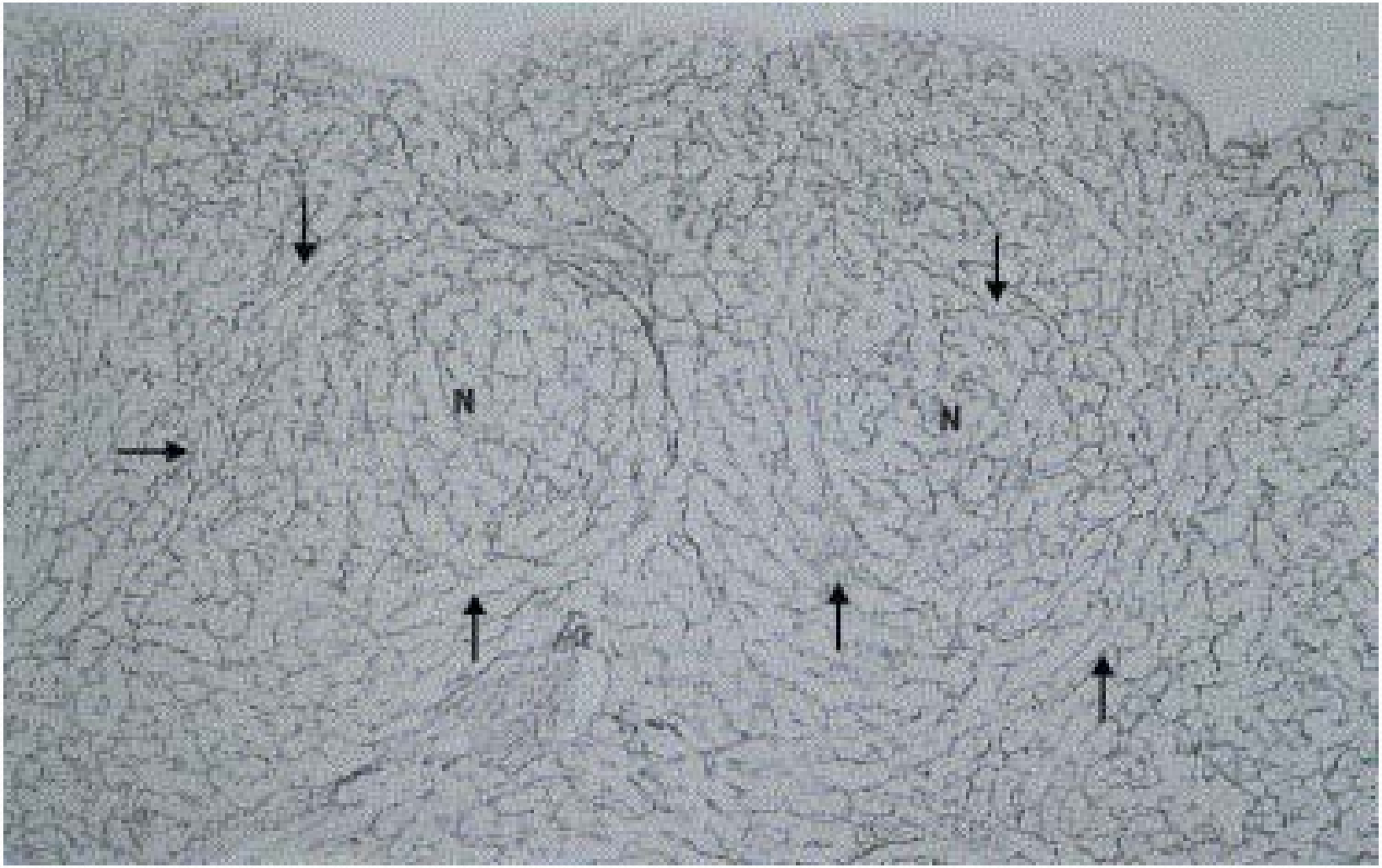
Nodular Regenerative Hyperplasia

Nodular Regenerative Hyperplasia

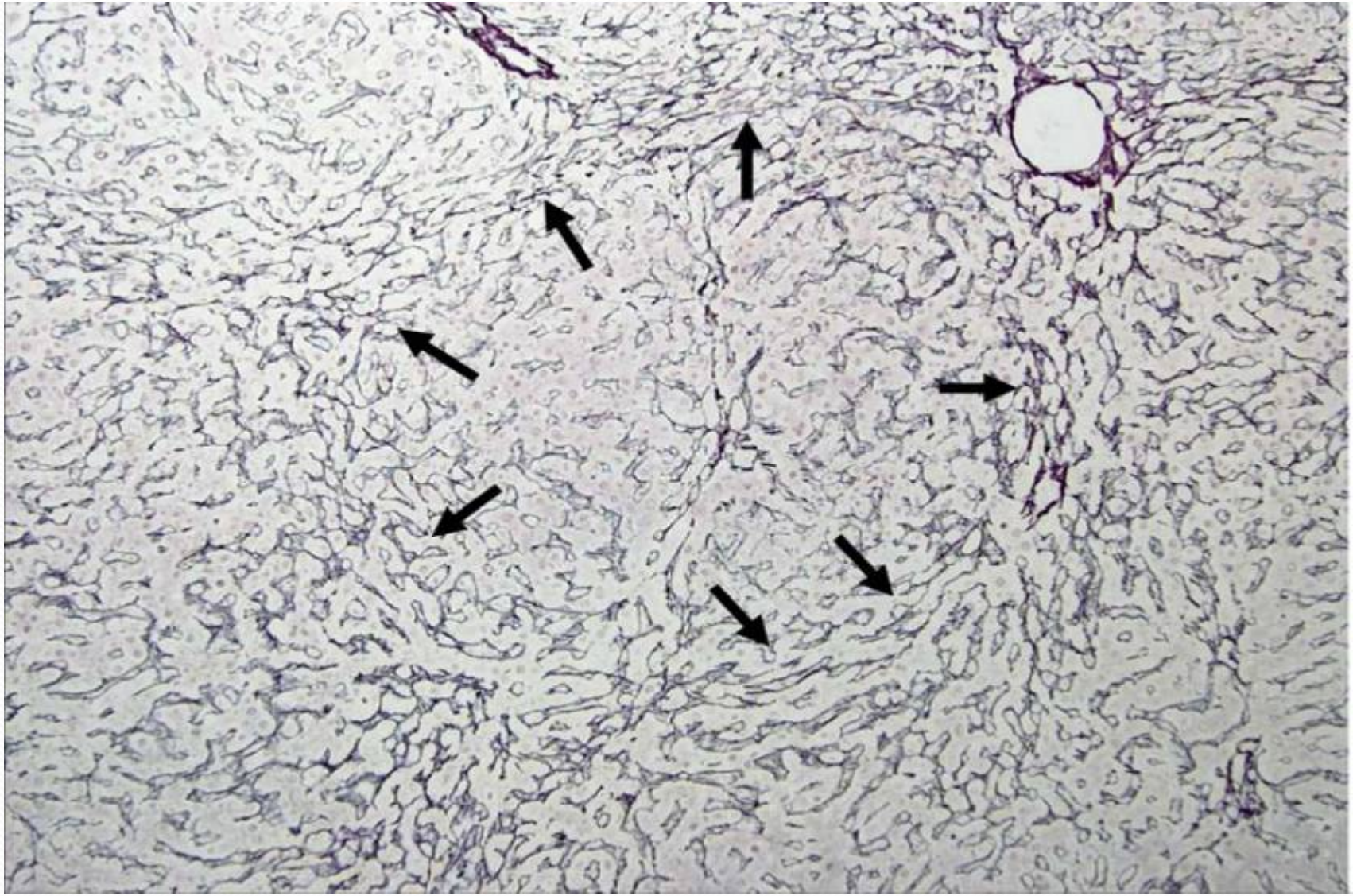
- Nodularity of the liver without cirrhosis
- Obliterative lesions in small portal veins typically present clinically with portal hypertension

- **Clinical Features**
  - Normal hepatic function but with complications of portal hypertension

- **Diagnosis**
  - Difficult to establish based on findings in small-needle biopsies
  - Radiologic evaluations often suggest normal liver
  - U/S reveals abnormal echogenecity; appears as well-defined hypodense nodules on CT
  - Reticulin stains are useful in identifying the unique structural features



http://thebileflow.com/2012/06/21/pathology-nodular-regenerative-hyperplasia/



Nodular Regenerative Hyperplasia

- Has been associated with a number of other diseases
  - Felty's Syndrome
  - RA
  - Primary hypogammaglobulinemia
  - SLE
  - Progressive systemic sclerosis
  - Sarcoidosis
  - Polymyalgia rheumatica
  - Polycythemia vera
  - Agnogenic myeloid hyperplasia

Nodular Regenerative Hyperplasia

- Medication-Induced
  - Azathioprine
  - Thioguanine
  - Didanosine
  - Stavudine
  - Isoplatin
  - Mercaptopurine
  - Vitamin A
  - Methotrexate?

Other Nodular Disorders

- **Macroregenerative Nodules**
  - May occur in advanced cirrhosis or after massive hepatic necrosis
  - Believed to be premalignant in presence of cirrhosis

- **Inflammatory Pseudotumor**
  - Rare; results from focal infection
  - Occurs particularly in young men
  - Leukocytosis, elevated ESR, and polyclonal hyperglobulinemia 50% of patients
  - May present as solitary or multiple lesion(s)
  - Mixture of chronic inflammatory cells with plasma cells predominating

Hepatic Cysts

Hepatic Cysts

- Abnormal fluid-filled spaces in the hepatic parenchyma and biliary tree

- **Three Main Types:**
  1. Fibrocystic Diseases of the Liver
  2. Cystadenomas and Cystadenocarcinomas
  3. Hydatid Cysts

Fibrocystic Diseases of the Liver

- Originate from abnormal persistence or defects in the progressive remodeling of the ductal plate during development resulting in dilated fluid-filled spaces

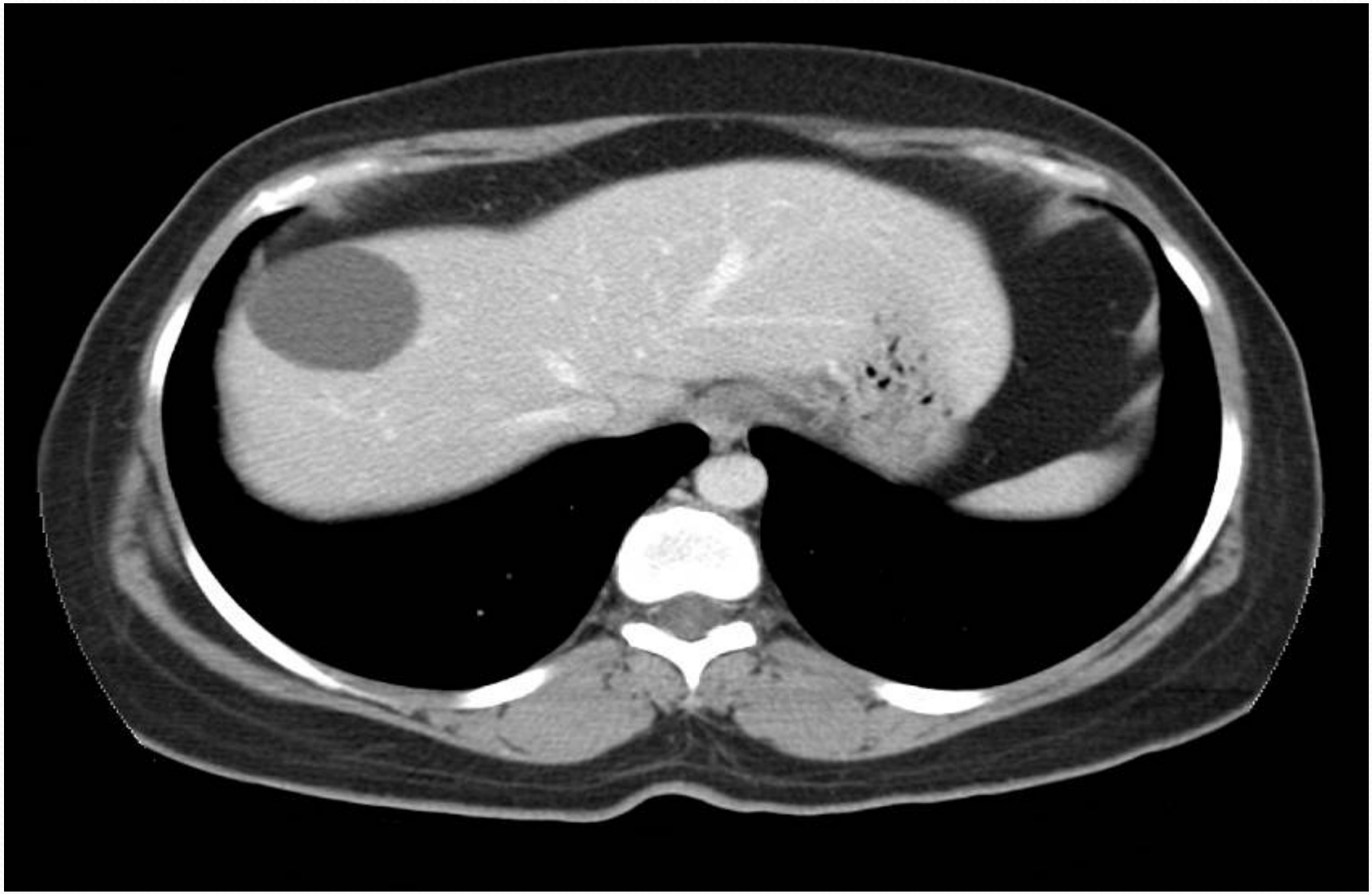
- Simple Hepatic Cysts
- Polycystic Liver Disease (PCLD)
- von Meyenburg Complexes
- Caroli's disease (Type V Choledochal Cyst)

Simple Hepatic Cyst

Simple Hepatic Cysts

- Thought to be congenital in origin
- Occur more often in women; prevalence increases with age
- Generally < 5cm; can have up to 3 before being considered part of PCLD
- Usually asymptomatic and found incidentally with imaging
- **Complications**: intracystic bleeding, infection, rupture, or compression

- **Treatment**
  - Should be left alone if patient asymptomatic
  - Percutaneous aspiration and sclerosis with EtOH or doxycycline; recurrence
  - Laparoscopic or open fenestration; seldom recur but greater morbidity



http://msc-spaichingen.de/fileadmin/hepatic-cyst

Polycystic Liver Disease

Polycystic Liver Disease

- Rare condition in which multiple cysts form in the hepatic parenchyma
- Usually in association with ADPKD but can appear as an isolated form
- Lined by a single layer of cuboidal or columnar epithelium, resembling that of bile ducts
- Rarely it can be lined with squamous but may develop into squamous cell carcinoma

Polycystic Liver Disease

- **Association with ADPKD**
  - Fairly common but kidney disease usually predominates the clinical course
  - Occurs in approximately 24% of patients in 3rd decade; 80% in 6th decade
  - Symptoms usually correlate with advancing age, severity of renal cysts, and renal dysfunction
  - Women tend to have larger and more numerous cysts
  - Correlation with number of pregnancies
  - Exogenous use of female sex hormones may accelerate growth and size of cysts

Polycystic Liver Disease

- **Association with ADPKD continued**
  - May coexist with other cystic liver diseases such as congenital hepatic fibrosis, Caroli's disease, or von Meyenburg complexes
  - Also associated with berry aneurysms, MVR, diverticular disease, and inguinal hernias
- **Isolated PCLD**
  - Rare; 7% of all PCLD
  - Linked to gene PRKCSH (protein kinase C substrate 80K-H) and SEC 63

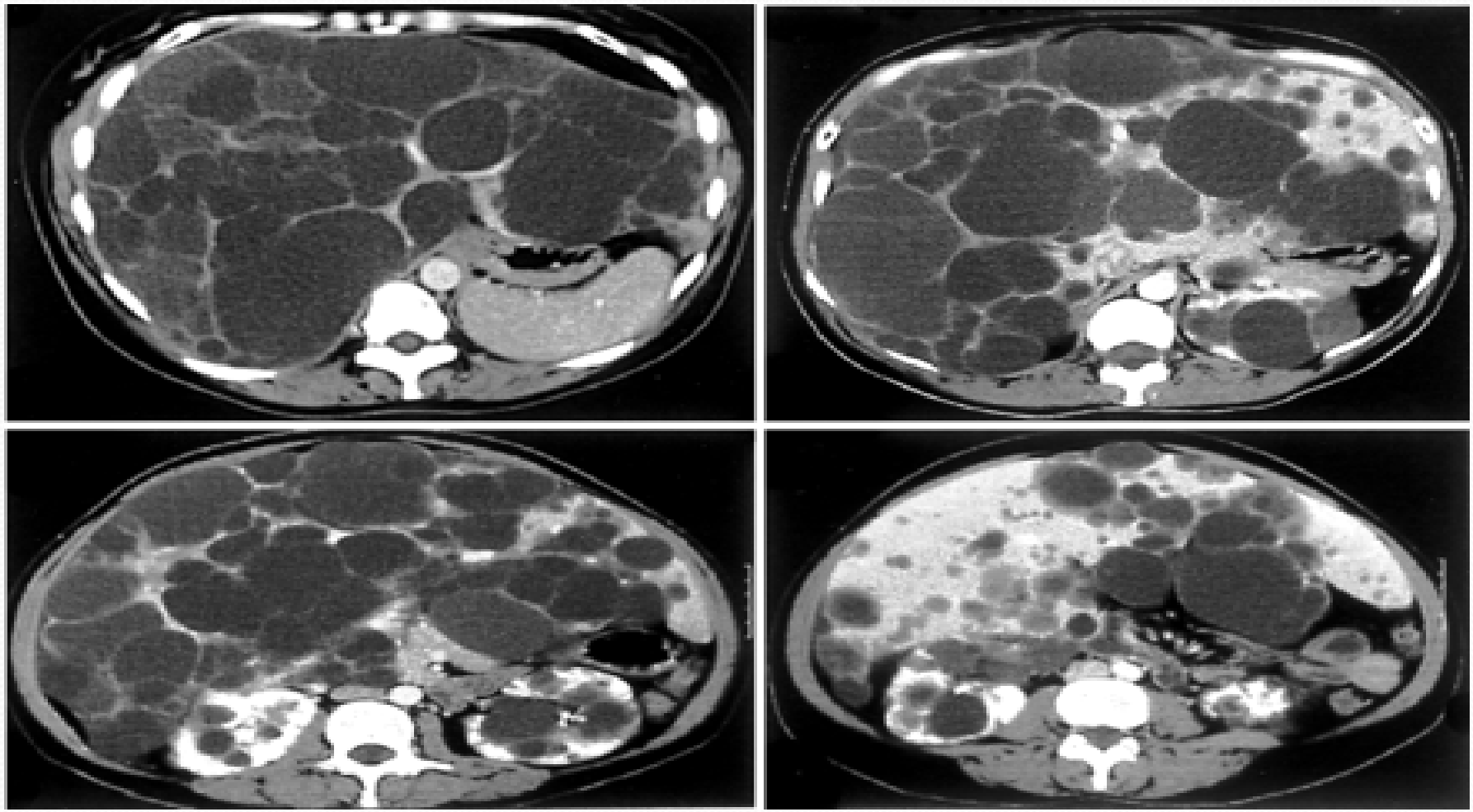
Polycystic Liver Disease

- **Clinical Features**
  - Usually asymptomatic but women tend to be more symptomatic than men
  - Severe pain may be experienced with rupture, infection, bleeding into cyst, or torsion of a pedunculated cyst
  - Jaundice if compression of major IH/EH bile ducts
  - Postprandial fullness
  - Ascites as a result of Portal HTN
  - Variceal bleeding rarely been reported

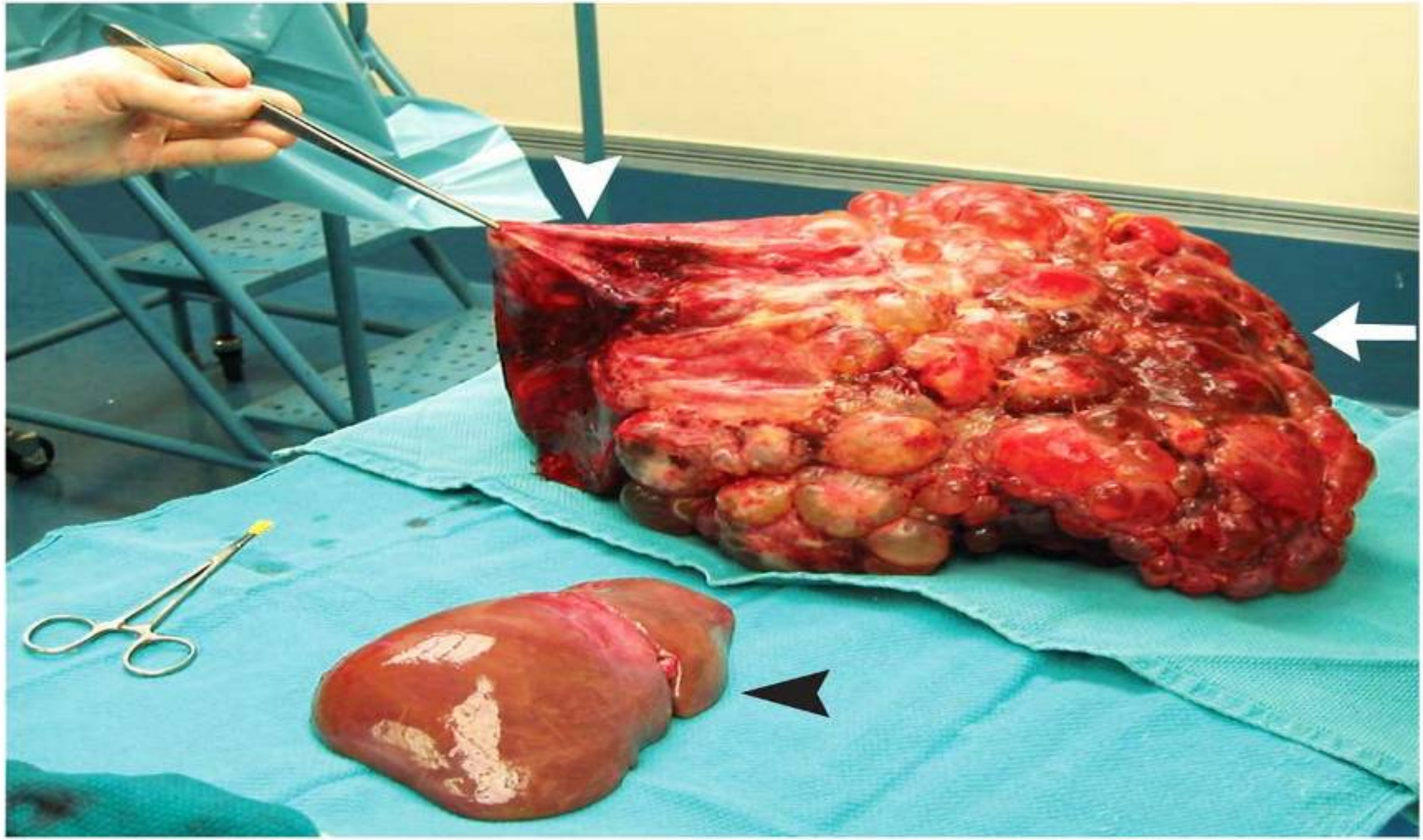
Polycystic Liver Disease

- **Diagnosis**
  - U/S, CT or MRI
  - LFTs generally normal
  - AP and GGTP may be increased
  - Raised right hemidiaphragm on CXR in severe PCLD

- **Treatment**
  - Fenestration (unroofing); high recurrence rate
  - Percutaneous injection of sclerosing agent
  - Partial hepatic resection
  - Liver transplantation



http://jasn.asnjournals.org/content/11/9/1767/F6.expansion



http://www.nejm.org/doi/full/10.1056/NEJMicm055470

Fibrocystic Disease associated with Autosomal Recessive Polycystic Kidney Disease

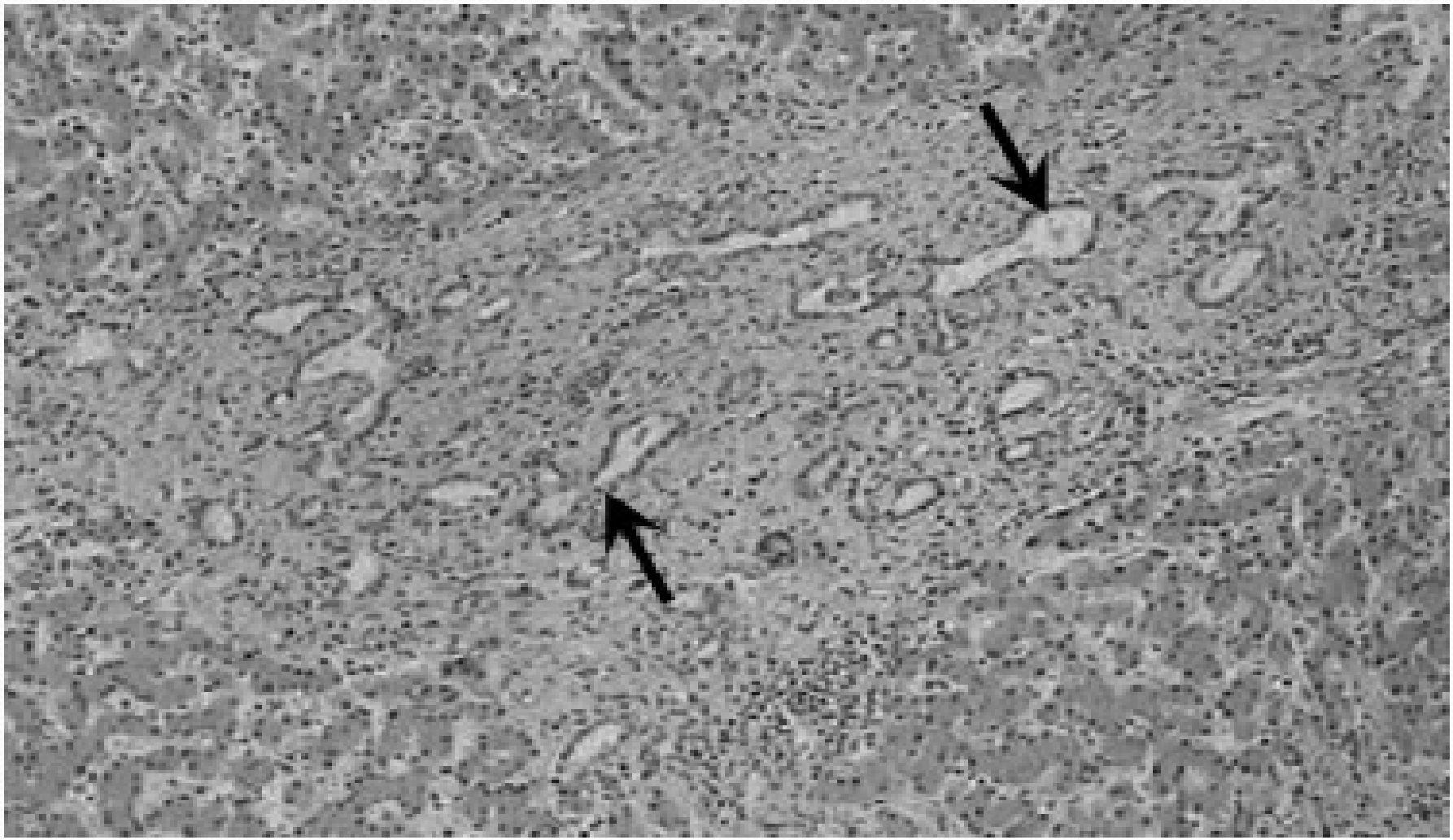
ARPKD

- May manifest in childhood and usually rapidly fatal
- Cysts are microscopic
- PKHD1 gene
- Proportion of patients maintain renal function into adulthood but complications of liver disease then predominate
- Complications of portal hypertension are the usual hepatic manifestations

Von Meyenburg Complexes

Von Meyenburg Complexes

- AKA biliary microhamartomas
- Common and do not produce symptoms
- Small and multiple
- Each complex is composed of cystically dilated intra- and interlobular bile ducts embedded in fibrous stroma
- May be complicated by development of peripheral cholangiocarcinoma



http://www.sciencedirect.com/science/article/pii/S1092913406001614

Caroli’s Disease

Caroli's Disease

- Rare disorder characterized by congenital nonobstructive gross dilatation of the segmental intrahepatic bile ducts

- **Epidemiology**
- Affects both men and women equally
- Usually become symptomatic in early adulthood with 80% before age 30

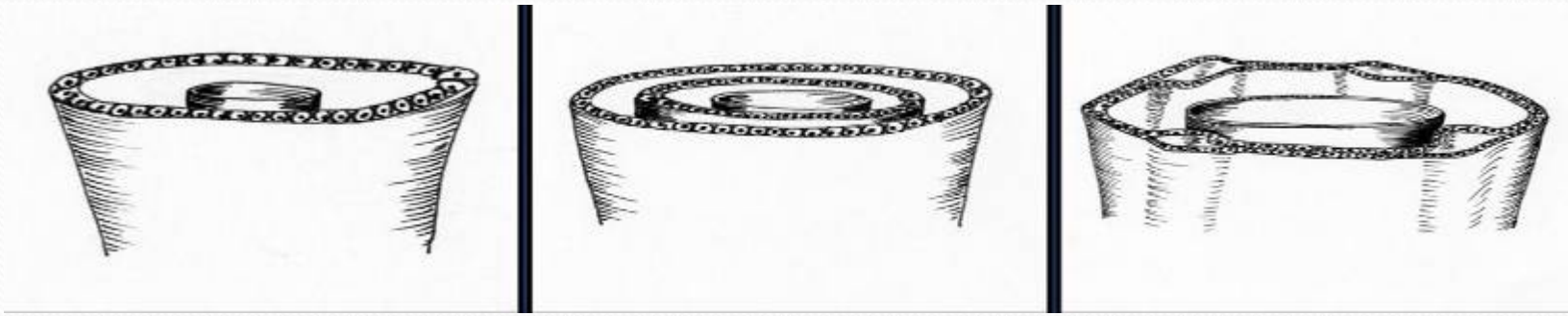
- **Pathogenesis**
- Believed to be caused by an intrauterine event that arrests ductal plate remodeling at the level of the larger IH bile ducts

- **Clinical Features**
- Recurrent episodes of cholangitis, abscess, or septicemia
- <10% can develop cholangiocarcinoma

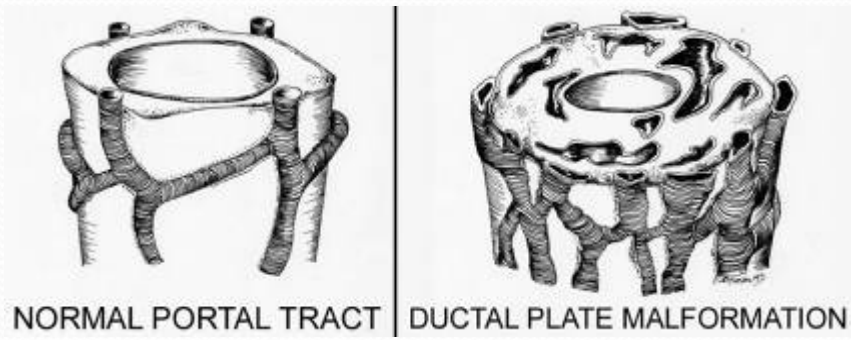
Caroli's Disease

- **Diagnosis**
  - Usually discovered during investigation of suspected cholangitis

- **Treatment**
  - Antibiotics
  - ERCP
  - Liver resection
  - Liver transplantation



Normal development of the ductal plate.
Embryologically each bile duct begins as a single layer of cells that surrounds a portal vein.
This layer then duplicates.
Portions of this double layer fuse and resorb leaving unfused portions that become the bile ducts.



So in the normal situation each portal vein is surrounded by interconnecting bile ducts (left image).
However if the patient has ductal plate malformation, the bile ducts are too numerous and they are ectatic (right image).
Whether or not we see this on imaging depends on which portion of the bile ducts is affected.
If the large ducts are involved, we see this as Caroli disease.
However if only the very small ducts are involved, the result is **congenital hepatic fibrosis**.
If all ducts are involved, then there is a combination of fibrosis and Caroli disease, which is also known as the Caroli syndrome.

http://www.radiologyassistant.nl/en/p49e17de25294d/biliary-ducts-benign-and-malignant-diseases.html

Question

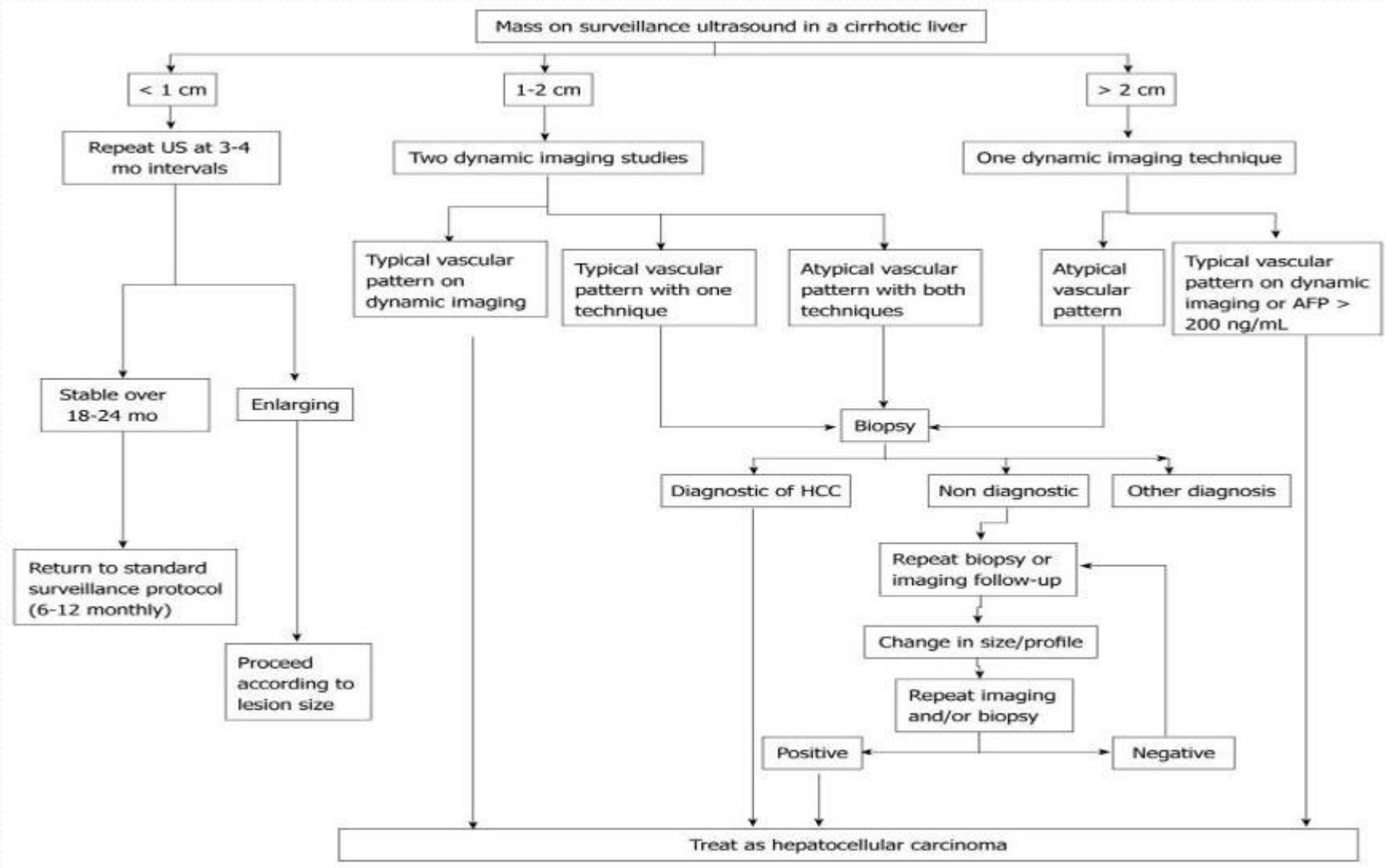
- A 42 y/o woman is incidentally noted to have a 4-cm cyst in the right lobe of the liver. She denies abdominal pain, fever, or recent travel. The cyst has no internal echoes on ultrasonography. Which is the most appropriate management?

- A) Aspiration
- B) Cyst cavity sclerosis
- C) Laparoscopic fenestration
- D) Observation only
- E) Percutaneous drain

Answer D

Simple hepatic cysts are though to be congenital in origin. The cysts usually are asymptomatic and discovered incidentally during upper abdominal imaging. They occur more often in women than in men, and their prevalence increases with age. Asymptomatic solitary hepatic cysts should be left alone. If intervention is required, percutaneous aspiration and sclerosis with alcohol or doxycycline will usually able the cyst, but recurrence is frequent. An alternative approach is laporoscopic fenestration, which is seldom followed by recurrence, but has a higher mortality rate.

Approach to Hepatic Mass



http://www.liverindia.com/liver-cancer.php